Role of IFN-γ induced genes in cell autonomous defence against *Legionellae*

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Abbreviations

Throughout this thesis the subsequent abbreviations have been used:

%	Percentage
~	Approximately
ΔdotA	*Legionella* DotA deletion mutant
ΔflaA	*Legionella* flagellin deletion mutant
°C	Degrees Celsius
µg	Microgram
µl	Microliter
µm	Micrometer
A600	Absorbance at 600 nm
ACES	N-(2-acetamido)-2-aminoethanesulfonic acid
ADP	Adenosine diphosphate
AIM2	Absent in melanoma 2
Akt	Protein kinase B
AM	Alveolar macrophage
AMP	Adenosine monophosphate
Arf	ADP-ribosylation factor
ATP	Adenosine triphosphate
ATPase	hydrolase enzymes that bind to ATP and hydrolyze it to ADP
BAL	Bronchoalveolar lavage
BCYE	Buffered charcoal yeast extract
BlaM	ß-lactamase
bp	Base pair
BSA	Bovine serum albumin
Cas	Caspase
CCF2 AM	FRET substrate used in ß-lactamase effector translocation assay
CCL	Chemokine (C-C motif) ligand
CCR	C-C chemokine receptor
CD	Cluster of differentiation
CFU	Colony forming unit
cm	Centimeter
CO_2	Carbon dioxide
CpG	cytosine-guanine dinucleotide DNA sequences
CRISPR	Clustered regularly interspaced short palindromic repeats
CXCL	Chemokine (C-X-C motif) ligand

Da	Dalton
DAMPs	Damage-associated molecular patterns
DC	Dendritic cell
DEG	Differentially expressed genes
dH2O	Distilled water
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
dNTP	Deoxynucleotide triphosphate
Dot	defect-in-organelle-trafficking
Dot/Icm	Defective for organelle trafficking /intracellular multiplication
dsRNA	Double-stranded RNA
DUB	Deubiquitinating enzyme
EDTA	Ethylenediaminetetraacetic acid
EEA-1	Early endosome antigen-1
EHEC	Enterohemorrhagic *Escherichia coli*
ELISA	Enzyme-linked immunosorbent assays
EPEC	Enteropathogenic *Escherichi coli*
ER	Endoplasmic reticulum
FACS	Fluorescence-activated cell sorting
FBS	Fetal bovine serum
FC	Fold change
FCS	Fetal calf serum
FDR	false discovery rate, p value adjusted for multiple testing
FRET	Fluorescence resonance energy transfer
GAP	GTPase activating protein
GBP	Guanylate-binding protein
GDP	Guanosine diphosphate
GEF	Guanine nucleotide exchange factor
GM-CSF	Granulocyte-macrophage colony-stimulating factor
GO	Gene ontology
GTP	Guanosine triphosphate
GTPases	hydrolase enzymes that bind to GTP and hydrolyze it to GDP
GVINs	Very large inducible GTPases
h	Hour(s)
HBSS	Hanks Balanced Salt Solution
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid
i.n.	Intranasal
iBMDM	Immortalized bone marrow-derived macrophages
Icm	Intracellular multiplication
IFN	Interferon
Ig	Immunoglobulin
IKK	IκB kinase

IL	Interleukin
iNOS	inducible nitric oxide synthase
IPTG	Isopropyl β-D-1-thiogalactopyranoside
IRF	Interferon regulatory factor
IRG	Immunity-related GTPases
IRG1	Immune-responsive gene 1
ISG15	Interferon stimulated gene 15
ISGases	Interferon-stimulated GTPases
ISGs	Interferon-stimulated genes
IκB	Inhibitor of NF-κB
kbp	Kilo base pair
kDa	Kilodalton
KO	Knockout
L. longbeachae +	*Legionella longbeachae* positive
LAMP-1	Lysosomal-associated membrane protein 1
LAMP-2	Lysosome Associated membrane protein 2
LB	Luria-Bertani
LC3	Microtubule-associated protein light chain 3
LCV	*Legionella* containing vacuole
LDH	Lactate dehydrogenase
Ll	*L. longbeachae*
Lp	*L. pneumophila*
LPS	Lipopolysaccharide
Lsp	*Legionella* secretion pathway
Lss	*Legionella* secretion system
Lvh	*Legionella* vir homologue
m^2	Square meter
MC	Monocyte-derived cell
MES	4-Morpholineethanesulfonic acid monohydrate
mg	Milligram
MHC	Major histocompatibility complex
MHCII	MHC class II
min	Minute(s)
ml	Milliliter
mm	Millimeter
mM	Millimolar
MOI	Multiplicity of infection
mRNA	Messenger RNA
MTT	3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide
MyD88	Myeloid differentiation primary response gene 88
NAD	Nicotinamide adenine dinucleotide
NADH	reduced form of Nicotinamide adenine dinucleotide

NADP	Nicotinamide adenine dinucleotide phosphate
NADPH	reduced form of Nicotinamide adenine dinucleotide phosphate
NF-κB	Nuclear factor kappa-light-chain-enhancer of activated B cells
ng	Nanogram
NK	natural killer cells
NLR	Nod-like receptor
NLRC	Nod-like receptor CARD domain containing
nm	Nanometer
NO	Nitric oxide
NOD	nucleotide-binding and oligomerization domain
NOS	Nitric oxide synthase
NOX2	NADPH oxidase 2
O_2	Oxygen
OD	Optical density
OD_{600}	Optical density at 600 nm
p.i.	Post-infection
PAGE	Polyacrylamide gel electrophoresis
PAMP	Pathogen-associated molecular pattern
PARP	poly (ADP-ribose) polymerases
pBMDM	primary bone marrow-derived macrophages
PBS	Phosphate buffered saline
PCA	Principal component analysis
PCR	Polymerase chain reaction
PCV	Pathogen-containing vacuole
Pen/Strep	antibiotic mix of Penicillin and Streptomycin
PFA	Paraformaldehyde
PH	Pleckstrin homology
PI	Propidium iodide
PI(3)P	Phosphatidylinositol (3)-phosphate
PI(3,4)P2	Phosphatidylinositol (3,4)-bisphosphate
PI(3,4,5)P3	Phosphatidylinositol (3,4,5)-trisphosphate
PI(4)P	Phosphatidylinositol (4)-phosphate
PI(4,5)P2	Phosphatidylinositol (4,5)-bisphosphate
PI3K	Phosphatidylinositol-3 kinase
PMA	Phorbol 12-myristate 13-acetate
PRR	Pattern recognition receptor
PTM	Post-translational modification
qRT-PCR	Real-time quantitative reverse transcription-PCR
RalF	*Legionella* effector of the Dot/Icm secretion system
RING	Really interesting new gene
RNA	Ribonucleic acid
RNAi	RNA inteference

RNAseq	RNA sequencing
RNS	Reactive nitrogen species
ROS	Reactive oxygen species
rpm	Revolutions per minute
RPMI	Roswell park memorial institute medium
RT	Room temperature
RTX	Repeats-in-toxins
s	Second
SCV	Salmonella containing vacuole
SD	Standard deviation
Ser	Serine
SidB	*Legionella* effector of the Dot/Icm secretion system
SidC	*Legionella* effector of the Dot/Icm secretion system
SidJ	*Legionella* effector of the Dot/Icm secretion system
SidM	*Legionella* effector of the Dot/Icm secretion system
spp.	Species
STAT	Signal transducer and activator of transcription
STAT1	Signal transducer and activator of transcription 1
STAT2	Signal transducer and activator of transcription 2
STAT3	Signal transducer and activator of transcription 3
T1SS	Type I secretion system
T2SS	Type II secretion system
T3SS	Type III secretion system
T4SS	Type IV secretion system
Tat	Twin arginine translocation
TBST	Tris Buffered Saline with Tween® 20
Thr	Threonine
TLR	Toll-like receptor
TNF	Tumour necrosis factor
Ub	Ubiquitin
USA	United States of America
V	Volt
v/v	Volume/volume
vATPase	Vacuolar H^+ATPase
w/v	Weight/volume
WB	Western blot
WHO	World Health Organization
WT	Wild type
α	Alpha
β	Beta
γ	Gamma
κ	Kappa

Abstract

L. pneumophila and *L. longbeachae* are ubiquitous environmental bacteria that can cause a severe pneumonia, known as Legionnaires' Disease, when contaminated aerosols are inhaled by susceptible humans. The co-evolution of the bacteria with their environmental hosts has equipped the bacteria with the ability to subvert the cell intrinsic host defence mechanisms in human cells, thereby allowing the pathogens to survive and replicate within the lung macrophages. During infection, *Legionella* establishes an intracellular niche, known as the *Legionella* containing vacuole (LCV). The biogenesis of the LCV is dependent on the defective organelle trafficking/intracellular multiplication (Dot/Icm) type IV secretion system, which translocates a large arsenal of bacterial effector proteins into the host cell. These effectors are known to modulate host metabolism and cell-autonomous defence, protect the integrity of the LCV and allowing the bacteria to acquire nutrients from the host to ensure intracellular survival and enable intracellular replication of the pathogen.

It is known that during *Legionella* lung infection, the mammalian host mounts a robust inflammatory response, producing cytokines, such as TNFα, IL-1α, IL-6, IL-12 as well as type I interferons and IFN-γ, which usually leads to the restriction of intracellular replication and culminates in the clearance of the infection. It was previously shown that IFN-γ is crucial for host defence against *Legionella* in mice, since disruption of IFN-γ signalling or IFN-γ deficiency results in a high replication of *Legionella* in the lung as well as a failure to clear the infection from the host, despite the activity of other inflammatory cytokines. Exposure of cells to interferons (IFN), including IFN-γ, results in the induction of a network of genes that combat infection, leading to so-called IFN-mediated cell-autonomous defence. This network is finely-tuned to balance efficient pathogen control while preventing collateral tissue damage. However, which interferon-induced genes and through what mechanism this strikingly potent restriction is mediated remains elusive for *Legionella*.

In this study, we shed some light on the mode of action of the IFN-γ induced host defence against *Legionella*. We identified a new mechanism of host defence mediated by interferon stimulated genes (ISGs), that results in the disruption of effector translocation

into host cells by the Dot/Icm secretion system. We demonstrated that this mechanism is uniquely triggered by interferon signalling and is independent of well-known host defence mechanisms such as host cell death, direct bactericidal activities, inflammasome activation as well as proteasome and autophagy-mediated degradation. By utilising mRNA sequencing of IFN-γ and type I interferon-stimulated macrophages, we identified possible factors that mediate this inhibition: ISG15 and PARPs. These proteins have not previously been implicated in *Legionella* host defence and represent a unique opportunity to increase our knowledge of interferon mediated cell-autonomous host defence.

Currently, more than 65 *Legionella* species are known and roughly half of them have been clinically associated with infection, frequently in immune compromised patients. After *L. pneumophila*, *L. longbeachae* is the second most common causative agent of Legionnaire's Disease worldwide and is the leading causative agent in Australia and south-east Asia. Despite this, knowledge about the pathogenesis of *L. longbeachae* is minimal. Therefore, during this study, we also aimed to provide new insights into the pathogenesis of *L. longbeachae* infection and characterise the impact of IFN-γ on immune control. We observed unique features of *L. longbeachae* infection in comparison to *L. pneumophila*, such as the ability to survive within a wider range of lung phagocytes, dampening of the cytokine response of the host and translocation of effectors into all lung phagocytes tested. These unique features may enable *L. longbeachae* to subvert the host defence more efficiently than *L. pneumophila* and thus replicate to higher numbers. Furthermore, we were able to show that IFN-γ is crucial for host defence against *L. longbeachae* in vivo, with neutrophils and monocyte derived cells dependent on IFN-γ signalling to mediate their bactericidal properties. In addition, we were able to demonstrate that IFN-γ stimulation restricts *L. longbeachae* Dot/Icm secretion system effector translocation into host cells.

Overall, this study substantiates the importance of IFN-γ in host defence against *Legionella* and supports the need to broaden research efforts to non-*L. pneumophila* species. Investigation and deeper understanding of critical host defence mechanisms can be used as a starting point to develop anti-infective agents against pathogens targeting the process of effector translocation or effector mediated manipulation of host function and cell-autonomous defence.

Declaration

This is to certify that:

1) This thesis comprises only my original work towards the Doctor of Philosophy except where indicated in the preface.

2) Due acknowledgement has been made in the text to all other material used.

3) This thesis is fewer than 100 000 words in length, exclusive of appendices, bibliographies, graphs and tables.

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Preface

This presented work is a thesis with publication

Heike L. Rafeld, Waldemar Kolanus, Ian R. van Driel and Elizabeth L. Hartland
"Interferon-induced GTPases orchestrate host cell-autonomous defence against bacterial pathogens"
Biochemical Society Transactions 49(3): 1287-1297
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and follows the guidelines defined by the University of Melbourne, such as a) the included publication is the PhD candidate's and the candidate contributed more than 50% of the work towards the publication and b) the co-authors have verified this and given their permission for the article to be included in this thesis. In fulfillment of these requirements, the necessary forms such as "Co-author authorisation" and the "Declaration for a thesis with publication" have been signed by co-authors and the primary supervisor respectively and have been submitted alongside this thesis. The candidate was the primary author of this publication and was the major contributor (approximately 85 %) to the development of this review's manuscript, graph design, incorporating revisions suggested by all the other co-authors, which also approved the final version for publication, as well as adjusting the manuscript following the journals revision process.

The publication was incorporated into the thesis's introductory chapter (chapter 1) and the original article's formatting was adjusted to align with the formatting guidelines predefined by the requirements for the jointly awarded degree of Doctor of Philosophy (PhD) between the University of Melbourne & The Rheinische Friedrich-Wilhelms-University Bonn. In addition, the original publication is also added as an appendix to this thesis.

Furthermore, in accordance with the regulations of the University of Melbourne and the Rheinische Friedrich-Wilhelms-University Bonn, I acknowledge the contribution of others to some of the work presented in this thesis. Specifically:

The *Legionella* strains over expressing the ß-lactamase-effector fusion proteins used for the ß-lactamase translocation assays in chapter 3, 4 and 5 have previously been created by various people, as indicated in the Material and Method chapter (Table 3).

The effector translocation assay of the *L. pneumophila* effector SidB in mouse macrophages (Chapter 3; Figure 5 A) was conducted by Dr. Sze Ying Ong.

The effector translocation assay in primary mouse macrophages deficient for GBP 1 and GBPs located on chromosome 5 (GBP chr5$^{-/-}$) (Chapter 3, Figure 22 B) were conducted by Dr. Garrett NG.

The sequencing of mRNA from interferon stimulated primary mouse macrophages was performed at the Next Generation Sequencing (NGS) Core Facility of the Medical Faculty at the University of Bonn. The subsequent sequence alignment to the mouse genome was performed by CF. Elzer and A. Buness from the Core Unit for Bioinformatics Data Analysis (CUBA) at the University of Bonn.

The remainder of this thesis comprises only my original work.

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of the most knowledge people I came across and I am very grateful for you taking the time to relay this abundance of knowledge to me. Furthermore, I am entirely grateful for your input and suggestions throughout my PhD and your ability to think outside the box. Without your help and guidance, I don't think this PhD would have been completed.

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List of Publications

This thesis contains material that is published or is currently in preparation for publication:

Rafeld, H. L., et al. (2021). "Interferon-induced GTPases orchestrate host cell-autonomous defence against bacterial pathogens." Biochem Soc Trans 49(3): 1287-1297.

Chapter 1: Introduction / Literature review

1.1 Legionellosis: Pontiac fever and Legionnaires' Disease

Gram-negative bacteria within the genus *Legionella* are known to be causative agents of severe and sometimes fatal pneumonia known as Legionnaires' Disease since 1977 [1-4]. After the initial identification of *Legionella* as the causative agent and of the first outbreak during the American Legion conference in Philadelphia, researchers found *Legionella* in clinic samples as far back as 1947 [4-6]. *Legionella* was later identified to cause a milder flu-like form of the disease, called Pontiac fever, named after the first outbreak in a health department facility in Pontiac, Michigan [5, 7].

Currently more than 65 species of *Legionella* are known with 80 serogroups, with new species being identified regularly [5, 8]. Within the confirmed species, 32 have been associated with human infections and disease [9]. While in most people *Legionella* causes a self-resolving infection, it can be life-threatening, with a mortality rate of 5- 10 % [10, 11]. Individuals with respiratory or immune compromising conditions, as well as smokers and elderly people, are at an increased risk of succumbing to Legionnaires' Disease [1, 12, 13].

Even though Legionnaires' Disease is a notifiable disease in many countries, Legionnaires' Disease is considered an underdiagnosed disease worldwide. Due to the fact that pneumonia caused by *Legionella* is indistinguishable clinically from other forms of community-acquired pneumonia [14, 15] and that patients with pneumonia are not being tested for *Legionella* infections routinely, with tests only performed when specifically requested [11, 13], it is believed that many cases of *Legionella* infection are missed. Furthermore, there is no worldwide standard for reporting these cases. Even though the burden of *Legionella* on the health system is considered to be a underestimated, reported cases are on the rise across the world including in Europe [16], America [17], Australia [18]. This might be due to the steadily increasing age average of the population and thus increasing the population size of potentially vulnerable people in these countries or due to increased awareness of Legionnaires' Disease and thus increased testing and reporting [5].

Across the globe, ~ 90% of diagnosed Legionnaires' Disease cases are caused by *L. pneumophila* [8, 19]. Furthermore, particular serogroups dominate disease incidence, such as *L. pneumophila* serogroup 1 causing ~90 % of *L. pneumophila* cases [8]. However, the identification of *L. pneumophila* as the leading causative agent is biased as the most commonly

used diagnostic test, the urinary antigen test, only detects *L. pneumophila* serogroup 1 reliably [8, 20-22]. The detection of other *Legionella* species is possible using direct fluorescent antibody staining and enzyme-linked immunosorbent assays (ELISA). However, these methods are not as reliable due to suboptimal sensitivity for non-pneumophila species and possible cross-reactivity between species [21, 23]. Furthermore, the detection of *Legionella* via cultivation on buffered charcoal yeast extract (BCYE) plates from sputum samples also favour the detection of *L. pneumophila,* due to the use of certain antibiotics. For instance, cefamandole is used to support a more selective growth of *Legionella* due to the growth restriction of normal oropharyngeal flora from the sputum sample, but it also inhibits the growth of certain *Legionella* spp. such as, *L. birminghamensis, L. bozemanii, L. erythra, L. jordanis, L. maceachernii, L. micadei, L. moravica, L. rubrilucens* and *L. santicrucis* [24]. The use of antibiotics in diagnostic growth settings can suppress or inhibit the growth of certain *Legionella* spp. and could therefore lead to false-negative results as well as misleading results for mixed infections [25]. As a consequence of these poor diagnostic strategies, species other than *L. pneumophila* are under-represented when determining the causes of Legionnaires' Disease [11, 13, 25-27]. As a result, the clinical relevance of these other species may be underestimated [8, 22, 25, 26, 28, 29]. Nonetheless, *L. longbeachae*, which was first isolated from a patient in 1981, is recognised as the predominant cause of Legionnaires' Disease in Australia, New Zealand and Thailand [19, 29-37] and was isolated for the first time in Australia in 1987 [38].

Currently, when patients are diagnosed with Legionnaires' Disease, the standard treatment is the administration of antibiotics. Even though Legionnaires' Disease is a disease prevalent worldwide, there are no common international standards for treatment and recommendations, and guidelines vary significantly between different nations [39]. Since *Legionella* are taken up by alveolar macrophages and other phagocytes, the range of effective antibiotics is limited to the ones that can penetrate cells such as fluoroquinolones, macrolides, pleuro-mutilins, rifampicin, streptogramins, tetracyclines and trimethoprim [39]. Fortunately, *Legionella* species have not acquired widespread resistance against antibiotics and reported cases with antibiotic resistance are limited to a few individual cases [40-42]. Testing for antibiotic efficacy or resistance is routinely done on *Legionella* being grown on BCYE agar which contains active charcoal, that can inhibit the potency of the drugs [39]. Thus, testing for antibiotic resistance via PCR might be an important alternative [43].

1.2 *Legionella*: environmental niche and intracellular life cycle

1.2.1 Morphology

Legionella are pleomorphic bacteria, usually ~3 µm long by 0.3-0.6 µm wide, and can range from coccoid, to coccobacillary, to short bacillus forms as well as long filamentous forms up to 50 µm [44]. These various forms are influenced by diverse factors such as growth media, host cells, temperature and available nutrients [22].

1.2.2 Environmental niche

Legionella are primarily environmental organisms, with *L. pneumophila* found mainly in natural and artificial aquatic environments. In its natural habitat, *L. pneumophila* depends on protozoan hosts for replication and survival [45-50], though it is currently argued if *Legionella* can survive and replicate extracellularly in biofilms [51-59]. The breadth of host species in which *Legionella* is suspected to be able to survive and replicate in has been demonstrated by co-culture and co-isolation experiments. The range of hosts, is extraordinarily vast and diverse, including 7 out of 8 protozoan phyla, nearly 30 % of all classes within these phyla and a quarter of all defined orders [60]. Some species of *Acanthamoeba* spp., *Hartmannella* spp., *Naegleria* spp. and *Vahlkampfia* spp., have been co-isolated with *Legionella* multiple times from varying environmental and man-made niches, indicating that these species might function as hosts in these systems and thus play an essential role in the epidemiology of *Legionella* [60]. Furthermore, *Legionella* has also been shown to replicate in slime-mould *Dictyostelium discoideum* as well as in the intestinal tract of *Caenorhabditis elegans* [25, 27, 28].

In contrast to the aquatic habitat of *L. pneumophila, L. longbeachae* is predominantly found in soil and can be isolated from potting soils [13, 30, 32, 61, 62]. Genome analysis of *L. longbeachae* shows that this bacterium is well adapted to a earth-dwelling lifestyle [63]. For instance, *L. longbeachae* encodes all the enzymes necessary for catabolizing plant cellulose as carbon source [63]. *L. longbeachae* possesses a pectin lyase to hydrolyse the pectin matrix in which cellulose is embedded, a 1,4-beta-xylanase to hydrolyse xylan the most common hemicellulose polymer in plants, as well as five endo-1,4-beta-glucanases, four cellobiohydrolases and three ß-glucosidases to convert cellulose into glucose [63]. Even though protozoans are crucial for *Legionella* lifecycle, it is still unknown which organism is the primary

environmental reservoir of *L. longbeachae* in soil, but it is known to replicate within the ciliate *Tetrahymena pyriformis* [28, 64].

Even though *Legionella* are ubiquitous in freshwater and soil environments, they are nutritionally fastidious in laboratory culture. Their replication is dependent on a variety of amino acids (Arg, Cys, Ile, Leu, Met, Thr and Val) as well as trace elements and ferric pyrophosphate added to the growth medium [59, 65-67].

1.2.3 Intracellular life cycle of *Legionella*

Of all disease-causing *Legionella*, *L. pneumophila* is the most comprehensively studied. In contrast, little is known about the mechanisms and characteristics of *L. longbeachae* infection despite the importance of this species in some countries [2]. Compared to *L. pneumophila*, *L. longbeachae* has significantly different ecological niches, modes of transmission, genetics, physiologies, virulence and infection patterns in mouse models and a different repertoire of Dot/Icm effectors [29, 35]. Despite these differences, *L. longbeachae* and *L. pneumophila* cause clinically indistinguishable respiratory diseases in humans [29]. Some aspects of the intracellular life cycle of *Legionella* are described in more detail in the following sections of this chapter.

1.2.3.1 Transmission and uptake of *Legionella*

Humans are considered accidental hosts, for *Legionella* infection and become infected, after inhaling contaminated aerosols [68]. Due to its aquatic habitat, *L. pneumophila* is mainly transmitted by inhaling contaminated water droplets. In contrast to *L. pneumophila*, *L. longbeachae* infection is acquired through inhalation of contaminated earth particles from potting soil and other decomposing materials [32, 61, 69-72]. Therefore people handling compost and potting soil are at greater risk of *L. longbeachae* infection [13, 28].

It is generally accepted that person-to-person transmission of *Legionella* does not occur and thus humans are accidental dead-end hosts for *Legionella* [73]. However, in 2016 the first possible person-to-person transmission of Legionnaires' Disease was reported [74]. This new transmission route might have an influence on precautions concerning the care of hospitalised patients with Legionnaires' Disease.

Upon inhalation of *Legionella*-contaminated aerosols, bacteria are taken up by alveolar macrophages [25]. Uptake of *L. pneumophila* has been described as occurring via coiling

phagocytosis in macrophages and amoebae [75, 76], although like other *Legionella* species, uptake by conventional phagocytosis also occurs [25].

Furthermore, it has been shown that effectors secreted by the Dot/Icm secretion system are necessary for the efficient uptake by the host cells, as Dot/Icm mutants show a decreased rate of phagocytosis compared to wild type *Legionella* in macrophages and *A. castellanii* [77].

1.2.3.2 Formation of the *Legionella* containing vacuole (LCV)

Following phagocytosis, *Legionella* reside in a vacuole from which they subvert and manipulate multiple host cell pathways and functions via countless Dot/Icm effectors, such as secretory pathway and retrograde trafficking, autophagy, cytoskeleton remodelling, ubiquitin machinery, host transcription, signal transduction and host cell death, to create an intracellular niche termed the *Legionella*-containing vacuole (LCV) [5, 78-81]. Especially the manipulation of the vesicle-trafficking pathway between the endoplasmic reticulum (ER) and Golgi is crucial to form a replication permissive LCV [82-86]. Furthermore, to ensure intracellular survival *L. pneumophila* actively avoids interaction of the LCV with the endocytic pathway, as the LCV membrane does not acquire endocytic markers and thus does not fuse with lysosomes [25, 82, 87-89].

The process of LCV formation by *L. pneumophila* is depicted in Figure 1. In short, as rapidly as 15 minutes after uptake, the *L. pneumophila* containing vacuole is surrounded by smooth vesicles derived from the ER, which appear to fuse with the phagosomal membrane [88]. Following this, mitochondria are also recruited to the cytoplasmic face of the LCV [88]. Around 4 hours after uptake, the smooth vesicles and mitochondria are replaced by rough vesicles derived from the endoplasmic reticulum and ribosomes [27, 88, 89]. This completes the transformation of the initial phagosome into the intracellular replicative niche, that allows *Legionella* to replicate to high numbers intracellularly [25, 82, 88, 89].

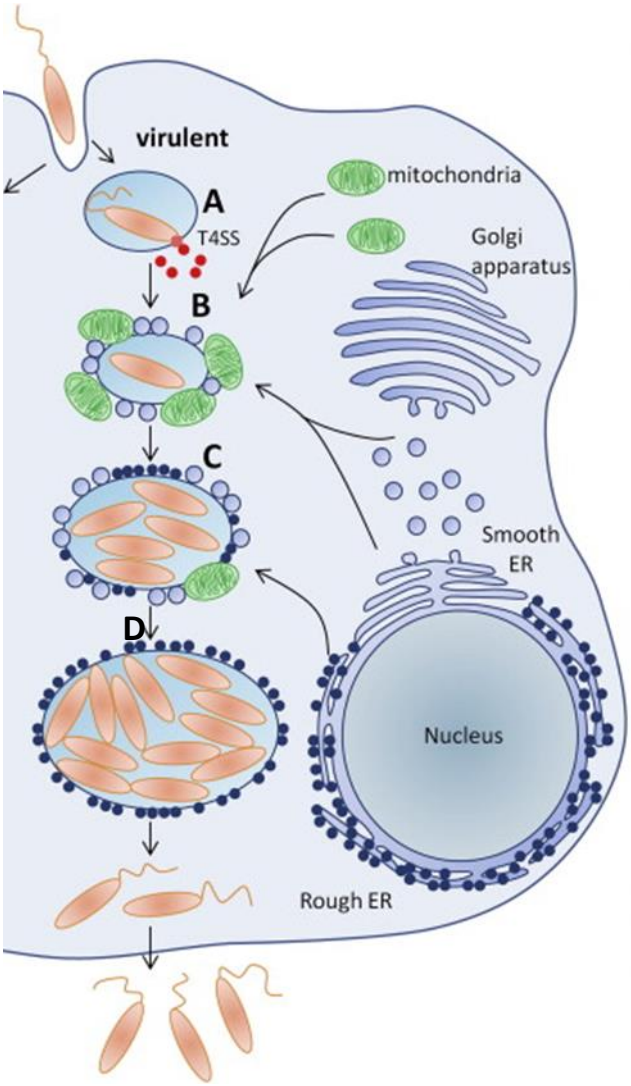

Figure 1: Formation of the *Legionella*-containing vacuole (LCV).
A) The bacterium resides in a phagosome after internalization. B) The LCV recruits mitochondria and smooth vesicles form the ER to its surface. C) Ribosomes are recruited to the LCV membrane and subsequently replace the mitochondria and smooth vesicles. D) Completed biogenesis of the LCV, in which *Legionella* replicates within to high numbers. Graph adapted from: **[68]**

While the process of LCV formation is similar for *L. pneumophila* and *L. longbeachae*, there are some differences. While *L. pneumophila* containing vacuoles do not gain endocytic markers, the *L. longbeachae* containing vacuole has been reported to acquire endocytic markers such as early endosomal antigen 1 (EEA1), Lysosome-associated membrane protein 2 (LAMP-2) and mannose 6-phosphate receptor (M6PR) [69]. At the same time, lysosome-associated protease Cathepsin D and vacuolar H^+ATPase (vATPase) were excluded from the *L. longbeachae* LCV, so that the *L. longbeachae* LCV avoids acidification [69]. Hence, the

L. longbeachae LCV may show some differences to *L. pneumophila* and this needs more characterisation [69, 90].

Successful formation of the LCV is dependent on a functional Dot/Icm secretion system, as it allows the bacteria to translocate effectors into the host cell cytoplasm during infection [91, 92]. In addition to orchestrating the avoidance of phagolysosomal degradation, *Legionella* utilises Dot/Icm effectors to establish the LCV by controlling the amount and composition of phosphoinositide (PI) lipids on its LCV membrane to anchor Dot/Icm effectors on the LCV surface and to interfere with the host cell membrane dynamics [93]. Phosphoinositide (PI) lipids can be phosphorylated and dephosphorylated at position 3', 4', and/or 5' of the D-myo-inositol head group by PI-kinases and PI-phosphatases, respectively, and are important components for subcellular compartment identity and vesicular traffic [94].
Upon internalisation the initial vacuole of both WT and Dot/Icm mutants are decorated with PtdIns(3,4,5)P_3. Shortly after uptake, this phosphoinositide gets converted to PtdIns(3)P, a marker for the endocytic pathway, by host cell PI-phosphatases [94-96]. However, vacuoles harbouring WT *Legionella* are increasingly accumulating PtdIns(4)P, a marker for Golgi apparatus, plasma membrane and secretory vesicles [96, 97], and decrease PtdIns(3)P on their LCV [93]. On the other hand, LCVs harbouring Dot/Icm defective mutants do not accumulate PtdIns(4)P and stay PtdIns(3)P positive [93]. It was recently shown that WT *L. pneumophila* are able to generate PtdIns(4)P de novo from phosphatidylinositol (PtdIns) utilising 3 different Dot/Icm effectors, wherein MavQ phosphorylates PtdIns to generate PtdIns(3)P, subsequently LepB phosphorylates PtdIns(3)P to produce PtdIns(3,4)P_2 and finally SidF removes the phosphate group at position 3 to yield PtdIns(4)P [98]. *L. pneumophila* maintains PtdIns(4)P on the LCV throughout the infection, which function as anchor points for other Dot/Icm effectors to enable LCV biogenesis and maintenance [93, 99-102]. It has also been shown that *L. longbeachae* utilises PtdIns(4)P to anchor Dot/Icm effectors (SidC) on the surface of the LCV [35].

1.2.3.3 Nutrient acquisition

In addition to establishing a replicative niche, successful survival and replication of intracellular *Legionella* is also dependent on the nutrient acquisition from the host, since *L. pneumophila* is auxotroph for seven amino acids Arg, Cys, Ile, Leu, Met, Thr and Val [65-67, 103]. The Dot/Icm effector AnkB is responsible for recruiting K48 linked polyubiquitinated proteins to

the LCV surface, where they are subsequently degraded into amino acids by host cell proteasome and aminopeptidases, which supplies the bacteria with the needed nutrients [104]. The acquisition of sufficient amounts of amino acids via AnkB and host cell mediated degradation of polyubiquitinated proteins is crucial to *L. pneumophila*, since AnkB mutants as well as chemical inhibition of proteasome and aminopeptidases activity results in defective intracellular replication in human macrophages [103, 105].

L. pneumophila also requires iron for proper intracellular growth and employs the Dot/Icm effector MavN to capture and transport iron across the LCV membrane [106, 107]. The acquisition of iron via the effector MavN is essential for *L. pneumophila* replication, since MavN mutants are defective in intracellular growth due to iron starvation [106].

In addition to acquiring amino acids, iron and other nutrients individually, *L. pneumophila* also effects the metabolism of the host cell on a greater scale. It was recently reported that the Dot/Icm secreted amylase LamA degrades glycogen to yield cytosolic hyper-glucose in amoeba and human macrophages [108]. In amoeba the natural host, the glycogen degradation via LamA prevents the amoeba from encystation and thus is beneficial for *L. pneumophila* growth [108]. On the other hand, the high levels of glucose in human macrophages prompt the cells to switch to aerobic glycolysis, which triggers proinflammatory M1-like differentiation of these cells and potentially restrict *L. pneumophila* growth [108]. Though, it was also suggested that the *L. pneumophila* effector MitF modulates mitochondria dynamics to trigger Warburg-like metabolism in human macrophages, which favours *L. pneumophila* replication [109]. The increase in glycolysis and thus available glucose does not benefit the bacteria directly, since it does not utilise glucose for its respiration but rather amino acids, it might instead benefits from this metabolic switch due to the increased production of glycolytic serine an amino acid essential for *L. pneumophila* growth [110].

1.2.3.4 Egress from host cells

Once host nutrients are depleted, *Legionella* egresses from the host cell and spreads to infect new host cells. Even though the details of LCV formation and host manipulation are well documented, the process regarding the exit of *Legionella* from different host cells is less well documented [111]. However, it has been reported, that *Legionella* becomes cytosolic prior to exiting the host cells, with ~70 % of cells showing cytosolic bacteria at 12 h p.i. and close to 100 % at 24 h p.i. [111]. Furthermore, it has been reported that IcmT is essential for pore

formation, which triggers cytolysis and subsequent egress of the bacteria from both mammalian and protozoan host cells [112].

1.3 Secretion systems

Bacterial secretions systems, especially the Dot/Icm secretion system, are crucial for the intracellular survival and replication of *Legionella* within their environmental hosts and human phagocytic cells [113]. *L. pneumophila* Dot/Icm mutants are unable to replicate within host cells, as they are unable to transform the phagosome into a replication permissive LCV [91, 92]. The Dot/Icm secretion system is also essential for *L. longbeachae* replication, as the mutation of the Dot/Icm components, results in a severe attenuation of *L. longbeachae* replication in *Acanthamoeba castellanii*, A/J and C57BL/6 mice as well has human macrophages [63, 90, 114]. Furthermore, Dot/Icm mutants are unable to avoid the accumulation of endocytic markers, which leads to their destruction via the endocytic pathway [90, 115, 116]. Dot/Icm effectors are transported across the LCV membrane during all the different stages of the intracellular lifecycle and are involved in a wide range of activities, including subversion, manipulation and exploitation of host cell metabolism [5, 78-81].

Aside from the Dot/Icm secretion system, *Legionella* possesses multiple other protein secretion systems. For instance, *L. pneumophila* strain Paris possesses a type I Lss secretion system, type V secretion pathway, type II Lsp (*Legionella* secretion pathway) and two type IV secretion systems (type IVA Lvh and type IVB Dot/Icm) [113]. Genome analysis of the *L. longbeachae* strain D-4968 has identified genes encoding for type I, II, IVA, and IVB secretion system homologs [29]. Despite the many secretion systems, only the type II and type IVB are thought to be crucial for the virulence of *L. pneumophila* [117].

1.3.1 Sec and Tat- dependent transport: transport into or across the inner membrane

The main secretion complex of the Sec pathway is composed of the Sec translocases (SecYEG), which form the membrane pore, a membrane-bound ATPase (SecA) and a chaperone (SecB) [113]. All sec genes, apart from *secG*, are present in *L. pneumophila* strain Philadelphia, though no further characterisation of this transport pathway has been undertaken [113].

In addition to the Sec-dependent transport, proteins can also be moved across the inner membrane via the twin-arginine translocation or Tat secretion pathway, which allows for the transport of folded proteins [113]. Tat-dependent proteins usually possess two arginine residues

in their signal sequence, which are recognised by TatB and TatC proteins and are transported through a pore formed by TatA proteins, though aberrant signal sequences are also recognised by the Tat system [113, 118]. Similar to the Sec secretion system, the Tat-pathway and function in *Legionella* is not well characterised, though it has been shown that TatC and TatB mutants exhibit a replication defect in *A. castellanii* and differentiated U937 cells [118].

1.3.2 Transport across the outer membrane: type I, type II secretion systems

1.3.2.1 Type I secretion system Lss

The type I secretions system transports substrates across the inner and outer membrane into the extracellular space in one step, without periplasmic intermediates [113]. This secretion system comprises three proteins: a dimerized inner-membrane ATPase (ATP-binding cassette, ABC-transporter), a trimerized membrane fusion protein spanning the periplasmic space and a trimerized outer-membrane protein [119, 120]. The assembly of this secretion system is initiated by the binding of a substrate to the ABC transporter in the inner membrane [121]. Type I secretion system substrates possess a C-terminal secretion signal and are proteins of varying size and function, such as pore-forming proteins, lipases, hemophores and proteases [121]. In *L. pneumophila* the type I secretion system locus is termed the *Legionella* secretion system (Lss), which comprises six genes (*lssXYZABD*) [122]. One of the best-studied type I substrates are the RTX (repeats-in-toxins) toxins, a family of proteins with varying functions and harbouring various repeats of the glycine-rich motif GGXGXDXXX [123]. The *L. pneumophila* RtxA protein is exported by a type I Lss system and is involved in host entry, intracellular survival in macrophages and *A. castellanii*, as well as virulence in mice [123-125]. Until very recently, it was thought that the type I secretion system is exclusively expressed in *L. pneumophila* strains, as non-*pneumophila* species seem to lack the periplasm spanning fusion protein LssD [120]. However in 2020, Brown et al. [120] described the RtxA type I secretion system in a novel *L. taurinensis* strain as well as four novel type I secretion systems. Furthermore, bioinformatic analysis of 45 *Legionella* whole genome sequences revealed *lssXYZABD* homologues in 19 species, although not in *L. longbeachae* [120].

1.3.2.2 Type II secretion system

In contrast to the one-step secretion via the type I secretion system, protein secretion into the extracellular space via the type II secretion system is a two-step process [126]. In the first step substrates are transported across the inner membrane into the periplasm via the Sec- or Tat-

dependent pathway, followed by transport across the outer membrane via the type II secretion system [126, 127]. In *Legionella*, the type II secretion system is encoded by the *Legionella* secretion pathway (lsp) genes *lspC, lspDE, lspFGHIJK, lspL, lspM* and *lspO* and is present in all sequenced species so far, though the sequence conservation varies greatly between the Lsp proteins and species [9, 113]. This secretion system consists of 12 core components which can be divided in four subcomplexes: an outer-membrane secretin pore consisting of 15 units of LspD, an inner-membrane assembly platform consisting of LspC, LspF, LspL, LspM, a pseudopilus consisting of a major pseudopilin Lsp G and minor pseudopilins LspH, LspI, LspJ, and LspK1 as well a hexameric cytosolic ATPase (LspE), [9, 128-130]. The outer-membrane secretin pore interacts with the inner-membrane proteins (LspF, LspL and LspM) to form a channel that spans the periplasm linked via LspC [130]. After processing via the prepilin peptidase, LspO, the pseudopilin proteins assemble inside the periplasmic channel to form a pilus like structure. This, acts as a piston or screw to push substrates through the secretin pore powered by the ATPase activity of LspE [9, 130].

Currently, 25 and 47 proteins have been identified as confirmed or putative substrates of the type II secretion system in *L. pneumophila*, respectively [9, 117]. Of these substrates, the vast majority is found in at least 32 other *Legionella* species, with nearly 10 % being present in all *Legionella* species, representing the current core effector repertoire of the type II secretion system [9]. So far 18 out of 22 *L. pneumophila* type II secretion system substrates have been identified in *L. longbeachae*, which is in stark contrast to the low conservation of type IV secretion system effectors [9]. The substrates secreted via the type II system show a plethora of enzymatic activities such as ribonucleases, lipases, metalloproteases, peptidases, chitinases, phosphatases, deoxyribonucleases and cellulases as well as some being eukaryotic-like proteins [9]. The type II secretion system and its substrates contribute to survival and replication in various amoebae species [131-134], mice [117, 135], macrophages and epithelial cells [136, 137], at low temperatures [138], dampening the cytokine and TLR signalling response of infected cells [136, 139], mucin degradation [140], biofilm colonisation [141, 142] and sliding motility [143].

1.3.3 Type IV secretion systems

Type IV secretion systems are multiprotein transport complexes, which span both the inner and outer membrane. These systems translocate proteins and nucleic acids into the recipient plant, animal and bacterial cells [119, 144]. The type IV secretion systems can be divided into three major subfamilies, the conjugation systems for transferring DNA between species, a system for uptake and release of DNA into the extracellular space and the translocation systems for transporting effector molecules [145]. These systems can be grouped into two classes A and B, and are based and defined on the prototypic *Agrobacterium tumefaciens* T-DNA transfer system (Vir system or type IVA system) and the IncP and IncN bacterial conjugation systems (Tra system or type IVB system) respectively [113].

1.3.3.1 The type IVA secretion system

The type IV A secretion system is encoded by 11 *lvh* (*Legionella vir* homologue) genes [146]. Surprisingly the Lvh secretion system is dispensable for the growth in *A. castellanii* as well as human macrophages [146]. Later though, it was shown to be involved in the intracellular replication of *Legionella* in human macrophages when cultured at 30 °C, suggesting the importance of this system under environmental growth conditions rather than laboratory conditions [147]. Furthermore, the Lvh system is involved in the conjugation of the RSF1010 plasmid and can substitute for some Dot/Icm components in the conjugation process, but not intracellular growth [146].

1.3.3.2 The type IVB secretion system: the Dot/Icm secretion system

1.3.3.2.1 Core structure

During the early nineties, two laboratories discovered *Legionella* mutants which were unable to replicate within host cells, defective in organelle trafficking as well as defective in inhibiting phagosome-lysosome fusion and termed the loci, which restored the defects of their respective mutants, *icm* (intracellular multiplication) [91] and *dot* (defective organelle trafficking) [92].
Proteins of these loci were later found to form a type IV B secretion system that was able to transfer DNA [148, 149] and bacterial proteins [150] into the host cell. In *L. pneumophila,* genes encoding the Dot/Icm secretion system are found in two regions in the genome, where region one encodes seven genes (*icmV, icmW, icmX, dotA, dotB, dotC,* and *dotD*), and region two encodes 18 genes (*icmT, icmS, icmR, icmQ, icmP/dotM, icmO/dotL, icmN/dotK, icmM/dotJ, icmL/dotI, icmK/dotH, icmE/dotG, icmG/dotF, icmC/dotE, icmD/dotP, icmJ/dotN,*

icmB/dotO, *icmF*, and *icmH/dotU*) [29, 48]. The majority of the Dot/Icm secretion system components are constitutively expressed and assembled during the intracellular life cycle of *L. pneumophila* [151]. Recently it was demonstrated that the Dot/Icm secretion system is assembled at both poles of the bacteria, with an average of 4.2 secretion systems per pole [152]. The specific process of effector translocation as well as the individual functions and interactions of the Dot/Icm components amongst themselves and with other host proteins e.g. effector proteins is currently still ambiguous, though some subcomplexes and functions have been identified in the last decades.

Vincent et al. [153] proposed that IcmG/DotF, IcmE/DotG, DotC, DotD, and IcmK/DotH form the core complex of the type IV secretion system, a multicomponent translocation machinery that spans both the inner and outer membranes. Wherein the proteins DotC, DotD, and IcmK/DotH localise to the outer membrane (DotH in DotC/D-dependent manner), forming a ring-/wheel-like structure with 13 fold symmetry embedded in the inner leaflet of the outer-membrane with a central ~6 nm wide pore and the proteins IcmG/DotF and IcmE/DotG localise to the inner membrane forming the membrane-spanning inner channel [154-157]. In addition, the proteins IcmH/DotU and IcmF are essential for the stability of the core complex via inhibiting the degradation of DotH and thus stabilizing the DotC-DotD-DotH outer-membrane subcomplex [158]. Furthermore, it has been shown that the inner-membrane core protein IcmG/DotF binds to effector proteins and might aid in their translocation [159, 160]. This goes hand in hand with a high sequence variability in the periplasmic region of DotF between different *Legionella* species, which possess vastly different effector repertoires [161]. Moreover, the membrane-spanning channel consisting of DotG and DotF possesses openings in the periplasm region, indicating that DotF might mediate the transport of effectors from the periplasm into the Dot/Icm machinery [157, 161].

1.3.3.2.2 Type IV secretion system ATPases

The type IV secretion is powered via three ATPases, the coupling ATPase DotL, the DotB ATPase and DotO ATPase. How these ATPases interact with each other to facilitate the translocation of substrates is currently unknown. However, the ATPase function of DotB is essential for polar targeting of DotB, as ATPase mutants remain cytoplasmic and are defective in polar localisation and interaction with the inner membrane complex of the type IV secretion system [155, 162]. Furthermore, the deletion of DotO or components of the core complex as well as components of the inner-membrane components (dotA and DotU) abrogate the polar

localisation of DotB, thus arguing a strong case of DotB interaction with the type IV secretion system [155]. In contrast the cycling of DotB between the cytoplasm and the membrane-bound type IV secretion system, the membrane and polar localisation of the ATPase DotO is constant and dependent on the core protein DotG as well as inner-membrane components DotI and DotU, but it is independent on ATPase DotL or DotB [155]. This suggests that the core structure and inner-membrane components of the type IV secretion system are assembled at the cell poles first, and subsequently DotO is recruited to the cell poles, which in turn recruits the ATP bound ATPase DotB to the secretion system [155]. Cryo-ET analysis revealed that the ATPases DotO and DotB form a cytoplasmic complex with an inner channel directly at the base of the core complex in the inner-membrane, consisting of two stacked hexameric discs made out of 6 homodimers of DotO and six units of DotB, respectively [155]. Interestingly the coupling complex was not associated with this structure consisting of the core complex and the cytoplasmic ATPase complex, thus the interaction of the coupling complex with the membrane-spanning core-complex might be transient and induced by recognising and binding of effectors to this coupling complex [155]. Furthermore, it was speculated that DotB might be involved in substrate recognition or transport, as different DotB alleles showed varying degrees of defects which might be consistent with an inability to translocate specific substrates [163]. However, this idea is at odds with the very high sequence conservation among different *Legionella* species, as one would expect a higher sequence variability that reflects the vastly diverse effecter repertoires of different *Legionella* species [161].

1.3.3.2.3 Other type IV Dot/Icm secretion system proteins

Currently, knowledge about the remaining proteins of the type IV secretion system, especially their role in substrate translocation as well as their interaction with other components of the type IV secretion system, is limited.

Even though the deletion mutants of *dotA* have been used historically as a model for Dot/Icm function studies [164], not much is known about the specific function of this protein. DotA is an inner-membrane protein with two large periplasmic domains and a small cytoplasmic region [165]. Recently, DotA was shown to be required for the polar targeting and recruitment of the cytoplasmic DotB ATPase to the Dot/Icm secretion system [155]. This might explain the loss of function phenotype observed in *dotA* mutants, as DotB is essential for the type IV secretion system function and intracellular replication of *Legionella* [162, 163]. Furthermore, this interaction might be mediated by the cytoplasmic C-terminal domain of DotA, as a DotA

derivative lacking the C-terminal domain was unable to complement the replication defect of a *dotA* mutant [165]. In addition to being an integral component of the Dot/Icm secretion system, DotA is secreted into the culture supernatant via the Dot/Icm system, wherein it forms ring-like structures [166]. Given the frequent recombination rate and low sequence conservation of DotA among *Legionella* species, it has been speculated that DotA might directly interact with the host, as a secreted protein, or interact with translocated effectors, as part of the Dot/Icm machinery [161, 167, 168].

Even though IcmQ and IcmR are essential for type IV secretion system function [169], similar to DotA not much is known about their specific function. It has been shown that IcmQ can associate with membranes and form pores in these vesicles via inserting an N-terminal domain into membranes [170, 171]. The pore size formed in these membranes ranges between 13 and 26 Å, as pores allow the efflux of calcein but not Dextran3000 [170]. In addition to this pore-forming ability, the C-terminal domain of IcmQ possesses structural homology with NAD^+ binding domains of secreted bacterial ADP ribosyltransferases [172]. Furthermore, IcmQ and IcmR are reported to interact with each other via the N-terminal of IcmQ and the middle region of IcmR [171]. Within this complex, IcmR exerts chaperone-like and regulatory functions on IcmQ, as binding prevents the aggregate formation of IcmQ and inhibits disruption of membranes via the N-terminal domain of IcmQ [170, 173].

Even though *L. longbeachae* carries 24 of the 25 *dot/icm* genes identified in *L. pneumophila* [29], the structure of the Dot/Icm secretion system of *L. longbeachae* may be different from that of *L. pneumophila*, as the gene encoding the core structure protein IcmE/DotG is ~1400 bp longer than that of *L. pneumophila* [29, 161]. Furthermore, a multiple copies of the gene *icmD/dotP* are found in *L. longbeachae* [174].

1.3.3.2.4 Substrate recognition and translocation

The translocation of proteins via the type IV secretion system requires multiple steps: firstly the recognition of the substrate, secondly the unfolding of the protein and thirdly the transport of the unfolded protein through the secretion system channel [175].

Some Dot/Icm substrates are recognised via a coupling protein complex, a complex consisting of IcmO/DotL, IcmP/DotM and IcmJ/DotN as well as IcmS and IcmW [176, 177]. Whitin the complex, DotL/IcmO functions as a type IV coupling protein interacting with a subcomplex consisting of IcmJ/DotN, IcmS, IcmW and LvgA, mediating the recognition and transport of substrates to the type IV secretion apparatus [175, 177-180]. Recently two new proteins, DotY

and DotZ have been identified as part of the coupling complex. Even though their respective mutants show defects in effector translocation, the specific function in coupling complex dependent translocation remains unknown [181]. It has also been suggested that the coupling complex might display a set of heterogeneous adaptors, such as IcmS/W exclusively, IcmS/W with LvgA or IcmS/W with yet unknown adaptors, with the different adaptors in turn being able to recognise a specific set of effectors [175]. This changing set of adaptors might explain how the Dot/Icm secretion system is able to interact and transport such a vast amount of different effectors [175]. Furthermore, the IcmP/DotM protein of the coupling complex seems to be responsible for recruiting effectors possessing a Glu-rich/E-block motif in their C-terminus [182]. This goes hand in hand with a high sequence variability in the cytoplasmic C-terminus region of DotM between *Legionella* species, which is supposed to mediate this interaction with the effectors [161].

The substrates of the Dot/Icm secretion system can currently be divided into four groups: 1st effectors that possess a C-terminal translocation signal composed of short and negatively charged amino acids [183-185] (though no specific consensus sequence has been identified [186]), 2nd substrates that possess regions rich in glutamate (E-block motif) in their C-terminus [187], 3rd substrates that require the cytosolic IcmS and IcmW "chaperone complex" for translocation [188-190] and 4th substrates that appear to be translocated via their C-terminal signal and the IcmS/W chaperon complex [191-193].

The expression of many type IV secretion substrates is induced during the transition from exponential intracellular replication to the stationary/transmissive phase, which makes them readily available for translocation immediately upon interaction with a new host cell [151]. However, some effectors, such as SidJ, appear to be expressed constitutively [194]. The mechanisms that regulate the timely export of specific effectors are currently unknown and do not purely rely on transcriptional regulation, as many effectors are upregulated in the post exponential growth phase but are still translocated in an orderly/ hierarchical manner indicating an additional control [195]. The selective translocation of effectors in this organised or hierarchical manner is further supported by the fact that even effectors which have been artificially overexpressed (e.g. effectors that manipulate Rab1) are still translocated into the host cell in an ordered fashion according to their known function in the manipulation cycle of Rab1 [195].

Even though the interactions between different Dot/Icm secretion system components and the exact mechanism of effector translocation into the host cell are still enigmatic, the transport of

effector proteins across the bacterial envelop to their respective site of action, is the most vital process for host interaction and manipulation to ensure intracellular survival and replication of *Legionella*. *Legionella* mutant with an inactive Dot/Icm secretion system are unable to establish the replicative LCV and can not avoid degradation via the phago-lysosomal pathway [116, 164, 196].

1.3.3.2.5 Dot/Icm substrates

Even though the Dot/Icm system is highly conserved among all species of *Legionella* the effector repertoire varies greatly between species, which is reflected by the immense number of 18 000 effectors identified in genome analysis of 58 *Legionella* species [197]. In a similar study analysing the effector repertoire of 38 different *Legionella* species, it was discovered that only seven effectors are shared between all the species [198]. In addition, Gomez-Valero et al. showed that only 24 Dot/Icm effectors are shared between *L. pneumophila, L. longbeachae, L. hackeliae, L. micdadei and L. fallonii* [199]. Similar observations were made when the effector repertoire of *L. pneumophila* and *L. longbeachae* were compared, where the substrates that are translocated by these two species vary significantly [29, 63, 90, 200, 201]. More specifically, *L. longbeachae* shares only 133 effectors or ~35% of its effector repertoire with *L. pneumophila* [63, 199]. To some extent, the variable repertoires of effectors found in different *Legionella* spp. is to be expected, since effectors mirror the adaption of the pathogen to a specialised ecological host niche [29]. Furthermore, the ability of *Legionella* to successfully infect protozoan as well as macrophages of mammalian hosts might be based on the fact that *Legionella* targets conserved cell signalling pathways [202-204].

Since most research has focused on *L. pneumophila*, the vast majority of effector functions are analysed in *L. pneumophila* strains. *L. pneumophila* strain Philadelphia-1 is predicted to have ~ 330 effectors and the majority of these are still functionally uncharacterised [82, 185, 205]. Interestingly, there is a high level of redundancy among them, as even the deletion of 31% of Dot/Icm substrates of *L. pneumophila* caused only marginal intracellular replication defects in mouse macrophages [206]. This high degree of genetic redundancy makes it difficult to study the function of individual effectors, since deletion of single effector genes rarely results in a phenotype [205-207]. It has been suggested, that this high amount of redundancy is an adaption of *Legionella* interacting and infecting a myriad of different hosts in the environment and thus particular effectors are used to facilitate optimal growth in a specific host [159, 208, 209]. This goes hand in hand with type II secretion system effectors, which have been shown to be

essential in some hosts but dispensable in others [131, 133, 134, 210]. Until now, ~110 putative Dot/Icm effectors have been found in *L. longbeachae* [35, 63, 200], with the majority remaining uncharacterised [35]. Like *L. pneumophila*, *L. longbeachae* harbours many effector proteins with eukaryotic-like domains [29, 63].

The ability to infect eukaryotic cells is most likely the result of co-evolution with the amoeba host and the acquisition of eukaryotic-like proteins [47, 208, 211]. Multiple substrates of the Dot/Icm secretion system contain eukaryotic-like domains, such as ankyrin repeats, leucine-rich repeats, F-box domains, U-box domains, Sel-1 domains and serine-threonine protein kinase domains [47, 197, 208, 211]. A genomic screen of 58 *Legionella* species actually discovered 137 different eukaryotic-like domains and 200 eukaryotic-like proteins [197]. Their acquisition is thought to have occurred via horizontal gene transfer from protozoa [48, 67, 82, 212, 213]. Many of these eukaryote-like effectors interfere with host cellular processes, such as the secretory vesicle trafficking machinery (including the small GTPases Arf, Rab and Ran families), autophagy machinery, ubiquitin machinery, vacuolar H-ATPase, NF-κB signalling and phosphoinositide (PI) lipids by mimicking functions of eukaryotic enzymes, in order to enable the intracellular survival and replication of the bacteria [35, 48, 79, 214-216].

Some of the best-characterized effectors of *L. pneumophila* manipulate enzymes belonging to the Ras superfamily of small GTPases, such as Ras, Rab and Arf GTPases [90]. Interestingly all the effectors, except for LepB, which manipulate Rab1 function (DrrA, AnkX, SidD, Lem3, DrrA, LepB and SidM) are absent in *L. longbeachae* [63].

The Sec7 domain protein, RalF, was the first Dot/Icm effector described and is widely used as a reporter for effector translocation. RalF dictates ARF-1 (ADP ribosylation factor-1) activity during *Legionella* infection [150]. ARF-1 is a small GTPase that regulates vesicle trafficking between the endoplasmic-reticulum (ER) and the Golgi [217]. RalF not only recruits ARF-1 to the LCV membrane, it also acts as a guanine nucleotide exchange factor (GEF), which converts inactive GDP-bound ARF-1 into active GTP-bound form [150]. Activation of ARF-1 leads to a conformational change and subsequent binding of ARF-1 to the LCV, thus enabling *L. pneumophila* to intercept the vesicular traffic between the ER and the Golgi to recruit vesicles to the LCV [82, 150, 217].

L. longbeachae also encodes a RalF homolog [63]. It shares only ~50 % identity with RalF of *L. pneumophila*, but it is still functionally similar as the Sec7 domain needed for the GEF function is conserved [90]. In addition, *L. longbeachae* possesses three additional Dot/Icm

effectors which contain a Ras family motif, a small GTP binding domain, which is rarely found in bacteria [29]. These small GTPase homologs could mimic the function of small host GTPases and thus directly recruit ER-derived vesicles to the LCV, while competing with host ARF-1 and Rab1 [29].

In summary, *Legionella* use a vast repertoire of Dot/Icm effectors to manipulate a wide range of host pathways and processes extensively, to enable intracellular survival and replication. *Legionella* may translocate effectors into host cells which interact with multiple proteins of the same signalling pathway, regulating these host processes either in collaborative or opposing fashion. In addition to *Legionella* effectors that manipulate host proteins, *Legionella* also translocates so called meta-effectors which interact and influence the function of other Dot/Icm effectors, which illustrates the intricated Dot/Icm effector network employed by *Legionella*. With the abundance and diversity of Dot/Icm effectors observed among the different *Legionella* species, novel mechanisms of host manipulation and unique enzymatic activities mediate by *Legionella* effectors are bound to be discovered.

1.4 Interferons and interferon stimulated genes (ISGs)

Interferons are a family of inducible signal proteins which are classified as cytokines[218]. They were discovered in 1957 and named after their ability to interfere with viral infection and multiplication [218-221]. To date ten mammalian interferons (interferon-alpha (IFN-α), interferon-beta (IFN-β), interferon-delta (IFN-δ), interferon-epsilon (IFN-ε), interferon-gamma (IFN-γ), interferon-kappa (IFN-κ), interferon-lambda (IFN-λ, also called IL-28 and IL-29) interferon-ny (IFN-ν), interferon-omega (IFN-ω), interferon-tau (IFN-τ) and interferon-zeta (IFN-ζ)) are known; though only seven interferons are found in humans, as indicated by those underlined [222, 223]. Based on genetic loci, homology in amino acid sequence and receptor binding, interferons are currently divided into three groups, namely type I (composed of IFN-α, IFN-β, IFN-δ, IFN-κ, IFN-ε, IFN-ν, IFN-ω, IFN-τ and IFN-ζ), type II (IFN-γ) and the recently discovered type III (IFN-λ) [224, 225]. Upon binding their specific receptors, interferons activate signal transduction pathways which modulate the transcription of up to 2000 IFN-stimulated genes (ISGs) [224, 226], resulting in immunomodulatory-, anti-proliferative- and anti-pathogenic-consequences [227].

The remainder of this introductory chapter comprises the author-accepted version of the candidate's review article titled: "Interferon-induced GTPases orchestrate host cell-autonomous defence against bacterial pathogens", published at Biochemical Society Transactions. (Rafeld H. L., Kolanus W., van Driel I. R., Hartland E. L.; Biochem Soc Trans; 2021; 49(3): p. 1287-1297; DOI: 10.1042/bst20200900).

1.5 Interferon-induced GTPases orchestrate host cell-autonomous defence against bacterial pathogens

Interferon (IFN)-induced guanosine triphosphate hydrolysing enzymes (GTPases) have been identified as cornerstones of IFN-mediated cell-autonomous defence. Upon IFN stimulation, these GTPases are highly expressed in various host cells, where they orchestrate anti-microbial activities against a diverse range of pathogens such as bacteria, protozoan and viruses. IFN-induced GTPases have been shown to interact with various host pathways and proteins mediating pathogen control via inflammasome activation, destabilising pathogen compartments and membranes, orchestrating destruction via autophagy and the production of reactive oxygen species (ROS) as well as inhibiting pathogen mobility. In this mini-review we provide an update on how the IFN-induced GTPases target pathogens and mediate host defence, emphasising findings on protection against bacterial pathogens.

1.5.1 IFN signalling and induction of IFN-stimulated genes

Exposure of cells to interferons (IFN) results in the induction of a network of genes that combat infections, leading to so called IFN-mediated cell-autonomous defence [224, 226, 228-230]. This network is a finely-tuned mechanism to balance launching an efficient pathogen control while preventing collateral tissue damage. In the last two decades, IFN-induced GTPases have become a focus of attention as key mediators of IFN-mediated host defence.

There is abundant evidence for the vital role of IFN in combating an array of pathogens, including key roles in defence against bacteria [218, 219, 221, 226, 231-244]. Ten mammalian IFNs are known, with seven found in humans [222, 223]. Based on genetic loci, homology in amino acid sequence and receptor binding, IFNs are currently divided into three groups, namely type I, II and III [224, 225].

Upon binding their specific receptors, IFNs activate signal transduction via the JAK/STAT pathway which leads to the formation of the transcription factor complex IFN-stimulated gene factor 3 (ISGF3), consisting of phosphorylated STAT1/STAT2 and IRF9, for type I and type III IFNs and the transcription factor Gamma-Activated Factor (GAF), a homodimer of phosphorylated STAT1, for type 2 IFN-specific signalling [245-247]. These activated transcription factors translocate into the nucleus and bind to their specific promotor elements, IFN-stimulated response element (ISRE) and gamma-activated sequence (GAS) for type I/III

and type II, respectively [245-247]. The binding of these transcription factors can modulate the transcription of up to 2,000 IFN-stimulated genes (ISGs) [224, 226, 228], resulting in immunomodulatory, anti-proliferative and anti-pathogenic consequences [226, 227]. Even though these IFNs possess distinct receptors, transcription factors and promotor binding sites, the activation of ISGs via IFNs is complex. All types of IFN show non-canonical signalling, some ISGs are also controlled by IFN regulatory factors (IRFs); which in turn are also ISGs; other ISGs are constitutively expressed at low levels in addition to being IFN-inducible and another portion ISGs are also induced by NF-κB signalling [247-253].

1.5.2 Families of IFN-induced GTPases

GTPases induced by IFN have been identified as crucial effectors in IFN-mediated pathogen control [254-274]. These large GTPases can be divided into four subfamilies based on their paralogy and molecular mass [275]. The four subfamilies are the 21–47 kDa immunity-related GTPases (IRGs), the 65–73 kDa guanylate-binding proteins (GBPs), the 72–82 kDa myxoma (MX) resistance proteins and the 200–285 kDa very large inducible GTPases (VLIGs/GVINs) [276-278]. In the following we will mainly focus on IRG and GBP GTPases and their functions in cell-autonomous defence against bacteria.

Mice have 23 IRGs and this family of genes has been mostly lost in humans, apart from IRGM1 and IRGC [279, 280]. The IRGs can be divided into two classes; the primarily cytosolic "GKS" IRGs which possess a conserved canonical GX4GKS sequence in the first nucleotide-binding motif (G1) and the predominantly membrane-bound "GMS" IRGs which possess the non-canonical GX4GMS sequence in their G1 nucleotide-binding motif [278, 279]. The "GMS" IRGs control the activity of "GKS" IRGs by controlling the GDP to GTP switch, thus acting as guanosine dissociation inhibitors (GDIs) [277, 281]. In the absence of "GMS" IRGs, "GKS" IRGs are constitutively active, form cytoplasmic aggregates and fail to localise to their respective cellular compartment, *T. gondii* parasitophorous vacuole and *C. trachomatis* inclusions [277, 281, 282].

Thus far, 7 human GBP (hGBP) genes (*GBP1-GBP7*) located on chromosome 1 and 11 mouse GBPs (mGBP) (*Gbp2b-Gbp11*) have been identified [267, 283-285]. The mouse GBPs are organised in clusters on chromosome 3 (*Gbp2b*, *Gbp2*, *Gbp3*, *Gbp5*, *Gbp7* and a pseudo*mGbp2b*) and chromosome 5 (*Gbp4*, *Gbp6*, *Gbp8*, *Gbp9*, *Gbp10*, *Gbp11* and a pseudo *mGbp2*) [286]. Transcription of human and mouse GBPs can be triggered by type 1 and 2 IFN

as well as other inflammatory cytokines and TLR ligands, although the quantitative responses vary substantially between the different GBPs and cytokines [267, 287, 288].

IFN-induced GTPases belong to the dynamin-protein family as judged by structural similarities and shared biochemical characteristics [275, 289, 290]. As members of the dynamin protein family, they possess a large GTPase domain (~ 300 amino acids), a middle domain and a GTPase effector domain (GED) [291]. In addition to these 3 domains, many IFN-induced GTPases also possess other domains and motifs for protein-protein and protein-membrane interactions [262, 291-293]. In contrast to dynamin, at least some IFN-induced GBPs can hydrolyse GTP to GDP and GDP to GMP, though their GTPase activation is still dependent on oligomerisation [291, 294, 295]. These dynamin-related characteristics enable IFN-induced GTPases to operate either as mechanoenzymes or as an assembly platform to coordinate diverse functions [275]. For instance, they govern vesicular trafficking and the coordination of protein complex assembly to stimulate autophagic, membranolytic, oxidative and inflammasome-related anti-microbial activities upon cytosolic bacteria as well as on pathogen-containing vacuoles [226, 275, 296-299].

1.5.3 Mechanisms of host defence by IFN-induced GTPases

1.5.3.1 Targeting of specific pathogens by GBPs and IRGs

To execute anti-microbial functions, GBPs and IRGs co-localise with pathogens invading the host cell. GBPs and IRGs are typically found in the cytosol, in vesicle-like structures and on endomembranes, but translocate to pathogen compartments and cytosolic bacteria which have escaped from the phagosome (Fig 1) [288, 293, 300, 301]. Bacteria shown to interact with GBPs and IRGs include *Listeria monocytogenes*, *Legionella pneumophila*, *Shigella flexneri*, *Mycobacterium bovis* BCG, *Chlamydia trachomatis*, *Francisella novicida*, *Salmonella Typhimurium*, *Brucella abortus*, *Yersinia pseudotuberculosis* and *Burkholderia thailandensis* [226, 256-258, 260-262, 265, 274, 283, 287, 302-314].

Even though the exact molecular mechanism which enables them to target and destroy pathogens is not fully understood, it has been shown that human and mouse GBPs form homo- and hetero- and polymers to fulfil their anti-microbial function [268, 315]. Kravets *et al.* [268] showed that mGBPs accumulate on *T. gondii* vacuoles in densely packed multimers consisting of several thousand monomers. Furthermore, these proteins seem to locate to the pathogens and associated membranes in a hierarchical manner, with GBP1, GBP2 and GBP5 leading the way due to a CaaX prenylation motif at the C-terminus of the protein, which enables them to bind

to membranes and to recruit non-prenylated GBPs to their location [268, 300]. In addition to targeting various pathogens and their vacuoles directly, in mouse cells "GMS" IRGs have been suggested to influence the localisation and activation of GBPs and "GKS" IRGs on target membranes via a "missing-self" signal [282]. This control of GBP and IRG activation and aggregation on host membranes via the "GMS" IRG family proteins (IRGM), is further supported by the targeting of GBPs and IRGs onto lipid droplets from which IRGM1 and IRGM3 have been removed independently of infection [282]. Based on this observation, it was suggested that a lack of IRGM proteins and therefore the mistargeting of self-membranes through activated GBPs and IRGs as well as the formation of cytosolic clusters leads to a diminished pool of available GBPs and IRGs which could effectively target *C. trachomatis* and *T. gondii* [282]. It should be noted that there is some data that is not consistent with the 'missing self' hypothesis [255, 262, 285], although some of this was refuted in later publications [316, 317].

Park *et al*. [318] proposed a "triple check" model for targeting of mouse GBPs and IRGs to pathogen vacuoles. This model suggests that pathogen vacuoles are targeted by the autophagy conjugation system by depositing microtubule-associated protein light chain 3 (LC3) and its homologues on the pathogen vacuole. IFN-γ stimulation would "trigger" LC3 on these membranes, either via posttranslational modifications or via the addition of factors such as ubiquitin, to act as a guanine nucleotide exchange factor (GEF) for GBPs and IRGs and activate them. Misguiding of GBPs to endo-membranes would be avoided through the protective function of IRGM proteins, which act as GDIs for GBPs and IRGs [281, 319]. How the LC3 conjugation system recognises pathogen vacuoles remains unknown. However, Brown *et al.* [320] has suggested that the autophagy conjugation complex or some upstream sensor of this complex recognises changes to the membranes occupied by pathogens, such as missing-self (e.g. lack of IRGM proteins), changed-self (e.g. rearranged protein and lipid composition) and non-self (e.g. pathogen effectors and secretion systems). It was also suggested that the binding of this complex to membranes might be facilitated via autophagy related-protein ATG5 [321], as ATG5 from the autophagy conjugation complex can bind membranes via an unknown lipid moiety [322]. This model is supported by the observations that ATG5 and LC3 are found on murine norovirus (MNV) membranous replication complexes [323] and also *T. gondii* vacuoles without prior IFN-γ stimulation in mouse macrophages [318, 324]. Furthermore, GBPs and IRGs are unable to target pathogen containing vacuoles and aggregate in the cytosol in cells lacking all ATG5 or all LC3 homologues [320, 324, 325]. Whether this model applies to other

pathogens and host species, especially with humans which lack most IRGs, remains to be investigated.

To what extent IRGs and GBPs cooperate in targeted co-localisation to pathogens or pathogen vacuoles remains unclear, as reciprocal dependence has been observed. For example, IRGM1 and 3 are needed for targeting of mGBPs to *T. gondii* vacuoles and pathogen control in MEFs, whereas they are dispensable for *Leishmania donovani* control [259, 270]. On the other hand, the localisation of IRGs can also be dependent on GBPs, as the targeting of IRGB10 and IRGB6, to *F. novicida*, *T. gondii* and *E. coli* are dependent on GBPs from chromosome 3, as these IRGs failed to co-localise with pathogen inclusions in cells lacking GBPs on mouse chromosome 3 [257, 326].

Different GBPs and IRGs have been shown to target specific pathogens, though the underlying mechanisms for this specificity is only now being uncovered [260, 270, 283, 312, 327]. Kohler *et al.* [307] have suggested that changes in the C-terminal polybasic motif (PBM) in primate GBP1s are responsible for the pathogen specificity towards *S. flexneri*. In line with this, it was shown that the unique triple arginine cassette in the PBM of hGBP1 is responsible for targeting *S. flexneri* [261]. The highly divergent C-terminal amino acid sequence in mGBPs might also indicate a non-redundant function in determining pathogen specificity [267]. In addition, alternative splicing variants of GBPs might play a role in specific pathogen targeting, since a splicing variant of mGBP5, mGBP5a, was present in *L. monocytogenes* infected mouse liver but absent in *T. gondii* infected liver [267]. Besides the co-localisation of GBPs and IRGs with particular pathogens, differences in GBP targeting of the same pathogens have also been observed in distinct cell types of the same host species. For example, hGBP1 co-localises with *T. gondii* in mesenchymal stromal cells and THP1 but not A549 cells [287, 314, 328, 329]. This remarkable diversity of targeting strategies for specific pathogens might be due to the diverse genetic backgrounds and proteomes of different host species and cell types as well as pathogen-specific virulence factors and intracellular life cycles.

1.5.3.2 Mechanisms of pathogen clearance by IFN-induced GTPases

The antimicrobial mechanisms of IFN-induced GTPases that are discussed below are represented in Figure 2.

1.5.3.2.1 Ubiquitination and lysosomal destruction mediated by GBPs and IRGs

GBPs and IRGs can mediate pathogen control by induction of autophagy and ubiquitin-mediated destruction of pathogen vacuoles [330-332]. mGBP7 interacts with and recruits the autophagy protein ATG4B to *Mycobacterium*-containing vacuoles [283], which promotes the expansion of autophagic membranes around the bacteria and damaged bacterial compartments [226, 275], leading to degradation of the pathogen via lysosome fusion [283]. Haldar *et al.* [259] demonstrated that IFN-γ-induced IRGM1 and IRGM3 control the recruitment of the E3 ligase tumour necrosis factor receptor-associated factor 6 (TRAF6) and subsequent ubiquitination of vacuoles of *T. gondii* and *C. trachomatis*. Following ubiquitination, GBPs co-localise with vacuoles in a sequestosome 1 (SQSTM1/p62)-dependent manner and mark these vacuoles for destruction [259]. IRGM-dependent autophagy was also shown for *Mycobacterium* infections though the exact mechanism remains unclear [263, 332]. It seems likely that "GMS" proteins IRGM1 and IRGM3 coordinate the localisation of other GKS IRGs to pathogen vacuoles, as virulent *T. gondii* strains and *C. muridarum* inhibit "GKS" IRG activity and vacuole co-localisation of these IRG proteins thereby avoiding ubiquitination of the replicative niche [259, 333-335].

In addition to mediating the ubiquitination of pathogen compartments and the subsequent lysosomal destruction via controlling the "GKS" IRGs activity, IRGM1 has been shown to target *M. tuberculosis* vacuoles directly [255, 283]. The recruitment of IRGM1 to pathogen containing vacuoles appears to facilitate fusion with lysosomes, as lysosomal fusion of *M. tuberculosis* vacuoles is impaired in *Irgm1*-deficient mutants [255]. The C-terminal amphipathic helix (αK) of IRGM1 binds to *Mycobacterium* vacuoles by interaction with phosphoinositide-3,4-bisphosphate (PtdIns[3,4]P_2) and PtdIns[3,4,5]P_3 [262].

For protection against the lung pathogen *L. pneumophila*, IRG-dependent as well as IRG-independent pathways have been described. Both IRGM1 and IRGM3, have been implicated in IFN-mediated control of *L. pneumophila* [234, 254]. Binding of IRGM1 to the intracellular replicative niche of *L. pneumophila*, the *Legionella*-containing vacuole (LCV), results in the

co-localisation of other IRG proteins and subsequent ubiquitination of the LCV, thereby leading to LCV degradation through autophagy [229]. GBP1 and GBP2 are involved in an IRGM-independent resistance against *L. pneumophila,* as the bacterial protein secretion system on the LCV is recognised as a PAMP, leading to binding of the cytosolic carbohydrate-binding protein galectin-3. The binding of galectin-3 to the LCV recruits GBP1 and GBP2 to the LCV, as well as subsequent ubiquitination and targeting by p62, which leads to the degradation of the bacteria via autophagy [311]. This IRGM-independent and GBP-dependent ubiquitination during *Legionella* infection is in contrast to the previously mentioned IRGM-dependent and GBP-independent ubiquitination of *T. gondii* vacuoles as well as *C. trachomatis* inclusions [259].

In most cases, the ubiquitination of pathogens and their compartments is a host-derived response which favours host survival and promotes pathogen control. In contrast to this, it was shown that the hGBP1-mediated, poly-ubiquitin coat on *S. flexneri* is not host-derived but mediated by a bacterial-derived E3 ubiquitin ligase IpaH9.8, which recognises, binds and ubiquitinates GBP1, GBP2 and GBP4 but not GBP3 and labels them for proteasome-mediated degradation [260, 261, 308]. This poly-ubiquitination reverses the GBP-mediated restriction and enables the bacteria to form actin tails and spread efficiently from cell to cell [260, 261, 308].

1.5.3.2.2 GBP mediated production of reactive oxygen species (ROS)

Another host resistance pathway that mediates IFN-induced pathogen control is the production of ROS. NOX2 is an NADPH oxidase that is able to generate superoxide, which has microbicidal properties [336]. During *L. monocytogenes* and *M. bovis* BCG infection, mGBP7 binds the membrane-bound heterodimer $gp91^{phox}$-$p22^{phox}$ (cytochrome b558) and cytosolic $p67^{phox}$ [283]. Thus, GBP7 acts as a linker between membrane-bound and cytosolic NOX2 components to assemble and activate the NOX2 holoenzyme on pathogen compartments after IFN-γ stimulation [283].

1.5.3.2.3 GBP mediated Inflammasome activation

Recent work has linked IFN-induced GTPases with inflammasome activation in various host cells and in response to a diverse range of pathogens. IFN-induced GTPases appear to influence inflammasome activation by promoting inflammasome complex assembly and targeting pathogens and their compartments to increase the access of PAMPs to cytosolic inflammasome components. These two mechanisms of inflammasome activation can work in concert to achieve adequate inflammasome activation and thus host defence.

GBP5 is involved in the assembly of the NOD-, LRR- and pyrin domain-containing 3 (NLRP3) inflammasome during *Listeria* or *Salmonella* spp. infections via tetramerisation of GBP5 [337-339]. Assembly of the NLRP3 inflammasome leads to the induction of pyroptosis in order to control bacterial infections. Deletion of single mGBPs from chromosome 3 revealed unique functions for GBPs; namely, GBP5 binding to the pyrin domain of NLRP3 and GBP2 binding of apoptosis associated speck-like protein containing a CARD (ASC) [339]. Due to their ability to form heterodimers, GBP2 and GBP5 thus facilitate the assembly of the NLRP3 inflammasome to activate caspase-1 [339].

Several observations have shown that GBPs activate inflammasomes by either directly sensing bacterial products or facilitating access to bacterial PAMPs. The induction of inflammasomes via GBPs and IRGs can result in canonical (caspase-1) or non-canonical (caspase-11, human caspase-4/5) mediated pyroptosis. It was shown that GBPs from mouse chromosome 3, namely GBP2, GBP5, as well as IRGB10 are essential for the activation of the AIM2 inflammasome in *F. novicida* infected macrophages, as cells lacking these IFN-induced GTPases showed decreased inflammasome activation [257, 305, 306]. GBPs from chromosome 3 also control the non-canonical activation of caspase-11 in response to *L. pneumophila* as well as pathogenic and non-pathogenic *E. coli* outer membrane vesicles and free LPS injected into the cytosol [254, 340, 341]. GBPs from chromosome 3 were also essential for caspase-1 activation and IL1-α as well as IL-1ß release in response to *Brucella abortus* and *Yersinia pseudotuberculosis* infections [265, 310]. It has been suggested that GBPs might be influencing the membrane dynamics of outer membrane vesicles and the integrity of pathogen membranes due to their dynamin-like activities thus exposing lipid A of LPS and other PAMPS to the cytosol, hence making them accessible for inflammasome activation [257, 340, 342].

In line with these previous observations suggesting GBPs mediate LPS release and/or recognition by the inflammasome, hGBP1 was recently identified as a novel cytosolic LPS sensor [287, 312-314]. hGBP1 binds to LPS via electrostatic interactions between the negatively charged LPS and positively charged amino acid residues of hGBP1 [312, 315]. Detection of LPS via hGBP1 results in the recruitment of hGBP2-4 to cytosolic *Salmonella*, this GBP coat in turn recruits and activates caspase-4 [287, 312, 313]. Based on these observations and their own, Kutsch *et al.* [315] presented a model of hGBP1 acting as a detergent on the bacterial LPS layer. hGBP1 was identified as a LPS sensing and binding protein, which disrupts the O-antigen barrier of Gram-negative bacteria through the insertion of the farnesyl tail of hGBP1 molecules into this layer, thereby disrupting the interactions between LPS molecules mediated by the O-antigens [315]. A triple-arginine motif in the C-terminal end of GBP1 mediates the binding of hGBP1 to the pathogen LPS O-antigen [261]. The insertion of hGBP1 into the LPS layer seemingly changes the membrane stiffness and fluidity, thus making the bacteria more accessible to caspase-4 activation and more susceptible to the anti-microbial activity of polymyxin B, as well as potentially influencing the function of other pathogen proteins inserted into the outer membrane such as *Shigella* IcsA [315].

Using different GBP1 catalytic mutants, Xavier *et al.* [343] identified a novel pathway of NLRP3 activation mediated by hGBP1. This group discovered that hGBP1 recruitment to *C. trachomatis* inclusions activates GTP hydrolysis to GMP and the subsequent generation of uric acid activates the NLRP3 inflammasome [343]. This novel pathway suggests that, in contrast to previous findings [287, 312-315], inflammasome activation can be independent of PAMP release in human cells, relying only on the hydrolytic activity of hGBP1 [343]. Whether this activation is unique to the *Chlamydia* inclusion or represents a more general response towards other pathogens, remains to be investigated.

1.5.3.2.4 IFN-induced GTPases and actin-based motility

Recent findings have demonstrated that IFN-induced GBPs can inhibit actin-based motility of intracellular bacteria. hGBPs target cytosolic *S. flexneri* after IFN-γ exposure and interfere with actin tail formation, which is required for cytosolic mobility and cell to cell spread [260, 261]. GBP1 is essential for IFN-γ mediated inhibition of actin tail formation as well as recruitment of GBP2, 3 and 4 to the pathogen [260]. GBP-mediated inhibition of actin tails hindered the bacteria from spreading efficiently from cell to cell and resulted in large microcolonies forming

in infected cells but significantly fewer cells becoming infected [260]. In addition to *S. flexneri,* hGBP1 also targets *B. thailandensis* through a C-terminal triple-arginine motif that binds O-antigen [261].

mGBPs also inhibit the formation of actin tails and the formation of multinucleated giant cells (MNGCs) during *B. thailandensis* infection by interfering with Arp2/3-mediated actin nucleation and cytoskeletal remodelling [304]. Cells lacking multiple GBPs from chromosome 3 as well as *Gbp2*$^{-/-}$ and *Gbp5*$^{-/-}$ cells showed an increased number of multinucleated giant cells and increased bacterial load [304].

1.5.4 Perspectives

Importance of the field

IFN-induced GTPases play a significant role in cell-autonomous defence against a wide variety of pathogens. They initiate and regulate a diverse range of host defence pathways and an appreciation of the roles of IFN-induced GTPases in host defence could lead to more effective anti-microbial treatments.

Current thinking

Individual IFN-induced GTPases possess unique functions that tailor the response to different pathogens and mediate their anti-microbial function by compromising the integrity of pathogen-related membranes, releasing PAMPS into the cytosol, inducing bactericidal small molecules, marking pathogens for destruction or inhibiting pathogen mobility.

Future directions

Identifying GTPase binding partners that mediate their specific function and regulate their activities, will be crucial in enhancing our understanding of how these GTPases mediate IFN-induced cell-autonomous defence against various pathogens.

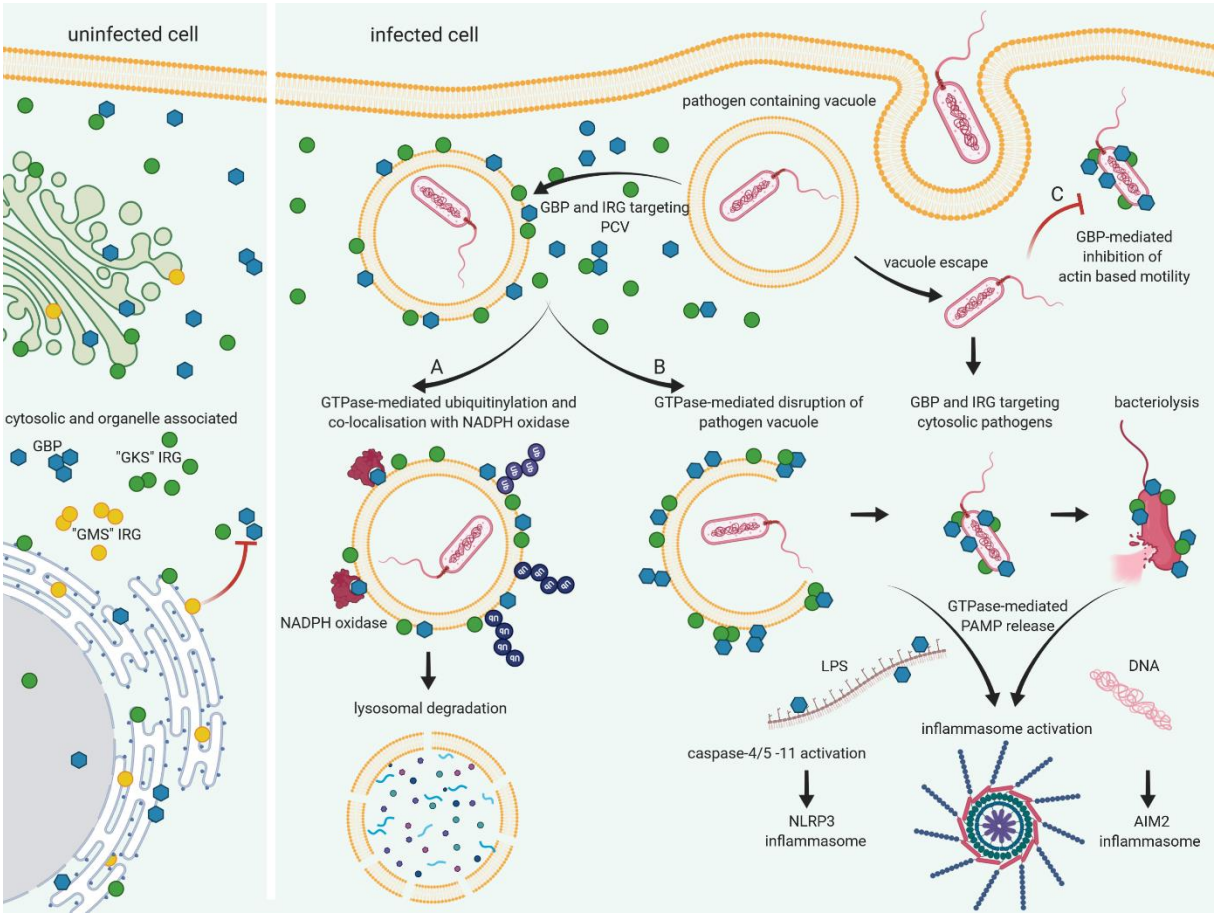

Figure 2: Mechanisms of pathogen clearance by IFN-induced GTPases.

In uninfected cells, GBPs and IRGs are found in the cytosol, in vesicle-like clusters, associated with endomembranes and the nucleus. “GMS” IRGs control the activation of GBPs and host membrane located “GKS” IRGs act as guanosine dissociation inhibitors.
During infection GBPs and IRGs co-localise with pathogen containing vacuoles (PCV) and cytosolic pathogens within minutes of pathogen entry.

A) GBP association with PCV may lead to the accumulation of ubiquitin and subsequent destruction of the invading pathogen. GBP7 is essential for NADPH oxidase holoenzyme assembly on PCV.
B) GBP and IRG co-localisation with the PCV and cytosolic bacteria leads to the disruption of vacuole and membrane integrity, releasing PAMPS into the cytosol. GBPchrom3, GBP1, GBP2, GBP3, GBP4 mediate activation of caspase4/5 or 11 during Salmonella, *Legionella* or *Chlamydia* infection by cytosolic LPS release leading to pyroptosis. Association with GBPs and IRGB10 leads to loss of membrane integrity and bacteriolysis with subsequent AIM2 activation during *Francisella* infection.
C) In addition to disrupting PCV and bacterial membrane integrity, GBPs also mediate host defence via the inhibition of actin-based motility of *Burkholderia* and *Shigella* pathogens.

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1.6 Aims

Even though it is known that the host triggers a strong inflammatory response upon detecting invading *Legionella*, little is known about how these inflammatory cytokines, especially IFN-γ, mediate host defence on a cell-intrinsic level. Although, *Legionella* can interfere with cell intrinsic immunity through the activity of Dot/Icm translocated effector proteins, an immune competent host usually overcomes this interference and restricts the intracellular replication of the invading pathogen. This suggests that cytokine responses can counter the activity of Dot/Icm effector proteins. Since inflammatory cytokines are essential in host defence against *Legionella*, we tested the impact of several inflammatory cytokines on *Legionella* Dot/Icm secretion system effector translocation, including IFN-γ and type I interferons IFN-α and IFN-β.

The importance of IFN-γ in host defence against *L. pneumophila* is well established. However, although *L. longbeachae* has been known since 1981 and is the dominant causative agent of Legionnaires' Disease in Australia and New Zealand, knowledge about the immune response to this important pathogen is extremely limited compared to *L. pneumophila*. We therefore also analysed the role of IFN-γ in host defence to *L. longbeachae* in vivo.

Chapter 2: Material and Methods

2.1 Materials

All common laboratory reagents and chemicals used in this study were purchased from Sigma Aldrich, Merck, Roth and ThermoFisherScientific. Components for *Legionella* media were obtained from Oxoid™ or the media preparation unit (MPU) of the Peter Doherty Institutes. Tissue culture media and supplements such as antibiotics and cytokines were obtained from ThermoFisherScientific, Gibco™, PANBiotech, Biolegend and Invitrogen. Fluorochrome conjugated antibodies and other components for FACS analysis were obtained from BD Bioscience.

2.1.1 Equipment

Table 1: Equipment used during this study

Equipment	Manufacturer
Microplate reader: ClarioStar® (Melbourne)	BMG LABTECH
Microplate reader: infinite 200Pro (Bonn)	Tecan
Homogenizer: ULTRA-TURRAX®	IKA
Imaging System: ChemiDoc™	BIO-RAD
BD LSRFortessa™ (Melbourne)	BD Bioscience
BD LSR II (Bonn)	BD Bioscience
PAGE: Mini protean tetra system	BioRad
PAGE-gel transfer system: iBlot™	Invitrogen™

2.1.2 Chemicals and Reagents

Table 2: Chemicals and reagents

Chemical / Reagent	Company	Reference
Tissue cell culture		
IMDM	PANBiotech	21980065
DMEM	ThermoFisher / Gibco™ or PAN™ Biotech	10566024
RPMI	ThermoFisher / Gibco™	61870127
FBS (heat inactivated)	PAN™ Biotech	P30-1302
PBS	PAN™ Biotech	
EDTA for cell culture	Sigma Aldrich	E7889
M-CSF	Immunotools	12343115

***Legionella* culture**		
BCYE plates	Oxoid™ or MPU Peter Doherty Institute	
Iron(III) nitrate ($Fe(NO_3)_3$	Sigma Aldrich	254223-50G
L-cysteine hydrochloride	Sigma Aldrich	C7880-100G
ACES	Sigma Aldrich	A9758-25G
Yeast extract	Oxoid™	LP0021B
FACS analysis		
BD FACS™ lysing solution	BD Bioscience	349202
Intracellular Fixation & Permeabilization Buffer Set	eBioscience™	88-8824-00
CaliBRITE™ APC-beads	BD Bioscience	340487
DNAse-I	Worthington Biochemical Corporation	
Collagenase-III	Worthington Biochemical Corporation	LS004182
Western Blot		
Bolt™ Bis-Tris Plus Gels		NW04120BOX
ECL Substrates for WB	Thermo Fisher Scientific	32106
ß-lactamase translocation assay		
LiveBLAzer™ loading kit with CCF2-AM	ThermoScientific/Invitrogen	K1032
Probenecid	Sigma Aldrich	P8761-25G
HEPES	PANBiotech	P05-01100
IFN-γ	Immunotools	12343536
IFN-α	Biolegend via BIOZOL	752804
IFN-β	Biolegend via BIOZOL	581303
MG123	Selleckchem	S2619
Bafilomycin A	Medchemexpress via BIOZOL	MCE-HY-100558
LPS	Sigma Aldrich	L4516
CpG		
TNF-α	Immunotools	12343014
IL-6	Immunotools	12340063
ISOLATE II RNA Mini Kit	Bioline via Biocat	BIO-52072-BL

2.1.3 *Legionella* strains and *Legionella* culture media

2.1.3.1 *Legionella* strains used throughout this study

The modified *L. pneumophila* strains used in this study are based on the clinical isolate *L. pneumophila* 130b (Serogroup 1; ATCC BAA-74) [344]. The modified *L. longbeachae* strains used in this study are based on the clinical isolate *L. longbeachae* NSW 150 [63].

Table 3: *Legionella* strains used in this study

***Legionella* strain and plasmids**	**Characteristics**	**Source / Reference**
	L. pneumophila	
L. pneumophila Δ*flaA*	in-frame deletion of *flaA*	[345]
L. pneumophila Δ*flaA* Δ*dotA*	in-frame deletion of *flaA* and *dotA* strain is unable to translocate any effectors	[345]
pxDC61	β-lactamase expression vector	[346]
pxDC61-RalF	ß-lactamase-RalF fusion protein	[347]
pxDC61-SidB	ß-lactamase-SidB fusion protein	[347]
L. pneumophila Δ*flaA* pxDC61-RalF (or SidB)	strain carrying plasmid with fusion protein, used in this study to determine effector translocation	[347]
L. pneumophila Δ*flaA* Δ*dotA* pxDC61-RalF (or SidB)	strain carrying plasmid with fusion protein, strain used as negative control in this study as it is unable to translocate any effectors	[347]
L. pneumophila Δ*flaA* pxDC61	strain carrying empty vector, used in this study as a negative control, as ß-lactamase is not translocated without fused effector	[347]
	L. longbeachae	
L. longbeachae Δ*dotB*	in-frame deletion of dotB strain is unable to translocate any effectors	[90]
pxDC61-RalF	ß-lactamase-RalF fusion protein	[90]
pxDC61-RelA	ß-lactamase-RelA fusion protein	[90]
pxDC61-RelB	ß-lactamase-RelB fusion protein	[90]
pxDC61-RelC	ß-lactamase-RelC fusion protein	[90]
pxDC61-RelD	ß-lactamase-RelD fusion protein	[90]
L. longbeachae pxDC61-RalF (or other effector)	strain carrying plasmid with fusion protein, used in this study to determine effector translocation	[90]
L. longbeachae Δ*dotB* pxDC61-RalF (or other effector)	strain carrying plasmid with fusion protein, strain used as negative control in this study as it is unable to translocate any effectors	[90]
L. longbeachae pxDC61	strain carrying empty vector, used in this study as a negative control, as ß-lactamase is not translocated without fused effector	[90]

2.1.3.2 *Legionella* culture media

2.1.3.2.1 Solid medium (BCYE plates)

Legionella were grown on buffered charcoal yeast extract BCYE plates and if required for ß-lactamase translocation assays, plates were supplemented with chloramphenicol (6 µg/ml). In Melbourne BCYE plates were sourced from the media preparation unit (MPU) at the Peter Doherty Institute (PDI) and in Bonn BCYE plates were purchased from Oxoid™.

2.1.3.2.2 Liquid culture medium for over-night *Legionella* culture

Legionella were grown in ACES [N-(2-acetamido)-2-aminoethanesulfonic acid]-buffered yeast extract (AYE) broth which consist of 1 % (w/v) ACES buffer and 1 % (w/v) yeast extract, and the pH of the solution is adjusted to pH 6.9 prior to autoclaving. After autoclaving, the solution is supplemented with sterile filtered solutions of 0.1 mM iron (III) nitrate ($Fe(NO_3)_3$ and 1 mM L-cysteine hydrochloride. Furthermore, if required for the ß-lactamase translocation assay, the medium was additionally supplemented with chloramphenicol (6 µg/ml) and isopropyl β-d-1-thiogalactopyranoside (IPTG, 10 mM) for the expression induction of the fusion protein.

2.1.4 Solutions used for *Legionella* infections

2.1.4.1 Solutions used during in vitro *Legionella* infections

Table 4: Substrate solution for ß-lactamase effector translocation assay

Solutions	Volumes for 1 sample
Hanks BSS (+ 25 mM HEPES)	100 µl
Solution C	15,8 µl
Solution B	1,08 µl
Probenecid (0.1M)	3 µl
CCF2 AM substrate	0,12 µl
Total	120 µl

2.1.4.2 Solutions used during in vivo *Legionella* infections

Table 5: Buffers used during in vivo *Legionella* experiments

Buffer / Solution	Composition
FACS buffer	PBS 0.1 % (w/v) BSA 2 mM EDTA
Digestion buffer	RPMI 3 % FCS 1 mg/mL DNase-I 1 mg/mL Collagenase-III in RPMI

Table 6: Cytokines detected with BD Bioscience Cytometric Bead Array (CBA) flex kit

Cytokine beads	Reference number
GM-CSF	558347
IFN-γ	558296
IL-10	558300
IL-12p70	558303
IL-17α	560283
IL-1α	560157
IL-2	558297
IL-6	558301
MCP-1	558342
TNF-α	558299

2.1.5 Buffers and solutions used for protein isolation and Western Blots

Table 7: Buffers and solutions used for protein isolation and Western Blots

Buffer / Solution	Composition
Cell lysis buffer	50 mM Tris, pH 8.0 150 mM NaCl 1 % Triton® X-100 1-2 µg/ml Aprotinin 0.5-2 µg/ml Leupeptin 50-100 µg/ml PMSF 1-20 mM Sodium Fluoride 1-100 mM Sodium Orthovanadate 2-10 mM EDTA 1-20 µM Pepstatin A
SDS-PAGE Sample buffer (2x)	125 mM, pH 6.8 Tris 4.0 % (v/v) SDS 10 % (v/v) Glycerol 0.02 % (v/v) Bromophenol blue 0.2 M DTT in dH_2O
TBST	10 mM Tris.HCl, 15 mM NaCl, 0.05 % Tween® 20 in dH_2O at pH 7.5
Running buffer (Bonn)	25 mM Tris base 190 mM Glycine 0.1 % SDS
Transfer buffer (Bonn)	50 mM Tris base 380 mM Glycine 0.1 % SDS 20 % (v/v) methanol in dH_2O pH 8.3

Ponceau S Solution (10x)	2 % /w/v) Ponceau S 30 % (v/v) Trichloroacetic acid 30 % (v/v) Sulfosalicylic acid
Membrane blocking solution	5 % (w/v) dry non-fat milk powder in TBST
Antibody solution	3-5 % BSA in TBST or PBS according to manufactures directions

2.2 Methods

2.2.1 Tissue culture

2.2.1.1 Reviving mammalian cells from frozen stocks

Aliquots of immortalised bone marrow-derived mouse macrophages (iBMDMs), HeLa CCL-2 epithelial cells or A549 lung epithelial cells were retrieved from cryogen storage and thawed at room temperature. To remove the DMSO, thawed cells were resuspended in 9 ml of PBS and harvested by centrifugation (RT, 5 min, 500 g). Subsequently, the supernatant was aspirated and the cell pellet resuspended in 7 ml of respective culture medium (Table 8). The resulting cell solution was transferred into tissue culture flasks and cells were cultured at 37 °C with 5 % CO_2. To ensure optimal cell health and phenotype, cells were passaged twice before they were used for any experiments.

For producing new stock aliquots, freshly revived cells were expanded and after reaching the desired number of cells and confluency, cells were detached from culture flasks and harvested by centrifuging for 5 min with 500 g at RT. Following the centrifugation, the supernatant was aspirated, the cell pellet resuspended in FCS containing 10 % (v/v) DMSO and the resulting cell solution was aliquoted in 1 ml vials for long-term cryo-storage.

Table 8: Tissue culture media used for mammalian cell culture

Primary cells / Cell line	Culture Media	Additives
iBMDMs	DMEM with GlutaMax™	10 % (v/v) heat-inactivated FCS
RAW 264.7	DMEM with GlutaMax™	10 % (v/v) heat-inactivated FCS
pBMDM	IMEM	10 % (v/v) heat-inactivated FCS recombinant M-CSF (10 ng/ml) 1 % (v/v) Pen/Strep
A549	RPMI	10 % (v/v) heat-inactivated FCS
HeLa CCL-2	DMEM with GlutaMax™	10 % (v/v) heat-inactivated FCS
THP1	RPMI	10 % (v/v) heat-inactivated FCS

2.2.1.2 Continues culture of mammalian cell lines

Cells were cultured in respective culture media (Table 8) at 37 °C with 5 % CO_2 and passaged whenever cell growth reached ~85-90 % confluency. Upon reaching appropriate confluency, culture supernatant was removed from adherent cells, cells were washed twice with 37 °C PBS and detached from wells either with a cell scraper (iBMDM, RAW 264.7) or enzymatically with trypsin (A549, HeLa CCL-2) at 37 °C. Detached cells were mixed with respective culture medium, appropriate numbers of cells were transferred into a new tissue culture flask and cultured until reaching ~85-90 % confluency again at 37 °C and 5 % CO_2. THP1 cells grow in suspension and were harvested for passaging by centrifugation (RT, 5 min, 500 g). Following centrifugation, the supernatant was aspirated and the cell pellet was washed twice with 37 °C PBS. THP1 cells were resuspended in culture medium, appropriate number of cells were transferred into new tissue culture flask and cells were cultured until reaching ~85-90 % confluency again.

To ensure consistency and cell health, cells were maintained for a maximum of 35 passages (except pBMDM, which were not passaged) before new cell aliquots are revived.

2.2.1.3 Culture of primary bone marrow derived macrophages (pBMDM)

Mice bones were harvested and the marrow extracted from the bones according to the protocol described in [348]. Following the marrow isolation, the marrow pellet was resuspended with culture medium (Table 8) and 10 ml of the cell mixture were added to a non-treated, non-tissue culture petri dishes (~10 cm diameter) at a concentration of $5x10^5$ cells/ml. Cells were cultured at 37 °C and 5 % CO_2 for 7 days and on day 3 10 ml fresh medium was added to each petri dish. After differentiation was completed, cells were harvested for experiments with the following steps: 1) aspirating culture media, 2) washing the cells twice with 37 °C PBS, 3) detaching cells by incubating cells with ice cold PBS containing 5 mM EDTA for 15-20 min, 4) cells were harvested by washing off cells from the petri dishes with repetitive pipetting using a 10 ml stripette and centrifugation at 500 g for 5 min at RT. After the centrifugation, the supernatant was removed, the cells were resuspended in culture media without Pen/Strep, if a *Legionella* infection was part of the following experiment, and cells were seeded at appropriate concentrations for planned experiments.

2.2.2 *Legionella* culture and preparation for infections

For each experiment *L. pneumophila* or *L. longbeachae* strains were sourced and reactivated from -80 °C glycerol stocks and cultured for 3 days aerobically at 37 °C on BCYE agar plates supplemented with chloramphenicol (6 µg/ml) if required. After initial culture on BCYE plates and in preparation for infections, *Legionella* were transferred into liquid culture and grown aerobically overnight at 37 °C with 180 rpm agitation in AYE broth.

In preparation for an infection (e.g. ß-lactamase translocation assay of replication assay), 1 ml of liquid *Legionella* culture was taken and centrifuged for 1 min with 12.000 g at RT (~23 °C). The supernatant was removed and the bacteria pellet was resuspended in 1 ml of cell culture medium. The optical density (OD) of this solution was measured at 600 nm (OD_{600}) with an OD of 1 representing 10^9 *Legionella*/ml. A solution of *Legionella* and appropriate cell culture media was mixed to achieve the desired multiplicity of infections (MOI); which is the ration between infectious agents (*Legionella*) and the targets of infection (cells); for the following experiment.

2.2.3 *Legionella* replication assay

Prior to infection, pBMDM were isolated and differentiated as previously described and 500 µl of cell mix was added into 24 well plates at a concentration of $5.6x10^5$ cells/ml 24. *L. pneumophila* was cultured and prepared for infection as previously described and pBMDM were infected with *L. pneumophila* at a MOI of 0.1. To synchronise infection, plates were centrifuged at 600 g for 10 min at RT (~23 °C). Following the centrifugation, cells were incubated at 37 °C and 5 % CO_2 for 1 h to allow cells to phagocytose bacteria. After the infection, supernatant was aspirated from cells and replaced with cell culture media containing 100 µg/ml gentamicin and incubated for 2 h at 37 °C with 5 % CO_2, to kill all extracellular non-phagocytosed bacteria. To remove the gentamicin, the supernatant was aspirated and pBMDM were washed twice with 37 °C warm PBS. Finally, 500 µl cell culture media was added to cells containing IFN-γ (50 U/ml), IFN-α (1000 U/ml), IFN-β (1000 U/ml) or IFN-α+β (1000 U/ml each) if required and plates were incubated at 37 °C with 5 % CO_2 to enable bacteria replication.

After 24 h or 48 h of replication the supernatant was collected and cells were lysed with 1 % (v/v) Saponin-PBS solution by incubating the cells at 37 °C and 5 % CO_2 for 30

minutes. Following the lysis of the cells, wells were scraped and the supernatant was mixed with the cell culture supernatant collected previously. Supernatant mixtures were vortexed and then serially diluted, with 25 µl of the diluted bacteria solution being spotted onto BCYE plates. Finally, BCYE plates were incubated at 37 °C for 3 days to enable CFU growth, following this the formed CFU were enumerated.

2.2.4 ß-lactamase translocation assay

Legionella strains used during ß-lactamase translocation assay were cultured as described (paragraph 2.2.2) previously. In general, per well 100 µl of cell mixture (for cell specific concentration and treatment please see Table 9) was added into clear bottom, black 96-well assay plates 24 h prior to infection, if cells did not need differentiation prior to infection, and cultured at 37 °C and 5 % CO_2. Since THP1 cells are differentiated into macrophages prior to infection, cells were seeded into wells 3 days prior to the ß-lactamase translocation assay and differentiated with 50 ng/mL phorbol 12-myristate 13-acetate (PMA). If cells were treated with IFN-γ or other stimuli, usually 100 µl of respective cell culture media mixed with cytokines or stimulants was added to wells prior to infection at indicated timepoints and final concentrations prior to infection (Table 10). To cells which were used as untreated controls, 100 µl of respective cell culture media was added.

Table 9: Cell and bacteria concentrations used for ß-lactamase translocation assay

Cell line	Concentration	MOI
iBMDM	$3.5x10^5$ cells/ml	40 for *L. pneumophila* 100 for *L. longbeachae*
RAW 264.7	$3.5x10^5$ cells/ml	40
pBMDM	$7x10^5$cells/ml	40
A549	$4x10^5$ cells/ml	40
HeLa CCL-2	$4x10^5$ cells/ml	125
THP1	$4x10^5$ cells/ml	40

Table 10: Treatment of cells prior to ß-lactamase translocation assay

Treatment	concentration	Incubation time prior to infection
IFN-γ	50 U/ml	over night ~17 h and shorter (1-12 h)
IFN-α	1 000 U/ml	over night ~17 h, 6 h, 4 h and 2 h
IFN-β	1 000 U/ml	over night ~17 h, 6h, 4 h and 2 h
MG123	5 µM	30 min
Bafilomycin A	160 nM	3 h
LPS	1, 5 and 10 ng/ml	over night ~17 h, 2 h, 4 h and 6
CpG	1 and 20 µM	over night ~17 h, 1 h
TNF-α	20 ng/ml	over night ~17 h, 2 h
IL-6	100 ng/ml	over night ~17 h

After cells were treated with the various stimulants, cells were infected with various *L. pneumophila* or *L. longbeachae* strains (Table 3) at indicated multiplicity of infections (Table 9). In order to synchronise the infections, plates were centrifuged at RT (~23 °C) with 600 g for 10 min and then incubated for 1 h (or 3 h *L. longbeachae* infection) at 37 °C and 5 % CO_2. Subsequently of the infection, cells were washed twice with 100 µl of 37 °C warm Hanks Balanced Salt Solution (HBSS) supplemented with 25 mM HEPES. After extracellular bacteria were removed by washing, 100 µl of CCF2-AM substrate solution (Table 4) was added to each well and plates were incubated at room temperature (~23 °C) for 1.5 h protected from light. Finally, the substrate solution was aspirated and replaced with 100 µl HBSS (Melbourne) or with 100 µl 2% PFA (Bonn). The effector translocation and thus ß-lactamase activity was immediately determined by measuring the fluorescence intensity of the translocation assay substrate CCF2-AM with the ClarioStar® (Melbourne) or TECAN Infinite® 200Pro (Bonn) microplate reader. The readers were set to measure in bottom-reading mode with the excitation filter set to 410 nm and the fluorescence intensity of the emission was detected with the filters set to 450 nm and 520 nm.

To assess the activity of the ß-lactamase and thus the amount of effector translocation, data analysis of raw values was performed. In order to determine the net fluorescence of each emitted wavelength, representing uncleaved substrate at 520 nm and cleaved substrate at 450 nm, the background fluorescence was obtained from wells only

containing substrate solution and respective values were subtracted from measured fluorescence intensities of each well/sample.

The resulting net fluorescence intensity at 450 nm was then divided by net fluorescence intensity at 520 nm, to obtain the blue to green ratio (cleaved to uncleaved substrate ratio) for each sample. Finally, this fluorescence ratio was normalised to the value obtained in the samples of the negative control (cells infected with strain carrying the empty pxDC61 vector) with values > 1 indicating β-lactamase activity and thus effector translocation.

2.2.5 Cell quantification assay

To quantify remaining cells after ß-lactamase effector translocation assay, supernatant was removed and cells were fixed with ice-cold methanol for 10 minutes. Following the fixation, cells were stained by adding 50 µl CellTag700 solution (1:10 000 in PBS) to wells and incubating for 20 min at RT (~23 °C) protected from light whilst shaking on an orbital shaker at 50 rpm. To remove any unspecific staining, cells were washed three time with PBS containing 10 % Tween for 5 min under the same conditions as previously used for staining the cells. Lastly, wells were toped up with 100 µl PBS and fluorescence was measured at 700 nm using the Licor Odyssey Imaging System. Similar to the data analysis of the ß-lactamase translocation assay, the net fluorescence of each well was calculated by subtracting background fluorescence, which was obtained by measuring wells which did not contain cells. Following the calculation of net fluorescence, the mean fluorescence of each triplicate was calculated and used for further data analysis and comparison of the different treatment groups.

2.2.6 Cell viability assay

To assess cell viability after the ß-lactamase assay or the *Legionella* replication assay, supernatant was removed from cells and 100 µl or 500 µl MTT (3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide) solution (0.5 µg/ml MTT in PBS) was added to cells respectively and incubated overnight (~18 h) at 37 °C with 5 % CO_2. After purple MTT formazan crystals have formed, these crystals were dissolved by adding 200 µl or 500 µl of solvent solution (acidified isopropanol, 4 mM HCL in isopropanol) respectively to each well. Plates were incubated on an orbital shaker (50 rpm) at RT (~23 °C) protected from light until formazan crystals were completely dissolved. Lastly, the absorbance is measured at 570 nm for formazan absorbance and at 690 nm to adjust for the optical

variation in the wells of the plates. During data analysis, the reference wavelength of each well was deducted from the absorbance value measured at 570 nm of each well, respectively. Following the adjustment with the reference wavelength, the net absorbance was calculated by deducting the mean of the background absorbance at 570 nm (taken from wells not containing cells) from each well. Following the calculation of net absorbance, the mean absorbance of each triplicate was calculated and used for further data analysis and comparison of the different treatment groups.

2.2.7 mRNA isolation and mRNA sequencing analysis

For the isolation of mRNA from pBMDM, the mRNA isolation kit of Bioline (ISOLATE II RNA Mini Kit) was used. In general, pBMDM were isolated and differentiated as previously described and seeded for mRNA isolation in 24 well plates in triplicates 24 h prior to infection. Cells were mock treated or treated with IFN-γ or IFN-α+β 2 h and 6 h prior to infection (Table 11). After treatment, cells were then either infected with *L. pneumophila* or mock infected and then treated as if a ß-lactamase translocation assay was conducted (Table 11). After the substrate incubation, cells were lysed and the mRNA isolation was performed according to manufacturer's protocol. The concentration and purity of isolated mRNA was measured with a NanoDrop spectrophotometer and samples meeting the quality criteria of the sequencing facility were selected for mRNA sequencing (for each treatment condition 3 different mice and isolations).

Table 11: Sample scheme for mRNA isolation

	unstimulated	**IFN-γ**	**IFN-α+β**
2 h	± *L. pneumophila*	± *L. pneumophila*	± *L. pneumophila*
6	± *L. pneumophila*	± *L. pneumophila*	± *L. pneumophila*

2.2.8 In vivo infections with *L. longbeachae* and *L. pneumophila*

2.2.8.1 Used mice

All mice (C57BL/6 WT mice and IFN-$\gamma^{-/-}$ mice (B6.129S7-*Ifng*^{tm1Ts}/J)) used during this study were bred and maintained under specific pathogen free conditions at the Bio21 Molecular Science and Biotechnology Institute. Furthermore, all mice experiments were conducted at the Bio21 in line with ethics approved by the University of Melbourne animal ethics committee.

2.2.8.2 Intranasal infection of mice with *L. longbeachae* or *L. pneumophila*

2.2.8.2.1 Intranasal infection

The *Legionella* strains used for the in vivo infections were cultivated on BCYE plates as previously described. The bacterial inoculum was prepared by collecting 3-5 *Legionella* colonies in PBS and adjusting the concentration to $5x10^6$ CFU/ml (*L. longbeachae*) and $5x10^7$ CFU/ml (*L. pneumophila*) via measuring the OD_{600} (OD of 1 = $1x10^9$ CFU/ml) and diluting the initial solution accordingly with PBS.

Mice were infected with *Legionella* via the intranasal route as previously described in [349]. During all experiments mice were infected with $2.5x10^5$ CFU (*L. longbeachae*) or $2.5x10^6$ CFU (*L. pneumophila*). The inoculum was administered under isoflurane induced anaesthesia by holding the mice gently at the scruff and applying 50 µl of the bacteria inoculum solution dropwise close to one nostril.

2.2.8.2.2 Daily health monitoring, organ harvest and BAL fluid collection

After intranasal infection, the health of mice and their body weight were monitored daily as required by the approved animal ethics.

At indicated days post-infection, mice were euthanized via CO_2 asphyxiation and organs or broncho-alveolar lavage (BAL) fluid were collected. To avoid cross contamination, the fur and skin of mice were drenched with 80 % ethanol prior to opening the body cavity with forceps and scissors. In order to determine the CFU burden, the right lung lobes and the spleen were collected and stored each in 2.5 ml ice cold PBS until further processing. For analysing cell populations involved in bacteria clearance during infections via flow cytometry, the left lung lobe was collected and stored in 3 ml ice cold FACS (Table 5) buffer.

In order to collect the BAL fluid, the trachea was exposed by removing the surrounding tissue and a small incision was made to insert a 20 G IV catheter attached to a 2 ml syringe. BAL fluid and cells were collected by injecting and removing 1 ml of ice-cold PBS twice into lungs and stored on ice until further use.

2.2.8.3 Quantification of *L. longbeachae* CFU in lung and spleen

Organs were harvested as described in the previous section and the tissue was then homogenised with the ULTRA-TURRAX® homogenizer (IKA). Following the tissue homogenisation, the cells were lysed by adding saponin solution (1 % v/v end concentration) to the homogenate and incubating the samples at 37 ℃ for 30 minutes. After cell lysis, samples were vortexed, serial diluted and then 25 µl of dilutant were spotted onto BCYE plates. These plates were then incubated for 3 days at 37 ℃, following bacteria growth resulting colonies were counted and numbers were extrapolated according to the dilutions used. The remaining non-permeabilised tissue homogenates were stored at -80 ℃ for future analysis such as cytokine analysis.

2.2.8.4 Quantification of cytokines in lung during *Legionella* infection with Cytometric Bead Array (CBA)

Lung tissue and BAL fluid were harvested and processed as previously described and to remove cells as well as debris for this analysis samples were centrifuged at 600 g for 5 min at 4 ℃. The clear supernatant was used to quantify the concentrations of various cytokines (Table 6) present in the lung during *L. longbeachae* and *L. pneumophila* infection, using the BD™ Cytometric Bead Array (CBA) mouse flexible kits according to manufacturers' protocol. Samples were subsequently analysed with the BD LSR Fortessa II.

2.2.8.5 Analysis of lung cell populations during *L. longbeachae* infections

2.2.8.5.1 Preparation of single cell solutions for FACS analysis

Lung tissue (left lung lobe) was harvested as previously described above and thoroughly minced with small scissors. This homogenised lung tissue was transferred into digestion buffer (Table 5) and incubated at 37 °C for 30 min with occasional mixing by pipetting to create a single cell solution. The resulting cell solution was filtered through a 70 µm cell strainers to remove any remaining cell clusters. To harvest the cells, samples were centrifuged at 600 g for 5 min at 4 °C and afterwards the supernatant was removed. Finally, the cell pellet was resuspended in PBS and cells stored at 4 °C until further use.

2.2.8.5.2 Cell staining for FACS analysis

After lungs were harvested and processed as previously described, cell viability was determined by staining cells with fixable viability dye (Table 12) for 30 min at RT (~23 °C). After the incubation with the viability dye, cells were washed with FACS buffer (Table 5) and then incubated with 50 µl antibody mixture for phagocyte differentiation (Table 12) for 30 min at 4 °C. Subsequently of cell staining, red blood cells were removed by lysing red blood cells with 1x BD FACS™ lysing solution for 7 min at RT (~23 °C). Following the red blood cell lysis, cells were fixed with fixation/permeabilization (eBioscience™) solution for 30 min at RT (~23 °C). In order to enable staining of intracellular *L. longbeachae*, fixed cells were permeabilised with 1x permeabilisation buffer (eBioscience™) containing primary anti-*L. longbeachae* antibody for 30 min at RT (~23 °C). During the final staining step, cells were incubated with secondary AlexaFluor488 or 594 conjugated anti-rabbit antibody for 30 min at RT (~23 °C). Finally, cells were washed with permeabilization buffer to remove unbound antibodies and stored at 4 °C in FACS buffer until flow cytometric analysis was conducted. To enable quantification of cells, $2x10^5$APC-labelled beads were added to each sample prior to FACS analysis using the BD LSR Fortessa II.

Table 12: Staining panel for lung phagocytes

Antigen / cell surface marker	Fluorochrome	Dilution
Ly6G	PerCP-Cy5.5	1/100
Ly6C	BV605	1/100
CD19	PE	1/100
CD11b	BV711	1/400
CD11c	PE-CF594	1/400
FceR1	PE-Cy7	1/100
Siglec-F	BV421	1/200
CD45	V500	1/100
CD103	BV786	1/100
CD64	A647	1/200
MHC-II	A700	1/400
Viability	APC-eFluor 780	1/1000
FcγII/III	Unlabelled	1/100
Legionella	Alexa 594 or 488	1/1000

2.2.8.5.3 Data analysis

All samples were measured with the BD LSR Fortessa II using BD FACSDiva™ Software. Fluorescence compensation was conducted using unstained samples, single fluorescence-stained cell samples as well as fluorescence minus one (FMO) samples. Following initial measurements at the BD LSR Fortessa II, subsequent data analysis was conducted using FlowJo™ Software.

2.2.8.6 Quantification of CFU in lung phagocytes

Mice were infected with *L. longbeachae* as previously described above and the whole lung was processed to generate single cell solutions. The collected cells were then stained with antibodies against cell surface markers (Table 13) for differentiation of the cell populations in the subsequent cell sorting process. In contrast to previous experiments dead cells were stained with 7-AAD. To be able to harvest enough alveolar macrophages, stained cells from 2 mice were pooled prior to cell sorting. Immediately before cell sorting, cell solutions were filtered through a 70 μm to remove any cell clumps and avoid clogging of the MoFlo Astrios cell sorter. Three cell populations were purified during cell sorting using cell surface markers as follows: alveolar macrophages (CD11c+Siglec F+), monocyte derived cells (CD11c+SiglecF-CD64+) and neutrophils (CD11c-Ly6G+CD64-Siglec F-). After cell sorting, samples are centrifuged and cell pellets are resuspended in PBS. Cell concentration as well as viable cells were determined by counting trypan blue

treated cells with haemocytometer. Subsequently, $2.5x10^4$ viable cells were lysed by adding saponin solution (1 % v/v end concentration) and incubating samples for 30 min at 37 °C. After cell lysis, samples were serial diluted and 25 µl of each dilution were spotted on BCEY plates. Bacteria were then cultured for 3 days at 37 °C and resulting CFU were enumerated.

Table 13: Staining panel for lung phagocyte cell sorting

Antibody	Fluorochrome	Dilution
Ly6G	FITC	1/100
CD11c	PE	1/100
Siglec-F	BV421	1/200
CD64	A647	1/200
FcγII/III	unlabelled	1/100

2.2.8.7 Quantification of *Legionella* RalF translocation in vivo

To determine the impact of IFN-γ on effector translocation in vivo, WT and IFN-γ deficient mice were infected as previously describe above with *Legionella* strains expressing the ß-lactamase-RalF fusion protein. Due to the fusion protein's expression being induced by IPTG, only a short infection was possible due the expression ceasing without IPTG stimulation in mice and thus substrate cleavage. To initiate migration of neutrophils and monocyte derived cells into the lungs, mice were treated intranasally with LPS (same procedure as intranasal infection) 48 h prior to infection. Subsequently, mice were infected with *L. longbeachae* or *L. pneumophila* expressing ß-lactamase-RalF fusion protein and 24 h post infection mice were euthanised and BAL fluid was collected as previously described. Cells were harvested form BAL fluid by centrifugation, red blood cells were lysed and cells were stained with cell surface markers as well as cell viability dye (Table 14) as previously described. After cell staining, cells were treated with ß-lactamase substrate solution (Table 4) for 1.5 h at RT (~23 °C). After substrate incubation, cells were fixed and immediately analysed via flow cytometry as ß-lactamase substrate leaks out of permeabilised cells. The different cell populations can be distinguished with the cell surface markers and the effector translocation within these populations can be tracked by measuring the fluorescence-intensity and -shift of the substrate from 520 nm to 450 nm.

Table 14: Staining panel for in vivo ß-lactamase translocation assay

Antibody	Fluorochrome	Dilution
Viability	eFluor780	1/1000
CCF2 (green) substrate	V500	NA
CCF2 (blue) substrate	eFluor450	NA
CD64	A647	1/200
Siglec-F	PE	1/100
CD11c	PE-CF594	1/200
CD11b	BV711	1/100
MHC-II	AF700	1/100
Ly6G	BV786	1/100
FcγII/III	unlabelled	1/100

2.2.9 Protein isolation, purification, PAGE and Western Blot

2.2.9.1 Protein isolation

In order to test if cells were responding to cytokine stimulation or inhibitor treatment, proteins were isolated and Western Blots were conducted to detect the protein of interest. After cells were treated for indicated timepoints, supernatant was removed and cells were lysed with cell lysis solution (Table 7) for 5 min on ice. After cell lysis, wells were scraped with a 100 µl pipette tip, supernatants were collected in 1.5 ml Eppendorf tubes and incubated on ice for 15 min with intermittent vortexing. After supernatant collection and incubation, samples were centrifuged at 4 °C for 10 min at 10000 rpm to remove cell debris. Following the centrifugation, supernatants were transferred into new 1.5 ml Eppendorf tube and mixed with sample buffer (Table 7) for Polyacrylamide gel electrophoresis (PAGE) and incubated for 7 min at 90 °C to denatured proteins. Samples were stored at -20 °C until further use.

2.2.9.2 PAGE

After proteins were isolated, samples were thawed and thoroughly mixed prior to adding samples to the sample pockets in the stacking gel of SDS polyacrylamide gels (amount applied varied depending on pocket size). Samples were separated in denaturing SDS gradient gels containing 4 to 20 % polyacrylamide (either bought or hand-cast) submerged in MES buffer and were run at 80 V for the stacking gel and subsequently with 120 V for the remaining resolving gel.

2.2.9.3 Western Blot

After the proteins were separated during PAGE, proteins were transferred onto nitrocellulose membranes by utilising either a semi dry (pre-cast gels, Melbourne, transfer according to manufactures recommendations) or a wet transfer system (hand-cast gels, Bonn, 2 h at 4 °C with 80 V, transfer buffer (Table 7)). After proteins were transferred from the polyacrylamide gel, proper protein transfer was verified by staining the proteins with ponceau solutions (Table 7) for 10 min at RT (~23 °C) on an orbital shaker (~50 rpm) and subsequently removing unspecific staining by incubating membrane in distilled H_2O under the same conditions as previous staining. Following the verification of protein transfer, membranes were incubated in blocking buffer (Table 7) at RT (~23 °C) on an orbital shaker (50 rpm) for at least 1 h to inhibit unspecific binding of antibodies. After membranes were blocked, membranes were washed 3x with TBST for 5 min at RT (~23 °C) on an orbital shaker (50 rpm). Following the washing steps, the membrane was incubated in antibody-solution against the protein of interest over night at 4 °C on orbital shaker (50 rpm). After the overnight incubation with the primary antibody, membranes were washed as previously described and incubated with the respective secondary antibody, which is conjugated to a horseradish peroxidase (HRP) enzyme, for 1 h at RT (~23 °C) on an orbital shaker (50 rpm). Following the binding of the secondary antibody to the primary antibody, membranes were washed again as previously described and subsequently membranes were treated with enhanced chemiluminescence (ECL) substrates and the emitted light was detected with the BIO-RAD ChemiDoc™ Imaging System. Lastly after the protein of interest was detected, as a loading control ß-actin amounts were detected for all samples by incubating the membrane with the primary antibody and subsequently with the secondary antibody solution for 1 h at RT (~23 °C) on an orbital shaker (50 rpm).

Table 15: Antibodies used for Western Blot

Antigen	Company	Reference
ß-actin	Sigma-Aldrich	A2066
pSTAT1	Cell Signaling Technology	7649S
STAT1	Cell Signaling Technology	9172P
pSTAT3	Cell Signaling Technology	9134S
STAT3	Cell Signaling Technology	12640S
pNFκB p65	Cell Signaling Technology	3033T
LC3B	Cell Signaling Technology	2775S
GBP5	ThermoScientific/Invitrogen	PA5-31236
Mono- and poly-ubiquitin	Enzo Life Sciences	BML-PW8810-0500
ß-lactamase	ThermoScientific/Invitrogen	MA1-10712
goat anti-rabbit HRP	Cell Signaling Technology	7074S
horse anti-mouse HPR	Cell Signaling Technology	7076S

Chapter 3: Influence of inflammatory cytokines and TLR signalling on *Legionella* Dot/Icm effector translocation into the host cell

3.1 Introduction

In an attempt to control infection, a strong inflammatory response is induced upon detecting pathogen associated molecular patterns (PAMPs) via pattern recognition receptors (PRRs). This triggers the expression of countless anti-pathogenic molecules designed to attack and overcome the invading pathogen. At the same time, this response attracts and activates immune cells of the innate and adaptive immune system to counteract the infection locally and systemically.

The environmental pathogen *Legionella* has the capacity to alter mammalian host metabolism and cell-autonomous defence to establish an intracellular replicative niche. However, generally infected immunocompetent hosts can mount an effective inflammatory response to *Legionella*, by recognising specific PAMPs. PRRs activate signalling cascades that culminate in eliminating the invading *Legionella* [350, 351]. PRRs that have been implicated in *Legionella* control are TLR2 [352, 353], TLR 2 and 4 [354], TLR 5 [355], TLR9 [356-358], Nod1 and Nod2 [359-361], Naip5/NLRC4 [362-365], RIG-I and MDA5 [366]. The recognition of *Legionella* PAMPs via these receptors triggers the production and release of inflammatory cytokines and chemokines such as: interleukin Il-1α, IL-1β, IL-6, IL-10, IL-12, IL-18, CXCL1, MCP-1, tumor necrosis factor alpha (TNFα), interferon IFN-α, IFN-β and IFN-γ [136, 235, 359, 366-369] and many of them mediate the restriction of *Legionella* growth in vivo [234, 370-378]. However, *Legionella* also inadvertently interferes with PRR signalling and cytokine production, due to the effects of Dot/Icm effector proteins on host cell biology. For example, *L. pneumophila* inhibits protein synthesis [379-382], dampens cytokine mRNA levels [136, 139], inhibits transcription [383, 384] and interferes with NF-κ-B signalling [385-387] as well as MAPK signalling pathways [388] all of which interfere with the host immune signalling. Such effector-mediated interference with host signalling pathways and metabolism can lead to so-called effector-triggered immunity (ETI) [389].

Even though it is known that the recognition of *Legionella* PAMPs via different PRR's and the activity of inflammatory cytokines results in reduced bacteria replication, the impact of innate immune signalling on *Legionella* Dot/Icm effector translocation, has not been fully explored. Therefore, here we analysed the effects of different inflammatory cytokines and TLR signalling on *Legionella* Dot/Icm effector translocation. During this study, we observed that stimulation

with type I and type II interferons inhibited the Dot/Icm effector translocation in macrophages. However, none of the other inflammatory cytokines and TLR ligands tested had any impact on the effector translocation. Furthermore, the observed reduction in effector translocation was not associated with host cell death or other bactericidal activities and not the result of augmented degradation of the translocated effector proteins. Thus, we discovered a novel mechanism for pathogen control for IFN mediated restriction of *Legionella* infection.

3.2 Results

3.2.1 Impact of IFN-γ on effector translocation

It previously has been shown that treatment of macrophages with IFN-γ results in a significantly reduced *Legionella* burden compared to untreated cells. Different aspects of IFN-γ mediated cell-autonomous defence against *Legionella* were observed, which contributed to the lower bacteria burden in IFN-γ stimulated cells such as increased pyroptosis, bactericidal activities via itaconic acid, inhibition of LCV remodelling to escape phagosome-lysosome fusion as well as antimicrobial action of GBPs [254, 311, 370, 374, 376].

However, none of these studies examined if the observed alterations to the LCV were influencing the ability of *Legionella* to translocate Dot/Icm effectors. Therefore, we analysed if IFN-γ stimulation had an influence on *Legionella* effector translocation, which might attribute to the IFN-γ mediated restriction of *Legionella* replication.

3.2.1.1 TEM-1 ß-lactamase reporter system for effector translocation

To analyse the possible impact of IFN-γ stimulation on *Legionella* Dot/Icm effector translocation, we used a well-established assay that enables the tracking of effector translocation into host cells via the TEM-1 ß-lactamase reporter system which uses FRET (Fluorescence Resonance Energy Transfer) substrates CCF2 AM or CCF4 AM [390]. To analyse translocation of a specific effector, the protein of interest is fused to the C-terminus of the TEM-1 ß-lactamase and translocation of the fusion protein is monitored via enzymatic cleavage of the FRET substrate's beta-lactam ring, which causes a shift in fluorescence from green (520 nm) to blue (450nm) (Figure 3 A). This shift in the FRET substrate emitted fluorescence can easily be observed in infected host cells and quantified. This reporter assay

was previously used to characterise secretion system dynamics as well as identify and define effectors from enteropathogenic and enterohemorrhagic *Escherichia coli* [390, 391], *Salmonella enterica* serotype Typhimurium [392], *Coxiella burnetii* [393], *Helicobacter pylori* [394], *Chlamydia trachomatis* [395], *L. longbeachae* [90] and *L. pneumophila* [195, 396-398]. To monitor changes in *Legionella* effector translocation upon treatment with various stimulants, we utilised the well characterised *Legionella* Dot/Icm dependent effector RalF for the TEM-1 ß-lactamase reporter system. For each effector translocation assay we used *Legionella* strains expressing the fusion protein TEM-1 RalF, an empty vector control and a strain that is unable to translocate any effectors into the host, due to a mutation in the Dot/Icm machinery (Δ*dotA*). After 1 h of infection and 1.5 h of substrate incubation, the fluorescence intensity of both the uncleaved (520 nm) and cleaved (450 nm) CCF2 AM substrate was measured and the ratio of fluorescence intensity 450/520 was used to assess the amount of effector translocation into the host cells (Figure 3 B).

3.2.1.2 Effector translocation in mouse macrophages

We first analysed the impact of IFN-γ stimulation on Dot/Icm effector translocation in mouse macrophages. Immortalised bone marrow derived macrophages (iBMDM) were stimulated with IFN-γ overnight prior to infection. In response to IFN-γ treatment iBMDM showed robust and swift phosphorylation of STAT1 (Figure 4 A), indicating that the cell line was responsive to IFN-γ. Subsequently, iBMDM were then infected with derivates of *L. pneumophila* for 1 h. Upon IFN-γ stimulation, we observed a significant reduction in fluorescence intensity at 450 nm and thus a lower 450 nm/520 nm fluorescence ratio. This indicated a reduced level of CCF2 AM cleavage, reflecting a reduced translocation of the TEM-1 RalF fusion protein compared to untreated cells (Figure 4 B).

We next wanted to test if this observed reduction in RalF effector translocation upon IFN-γ stimulation during *L. pneumophila* infection would be applicable to other *Legionella* species. Since *L. longbeachae* is also an important causative agent of Legionnaires' Disease in Australia and New Zealand, we decided to test the impact of IFN-γ on *L. longbeachae* Dot/Icm effector translocation in iBMDM. Since the Dot/Icm effector RalF is also expressed by *L. longbeachae*, we tested the translocation of *L. longbeachae* RalF translocation in IFN-γ stimulated macrophages. In accordance with our previous observations during *L. pneumophila* infection, IFN-γ stimulation significantly reduced the translocation of *L. longbeachae* RalF and therefore

reduced the fluorescence shift of CCF2 AM (Figure 4 C). Therefore, IFN-γ mediated disruption of effector translocation into the host cell is not a specific response to *L. pneumophila* infection but also applies to *L. longbeachae*.

To determine if the observed impact on effector translocation was specific to RalF or whether IFN-γ influenced Dot/Icm effector translocation more broadly, we tested further *L. pneumophila* and *L. longbeachae* Dot/Icm effectors. We were able to show that the translocation of *L. pneumophila* effector SidB was also reduced upon IFN-γ stimulation (Figure **5** A). However, all the *L. longbeachae* effectors selected (SnpL, RelA, RelB, RelC and RelD) were translocated at low levels, resulting in a very low 450 nm/520 nm fluorescence ratio which made them unsuitable for further analysis in which their translocation might be even further reduced (Figure 5 B).

Overall, the observed inhibition of effector translocation upon IFN-γ treatment was not limited to one specific effector nor was it specific to *L. pneumophila*, indicating a more general interference with the Dot/Icm effector translocation machinery or its transport mechanism was at play.

3.2.1.3 Effector translocation in human cells

L. pneumophila has been previously shown to replicate within human macrophages and this replication is inhibited by IFN-γ [376, 399]. We therefore tested if IFN-γ stimulation of human cells also influenced *Legionella* effector translocation similar to mouse macrophages. We analysed the impact of IFN-γ stimulation on effector translocation in the well-established human macrophage cell line THP1. For the translocation assay, THP1 cells were differentiated with PMA for 3 days and then treated with IFN-γ overnight prior to *Legionella* infection. Upon stimulation with human IFN-γ, THP1 expressed GBP5 a IFN-γ induced protein, thus responding to the IFN-γ stimulation after differentiation with PMA (Figure 6 D). However, to our surprise, IFN-γ stimulation did not reduce effector translocation in THP1 macrophages of *L. pneumophila* or *L. longbeachae* (Figure 6 A), which contrasts with what we had previously observed in mouse macrophages (Figure 4). To rule out a cell line specific phenotype, we also analysed the *L. pneumophila* effector translocation in human epithelial cells (HeLa CCL-2 and A549) upon IFN-γ stimulation. Both cell lines responded to human IFN-γ stimulation which was detected either by GBP5 expression or phosphorylation of STAT1 (Figure 6 E-F). In line with the phenotype observed in THP1 macrophages, neither Hela CCL-2 cells or A549 lung

epithelial cells showed reduced the translocation of *L. pneumophila* RalF upon IFN-γ stimulation (Figure 6 B-C).

The inability IFN-γ stimulation to reduce effector translocation in human cells was not based on signalling defects, as all three cell lines responded by expressing IFN-γ induced GBP5 or by phosphorylation of STAT1. Thus, IFN-γ mediated reduction in effector translocation seems to be a mouse-specific phenotype. However, further testing with primary human macrophages would have to be conducted first to confirm the mouse-specific phenotype.

3.2.2 Effects of IFN-γ stimulation on cell survival and bactericidal activities

3.2.2.1 Cell survival

Upon infection, the recognition of *Legionella* PAMPs as well as the actions of IFN-γ stimulated genes (ISG) lead to a strong inflammatory response, which can result in enhanced cell death of in an attempt to control the infection [201, 254, 342, 400-402]. It has been previously shown that IFN-γ stimulation and *Legionella* infection can lead to cell death [254, 370]. Therefore, we wanted to analyse if the reduced fluorescence intensity ratio of 450 nm/520 nm of the FRET substrate might be due to enhanced cell death during the assay, rather than the inhibition of effector translocation per se. Under normal conditions, live macrophages show a stretched-out morphology and adhere firmly to the cell culture wells. In contrast, activated, dead or dying cells round up and detach from the wells. During the translocation assay, the cells are washed and the culture media is changed twice, thus any loosely attached or dead non-adherent cells would be removed from the wells. This could contribute to a lower 450 nm/520 nm ratio, if infected and thus "blue" cells died and detached from the wells, thereby increasing the ratio of "green" cells to "blue" cells in the remaining cell pool. Therefore, we examined the number of cells remaining in the cell culture wells after the assay, via fluorescence cell staining and MTT assay. In all the different sample groups (uninfected, infected with *L. pneumophila* Δ*flaA* Δ*dotA* pxDC61-RalF, infected with *L. pneumophila* Δ*flaA* pxDC61 or infected with *L. pneumophila* Δ*flaA* pxDC61-RalF) that are analysed after the effector translocation assay, none of the IFN-γ the treated cell populations showed a decrease in cell numbers (Figure 7). In fact, there is a slight increase observed in the treated populations, which would go hand in hand with IFN-γ induced genes executing functions and mechanisms which favour host cell survival. These observations are also in line with observations made by Naujoks et al. and Pilla et al. which only observed an increase in cell death at later time points [254, 370]. Therefore, the observed

reduction in fluorescence ratio 450 nm/520 nm upon IFN-γ stimulation compared to untreated samples is not based on a reduction in cell viability in IFN-γ treated and infected cells. This indicates that the mechanism by which ISGs are interfering with the effector translocation is independent of host cell death.

3.2.2.2 Bactericidal activities

During infection, the host induces the production of antibacterial proteins and reactive oxygen and nitrogen species in an attempt to control the pathogens [283, 336, 403]. IFN-γ stimulation has been shown to increase the bactericidal properties of host cells against *Legionella* [370, 372, 404]. We therefore tested the hypothesis, that IFN-γ stimulation leads to increased bactericidal activity in macrophages and hence a decline of viable bacteria. After the effector translocation assay was performed, macrophages were lysed and released bacteria were cultured on BCYE plates to enumerate viable bacteria. Colony forming units (CFU) from untreated and IFN-γ treated macrophages were counted 3 days later. During the translocation assay, macrophages were washed multiple times and the media is changed twice, thus removing most extracellular bacteria. For both *L. pneumophila* as well as *L. longbeachae* no significant reduction in viable bacteria was observed in IFN-γ stimulated iBMDM compared to untreated cells during the infection period (Figure 8). Consequently, the observed reduction in effector translocation was independent of increased bactericidal activities of the host cells.

The autonomy of this phenotype from host cell death and bactericidal activity implied a directed and fine-tuned mechanism geared toward the disruption of Dot/Icm translocation machinery or levels of effector proteins.

3.2.3 Effects of IFN-γ induced autophagy and proteasomal degradation

In addition to bactericidal activity and host cell death as innate immune mechanisms, the host is able to control infections through the degradation of pathogen compartments via autophagy, ubiquitination and subsequent proteasomal degradation as well [258, 330, 405-408]. *Legionella* is known to actively subvert autophagy and ubiquitination to accomplish intracellular survival [214, 216, 409-413], although how these processes affect Dot/Icm effector translocation is unknown. Since IFN-γ can enhance autophagy and proteasomal degradation, we tested if the IFN-γ mediated reduction in cleaved CCF2 AM was caused due to degradation of the bacterial effectors, rather than the disruption of the effector translocation into the host cell.

3.2.3.1 Proteasomal degradation

In order to analyse if proteasomal degradation of Dot/Icm effectors was behind the IFN-γ mediated decrease in CCF2 AM cleavage, we blocked proteasomal degradation via the specific inhibitor MG132.

Neither MG132 nor DMSO treatment of macrophages prior to infection had an influence on the effector translocation compared to untreated cells (Figure 9 A). Furthermore, MG132 mediated inhibition of the proteasome did not restore the effector translocation in IFN-γ stimulated macrophages compared to untreated cells (Figure 9 A). Efficient inhibition of the proteasome was shown by an increase in poly-ubiquitinated proteins via immunoblot (Figure **9** B).

This observation suggests that the decreased substrate cleavage is not caused due to enhanced *Legionella* effector degradation in IFN-γ treated cells.

3.2.3.2 Degradation via autophagy

In addition to the proteasomal degradation, the host cell can inactivate pathogens and their components via autophagy and lysosomal degradation. In order to test if these processes were responsible for the IFN-γ mediated decrease in CCF2 AM cleavage, we blocked the maturation of the autophagosome with the vacuolar-type H^+-ATPase (V-ATPase) inhibitor Bafilomycin A1. In line with the MG132 treatment, Bafilomycin A1 or DMSO treatment did not alter the Dot/Icm effector translocation compared to unstimulated cells (Figure 10 A). In addition, the Dot/Icm effector translocation was also not restored in IFN-γ stimulated and Bafilomycin A1 treated macrophages compared to unstimulated macrophages (Figure 10 A).

Cells responded to Bafilomycin A1 with an increased amount of LC3B II, a well-known marker for autophagy [414-418], which was visualised via immunoblot (Figure 10 B).
Hence, the reduction in cleaved CCF2 AM substrate and the subsequently observed reduction in 450 nm/520 nm fluorescence ratio was not caused by targeted degradation of the TEM-1-RalF fusion protein via the phagosomal/lysosomal degradation pathway.

These observations indicate that, even though the degradation of pathogen related proteins and compartments via the proteasome and autophagy are established mechanisms of host defence, IFN-γ stimulation did not seem to trigger an enhanced degradation of *Legionella* Dot/Icm effector molecules via these processes.

Overall, these results suggested that the observed reduction of Dot/Icm effector translocation in IFN-γ stimulated macrophages was caused by the direct or indirect disruption of the translocation process across LCV membrane.

3.2.4 Effects of other inflammatory cytokines and TLR ligands on *Legionella* Dot/Icm effector translocation

We previously observed that the stimulation of macrophages with IFN-γ led to a significant reduction in Dot/Icm effector translocation, which was independent of a variety of well-known host defence mechanisms and thus represented a novel mechanism of cell-autonomous defence against *Legionella* intracellular replication. However, aside from IFN-γ, various other inflammatory cytokines are produced upon detection of *Legionella* infection. We wondered if a similar reduction in Dot/Icm effector translocation could be triggered by other inflammatory cytokines and PRRs. We therefore analysed the impact of other inflammatory cytokines as well as classic PAMP triggered PRR signalling on the Dot/Icm dependent effector translocation.

3.2.4.1 Influence of Toll like receptor (TLR) ligands on Dot/Icm effector translocation

As previously mentioned, the detection of PAMPs via PRRs or pathogen associated activities leads to the upregulation of inflammatory signals and thus results in the inhibition of pathogen replication. As some of the IFN-γ stimulated factors are also produced by other inflammatory stimuli as well as TLR mediated transcription factors [248, 249, 253], we tested if other cytokines or TLR ligands are able to trigger a similar effect on the *Legionella* Dot/Icm effector translocation.

3.2.4.1.1 Lipopolysaccharides (LPS) TLR 4 ligand

LPS is a gram-negative bacteria cell membrane component and thus is one of the classic PAMPs recognised by the host TLRs. Binding of LPS to TLR 4 results, amongst other things, in the translocation of NF-κB into the nucleus and the transcription of proinflammatory cytokines [352, 353, 356]. Hence, we tested if TLR 4 signalling triggered *E. coli* LPS would inhibit the Dot/Icm effector translocation during *Legionella* infection of macrophages. Surprisingly, the treatment of macrophages with LPS did not induce a reduction in *Legionella* Dot/Icm effector translocation (Figure 11 A-B), as previously observed in IFN-γ stimulated macrophages, thereby ruling out multiple NF-κB dependent factors. The phosphorylation of NF-κB p65 confirmed the responsiveness of iBMDM towards *E. coli* LPS (Figure 11 C).

3.2.4.1.2 CpG TLR 9 ligand

The high frequency of unmethylated cytosine-guanine dinucleotide (CpG) in bacterial DNA is recognised as a PAMP that triggers TLR 9 [419-421]. It has been shown previously that TLR 9 signalling is essential for host defence against *Legionella*, as TLR $9^{-/-}$ mice show increased mortality compared to WT mice and decreased IL-12 production, a cytokine triggering IFN-γ production [357, 358]. Furthermore, administering CpG to A/J mice enhanced immunity against *Legionella* [358]. We therefore tested if TLR9 signalling triggered by CpG would inhibit the Dot/Icm effector translocation during *Legionella* infection. However, CpG stimulation of macrophages did not impact Dot/Icm effector translocation during the subsequent *L. pneumophila* infection compared to untreated cells (Figure 11 D). Macrophages stimulated with CpG responded swiftly with the phosphorylation of NF-κB p65, confirming initiation of TLR9 dependent gene transcription (Figure 11 E).

In summary, neither LPS nor CpG stimulation and the subsequent activation of pro-inflammatory factors via TLR 4 or TLR 9 signalling reduced the Dot/Icm effector translocation into host cells. In addition, the observed phenotype was independent of TLR 5 signalling, since a flagellated mutant (Δ*flaA*) strain of *L. pneumophila* was used for the effector translocation assays.

3.2.4.2 Influence of inflammatory cytokines on *Legionella* effector translocation

3.2.4.2.1 TNFα stimulation

TNFα plays an essential role in mediating host defence against *Legionella*. Mice deficient in TNF signalling showed increased CFU burden in the lung compared to WT mice and treatment of macrophages with TNFα inhibits *Legionella* replication [373, 375, 404, 422-426]. Furthermore, *L. pneumophila* actively inhibits the secretion of TNFα via one of its effectors called RomA [383], thus supporting a role of TNFα in host defence against *L. pneumophila*. We therefore analysed if TNFα stimulation caused a reduction in *L. pneumophila* effector translocation in macrophages but observed that TNFα did not reduce Dot/Icm effector translocation compared to untreated macrophages (Figure 12 A). This was despite the fact that macrophages stimulated with TNFα responded with a strong phosphorylation of NF-κB p65 (Figure 12 B). Hence, even though TNFα is essential for host defence against *Legionella*, it does not interfere with the process of Dot/Icm effector translocation.

3.2.4.2.2 IL-6

Another prominent cytokine produced in response to *Legionella* infection is IL-6 [136, 427-430] and signal transduction is mediated through the formation of a STAT3 homodimers. This signalling is closely related to the signal transduction by IFN-γ and type-1 interferons, which also signal via STAT proteins [245, 247]. Non-canonical signalling via different STAT combinations has been reported previously [248]. Furthermore, *L. pneumophila* also interferes with the transcription of IL-6 via the mechanism observed for TNFα transcription inhibition [383]. We therefore analysed if IL-6 stimulation would recapitulate the reduction in Dot/Icm effector translocation observed upon IFN-γ stimulation. Despite a rapid response to IL-6 (Figure 12 D), macrophages no reduction in Dot/Icm effector translocation was observed compared to untreated macrophages (Figure 12 C). Thus, the Dot/Icm effector translocation across the LCV was not altered by IL-6 mediated signalling.

Since the stimulation of macrophages with classic PAMPs or pro-inflammatory cytokines such as TNFα or IL-6 did not result in a reduction in Dot/Icm effector translocation, it is tempting to speculate that this phenotype is exclusively mediated by IFN-γ, which would underpin its importance in host defence against *Legionella*. However, given the overlap in ISGs produced in response to IFN-γ and type I interferons, we next tested whether type I interferon stimulation also reduced Dot/Icm effector translocation.

3.2.5 Influence of type I interferon on *Legionella* effector translocation

The type I interferons IFN-α and IFN-β have previously been implicated in host defence against *Legionella* [234, 368, 370]. We decided to test these cytokines for their ability to interfere with *Legionella* Dot/Icm effector translocation in macrophages to compare to the IFN-γ induced reduction of effector translocation already observed.

Initially, iBMDM were stimulated with type I interferons IFN-α and IFN-β. However, unexpectedly iBMDMs did not respond to type I interferons, as no STAT1 phosphorylation nor GBP5 production was detected via immunoblot (Figure 13 A).

Based on these results, we switched to a different macrophage cell line RAW 264.7 macrophages, as they are permissive to *Legionella* infection and well described. Subsequently, we tested if RAW 264.7 macrophages responded to the interferons IFN-γ, IFN-α and IFN-β. All three interferons rapidly induced the phosphorylation of STAT1 (Figure 13 B). Thus, we

used this new macrophage cell line for our subsequent Dot/Icm translocation experiments. Similar to iBMDM cells, IFN-γ stimulated RAW 264.7 macrophages interfered with the Dot/Icm effector translocation and showed a reduced 450 nm/520 nm fluorescence ratio compared to untreated macrophages (Figure 13 C-D). However, neither IFN-α and IFN-β restricted the Dot/Icm translocation as seen for IFN-γ (Figure 13 C-D). In order to exclude any cell death-related phenotypes, we analysed cell viability after the translocation assay in RAW 264.7 macrophages. In line with our previous observation in iBMDM, stimulation with IFN-γ, IFN-α or IFN-β did not cause an increase in cell death during the effector translocation assay (Figure 13 E). Based on this experiment, we initially inferred that the phenotype of reduced Dot/Icm effector translocation into host cells was caused by factors solely induced by IFN-γ.

As I am a PhD student in "The Bonn and Melbourne Research and Graduate School Immunoscience" which is a collaboration between the University of Bonn in Germany and the University of Melbourne in Australia, I left the laboratory of Prof. Elizabeth Hartland in Melbourne and continued my studies under the supervision of Prof. Waldemar Kolanus in Germany.

Since RAW 264.7 macrophage are such a well-established and commonly used cell line worldwide, we did not to export the cells from Melbourne to Bonn and instead established the Dot/Icm effector translocation assay with a batch of RAW 264.7 macrophages stored in the laboratory of Prof. Kolanus. In line with the "Melbourne" RAW 264.7 macrophages, the German "LIMES" macrophages rapidly responded to type I interferons IFN-α and IFN-β as well as IFN-γ with phosphorylation of STAT1. However, to our surprise, the German "LIMES" macrophages could not recapitulate the IFN-γ mediated reduction in Dot/Icm effector translocation (Figure 14 B). We therefore acquired RAW 264.7 macrophages from a different source and these German "Venusberg" RAW 264.7 macrophages responded to IFN-α, IFN-β and IFN-γ stimulation with a rapid phosphorylation of STAT1. In line with our previous observations in Melbourne, we could observe IFN-γ mediated reduction in Dot/Icm effector translocation that was not mediated by IFN-α or IFN-β (Figure 14 C). Again these results suggested that the observed IFN-γ mediated reduction in Dot/Icm effector translocation was a mechanism uniquely induced by IFN-γ and seems to be independent of the inflammasome, as these macrophages do not express the apoptotic speck-like protein [431].

Due to the observed inconsistencies within the RAW 264.7 macrophage derivates and to determine if the observed phenotype of IFN-γ mediated impairment of Dot/Icm effector translocation could be observed in non-immortalised cells, we tested if primary mouse macrophages would display the same phenotype upon interferon stimulation. Bone marrow derived macrophages (pBMDM) were generated from C57BL/6 mice and their response to the different interferons was tested. In contrast to RAW 264.7 macrophages, a reduction in Dot/Icm effector translocation was observed upon IFN-γ as well as IFN-α and IFN-β stimulation (Figure 15 A). All three interferons were shown to induce robust phosphorylation of STAT1 shortly after the stimulation and did not affect bacterial viability over the course of the Dot/Icm effector translocation assay (Figure 15 B-C).

Since a reduction in effector translocation could be observed for both types of interferons, we aimed to identify the interferon induced factors responsible from a pool of genes induced by both types of interferon. Interferon-induced genes (ISGs) are induced in two "waves", the primary response includes a variety of transcription factors (e.g. IRF-1) which in turn activate the transcription of the secondary response genes (e.g. GBPs) [432]. Hence, we analysed the dynamics of the inhibition of effector translocation. Therefore, pBMDM were stimulated with IFN-γ over a range of decreasing incubation periods, starting with 16-18 h, prior to infection. A significant reduction in Dot/Icm effector translocation was detectable after 4 h of IFN-γ treatment and this decreased further with longer incubation times, prior to *Legionella* infection (Figure 15 D). We also monitored the cell viability during this time course, to exclude a cell death related contribution to this phenotype. In line with our previous results in the macrophage cell lines iBMDM and RAW 264.7, no increased cell death was detected in IFN-γ stimulated pBMDM compared to untreated cells (Figure 15 D). In addition, we analysed the expression of the secondary response protein, GBP5, to estimate the timepoint at which the repertoire of IFN-γ induced ISGs might be present. Proteins from pBMDM treated with IFN-γ were analysed over increasing incubation periods prior to cell lysis. GBP5 was detectable via immunoblot after 8 h of IFN-γ stimulation (Figure 15 E). In addition, analysed if the reduction in Dot/Icm effector translocation correlated with a reduction in *Legionella* replication. We observed a reduction in *L. pneumophila* replication upon IFN-γ stimulation but not in type I stimulated macrophages (Figure 15 F). A reduced potency of type I interferons compared to IFN-γ in restricting the replication of *L. pneumophila* has been reported previously [234, 368]. This might indicate that the interruption of Dot/Icm effector translocation and the host restriction of

replication is mediated by different interferon-stimulated factors, hinting at a multifaceted control of pathogen replication.

Based on the observations, that neither classic TLR ligands nor other inflammatory cytokines induced a reduction in *Legionella* Dot/Icm effector translocation, it is tempting to speculated that this phenotype represents a novel host defence mechanism mediated by interferon-stimulated genes.

3.3 Discussion

The ability to manipulate the host and thus achieving the survival and replication of intracellular *Legionella*, relies on the uninterrupted transport of effector proteins across the bacterial envelope and the LCV membrane. This is intracellular replication is accomplished by a myriad of effector proteins orchestrating a fine-tuned network of host protein manipulation via inhibiting or repurposing their function for the benefits of the *Legionella* survival inside the host.

After pathogen invasion, the recognition of PAMPs or pathogen-associated activities launches the production of various pro-inflammatory cytokines, triggering a myriad of anti-pathogenic responses that orchestrate a multilayered attack on the invading pathogen. In the case of *Legionella*, which resides in a membrane-bound compartment and heavily interferes with host processes, the host must either destroy the replicative niche and thus expose the bacteria to the cytosol or overcome the effector mediated inhibition of lysosomal fusion with the LCV [433]. The mechanistic details of how this is achieved, especially facing a pathogen that actively manipulates host cell-autonomous defence remains enigmatic. However, in the last decades, some light has been shed on cell-intrinsic anti-pathogenic mechanism, especially the activities of interferon-regulated proteins.

In this study, we were able to identify a novel facet of host defence mediated by interferon. We observed that upon IFN-γ stimulation of mouse macrophages, the translocation of Dot/Icm effector proteins into the host cell cytosol was significantly reduced. Furthermore, we later identified that this novel mechanism was specifically mediated by interferon-induced factors, since the type I interferons, IFN-α and IFN-β, were able to elicit the same phenotype. In contrast, all other analysed pro-inflammatory cytokines as well as TLR ligands were unable to reduce Dot/Icm effector translocation into the host cells. In addition, we were able to demonstrate that this novel mechanism was not the result of host cell death, nor due to a decrease in *Legionella* viability or targeted degradation of effector proteins via autophagy or proteasomal activities. These observations suggested a specific interruption of Dot/Icm effector translocation across the LCV membrane itself and thus disruption of a core element of *Legionella* infection, the transport of effector proteins into the host cell.

Even though *Legionella* pathogens have been known since the late 1970s, and their dependence on the Dot/Icm secretion system for intracellular survival since the late 1990s, much remains unknown regarding the Dot/Icm secretion system itself and the process of effector translocation

into the host cells. For example, only recently has the Dot/Icm secretion system core complex structure been established in situ [156, 157, 434, 435]. Furthermore, despite the fact that Dot/Icm effector translocation is a crucial part of *Legionella* pathogenesis, not much is known about the actual process of effector transport across membranes and which factors influence this function. For an effector to reach its site of action, it must cross three membranes, the bacterial inner and outer membrane and the LCV membrane. It is currently suggested that the transport of effectors across the bacterial membrane via the type IV secretion core complex occurs in an unfolded state [175, 181, 436]. This transport of effector molecules also seems to depend on ATPase activity, since ATPase mutants cannot translocate effectors into the host cell [155, 162-165]. This is further substantiated by the fact that small molecules which disrupt the bacterial membrane proton motive force and thus inhibit ATPase activity, inhibit the effector translocation into host cells [397]. In addition to ATPase activity, it has been shown that for efficient host manipulation and intracellular survival, the Dot/Icm secretion system components and effectors have to be targeted to the poles of the bacteria [152].

Knowledge about the effector transport across the LCV membrane is even further limited. So far, it has been established that Dot/Icm effector translocation is initiated upon host contact [183, 437] and already occurs during the internalisation process. This indicates that an extracellular host factor might trigger effector translocation via the Dot/Icm secretion system [183]. This initiation early upon host contact, might also be an indication of how *Legionella* is able to manipulate host processes immediately after uptake [183]. The requirement of intimate host contact for effector translocation has been further validated by the observation that small molecules which disrupt host phagocytosis by interacting with cytoskeleton components inhibit Dot/Icm effector translocation as well [397].

Apart from the necessity of intimate host contact to initiate the Dot/Icm effector translocation, nothing is known how effectors are transported across LCV the membrane into the host cytosol. All the structural analysis of the Dot/Icm secretion system as well as observations via microscopy have not yet indicated a structure or attachment extending from the core complex beyond the bacteria outer membrane which might mediate host contact and thus effector translocation across the LCV membrane. The requirement for host contact and the ability of *Legionella* to translocate the effectors shortly after uptake, indicates either an extremely rapid assembly or formation of the structure which allows the transport across the host membrane, or the manipulation of a host complex already present in the host plasma membrane to enable effectors to cross the LCV membrane.

Even though the exact mechanism of effector translocation into the host cells remains enigmatic, since the genes encoding the type IV secretions system are highly conserved among the different *Legionella* species [63, 438] and we have shown interferon-stimulated genes are able to disrupt the effector translocation in two different species, it is tempting to speculate that the process of effector translocation into the host cell as well as the components involved, are conserved across all *Legionella* species.

In the accidental human host *L. pneumophila* has been previously shown to replicate within macrophages and that this replication is inhibited by IFN-γ [376, 399]. Since IFN-γ is capable of restricting the replication of *L. pneumophila* in mouse and human cells, we tested if IFN-γ treatment of human cells would also trigger the reduction of Dot/Icm effector translocation. To our surprise IFN-γ stimulation did not restrict the Dot/Icm effector translocation in human cells, although it remains to be investigated if this also applies to primary human macrophages. However, host defence differences against the same pathogen between mice and humans have been reported before [335, 439]. Even differences in host defence among various cell types of the same host have been reported prior [328, 329]. The difference observed between mice and humans, might be based on the genomic differences between the species, as for example humans lack an entire group of interferon-stimulated GTPases (IRGs) compared to mice. These observations emphasise that the immune response between different host species as well as cell types can vary greatly even when infected with the same pathogen, thus caution is required when inferring functions/mechanisms from one organism to another.

Since *Legionella* can replicate within human hosts and an intimate contact between bacteria and host cells is needed to initiate the translocation, a systematic screen with 2500 small molecules was used to identify human host factors necessary for efficient effector translocation [397]. Some of these host factors are proteins involved in phagocytosis (actin, tubulin and phosphoinositide 3-kinases), which is in line with previous results suggesting effector translocation depends on intimate host contact and phagocytosis [183, 437]. However, it has been reported that IFN-γ stimulation can impact phagocytosis, usually enhancing phagocytic activity [440-442]. A reduced rate of phagocytosis is thus not likely the cause for the observed reduction in Dot/Icm effector translocation, since no significant reduction of *Legionella* CFU was observed in IFN-γ treated macrophages compared to untreated macrophages. In addition, since we observed that both type I and type II interferons are able to restrict the Dot/Icm effector translocation independent of CFU, different rates of phagocytosis are most likely not

responsible for the observed reduction in Dot/Icm effector translocation, as IFN-α, IFN-β and IFN-γ can have opposing effects on phagocytosis [443].

This chemical screen also identified the host receptor protein tyrosine phosphate phosphatases CD45 and CD148 as essential for effector translocation [397]. Based upon our mRNA sequencing (discussed in the next chapter), CD45 as well as CD148 most likely do not play a role in the reduction of effector translocation, as CD148 was not induced significantly upon IFN stimulation compared to unstimulated samples and CD45 was only marginally upregulated in macrophages. Furthermore, one would rather expect a downregulation of this factor rather than upregulation, to mirror the previously observed reduction in Dot/Icm effector translocation upon deletion of this gene [397].

It was previously shown that IFN-γ can mediate the restriction of intracellular pathogens such as *Mycobacterium tuberculosis* [330] *Chlamydia trachomatis* [258, 405] *Toxoplasma gondii* [407] via autophagy-related mechanisms. Even though we found no involvement of autophagy in the IFN-γ mediated reduction of Dot/Icm effector translocation, one might argue that autophagy inhibition via Bafilomycin A1 only inhibits this process at its last stage. Though testing the inhibition of autophagy at an earlier stage via the classic autophagy inhibitors Wortmannin, LY294002 or 3-MA was not optimal, as they are phosphoinositide 3-kinases inhibitors and phosphoinositide 3-kinases are essential for *Legionella* uptake [397, 444]. As an alternative, we tried to establish a translocation assay with the autophagy inhibitor Spautin-1, which inhibits autophagy initiation via degradation of beclin-1 [445]. Unfortunately, we could not establish a functional effector translocation assay with potent inhibition due to increased cell death (data not shown). Hence, the role of autophagy, in its initiation stage, in IFN-γ mediated reduction of Dot/Icm effector translocation remains to be investigated. Even though the impact of autophagy on effector stability was not specifically analysed in our studies, Pilla et al. [254] as well as Lippmann et al. [234] were able to show that autophagy does not mediate the restriction of *L. pneumophila* replication observed upon interferon stimulation, indicating that it likely does not play a role in our observed phenotype.

It has been previously demonstrated that the recognition of *Legionella* PAMPs triggers type I interferons resulting in an autocrine loop, which results in a reduced intracellular replication of *L. pneumophila* [235, 368]. This autocrine loop would in turn have the potential to restrict Dot/Icm effector translocation upon induction of interferon stimulate genes. During our studies, we examined the influence of classic PAMPs such as LPS and CpG on effector translocation.

A pre-treatment of iBMDM with LPS or CpG for ~17 h prior to infection did not result in a reduction of effector translocation, suggesting that the induction of interferon-stimulated genes via the autocrine loop is either not strong enough or interrupted. We later discovered that our iBMDM cell line does not display the type I interferon receptor on their cell surface (Sarah Straub, personal communication), thus resulting in a disrupted autocrine loop. Whether stimulation of pBMDM with LPS or CpG would trigger the production of type I interferons and thus trigger the autocrine loop and inhibit Dot/Icm effector translocation remains to be analysed. However, we have demonstrated that pBMDM are capable of reducing Dot/Icm effector translocation upon external stimulation with type I interferons IFN-α and IFN-β.

Overall, our data emphasises the crucial role of interferon in host cell defence against *Legionella*. Here we were able to show that interferon stimulated factors inhibit the Dot/Icm effector translocation of *L. pneumophila* and *L. longbeachae* into host cells. Furthermore, this inhibition is specific for interferon stimulation, as all other inflammatory cytokines and TLR ligands tested failed to inhibit Dot/Icm effector translocation and is independent of host cell death, inflammasome activity as well as proteasome and autophagy mediated degradation. The inhibition of Dot/Icm effector translocation thus constitutes a novel cell autonomous defence mechanism mediated by ISGs.

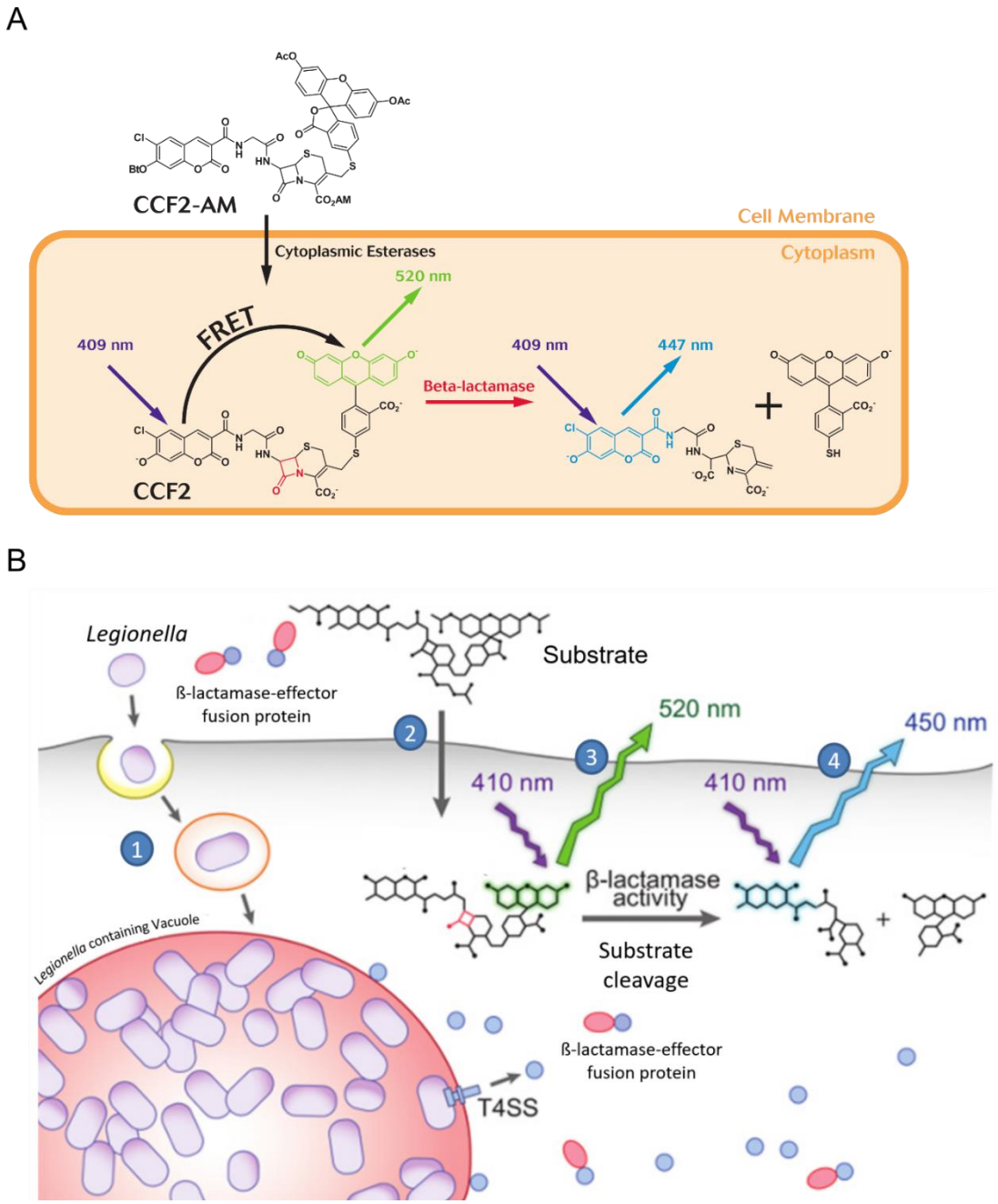


Figure 3: Schematic representation of ß lactamase reporter system with FRET substrate CCF2 AM

A) Schematic representation of FRET substrate CCF2-AM cleavage, Graph adjusted from: https://assets.fishersci.com/TFS-Assets/LSG/brochures/B12269%20GeneBLAzer%20FINAL.pdf

B) Schematic representation of ß-lactamase effector translocation during *Legionella* infection. 1) Cells were infected with *Legionella* strains over-expressing effector-ß-lactamase fusion proteins (TEM-1 β-lactamase fused to the N-terminus) or respective controls. 2) Infected cells were incubated with FRET substrate solution for 1.5 h at room temperature. 3) Uncleaved FRET substrate fluoresces at 520 nm when exited at 410 nm. 4) If effector translocation into the host cells, including the ß-lactamase-effector fusion

protein, takes place the FRET substrate is cleaved by the ß-lactamase and cleaved substrate fluoresces at 450 nm when exited at 410 nm. Graph adapted from Newton et al. (2016) [393]

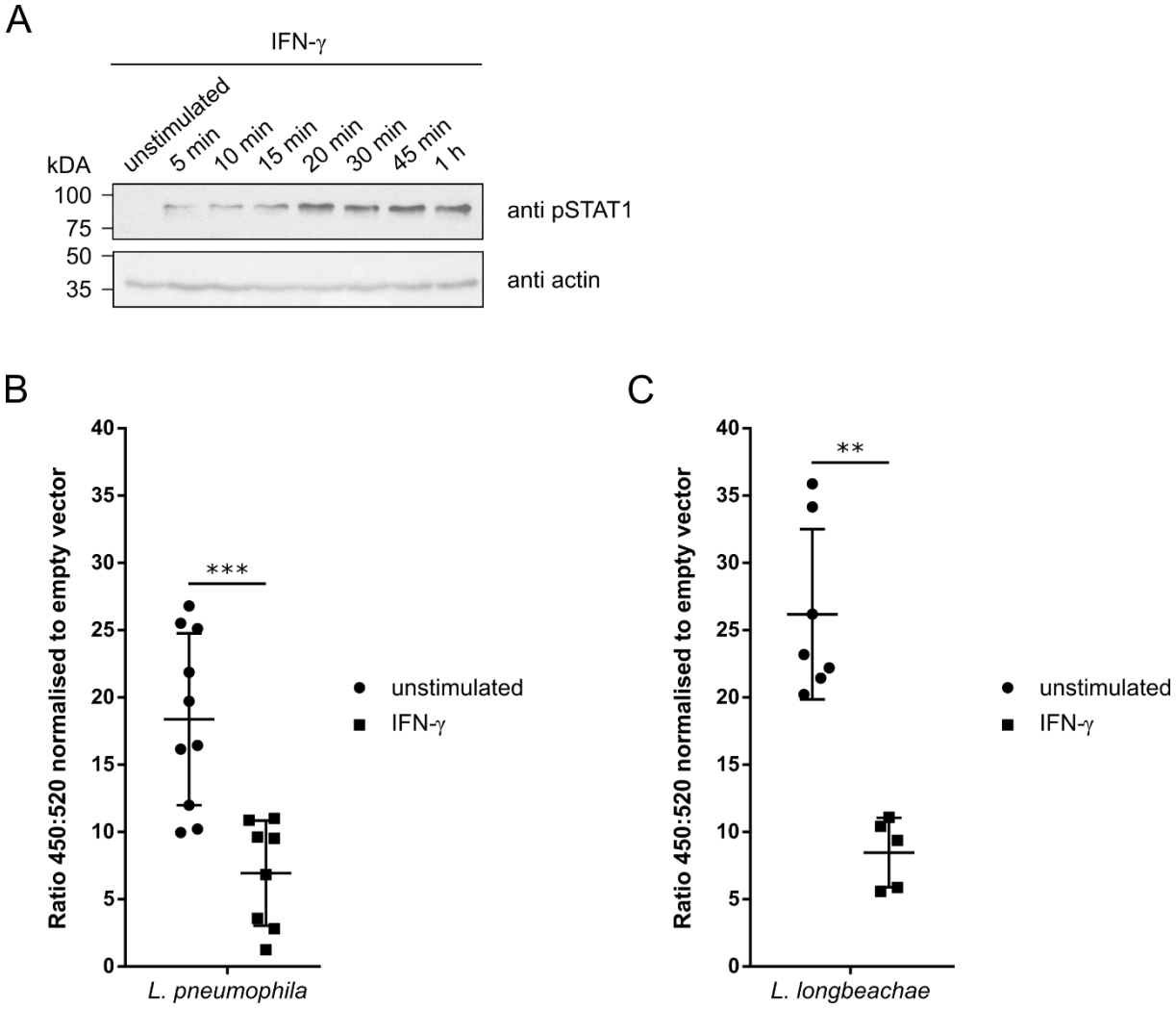


Figure 4: Impact of IFN-γ on *Legionella* RalF effector translocation in iBMDM

A) To test responsiveness toward IFN-γ, mouse iBMDM were treated with 50 U/ml IFN-γ or mock treated, cells were lysed after indicated timepoints and proteins were extracted. Protein levels were analysed via WB with anti-pSTAT1 and anti-actin antibodies. Representative immunoblot of at least three independent experiments is shown.

B) iBMDM were treated with IFN-γ (50 U/ml) overnight prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation reporter system. Results are shown as mean ± SD of $n \geq 8$ independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

C) Same as B) but instead cells are infected with *L. longbeachae* NSW 150, carrying pxDC61-RalF plasmid, for 3 h. Subsequently, $RalF_{Ll}$ effector translocation was quantified using TEM-1 β-lactamase translocation reporter system. Results are shown as mean ± SD of $n \geq 5$ independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** ≤ 0.0001, Mann Whitney test)

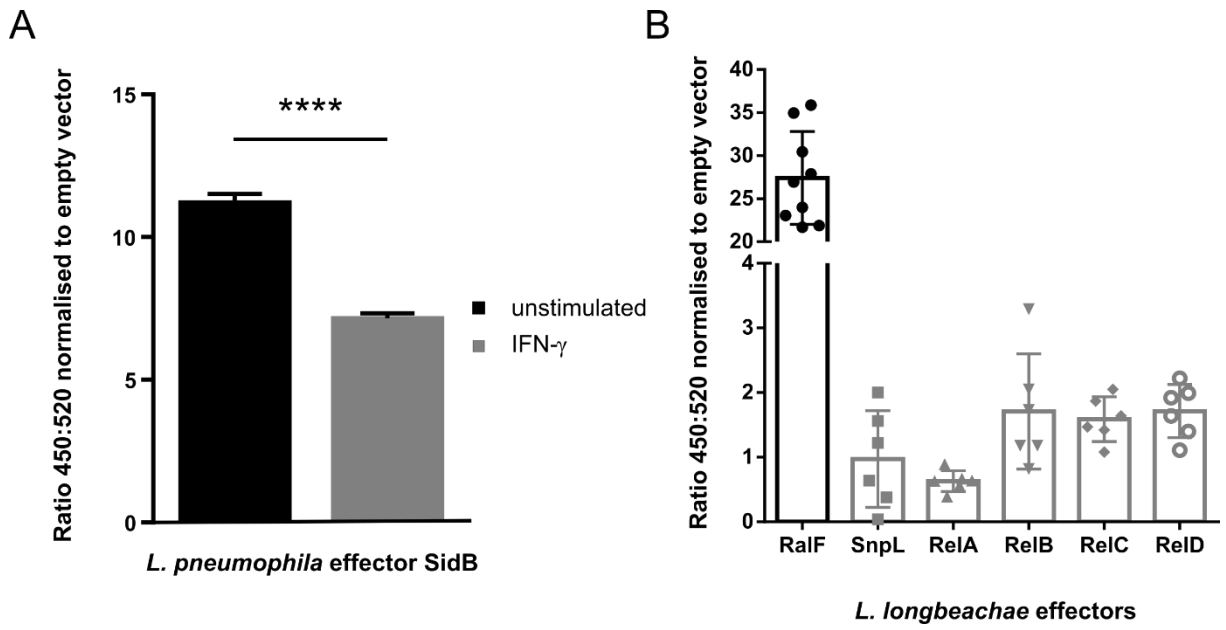


Figure 5: Impact of IFN-γ on *Legionella* Dot/Icm effector translocation in iBMDM

A) iBMDM were treated with IFN-γ (50 U/ml) overnight prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-SidB plasmid, for 1 h. Subsequently, $SidB_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation reporter system. Results are shown as mean ± SD of n = 3 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** ≤ 0.0001, unpaired t-test)

B) Untreated iBMDM were infected with *L. longbeachae* NSW 150, carrying pxDC61-RalF (or pxDC61-SnpL, -RelA, -RelB, -RelC or -RelD) plasmid, for 3 h. Subsequently, effector translocation of indicated effectors were quantified using TEM-1 β-lactamase translocation reporter system. Results are shown as mean ± SD of n = 6 independent experiments carried out in technical triplicates.

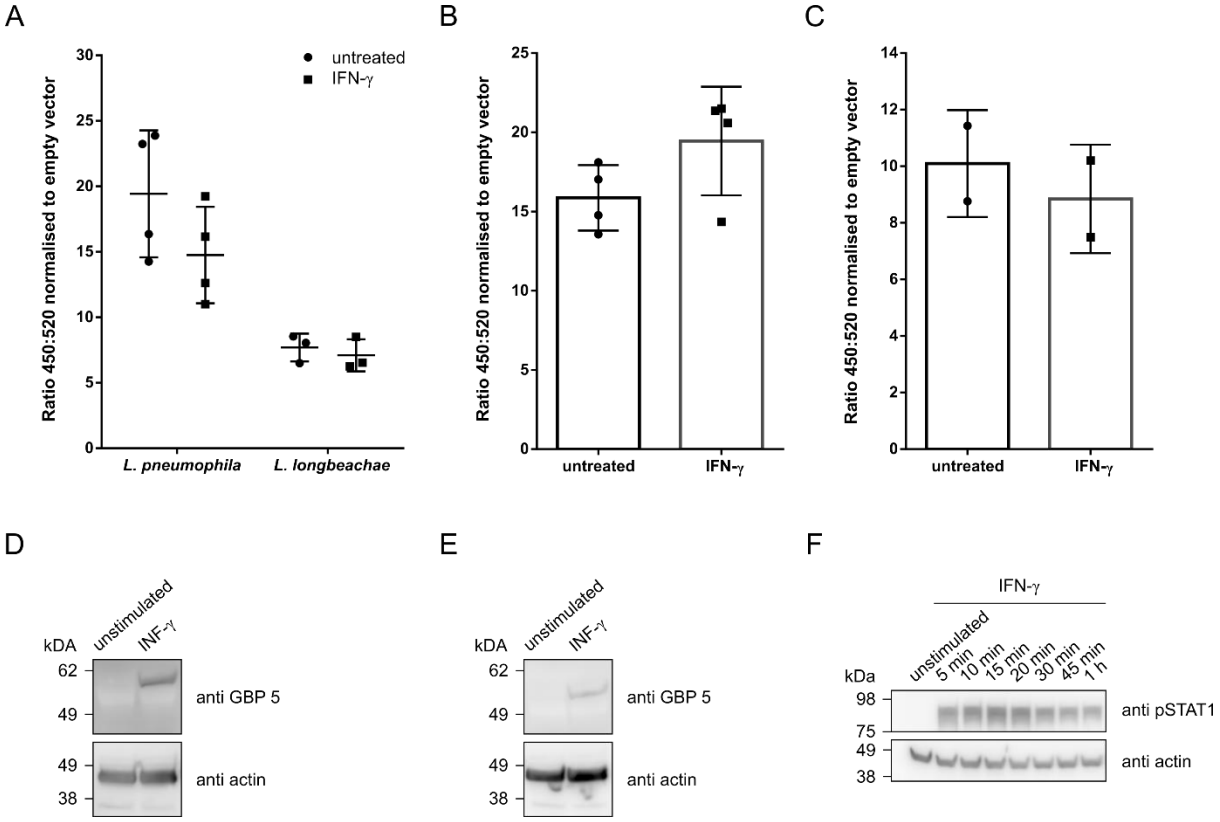


Figure 6: Impact of IFN-γ on *Legionella* RalF effector translocation in human cells

A) THP1 cells were differentiated into macrophages with PMA and treated with IFN-γ (50 U/ml) prior to infection with *L. pneumophila* 130b Δ*flaA* or *L. longbeachae* NSW 150, each carrying pxDC61-RalF plasmid, for 1 h or 3 h, respectively. Subsequently, $RalF_{Lp}$ or $RalF_{Ll}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of $n \geq 3$ independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test, results were statistically non-significant)

B) HeLa CCL-2 epithelial cells were treated with IFN-γ (50 U/ml) prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 4 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test, results were statistically non-significant)

C) A549 lung epithelial cells were treated with IFN-γ (50 U/ml) prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 2 independent experiments carried out in technical triplicates.

D) THP1 cells were differentiated into macrophages with PMA and stimulated with IFN-γ overnight. Cells were lysed and proteins from treated and untreated (mock) cells were harvested. Protein levels of GBP5 (IFN-γ induced protein) and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

E) HeLa CCL-2 cells were treated with IFN-γ overnight and subsequently cells were lysed and proteins from treated and untreated (mock) cells were harvested. Protein levels of GBP5 (IFN-γ induced protein) and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

F) A459 cells were stimulated with IFN-γ for the indicated time. Cells were lysed and proteins from treated and untreated (mock) cells were harvested. Protein levels of pSTAT1 and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

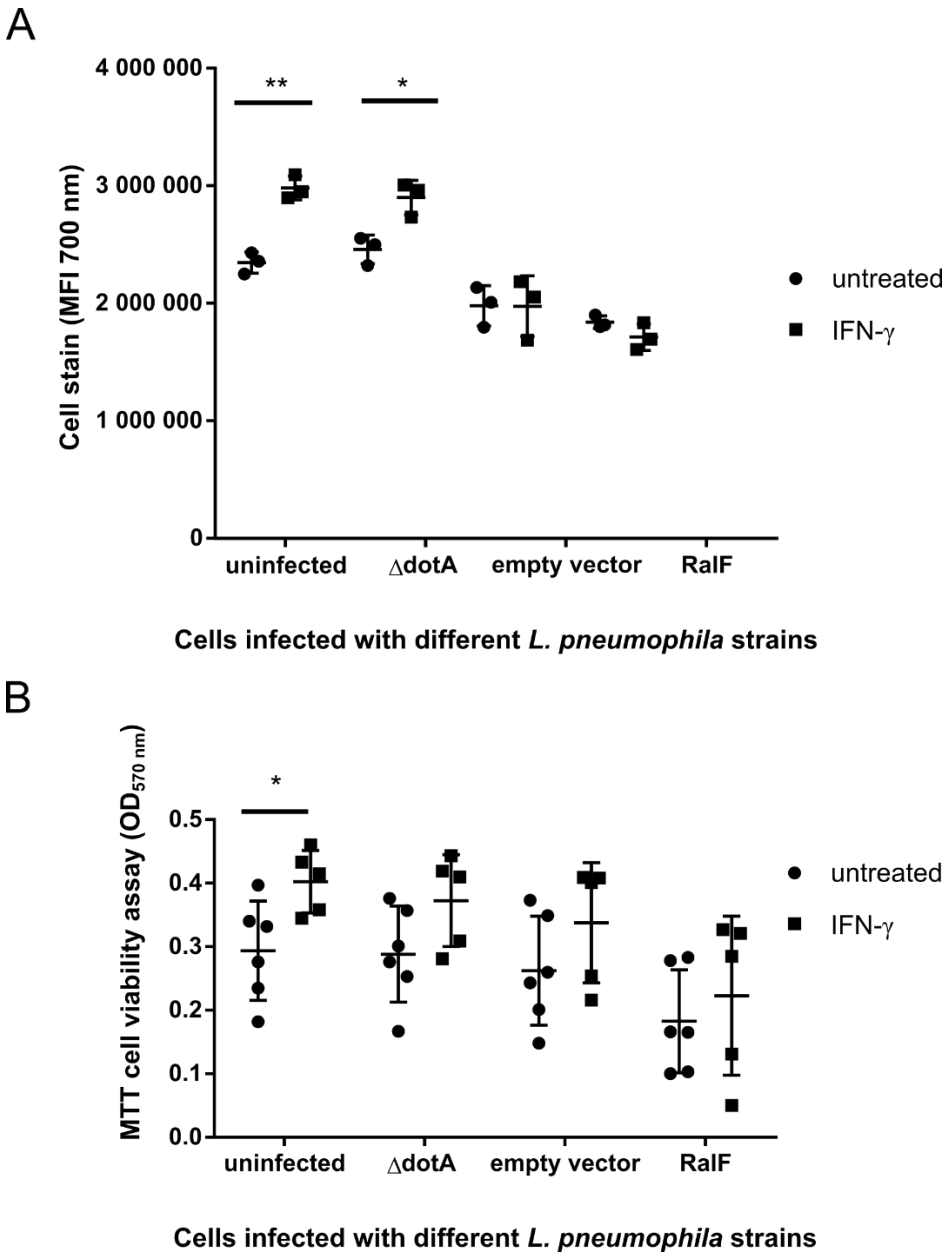


Figure 7: Impact of IFN-γ treatment on cell viability of iBMDM during ß-lactamase effector translocation assay

A) Following the quantification of *L. pneumophila* $RalF_{Lp}$ effector translocation described previously, iBMDM cells were stained with CellTag™ 700 Stain to quantify cells remaining after the translocation assay. Results are shown as mean ± SD of n = 3 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Unpaired t test with Welch's correction)

B) Following the quantification of *L. pneumophila* $RalF_{Lp}$ effector translocation described previously, iBMDM cells were treated with MTT solution to quantify viable cells remaining after the translocation assay. Results are shown as mean ± SD of $n \geq 5$ independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

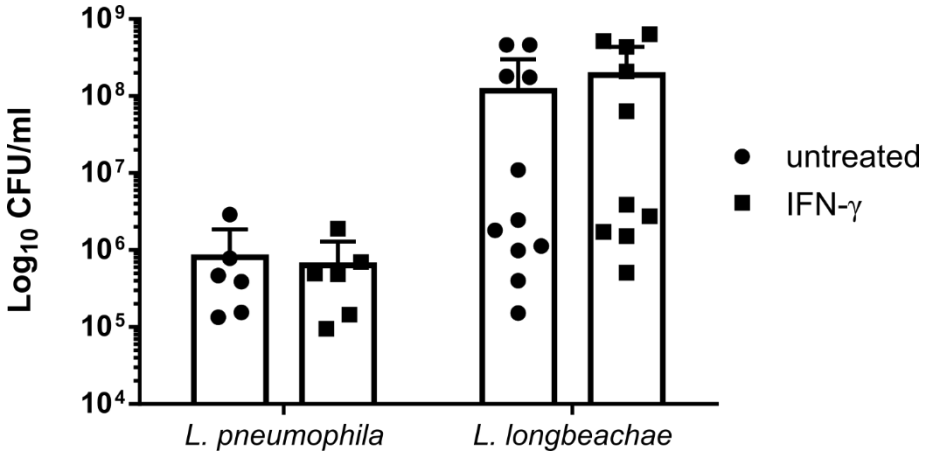


Figure 8: Impact of IFN-γ treatment on *Legionella* viability during ß-lactamase effector translocation assay

Following the quantification of RalF effector translocation previously described, iBMDM cells were lysed and viable *Legionella* were plated and cultured on BCYE plates at 37 °C for 3 days, subsequently resulting CFU were quantified. Results are shown as mean ± SD of $n \geq 6$ independent experiments carried out in technical duplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test, results were statistically non-significant)

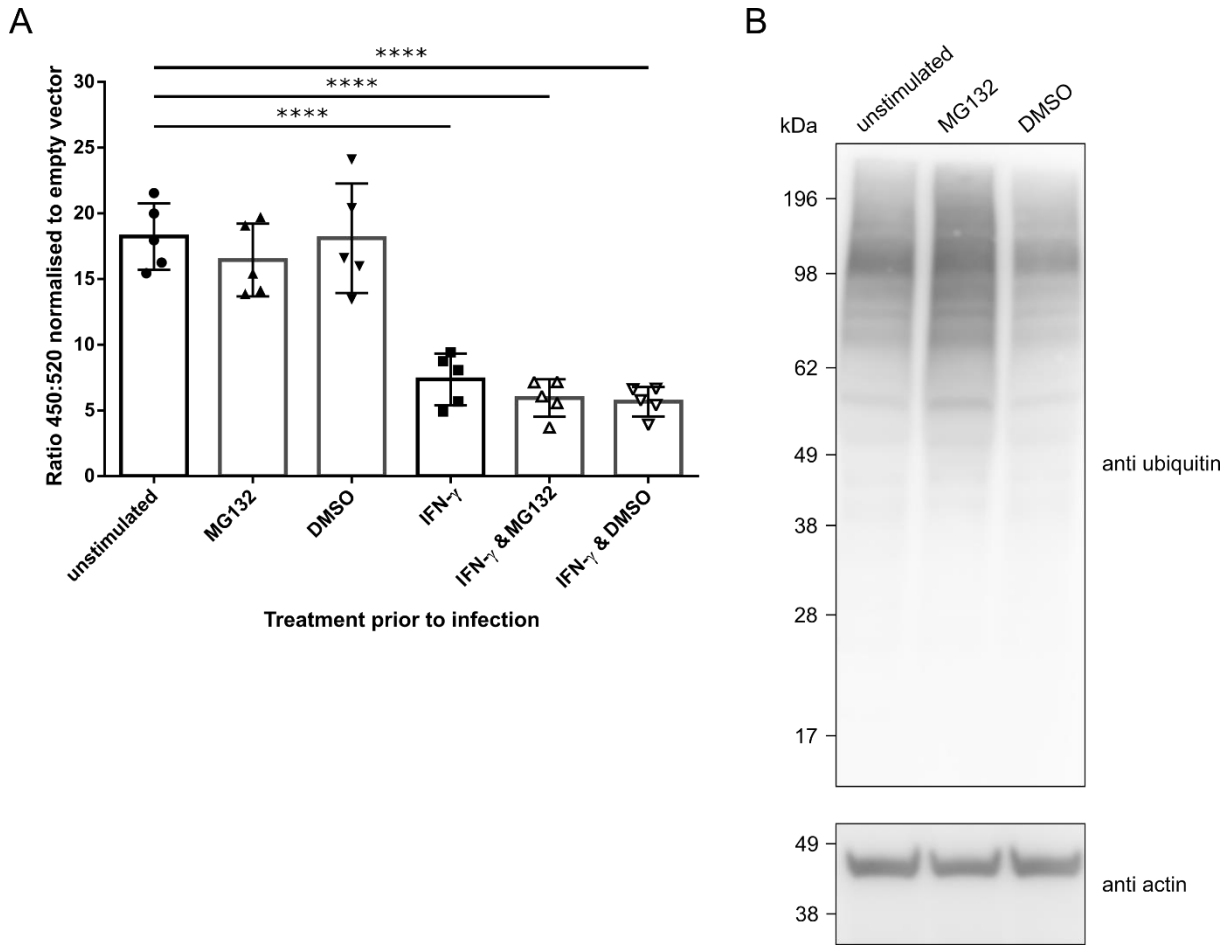


Figure 9: Role of proteasomal degradation in IFN-γ mediated reduction of *Legionella* Dot/Icm effector translocation

A) iBMDM mouse macrophages were stimulated with IFN-γ overnight and/or treated with the proteasome inhibitor MG132 or DMSO for 30 min prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 5 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

B) iBMDM cells were stimulated with MG132 or DMSO for 30 min and subsequently cells lysed. Proteins from treated and untreated (mock) cells were harvested and levels of poly-ubiquitinylated proteins were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

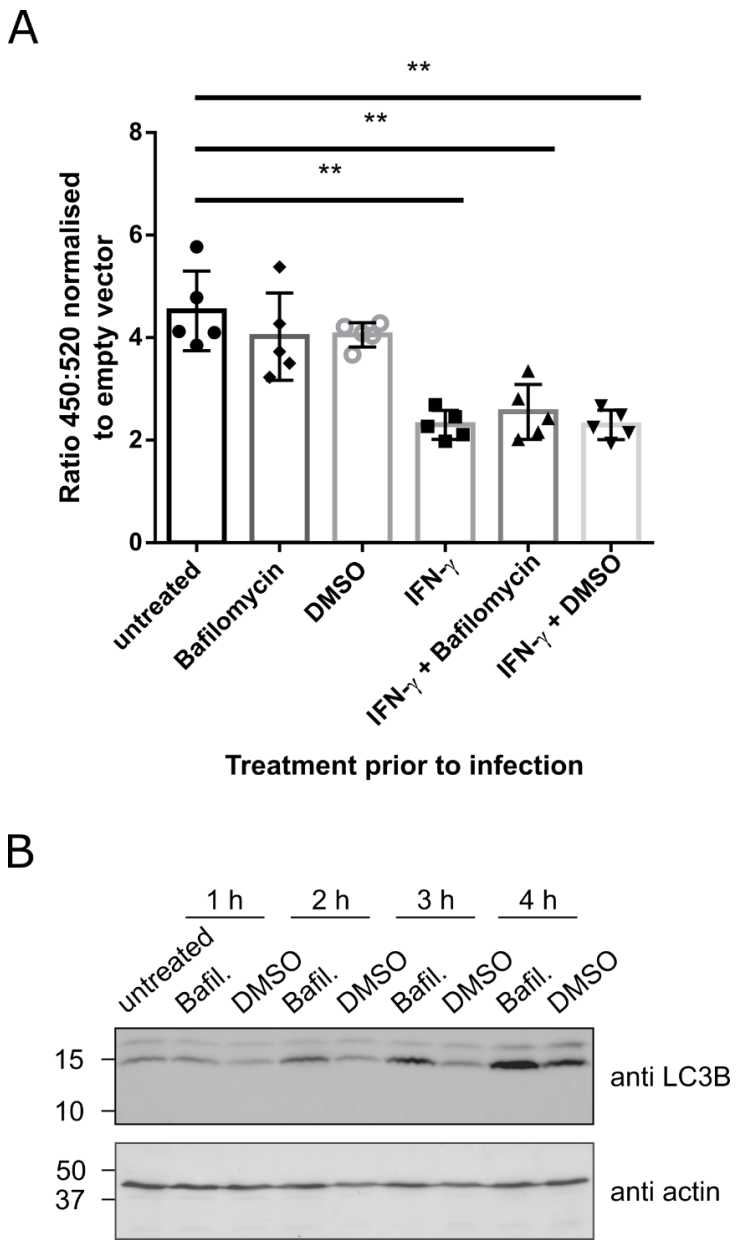


Figure 10: Role of autophagy in IFN-γ mediated reduction of *Legionella* Dot/Icm effector translocation

A) iBMDM mouse macrophages were stimulated with IFN-γ overnight and/or treated with autophagy inhibitor Bafilomycin A or DMSO for 3 h prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 5 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

B) iBMDM cells were stimulated with Bafilomycin A1 or DMSO for indicated times. Subsequently cells were lysed and proteins from treated and untreated (mock) cells were harvested. Accumulation of LC3B II protein levels were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

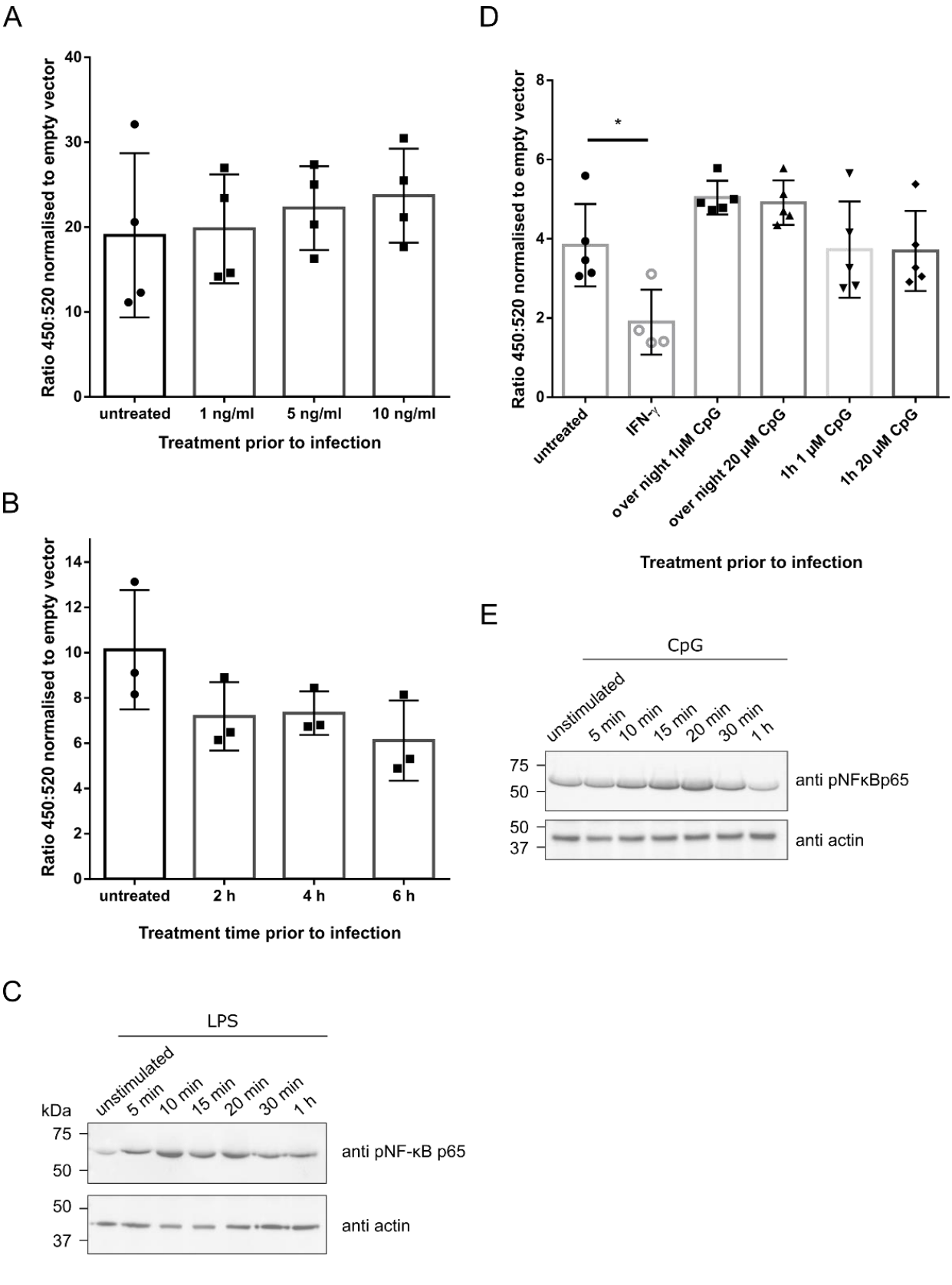

A
Ratio 450:520 normalised to empty vector
40
30
20
10
0
untreated
1 ng/ml
5 ng/ml
10 ng/ml
Treatment prior to infection
B
Ratio 450:520 normalised to empty vector
14
12
10
8
6
4
2
0
untreated
2 h
4 h
6 h
Treatment time prior to infection
C
LPS
kDa
unstimulated
5 min
10 min
15 min
20 min
30 min
1 h
75
50
anti pNF-κB p65
50
37
anti actin
D
Ratio 450:520 normalised to empty vector
8
6
4
2
0
*
untreated
IFN-γ
over night 1μM CpG
over night 20 μM CpG
1h 1 μM CpG
1h 20 μM CpG
Treatment prior to infection
E
CpG
unstimulated
5 min
10 min
15 min
20 min
30 min
1 h
75
50
anti pNFκBp65
50
37
anti actin

Figure 11: Impact of LPS and CpG treatment on Dot/Icm effector translocation in mouse macrophages

A) iBMDM mouse macrophages were treated with *E. coli* LPS overnight at indicated concentrations prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 4 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

B) iBMDM mouse macrophages were treated with *E. coli* LPS for up to 6h prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 3 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Unpaired t test with Welch's correction)

C) iBMDM cells were stimulated with LPS for the indicated time and subsequently cells were lysed. Proteins from treated and untreated (mock) cells were harvested and protein levels of pNF-κB p65 and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

D) iBMDM mouse macrophages were treated with CpG for the indicated time prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF, for 1 h. Subsequently $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n ≥ 4 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

E) iBMDM cells were stimulated with CpG for the indicated time and subsequently cells were lysed. Proteins from treated and untreated (mock) cells were harvested and protein levels of pNF-κB p65 and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

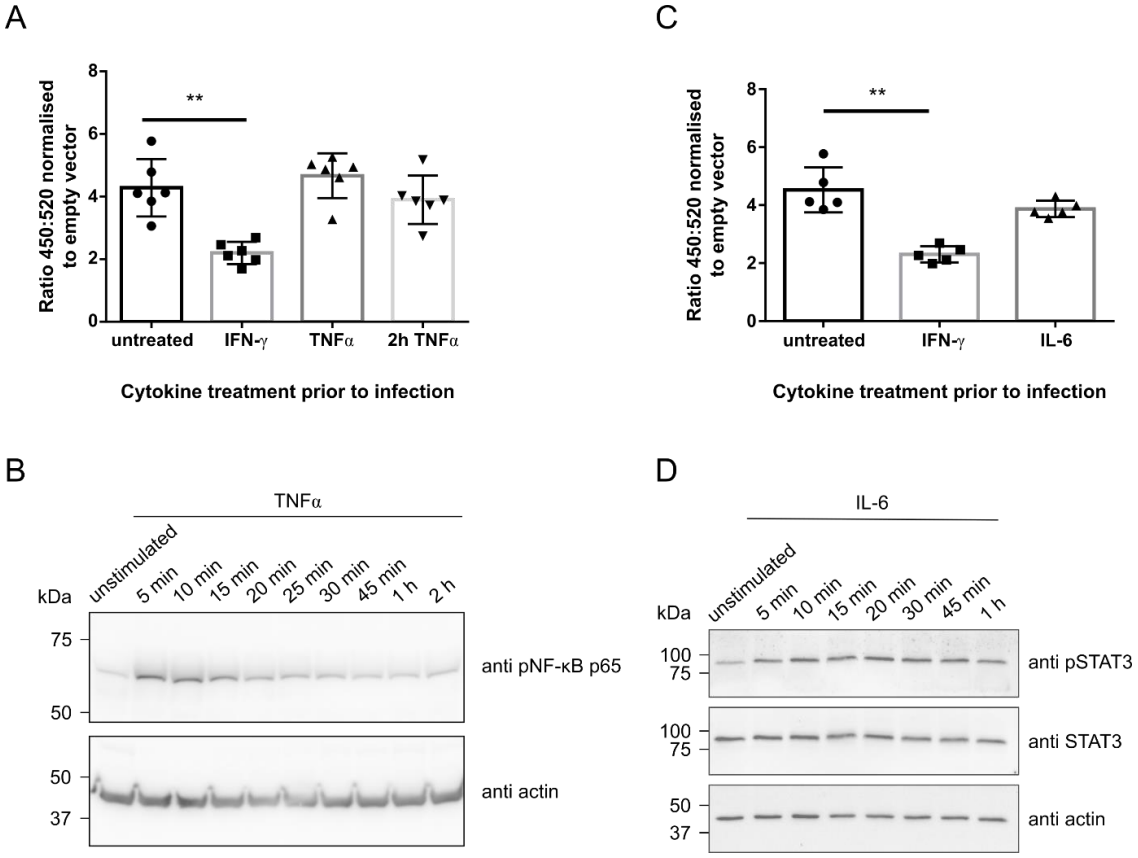


Figure 12: Impact of TNFα and IL-6 treatment on Dot/Icm effector translocation in mouse macrophages

A) iBMDM mouse macrophages were treated with TNFα overnight and at indicated times prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 6 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

B) iBMDM cells were stimulated with TNFα for the indicated time and subsequently cells were lysed. Proteins from treated and untreated (mock) cells were harvested and protein levels of pNF-κB p65 and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

C) iBMDM mouse macrophages were treated with IL-6 overnight prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 5 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

D) iBMDM cells were stimulated with IL-6 for the indicated times and subsequently cells were lysed. Proteins from treated and untreated (mock) cells were harvested and protein levels of pSTAT3, STAT3 and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

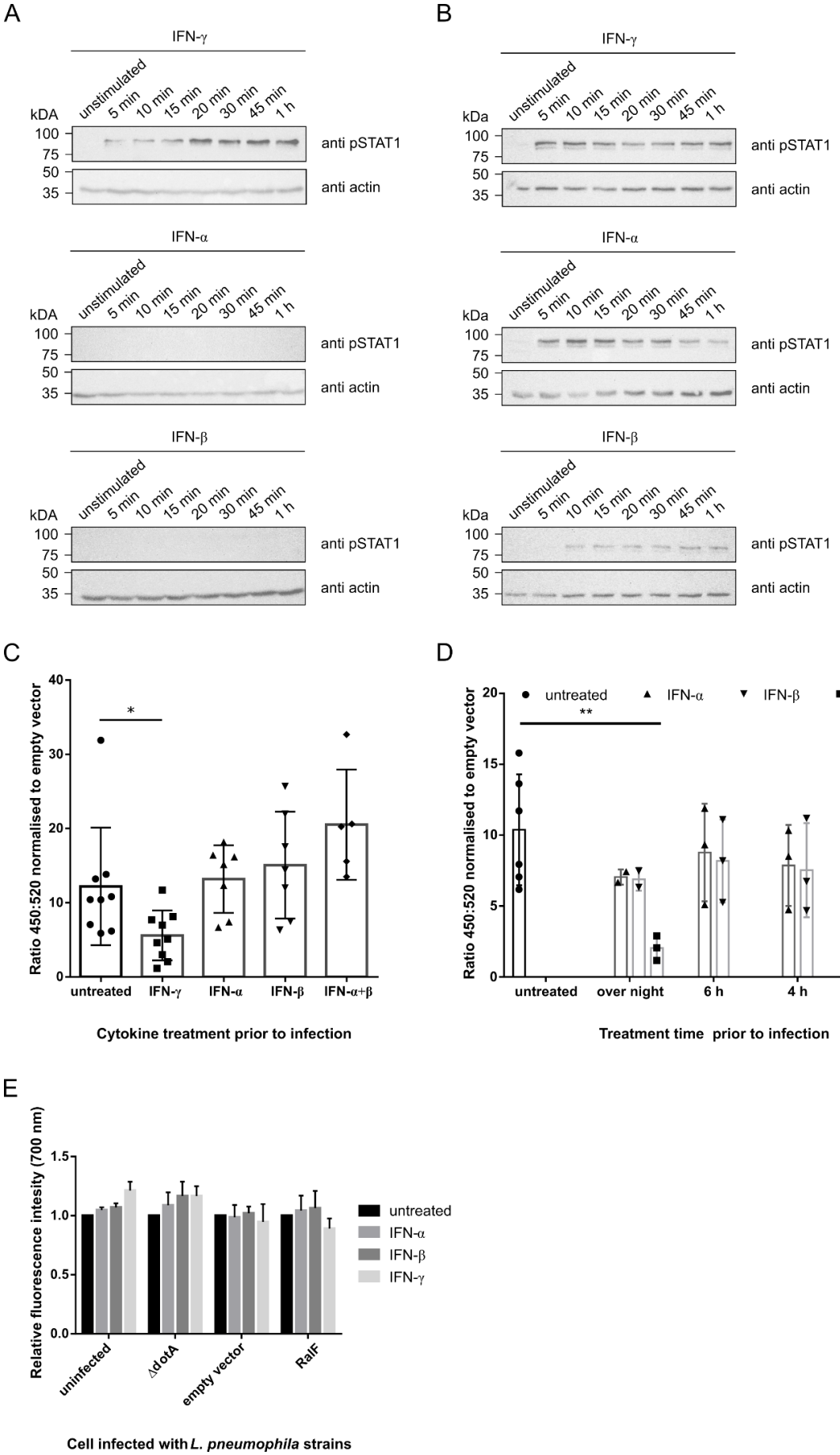

A
B
IFN-γ
IFN-α
IFN-β
unstimulated
5 min
10 min
15 min
20 min
30 min
45 min
1 h
kDA
100
75
50
35
anti pSTAT1
anti actin
C
Ratio 450:520 normalised to empty vector
*
untreated
IFN-γ
IFN-α
IFN-β
IFN-α+β
Cytokine treatment prior to infection
D
untreated
IFN-α
IFN-β
IFN-γ
**
over night
6 h
4 h
2 h
Treatment time prior to infection
E
Relative fluorescence intesity (700 nm)
uninfected
ΔdotA
empty vector
RalF
Cell infected with L. pneumophila strains

Figure 13: Impact of type I interferon on Dot/Icm effector translocation in RAW 264.7 macrophages

A) iBMDM mouse macrophages were stimulated with interferons (IFN-γ 50 U/ml, IFN-α and IFN-β 1000 U/ml) for the indicated time. Cells were lysed and proteins from treated and untreated (mock) cells were harvested. Protein levels of pSTAT1 and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

B) RAW 264.7 cells were stimulated with interferons (IFN-γ 50 U/ml, IFN-α and IFN-β 1000 U/ml) for the indicated time. Cells were lysed and proteins from treated and untreated (mock) cells were harvested. Protein levels of pSTAT1 and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

C) RAW 264.7 mouse macrophages were treated with IFN-γ (50 U/ml), IFN-α (1000 U/ml), IFN-β (1000 U/ml) and IFNα+β (each 1000 U/ml) overnight prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF, for 1 h. Subsequently $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n ≥ 5 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

D) RAW 264.7 mouse macrophages were treated with IFN-γ (50 U/ml), IFN-α (1000 U/ml) and IFN-β (1000 U/ml) for up to 6h prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified with TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n ≥ 2 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Unpaired t test with Welch's correction)

E) Following the quantification of *L. pneumophila* RalF effector translocation described previously, RAW 264.7 cells were stained with CellTag™ 700 Stain to quantify cells remaining after the translocation assay. Results are shown as mean ± SD of n = 3 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Unpaired t test with Welch's correction)

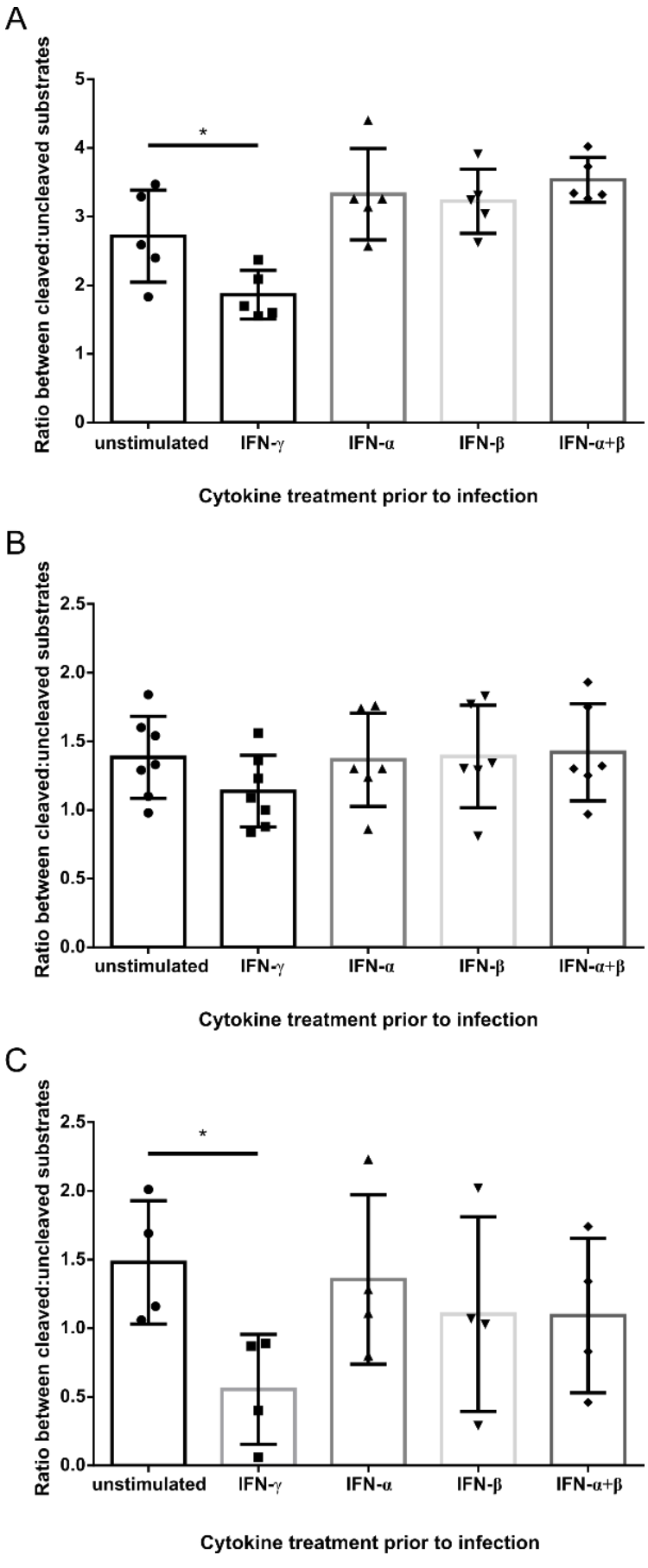

A
Ratio between cleaved:uncleaved substrates
5
4
3
2
1
0
*
unstimulated
IFN-γ
IFN-α
IFN-β
IFN-α+β
Cytokine treatment prior to infection
B
Ratio between cleaved:uncleaved substrates
2.5
2.0
1.5
1.0
0.5
0.0
unstimulated
IFN-γ
IFN-α
IFN-β
IFN-α+β
Cytokine treatment prior to infection
C
Ratio between cleaved:uncleaved substrates
2.5
2.0
1.5
1.0
0.5
0.0
*
unstimulated
IFN-γ
IFN-α
IFN-β
IFN-α+β
Cytokine treatment prior to infection

Figure 14: Impact of type I interferon on Dot/Icm effector translocation in different RAW 264.7 macrophage batches

A) RAW 264.7 mouse macrophage batch "Melbourne" was treated with IFN-γ (50 U/ml), IFN-α (1000 U/ml), IFN-β (1000 U/ml) and IFN-α+β (each 1000 U/ml), overnight prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n ≥ 5 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

B) RAW 264.7 mouse macrophage batch "LIMES" was treated with IFN-γ (50 U/ml), IFN-α (1000 U/ml), IFN-β (1000 U/ml) and IFN-α+β (each 1000 U/ml) overnight prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 7 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

C) RAW 264.7 mouse macrophage batch "Venusberg" was treated with IFN-γ (50 U/ml), IFN-α (1000 U/ml), IFN-β (1000 U/ml) and IFN-α+β (each 1000 U/ml), overnight prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 4 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

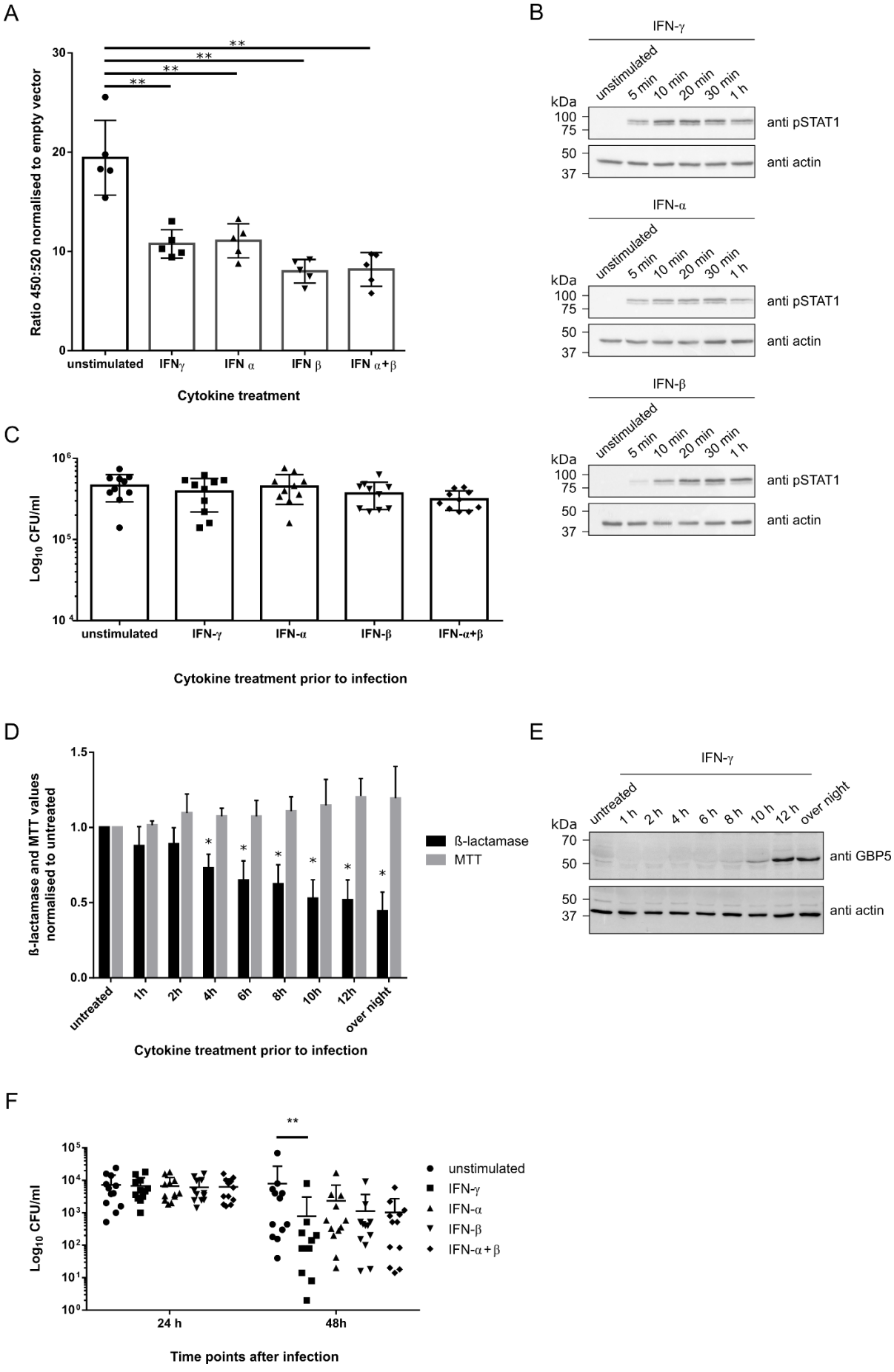

A
Ratio 450:520 normalised to empty vector
unstimulated
IFNγ
IFN α
IFN β
IFN α+β
Cytokine treatment
B
IFN-γ
IFN-α
IFN-β
unstimulated
5 min
10 min
20 min
30 min
1 h
kDa
anti pSTAT1
anti actin
C
Log10 CFU/ml
unstimulated
IFN-γ
IFN-α
IFN-β
IFN-α+β
Cytokine treatment prior to infection
D
ß-lactamase and MTT values normalised to untreated
ß-lactamase
MTT
untreated
1h
2h
4h
6h
8h
10h
12h
over night
Cytokine treatment prior to infection
E
IFN-γ
untreated
1 h
2 h
4 h
6 h
8 h
10 h
12 h
over night
anti GBP5
anti actin
F
Log10 CFU/ml
unstimulated
IFN-γ
IFN-α
IFN-β
IFN-α+β
24 h
48h
Time points after infection

Figure 15: Impact of interferon stimulation on *Legionella* Dot/Icm effector translocation into primary BMDM

A) Primary BMDM were treated with IFN-γ (50 U/ml), IFN-α (1000 U/ml), IFN-β (1000 U/ml) and IFN-α+β (1000 U/ml each) overnight prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of n = 5 independent experiments carried out in technical triplicates, each dot representing a mouse.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

B) Primary BMDM were stimulated with IFN-γ (50 U/ml), IFN-α (1000 U/ml), IFN-β (1000 U/ml) for the indicated time. Cells were lysed and proteins from treated and untreated (mock) cells were harvested. Protein levels of pSTAT1 and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

C) Following the quantification of $RalF_{Lp}$ effector translocation previously described, pBMDM cells were lysed and viable *L. pneumophila* were plated and cultured on BCYE plates at 37 °C for 3 days for CFU enumeration. Results are shown as mean ± SD of n = 5 independent experiments carried out in technical duplicates, each dot representing a mouse. (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

D) pBMDM mouse macrophages were treated with IFN-γ (50 U/ml) prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for the indicated duration. Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Subsequent of the ß-lactamase effector translocation assay, cell viability was quantified using a MTT assay. Results are shown as mean ± SD of n = 4 independent experiments carried out in technical triplicates.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

E) pBMDM cells were stimulated with IFN-γ (50 U/ml) for the indicated duration. Subsequently cells were lysed and proteins from treated and untreated (mock) cells were harvested. Protein levels of GBP5 and ß-actin were analysed via immunoblotting. Results are representative images of at least 3 independent stimulations.

F) Primary BMDM were infected with *L. pneumophila* 130b Δ*flaA* for 1 h at 37 °C and subsequently treated with Gentamicin for 2 h at 37 °C to kill extracellular bacteria. After the Gentamicin treatment, pBMDM were stimulated with interferons (IFN-γ 50 U/ml, IFN-α, IFN-β and IFN-α+β 1000 U/ml) for the duration of the replication assay. Cells were lysed at indicated times and viable *Legionella* were cultured on BCYE plates for 3 days at 37 °C and resulting CFU were enumerated. Results are shown as mean ± SD of n = 5 independent experiments carried out in technical duplicates, each dot representing a mouse.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

Chapter 4: Identification of candidate interferon stimulated genes conferring the reduction in *Legionella* Dot/Icm effector translocation

4.1 Introduction

Interferon stimulated genes (ISGs) and their role in host defence have been of interest since the discovery of their inducing molecules in 1957 [218-221]. During the last couple of decades, an intricate network of ISGs has been discovered that mediates host defence upon pathogen detection. Interferon stimulated GTPases especially have been recognised as a core protein family within this network [446].

IFN-γ has been known to restrict the replication of *Legionella* since the mid-nineties' [371, 447], though the mechanisms underlying this restriction were only discovered piece by piece in the last decade. Starting with the observation that nitric oxide has bactericidal effects on *L. pneumophila* [448], and was followed by linking Irgm1 to IFN-γ mediated control [234]. Subsequently, caspase11 was identified as a crucial component of IFN-γ mediated restriction as well as the discovery of some functional redundancy mediate by Nos2 and Nox2 as well as Irgm1 and Irgm3 [254]. Finally, immune-responsive gene 1 (Irg1) was linked to the production of anti-microbial itaconic acid [370].

Recently, Price et al. described a mouse mutant that lacked all six genes previously implicated in host defence against *L. pneumophila* [372]. They demonstrated that pBMDM derived from mice lacking all six IFN-γ stimulated factors (iNOS, NOX2, IRGM1, IRGM3, IRG1, CASP11) were unable to restrict intracellular replication of *L. pneumophila* upon IFN-γ stimulation [372]. This observation substantiates the multifaceted host defence against a single pathogen mediated by IFN-γ, with multiple factors involved and even some functional redundancies.

However, if these six genes also mediate the reduction in effector translocation remains to be investigated. Though it is possible that the genes which mediate the restriction of *L. pneumophila* intracellular replication are distinct from those mediating the reduction in Dot/Icm effector translocation, since we and others [234, 368] observed a weaker potential of type I interferon to restrict the replication of *L. pneumophila* compared to IFN-γ. However, type I interferons restrict the Dot/Icm effector translocation as potently as IFN-γ does, thus

suggesting either different mechanisms or, more likely, an overlap in the genes responsible for inhibiting Dot/Icm effector translocation.

Based on our previous observations, in this chapter we aimed to identify the ISGs which are responsible for the observed reduction in Dot/Icm effector translocation. Since this novel mechanism might be mediated by interferon stimulated factors distinct from those which inhibit *L. pneumophila* replication, and thus most likely have not been directly linked to host defence against *Legionella* yet, we decided to take an unbiased approach to identify candidate interferon induced factors by utilizing mRNA sequencing of interferon-stimulated macrophages. Using comparative analysis, we were able to identify ISGs which were uniquely induced by either IFN-γ or type I interferon in pBMDM as well as the genes which were induce by both IFNs, the latter representing candidates for the inhibition of Dot/Icm effector translocation. Via gene ontology enrichment analysis, we identified ISG15 (interferon stimulated gene 15) as well as the family of PARPs (poly (ADP-ribose) polymerases) as possible factors leading to the reduction in *Legionella* Dot/Icm effector translocation into host cells.

4.2 Results

Since interferon stimulation can lead to the expression of thousands of genes, we wanted to narrow down the number of possible targets by comparing mRNA sequencing data from interferon-stimulated pBMDM. The web tool INTERFEROME, is a collection of ISGs induced via a diverse range of interferons in humans and mice, but currently does not harbour a complete set of type I and IFN-γ stimulated primary mouse macrophages. Hence, we performed our own mRNA sequencing to identify possible factors mediating the reduction in Dot/Icm effector translocation and in this way also hope to learn more about the interferon induced response in macrophages during *Legionella* infection.

4.2.1 mRNA sequencing of interferon stimulated macrophages

For mRNA sequencing we isolated and differentiated macrophages from C57BL/6 mouse bone marrow and stimulated these pBMDM with IFN-γ or a mixture of IFN-α and IFN-β. These cells were subsequently either infected with *L. pneumophila* Δ*flaA* carrying pxDC61-RalF plasmid or mock-treated with media and a ß-lactamase Dot/Icm effector translocation assay was

performed as previously described in chapter 3 and material methods chapter. Immediately following the translocation assay, cells were lysed and mRNA was isolated, a summary of the different treatment groups is listed in (Table 11). These samples (in triplicate) were sent for RNA sequencing and the subsequent alignment of the sequencing snips to the mouse genome (Mus_musculus.GRCm38.94.gtf) was performed by CF. Elzer and A. Buness from the "Core Unit for Bioinformatics Data Analysis (CUBA)" at the University of Bonn. The resulting counting matrix was subsequently analysed with the genomic analysis software Partekflow, to identify interferon-stimulated genes.

4.2.2 Principal component analysis (PCA)

We performed a principle component analysis [449] to create a visual summary of all sequenced samples based on their diverse and common attributes. Based on this analysis, we showed that the samples cluster by treatment group and not by origin (i.e. individual mouse), thus indicating the reproducibility of the treatment results (Figure 16 A-B). Furthermore, a clustering based on *L. pneumophila* infection was not apparent, suggesting that infection with *L. pneumophila* for such a short time (1 h) did not seem to alter mRNA expression dramatically, compared to interferon treatment (Figure 16 C). Somewhat surprisingly, the incubation time with interferon did not seem to have a significant impact on the transcriptome either, as the different time points within the treatment classes did not cluster according to treatment either. Based to these observations, 4 samples initially belonging to interferon treated groups, were identified as untreated and thus excluded from the analysis.

4.2.3 Analysis of differential expressed genes upon IFN-γ and type I interferons IFN-α and IFN-β stimulation of pBMDM

To identify differentially expressed genes, differential expression analysis via the DeSeq2 algorithm was performed with the count matrix resulting from the previous genome alignment step. For the analysis a log2 fold-change value of $-2 \leq FC \geq 2$ as well as an adjusted P-value (corrected for multiple comparisons with the Benjamini-Hochberg procedure) of $FDR \leq 0.05$ were set as thresholds. Genes meeting both criteria were considered to be differentially expressed and used for subsequent analysis. Comparing IFN-γ treated samples to the untreated samples resulted in 1 903 differentially expressed genes, with the majority (1 155) being upregulated and only 748 genes down regulated (Figure 17 A&C and Appendix 3). Similar results were obtained from type I interferon stimulated samples, with 2 880 genes differentially

expressed compared to untreated samples, consisting of 1 736 upregulated and 1 144 downregulated genes (Figure 17 B&C and Appendix 2). These data indicate that stimulation with interferons extensively changes the host transcriptome and thus proteome to clear invading pathogens. Due to the observation that both types of interferon can interrupt the translocation of *Legionella* Dot/Icm effectors, differentially expressed genes of both interferon types were compared and jointly as well as uniquely stimulated ISGs were identified (Figure 17). In total 1 276 genes were differentially express upon stimulation with both types of interferons, with 843 upregulated and 433 downregulated genes (Figure 17 C and Appendix 1). These jointly stimulated genes were used for subsequent analysis.

4.2.4 Gene ontology enrichment analysis of IFN-γ and type I interferon stimulated genes

In order to identify essential biological functions and processes executed by the differentially expressed genes, previously identified as being part of the gene set induced by both types of interferons, we conducted a gene ontology enrichment analysis using the web-based tool gProfiler [450]. The enrichment analysis was done using the recommended settings of gProfiler, the g:SCS algorithm for multiple testing corrections, which also has been previously used by Naujoks et al. for their analysis of the LCV proteome [370]. The gene ontology terms which were identified as being overrepresented in the list of commonly induced ISGs belonging to the groups of biological processes (BP), molecular function (MF), cellular compartment (CC) as well as Reactome pathways are depicted in (Figure 18, Figure 19, Figure 20, Figure 21). Each of the commonly stimulated ISGs could be categorised into multiple groups as well as GO terms.

Unsurprisingly, the group of biological processes (BP) is highly enriched with host defence processes and cytokine responses such as: defence response to other organisms ($2.2*10^{-56}$), innate immune response ($2.7*10^{-54}$), cellular response to cytokine stimulus ($4.1*10^{-46}$) and response to bacterium ($9.1*10^{-21}$) (Figure 18), which is in line with previous observations regarding the function of ISGs. One of the cellular compartments highly enriched in the ISGs analysis, was the symbiont-containing vacuole ($3.6*10^{-15}$), indicating that some ISGs might directly target and act upon the LCV (Figure 20). Regarding the enrichment of certain functions mediated by common ISGs, a diverse range of molecular functions relating to nucleotide binding, antigen processing, metal binding, ubiquitin and ubiquitin-like protein transfer as well as cytokine receptor signalling were identified (Figure 19). These functions go hand in hand with host cell defence against an invading pathogen via limiting essential nutrient acquisition,

marking pathogen components with ubiquitin-like proteins for degradation, and processing the pathogen for antigen presentation. Some of these molecular functions are directly linked to REACTOME pathways, such as antigen processing-cross presentation, nicotinamide salvaging and ISG15 antiviral mechanisms (Figure 21), indicating that these particular molecular functions and pathways might have a role in restricting the *Legionella* effector translocation into host cells. We therefore wanted to analyse if some of these molecules and pathways restricted the Dot/Icm effector translocation in vitro. However, due to the immense negative impact of the SARS-CoV-2 pandemic on the work and progress of this thesis, we were not able to test many possible targets in vitro. Nonetheless, we have explored the possible involvement of these factors in the interferon induced inhibition of Dot/Icm effector translocation in the discussion section of this chapter.

4.2.5 Role of interferon induced GTPases in *Legionella* effector translocation

One of the gene ontology terms which was prominent due to its very high enrichment score, was the molecular function revolving around the binding and hydrolysing of guanyl nucleotide (Figure 19). This is in line with GTPases known as guanylate binding proteins (GBPs) or interferon regulated GTPases (IRGs) being one of the most highly induced proteins in IFN-γ and type I interferon stimulated macrophages (Appendix 1, 2 and 3). Furthermore, this is in agreement with previous observations that GTPases (GBPs and IRGs) are one of the most highly induced protein groups upon interferon stimulation [288]. In addition, GBPs and IRGs have been shown to be involved in a variety of host defence processes against a large range of pathogens [446] including *Legionella* [229, 234, 254, 311]. We therefore analysed the expression values of the different GBPs and IRGs in our samples. All the GBPs and IRGs were highly induced upon IFN-γ and type I interferons, with the exception of GBP 10 and Irgc 1, which were excluded from the differential expressed genes due to very low expression across all samples (Figure 22 A). The induction of the GTPases with the different interferons was higher upon induction IFN-γ stimulation compared to type I interferons, and this was especially pronounced with GBP 2, GBP 4-6, GBP 11, Irga 6 and Irgb 6 which showed roughly double the expression compared to type I interferon (Figure 22 A and Table 16). The highest induction was observed for Irga6 followed by GBP 4 and GBP11, whereas Irgb 4/5 and GBP1 showed the smallest change in expression (Figure 22 A and Table 16).

Based on their high levels of induction, the high enrichment for GTPase function in our mRNA sequencing analysis and the ability of GBPs to directly target the LCV during infection, we

analysed their impact on *L. pneumophila* Dot/Icm effector translocation into host cells. A thoughtful donation from Prof. Pfeffer's laboratory at the University of Düsseldorf enabled us to isolate and test pBMDM from WT, GBP2$^{-/-}$ and GBP5$^{-/-}$ C57BL/6 mice in Germany, while in Melbourne at the Hudson Institute of Medical Research Dr. Garrett Ng was able to test GBP1$^{-/-}$ and GBPchr5$^{-/-}$ mice (GBP 4,8,9$^{-/-}$). We isolated and differentiated pBMDM from these mice and conducted a *L. pneumophila* Dot/Icm effector translocation assay following IFN-γ stimulation. None of the GBP deficient macrophages showed differences in Dot/Icm effector translocation compared to WT cells in untreated or IFN-γ treated cells (Figure 22 B). These experiments suggest that the tested GBPs are not involved in the reduction of Dot/Icm effector translocation into host cells or may indicate that multiple GBPs are involved in this phenotype. However, more repeats are needed and more knockout pBMDM should be tested to define the role, if any, of GBPs and IRGs in the interferon mediated inhibition of Dot/Icm effector translocation.

4.3 Discussion

It has previously been shown that infection with *L. pneumophila* leads to transcriptional changes in host cells. These changes are triggered via the detection of *Legionella* PAMPs or *Legionella* associated activities, such as the inhibition of host protein translation or via the translocation of effectors that modulate the host transcriptional activity directly [202, 380, 451-453]. For the latter case, a couple of effectors have been identified for example, the *L. pneumophila* effector SnpL binds to the eukaryotic transcription elongation factor, Suppressor of Ty5 (SUPT5H)/Spt5, which in turn leads to a massive upregulation of gene transcription [384]. The *L. pneumophila* effector AnkH also impacts host transcription, via interacting with LARP7 a component of the 7SK small nuclear ribonucleoprotein (snRNP) complex. This interaction disrupts the association of LARP7 with the snRNP complex, which in turn leads to a blockage of the transcriptional elongation by polymerase (Pol) II [454]. Another example for extensive host transcriptional manipulation is the manipulation of the Hippo pathway, due to functional mimicry of the host Hippo kinase via effector LegK7 [455]. On the other hand, the *L. pneumophila* effector RomA translocates to the nucleus and methylates histone H3, thereby repressing host transcription, including host defence genes [383]. These studies appear to be at odds with our observations, since *L. pneumophila* infection did not have a great impact on host transcription and thus our samples did not cluster into infected and uninfected groups respectively in the PCA plots. However, all these previous experiments and analyses were performed after a much longer infection time ranging from 7 h to 12 h for ectopically expressed effectors [384] and 4 h to 8 h for infection related analyses [383, 452, 453, 455, 456]. These differences in the duration of *L. pneumophila* infection compared to our short infection period, at just one hour of infection and a further 1.5 h of substrate incubation, could explain the differences observed and indicate that a significant shift in the transcriptome is only detectable after a longer infection time.

As previously mentioned, interferon-inducible GTPases have been identified as a cornerstone of interferon-mediated host defence. It was demonstrated prior that these GBPs and IRGs are up-regulated in various cell types upon IFN-γ stimulation and other stimuli, though their levels of induction vary among the different GTPases and upon different stimulations, such as IFN-γ or type I interferons, and stimulation times [267, 287, 288, 306]. In contrast to the observations made in ANA-1 macrophages [267], we detected expression of all GBPs (except for *Gbp10*) upon IFN-γ as well as type I interferon stimulation. These discrepancies might be due to using

different cells, as differences in GTPase expression has been observed among different cells types of the same species e.g. THP1 vs primary human monocyte derived cells vs human endothelial cells [287, 288]. These observations indicate the need to test the effects/mechanisms of target proteins in multiple cell types and species, as these differences in gene induction between cell lines might also apply to our observations regarding the differences in the interferon-mediated inhibition of Dot/Icm effector translocation in human vs mouse cells.

Even though the GBPs were readily expressed in macrophages, we were not able to show an impact on effector translocation using GBP knockout pBMDM. However, these results are only preliminary observations, since we were not able to complete all repeats due to the restricted availability of GBP deficient mice. Hence, these observations might change upon repeating the Dot/Icm effector translocation in GBP deficient pBMDM as well as analysing other GBP deficient macrophages as soon as they are available to us, including mice deficient in multiple GBPs and other GTPases e.g. the GBP clusters on chromosome 3 or the GTPases which are absent in humans (GBP 8-11, IRGs). Furthermore, it has been shown that GBPs interact with each other and other host proteins in order to mediate the anti-pathogenic effects [268], which may not be well represented in a single gene knockout. The full complement of GBP and IRG deficient mice would allow us to analyse their involvement in Dot/Icm effector translocation inhibition, intracellular replication and LCV biogenesis in vitro as well as the role of GBPs and IRGs in the immune response in vivo.

Since the translocation of Dot/Icm effectors is initiated upon host contact [183, 437], inhibition of effector translocation would be most effective, if initiated upon uptake of *Legionella* into host cells. This would immediately mitigate the extensive manipulation of host cell biology resulting from the activity of translocated Dot/Icm effectors. The interferon-stimulated GTPases would be ideal candidates, since they are highly induced upon interferon stimulation and both GBP and IRG family members have been shown to locate to pathogen containing vacuoles within a few minutes of pathogen invasion [267, 274, 311, 457, 458]. Furthermore, it has been shown that the accumulation of GBPs and IRGs on pathogen vacuoles results in membrane instability and subsequent rupture of the vacuole [257, 268, 333, 459], starting at the poles of the parasites [460]. Recently it has been demonstrated that the *Legionella* Dot/Icm secretion system is also located at the poles of the bacteria and the polar delivery of effectors is crucial for the manipulation of the host cell and bacterial survival [152, 156]. Even though direct rupture of the LCV has not been observed upon IFN-γ stimulation, considering that these observations were made early on during the infection cycle [234, 254, 370], it is possible that

the polar localisation of GBPs and IRGs on the LCV could target the Dot/Icm secretion system and subsequently disrupt effector translocation. In support of this hypothesis, it recently has been shown that binding of hGBP1 results in the disruption of membrane dynamics, which interferes with the polar targeting of the *Shigella* autotransporter IcsA and its binding partners, subsequently leading to the an interrupted bacterial actin-based motility [315]. GTPases might therefore interfere with the function or assembly of the entity which is used to transport effectors across the LCV. It was recently demonstrated that GBP2 and GBP5 inhibit the proteolytic function of the protease furin [271]. Furthermore, a splicing variant of hGBP3 disrupts the function of the influenza A viral polymerase complex and thus inhibit the transcription and replication of influenza A virus [273]. To test if GBPs impact the Dot/Icm effector translocation of *Legionella* by interrupting the membrane dynamics or protein function, the analysis should also include different *Legionella* strains and species, since it has been shown that specific GTPases target different pathogens [270, 274, 283, 312] and some pathogens actively interfere with the function or colocalization of the GTPases such as *C. muridarum* [333] or *Chlamydia trachomatis* [335, 461], *Toxoplasma gondii* [334, 462-465] and *Shigella flexneri* [260, 261, 308].

Although we focussed on the possible role of selected GBPs in the interferon-induced inhibition of Dot/Icm effector translocation, it is equally possible that other ISGs are responsible for the phenotype we observed.

Another interferon-induced protein that might interfere with the Dot/Icm effector translocation was identified during the REACTOME pathway enrichment analysis of the commonly induced genes based on the mRNA sequencing; namely ISG15 (interferon-stimulated gene 15) (Figure 21).

ISG15 was first identified in 1979 [466] and was classified as a ubiquitin-like protein since it consists of two ubiquitin-like domains, linked via a short hinge, with roughly 33 % sequence homology to ubiquitin [467]. Even though ISG15 is classified as a ubiquitin-like protein, the sequence of ISG15 varies greatly between mammalian species, ranging from 42 % to 98 % amino acid identity, in contrast to the high sequence conservation of ubiquitin which is conserved close to 100 % among species [467]. These differences in sequence identity resulting in different binding/interacting partners might explain the differences we observed in human and mouse stimulated macrophages. Although the sequence is quite variable between species, the C-terminal LRLRGG sequence needed for conjugation is conserved across all species [467]. The attachment of ISG15 to a target protein is termed ISGylation and is controlled by an enzyme cascade very similar to ubiquitin [467]. So far, only a few proteins have been identified as ISG15 components of the transfer machinery, ISG15 is activated by E1 UBE1L [468], Ubc8 acts as an E2 conjugating enzyme [469, 470] and three E3 ligases EFP (estrogen-responsive finger protein; TRIM25) [471], HERC5 (HECT E3 enzyme) [472] and HHARI (human homolog of Drosophila ariadne) [473] mediate the transfer of ISG15 onto a target protein. On the other hand, the removal of ISG15 (de-ISGylation) is controlled by a ubiquitin-specific protease UBP43 (USP18) [467, 474]. All the mouse homologue components needed to attach ISG15 and remove ISG15 as well as ISG15 itself were upregulated upon treatment with both types of interferon (Table2&3) in mouse macrophages, which is in line with previous observations [475]. Furthermore, all of these proteins are found on the LCV during infection [370] and also have been shown to be induced upon *L. pneumophila* infection in vivo [234], which suggests a possible role in host defence against *L. pneumophila*.

The function or consequence of the post-translational modification of a protein with ISG15 remains enigmatic, though some functional insights have been gained in the last couple of years. It has been shown that ISG15 can interact with other proteins in mainly two modes, as free

ISG15/non-covalently bound (extracellular or intracellular) or covalently bound to a target protein (ISGylation).

Intracellular ISG15 can disrupt protein-protein interactions and thus disrupts the protein oligomerization necessary to form protein complexes. For example, in cells infected with influenza B, ISG15 binds to viral nucleoproteins which inhibits the oligomerization of nucleoproteins and thus leads to the disruption of viral ribonucleoprotein formation culminating in reduced viral replication [476]. Furthermore, it has been shown that ISG15 also interrupts the building of human papillomavirus (HPV) particles via the binding of ISG15 to HPV L1 capsid protein [477]. The ISGylation of only a fraction of the HPV L1 capsid proteins results in a 30 % reduction of viral particle production and 70 % loss of infectivity compared to un-ISGylated virus particles [477]. This indicates that even a small number of ISGylated proteins can significantly affect a pathogen's replication and survival. It might be possible that the ability of ISG15 to interrupt protein-protein interactions and protein complex assembly might interfere with Dot/Icm effector translocation. Since the Dot/Icm secretion system of *Legionella* is a highly intricate protein complex and even the loss of a single secretion system component (e.g. DotA) leads to a non-functional complex, binding of ISG15 to one protein of this complex might interrupt the protein-protein interactions in the Dot/Icm secretion system and lead to a disrupted translocation of effectors. Alternatively, ISG15 might directly or indirectly disrupt putative protein-protein interactions in the translocation pore which allows the transport of effectors across the LCV membrane.

Since ISG15 can be secreted from cells [478], another possibility of ISG15 mediated disruption of Dot/Icm effector translocation is via free extracellular ISG15. The interferon-mediated inhibition of Dot/Icm effector translocation starts shortly after the pathogen contact/invasion, as we have observed the disruption of RalF translocation and RalF is one of the first Dot/Icm effectors translocated into host cells. Hence, free extracellular ISG15 might disrupt the Dot/Icm secretion system of *Legionella* upon host contact, which would support the early interference with Dot/Icm effector translocation that we observed.

Another mechanism by which ISG15 may disrupt the Dot/Icm effector translocation is by interacting with the ubiquitin system of the host. It has been shown that ISG15 competes with ubiquitin for ubiquitin-binding sites on target proteins and also binds to ubiquitin forming mixed ubiquitin-ISG15 chains [479, 480]. This, in turn can modulate the degradation of proteins via the proteasome as well as disrupting the ubiquitin chain mediated fate/signalling of the

target protein [479, 480]. However, this mechanism is unlikely to play a role in our model, as we found that the inhibition of the proteasome activity via MG123 in IFN-γ stimulated macrophages did not restore Dot/Icm effector translocation.

In addition to manipulating the ubiquitin code on a target protein, it has been shown that ISG15 can interact with the enzymes mediating the transfer of ubiquitin. For example, binding of ISG15 to the E2 enzymes, UbcH6, UbCH8 and Ubc13, leads to the disruption of their conjugation activity and thus rendering the proteins inactive [481, 482]. ISG15 has also been shown to interact with ubiquitin ligase E3 Nedd4, which leads to the interruption of the protein-protein interaction between ubiquitin, Nedd4 and E2 enzymes, accumulating in a failed ubiquitin transfer from E2 to E3 [483, 484].

In 2021 Ong et al. demonstrated that *L. pneumophila* relies on some of the E2 and E3 host ubiquitin ligases to translocate Dot/Icm effectors efficiently [485] and ISGylation my interfere with the function of many of these ubiquitin components. For example siRNA based silencing of the host E2 ubiquitin conjugating enzyme UBE2E1 and the E3 ubiquitin ligase CUL7 led to reduced Dot/Icm effector translocation by *L. pneumophila* and compromised intracellular replication [485]. Since these enzymes are important for the survival of *L. pneumophila* and are also located on the LCV, ISG15 might interact with host ubiquitin enzymes at the LCV and therefore disrupt their function leading to a reduced Dot/Icm effector translocation into host cells. Given the associations outlined here, further investigation of the role of ISGylation in interferon mediated inhibition of Dot/Icm effector translocation is warranted.

Another protein family of interest in elucidating the mechanism of interferon-induced reduction in Dot/Icm effector translocation, was identified as part of the enriched REACTOME pathway of Nicotinamide salvaging (Figure 21).

These proteins belong to the enzyme family of poly (ADP-ribose) polymerases (PARPs) and transfer either mono ADP-ribose units (MARylation) or poly ADP ribose units (PARylation) onto target proteins using nicotinamide adenine dinucleotide (NAD^+) as a substrate [486]. Various amino acids are used for the attachment of ADP ribose units and similar to the ubiquitin code, ADP ribose attachments can be extended to long linear or branched chains of ADP ribose units, conferring different biological functions [487, 488]. Like many other posttranslational modifications, attachment of ADP ribose is recognised by other proteins and can be removed by ADP ribosyl-hydrolases, with some of these hydrolases having specificity for poly ADP ribose or mono ADP ribose and others that can remove both types of modification [489, 490]. The enzymes catalysing the "lifecycle" of the post-translational modification of ADP ribosylation are also called writers, readers and erasers [488, 491]. The family members of PARPs are highly diverse in structure, subcellular location and function, though all family members possess a PARP domain [486]. In line with a diverse structure, a rapid evolution of PARPs has been suggested from analysing PARP sequences in all primates, indicating an important role in the hosts arms race against pathogens [492].

PARP activity, the selection of target proteins and interaction with other cellular components are determined by the various domains of PARP proteins [493]. In addition to the vast range of possible interaction partners influenced by these domains, subcellular location of PARP proteins is dependent on cellular environment and can change upon infectious or chemical triggers, thus extending their range of activity even further [494, 495]. Even though these enzymes were discovered decades ago, the impact of MARylation and PARylation on target proteins remains enigmatic and manifold.

Since the discovery of the PARP family number of studies have focused on the function of PARP1 and PARP2 in DNA damage repair, though functions for other PARPs have emerged in recent years. Almost all focus on PARP1 function, either by studying PARP1 deficient animals and cells or by chemically inhibiting the PARP1 function (reviewed in [496]) and unfortunately, studies analysing the involvement of PARPs in bacterial infections are limited. Nonetheless some of these publications have identified a role for PARP1 in regulating the pro-inflammatory responses upon infection, such as observing a reduction in pro-inflammatory cytokines e.g. TNFα, IL1 β, IL 6, IFN-γ, MIP-2 and M-CSF [496]. So far, only one study

showed a direct impact of PARP function on bacterial burden at a cellular level [496], where an increased burden of *Salmonella enterica* serovar Typhimurium in PARP14 deficient macrophages was observed [497]. This reduction was linked to reduced transcription of IFN-β as well as other secondary anti-pathogen genes and reduced production of NO [497].

Our mRNA sequencing analysis showed that genes encoding PARP proteins were highly upregulated upon stimulation with both IFN-γ and type I interferons (Table 3), which is in line with previous observations [486, 497]. A comparison of these enzyme IDs with the LCV proteome data created by Naujoks et al.[370] revealed that PARP enzymes were associated with the LCV. In addition, it has previously been shown that IFN-γ stimulation of macrophages leads to an increase in poly ADP ribosylation signals [498-500] Since PARP proteins and their resulting ADP-ribosylation activity are highly up-regulated upon interferon stimulation and the proteins are targeted to the LCV during infection, we speculate that these enzymes are candidates for a role in host defence against *Legionella*.

MARylation or PARylation can influence the function and activity of targeted proteins as well as trigger the interaction/localisation with other proteins. For example, ADP-ribosylation of a target protein can act as a pattern or signal for other proteins (ADP-ribosylation readers), leading to ubiquitination of the PARylated protein [501, 502]. ADP-ribosylation is recognised by a WWE domain and since many E3 ubiquitin ligases contain WWE domains, this may be a broadly used mechanism of modifying PARylated proteins with ubiquitin [501, 502]. In line with this, it was demonstrated that PARP 12 is able to disrupt the replication of Zika virus by mediating ADP-ribosylation of the non-structural viral proteins NS1 and NS3, leading to their ubiquitination and degradation via the proteasome [503].

However, the relationship between ADP-ribosylation and ubiquitin is far more complex than simply triggering the degradation of MARylated or PARylated proteins. PARP10 exemplifies another important link between ADP-ribosylation and the ubiquitin machinery. PARP10 possesses two unique ubiquitin interaction motifs which are able to recognise and bind to K63-linked poly-ubiquitin [478]. PARP10 binds to and ADP-ribosylates NEMO, an upstream activator of NF-κB [478], which leads to inhibition of the ubiquitination of NEMO and thus the downstream activation NF-κB [478]. Thus, ADP-ribosylation can also inhibit ubiquitination of a target protein and the pro-inflammatory response.

Furthermore, ADP-ribosylation can also lead to changes is E3 ligase activity. It has recently been demonstrated that PARPs have an impact on type I interferon signalling strength via MARylation of the ubiquitin E3 ligase β-TrCP (β-transducin repeat-containing protein) by

PARP11 [504]. This MARylation promotes the ubiquitination and subsequent degradation of type I receptor subunit 1 (IFNAR1), culminating a weaker interferon response [504]. In contrast, to these stimulating effects of MARylation, PARP9 can inhibit the ubiquitination activity of the E3 ligase Dtx3L [505]. PARP 9 heterodimerizes with the E3 ligase Dtx3L and this dimerization triggers the MARylation of ubiquitin on the carboxyl group of Ub Gly76 [505]. Since this position is usually used to attach ubiquitin to the substrate, modifying ubiquitin at this residue via ADP-ribosylation eliminates the ubiquitination activity of Dtx3L [505].

Besides influencing the ubiquitin status of a target protein as well as influencing its enzymatic activity, ADP-ribosylation can also lead to a changed susceptibility for additional post-translational modifications. It has been demonstrated that PARP9 and PARP14 regulate macrophage activation in an opposing manner due to regulating the MARylation of STAT1 [499]. Whereas PARP14 activity results in MARylation of STAT1 which subsequently reduces STAT1 phosphorylation resulting in blunted IFN-γ signal transduction and on the other hand PARP9 activity inhibits PARP14 mediated MARylation of STAT1, thereby promoting IFN-γ signal transduction [499].

Another interesting connection between ubiquitin and MARylation is based on a unique ubiquitination mechanism mediated by the SidE family of *L. pneumophila* effectors. SidE effectors are able to transfer ubiquitin to a target protein without utilising the E1 and E2 enzymes and independently of ATP [506]. Instead, these effectors activate ubiquitin via MARylation of the Arg42 residue of ubiquitin using NAD as energy source [506]. The MARylated ubiquitin is then transferred to the target protein via the activity of a phosphodiesterase domain in SidE, that cleaves the phosphodiester bond of ADP-ribose ubiquitin, releasing AMP and attaching the phosphoribosylated ubiquitin to a serine residue via a phosphodiester bond to the target protein [507, 508]. Furthermore, MARylated ubiquitin released from SidE cannot be processed adequately by host E1 and E2 enzymes, thus leading to overall decreased ubiquitination in host cells [508]. Thus, the MARylation of ubiquitin via SidE has a major impact on the host ubiquitin machinery and host signalling influenced by ubiquitin. These observations are similar to the PARP9/Dtx3L mediated MARylation of ubiquitin, since this also results in a MARylated ubiquitin which cannot be processed for canonical ubiquitination reactions. However, this complex is dependent on E1 and E2 enzyme activity and uses a different amino acid to attach the ADP-ribose [505].

Since the function of PARPs are so manifold and the PARPs are targeted to the LCV upon *Legionella* infection, we speculated that these enzymes may ADP-ribosylate Dot/Icm or host components necessary for effector translocation. Protein modification via MARylation or PARylation might influence their enzymatic function, disrupt protein-protein interactions within this complex or trigger their degradation, as observed with other ADP-ribosylated proteins. Since MARylation as well as PARylation can be generated and dismantled within seconds [491] and can be recognised by a wide variety of readers, these ADP ribose structures can act as a transient scaffold to recruit proteins to a specific site of action [491]. Thus, the modification of proteins with ADP-ribose on the LCV may trigger the recruitment of factors which in turn act upon the complex that mediates Dot/Icm effector translocation across the LCV membrane. This is supported by the observation that PARP10 as well as PARP14 interact with p62/SQSTM1 and that some of these interactions occur in structures consisting amongst other things of poly-ubiquitin and poly ADP-ribose [495, 509].

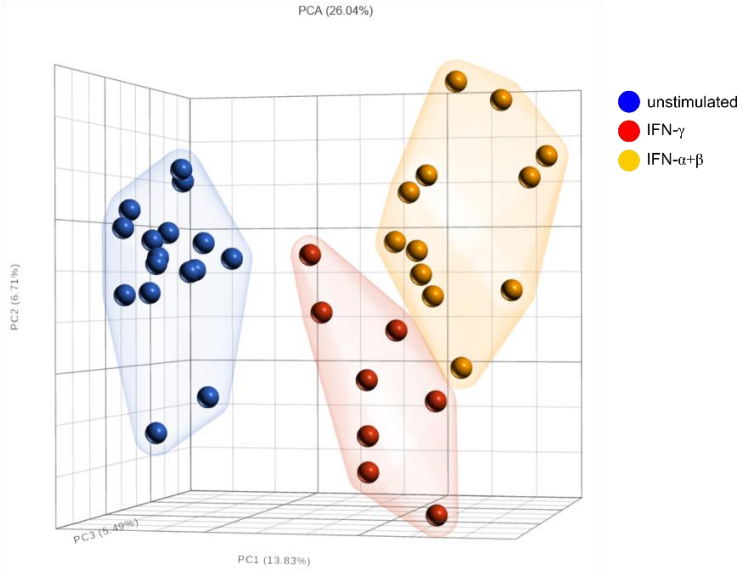
Another mechanism by which PARPs might interfere with Dot/Icm effector translocation is the modulation of ubiquitin signals and enzymes. As previously mentioned, *Legionella* manipulates the ubiquitin machinery of the host extensively to advance its own survival (revied by [214]). In addition, ubiquitination as a process is known to enhance Dot/Icm effector translocation [485]. Since it was previously shown that PARPs extensively interact with the host ubiquitin machinery, it is possible that ADP-ribosylation of host proteins normally targeted by Dot/Icm effectors or host proteins utilised during effector translocation interferes with Dot/Icm secretion system function.

In summary, here we identified possible mediators of interferon-induced disruption of effector translocation into host cells by utilising mRNA sequencing of interferon stimulated macrophages. With the aid of gene ontology enrichment analysis, well-known anti-pathogen proteins such as interferon induced GTPases and factors not yet implicated in defence against *Legionella* such as ISG15 and PARPs were identified as possible factors mediating the observed inhibition of Dot/Icm effector translocation. We were only able to test a small fraction of GBPs for their involvement in the inhibition of effector translocation and did not observe any impact of these proteins. However, further analysis is needed to confirm these observations for a broader range of GTPases. In the case of ISG15 and PARPs in vitro analysis was unfortunately not possible due to the laboratory closures during the COVID-19 pandemic. Thus, many questions regarding the role of these proteins remain, such as a) do these proteins have a direct

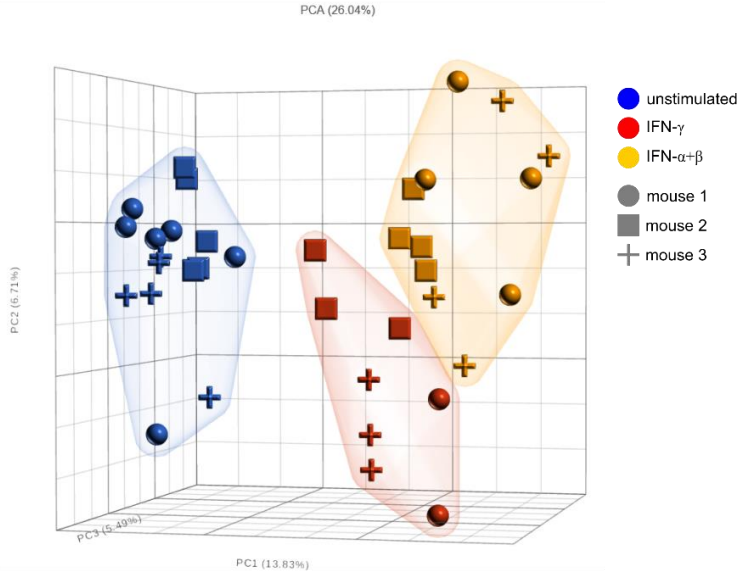
effect on Dot/Icm effector translocation, b) which proteins are targeted by these posttranslational modifications, c) are ISGylated or PARylated proteins enriched on the LCV, d) does *Legionella* express effectors that are able to remove ISG15 or ADP-ribose from targeted proteins or counteract their consequences?

The identification of interferon-induced factors that mediate the interferon-induced reduction of *Legionella* Dot/Icm effector translocation would further increase our understanding of interferon-mediated host defence against *Legionella* and potentially other pathogens that translocate effector proteins into the host cells. Identifying a more general mechanism of host defence represent a unique opportunity to develop effective and potent anti-infective drugs against a range of pathogens.

A


PCA (26.04%)
PC2 (6.71%)
PC3 (5.49%)
PC1 (13.83%)
unstimulated
IFN-γ
IFN-α+β

B


PCA (26.04%)
PC2 (6.71%)
PC3 (5.49%)
PC1 (13.83%)
unstimulated
IFN-γ
IFN-α+β
mouse 1
mouse 2
mouse 3

C

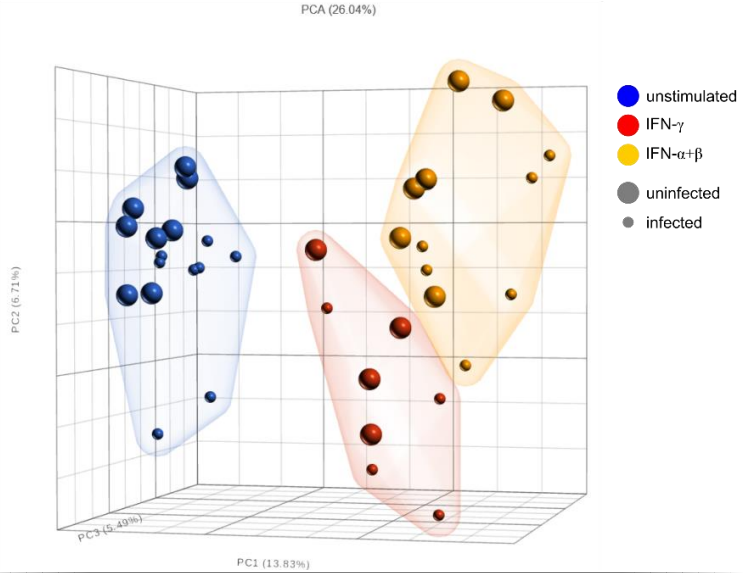

PCA (26.04%)
PC2 (6.71%)
PC3 (5.49%)
PC1 (13.83%)
unstimulated
IFN-γ
IFN-α+β
uninfected
infected

Figure 16: PCA of mRNA sequencing samples

Principal component analysis (PCA) graph to visualize the differences and common features of each sample. pBMDM were stimulated and infected (or mock treated and uninfected) as previously described in the methods material chapter before mRNA was isolated. For each condition (Table 11) triplicates were sent for mRNA sequencing. All samples used for mRNA sequencing analysis are depicted in each small PCA graph. A) only treatment conditions are highlighted; B) distribution of IFN treatment and mice origin, C) distribution and clustering of IFN treatment and infection depicted

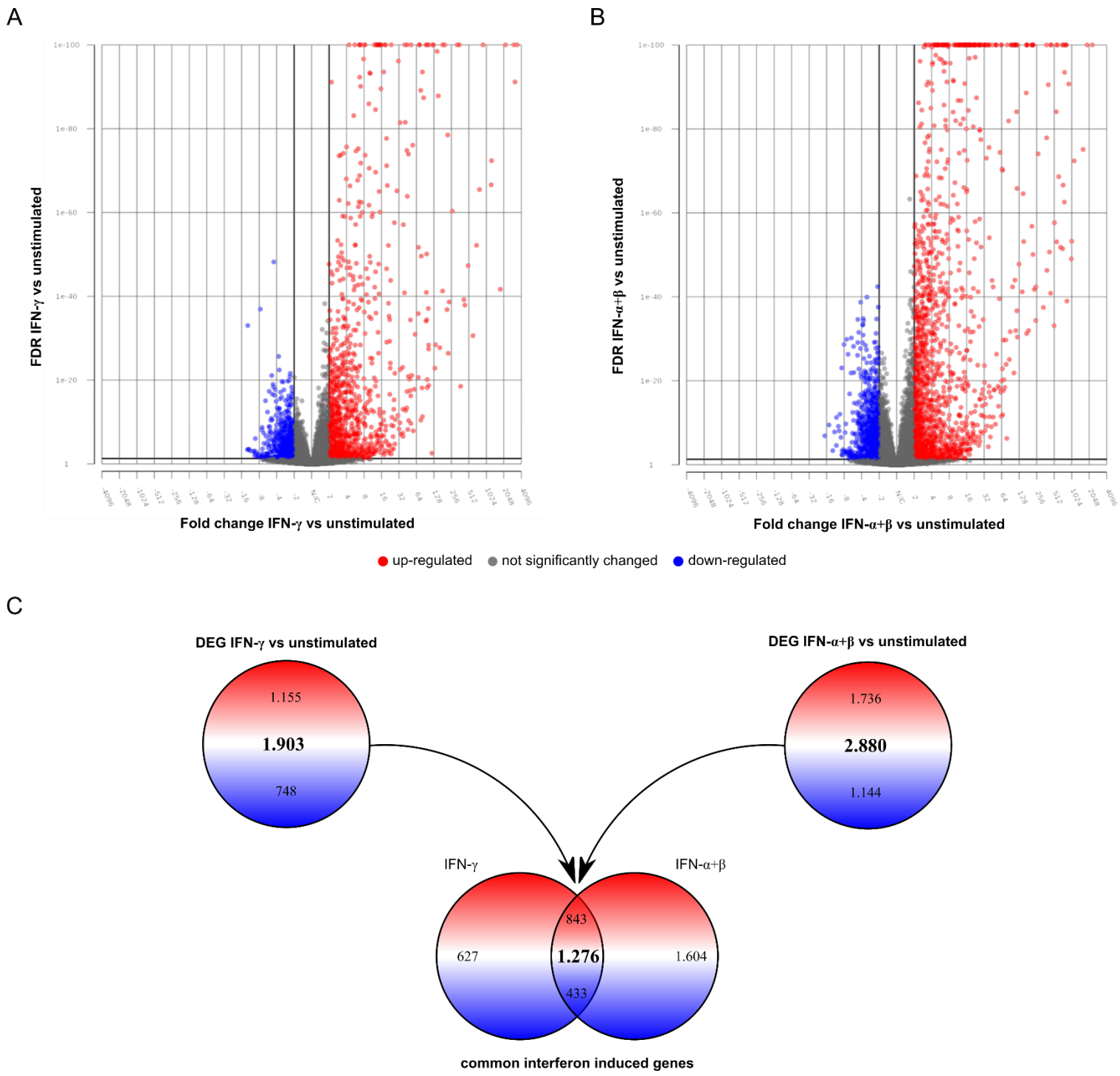

A
B
FDR IFN-γ vs unstimulated
Fold change IFN-γ vs unstimulated
FDR IFN-α+β vs unstimulated
Fold change IFN-α+β vs unstimulated
up-regulated
not significantly changed
down-regulated
C
DEG IFN-γ vs unstimulated
1.155
1.903
748
DEG IFN-α+β vs unstimulated
1.736
2.880
1.144
IFN-γ
IFN-α+β
843
627
1.276
1.604
433
common interferon induced genes

Figure 17: Identification of differentially expressed genes (DEG) based on the mRNA sequencing analysis of interferon stimulated pBMDM

A) Volcano plot of DEG of IFN-γ stimulated genes compared to untreated pBMDM. Significant threshold set at FDR ≤ 0.05 and Foldchange -2 ≤ FC ≥ 2, wherein blue dots are significantly downregulated and red dots are significantly upregulated genes.

B) Volcano plot of DEG of IFN-α+β stimulated genes compared to untreated pBMDM. Significant threshold set at FDR ≤ 0.05 and Foldchange -2 ≤ FC ≥ 2, wherein blue dots are significantly downregulated and red dots are significantly upregulated genes

C) Identification of common DEG induced by both interferon as basis for gene ontology enrichment analysis. Each circle representing the number of differential expressed genes (DEG), total numbers of DEGs depicted in the middle and up and down regulated at the top and bottom of each circle, respectively (IFN-γ DEG top left circle, IFN-α+β top right circle). Venn diagram at the bottom represents the genes which are differentially expressed in both interferon types. Total numbers of common DEG in the overlapping area and genes uniquely induced by either interferon at the edge of the circles.

GO:BP		stats	
Term name	Term ID	p_{adj}	$-\log_{10}(p_{adj})$ 0 ≤16
defense response to other organism	GO:0098542	2.241×10^{-56}	
defense response	GO:0006952	6.079×10^{-55}	
innate immune response	GO:0045087	2.723×10^{-54}	
response to other organism	GO:0051707	2.200×10^{-53}	
response to external biotic stimulus	GO:0043207	2.666×10^{-53}	
immune system process	GO:0002376	1.848×10^{-52}	
response to biotic stimulus	GO:0009607	2.590×10^{-52}	
biological process involved in interspecies interaction betwe...	GO:0044419	5.051×10^{-51}	
response to cytokine	GO:0034097	3.196×10^{-50}	
immune response	GO:0006955	4.604×10^{-49}	
cellular response to cytokine stimulus	GO:0071345	4.092×10^{-46}	
response to interferon-beta	GO:0035456	3.262×10^{-45}	
cellular response to interferon-beta	GO:0035458	1.253×10^{-44}	
response to virus	GO:0009615	1.915×10^{-39}	
response to stress	GO:0006950	3.631×10^{-39}	
regulation of response to biotic stimulus	GO:0002831	3.096×10^{-38}	
defense response to virus	GO:0051607	8.087×10^{-38}	
defense response to symbiont	GO:0140546	8.087×10^{-38}	
response to external stimulus	GO:0009605	2.432×10^{-37}	
regulation of defense response	GO:0031347	8.841×10^{-36}	
regulation of immune system process	GO:0002682	4.594×10^{-30}	
regulation of response to external stimulus	GO:0032101	1.893×10^{-28}	
regulation of innate immune response	GO:0045088	4.790×10^{-28}	
cellular response to organic substance	GO:0071310	1.080×10^{-25}	
regulation of immune response	GO:0050776	3.955×10^{-25}	
regulation of response to stress	GO:0080134	1.270×10^{-24}	
response to interferon-gamma	GO:0034341	7.039×10^{-24}	
cellular response to chemical stimulus	GO:0070887	3.176×10^{-21}	
response to bacterium	GO:0009617	9.136×10^{-21}	
response to organic substance	GO:0010033	2.331×10^{-20}	
cellular response to interferon-gamma	GO:0071346	9.070×10^{-20}	

Figure 18: Gene ontology enrichment analysis: biological processes (BP)

Genes which were differentially expressed both in IFN-γ and IFN-α+β were used for gene ontology analysis with the web-based tool gProfiler The enrichment analysis was done using the recommended settings of gProfiler, the g:SCS algorithm for multiple testing corrections. Gene ontology terms which were identified as being overrepresented in the list of commonly induced ISGs belonging to biological processes (BP) are depicted here (the top 30 with highest enrichment scores).

GO:MF		stats	
Term name	Term ID	p_{adj}	$-\log_{10}(p_{adj})$ 0 ≤16
GTPase activity	GO:0003924	1.010×10^{-14}	
guanyl ribonucleotide binding	GO:0032561	4.466×10^{-13}	
guanyl nucleotide binding	GO:0019001	4.466×10^{-13}	
GTP binding	GO:0005525	4.514×10^{-13}	
carbohydrate derivative binding	GO:0097367	7.492×10^{-12}	
nucleoside-triphosphatase activity	GO:0017111	1.007×10^{-11}	
pyrophosphatase activity	GO:0016462	1.232×10^{-11}	
hydrolase activity, acting on acid anhydrides, in phosphorus...	GO:0016818	2.010×10^{-11}	
hydrolase activity, acting on acid anhydrides	GO:0016817	2.109×10^{-11}	
purine ribonucleoside triphosphate binding	GO:0035639	4.136×10^{-11}	
ribonucleotide binding	GO:0032553	4.922×10^{-11}	
purine ribonucleotide binding	GO:0032555	5.053×10^{-11}	
nucleotide binding	GO:0000166	5.484×10^{-11}	
nucleoside phosphate binding	GO:1901265	5.484×10^{-11}	
purine nucleotide binding	GO:0017076	9.317×10^{-11}	
anion binding	GO:0043168	2.572×10^{-10}	
small molecule binding	GO:0036094	4.367×10^{-9}	
pentosyltransferase activity	GO:0016763	5.799×10^{-9}	
double-stranded RNA binding	GO:0003725	7.065×10^{-9}	
identical protein binding	GO:0042802	1.665×10^{-8}	
heterocyclic compound binding	GO:1901363	5.000×10^{-8}	
organic cyclic compound binding	GO:0097159	1.069×10^{-7}	
NAD+ ADP-ribosyltransferase activity	GO:0003950	3.883×10^{-7}	
protein ADP-ribosylase activity	GO:1990404	3.930×10^{-7}	
catalytic activity, acting on DNA	GO:0140097	1.385×10^{-6}	
adenylyltransferase activity	GO:0070566	2.006×10^{-6}	
2'-5'-oligoadenylate synthetase activity	GO:0001730	2.225×10^{-6}	
catalytic activity	GO:0003824	2.644×10^{-6}	
hydrolase activity	GO:0016787	4.325×10^{-6}	
adenyl ribonucleotide binding	GO:0032559	2.423×10^{-5}	
ATP binding	GO:0005524	3.039×10^{-5}	
adenyl nucleotide binding	GO:0030554	3.835×10^{-5}	
ion binding	GO:0043167	1.050×10^{-4}	
immune receptor activity	GO:0140375	1.300×10^{-4}	
protein homodimerization activity	GO:0042803	1.866×10^{-4}	
TAP binding	GO:0046977	4.483×10^{-4}	
transferase activity	GO:0016740	6.696×10^{-4}	
peptide antigen binding	GO:0042605	7.869×10^{-4}	
cytokine receptor binding	GO:0005126	9.018×10^{-4}	
DNA secondary structure binding	GO:0000217	1.043×10^{-3}	
CARD domain binding	GO:0050700	1.664×10^{-3}	
CXCR3 chemokine receptor binding	GO:0048248	1.711×10^{-3}	
protein binding	GO:0005515	2.804×10^{-3}	
ubiquitin-protein transferase activity	GO:0004842	2.948×10^{-3}	
nucleotidyltransferase activity	GO:0016779	3.153×10^{-3}	

Figure 19: Gene ontology enrichment analysis: molecular function (MF)

Genes which were differentially expressed both in IFN-γ and IFN-α+β were used for gene ontology analysis with the web-based tool gProfiler The enrichment analysis was done using the recommended settings of gProfiler, the g:SCS algorithm for multiple testing corrections. Gene ontology terms which were identified as being overrepresented in the list of commonly induced ISGs belonging to molecular fuction (MF) are depicted here (the top 45 with highest enrichment scores).

GO:CC		stats	
Term name	Term ID	p_{adj}	$-\log_{10}(p_{adj})$ 0 ≤16
symbiont-containing vacuole	GO:0020003	3.588×10^{-15}	
host cell cytoplasm	GO:0030430	3.588×10^{-15}	
host intracellular region	GO:0043656	3.588×10^{-15}	
host intracellular part	GO:0033646	3.588×10^{-15}	
host cell cytoplasm part	GO:0033655	3.588×10^{-15}	
host cell part	GO:0033643	8.965×10^{-15}	
host cellular component	GO:0018995	7.316×10^{-14}	
host cell	GO:0043657	7.316×10^{-14}	
symbiont-containing vacuole membrane	GO:0020005	4.187×10^{-12}	
cytosol	GO:0005829	2.305×10^{-11}	

Figure 20: Gene ontology enrichment analysis: cellular compartment (CC)

Genes which were differentially expressed both in IFN-γ and IFN-α+β were used for gene ontology analysis with the web-based tool gProfiler The enrichment analysis was done using the recommended settings of gProfiler, the g:SCS algorithm for multiple testing corrections. Gene ontology terms which were identified as being overrepresented in the list of commonly induced ISGs belonging to cellular compartment (CC) are depicted here (the top 10 with highest enrichment scores).

REAC		stats	
Term name	Term ID	p_{adj}	$-\log_{10}(p_{adj})$ 0 ≤16
Antiviral mechanism by IFN-stimulated genes	REAC:R-MMU-1...	4.094×10^{-5}	
ISG15 antiviral mechanism	REAC:R-MMU-1...	1.554×10^{-4}	
Nicotinamide salvaging	REAC:R-MMU-1...	1.749×10^{-4}	
Interferon Signaling	REAC:R-MMU-9...	1.053×10^{-3}	
Nicotinate metabolism	REAC:R-MMU-1...	1.849×10^{-3}	
Cytokine Signaling in Immune system	REAC:R-MMU-1...	3.366×10^{-3}	
Antigen processing-Cross presentation	REAC:R-MMU-1...	1.337×10^{-2}	
Interleukin-2 family signaling	REAC:R-MMU-4...	1.658×10^{-2}	

Figure 21: Gene ontology enrichment analysis: REACTOME pathway

Genes which were differentially expressed both in IFN-γ and IFN-α+β were used for gene ontology analysis with the web-based tool gProfiler The enrichment analysis was done using the recommended settings of gProfiler, the g:SCS algorithm for multiple testing corrections. Gene ontology terms which were identified as being overrepresented in the list of commonly induced ISGs belonging to Reactome pathways are depicted here.

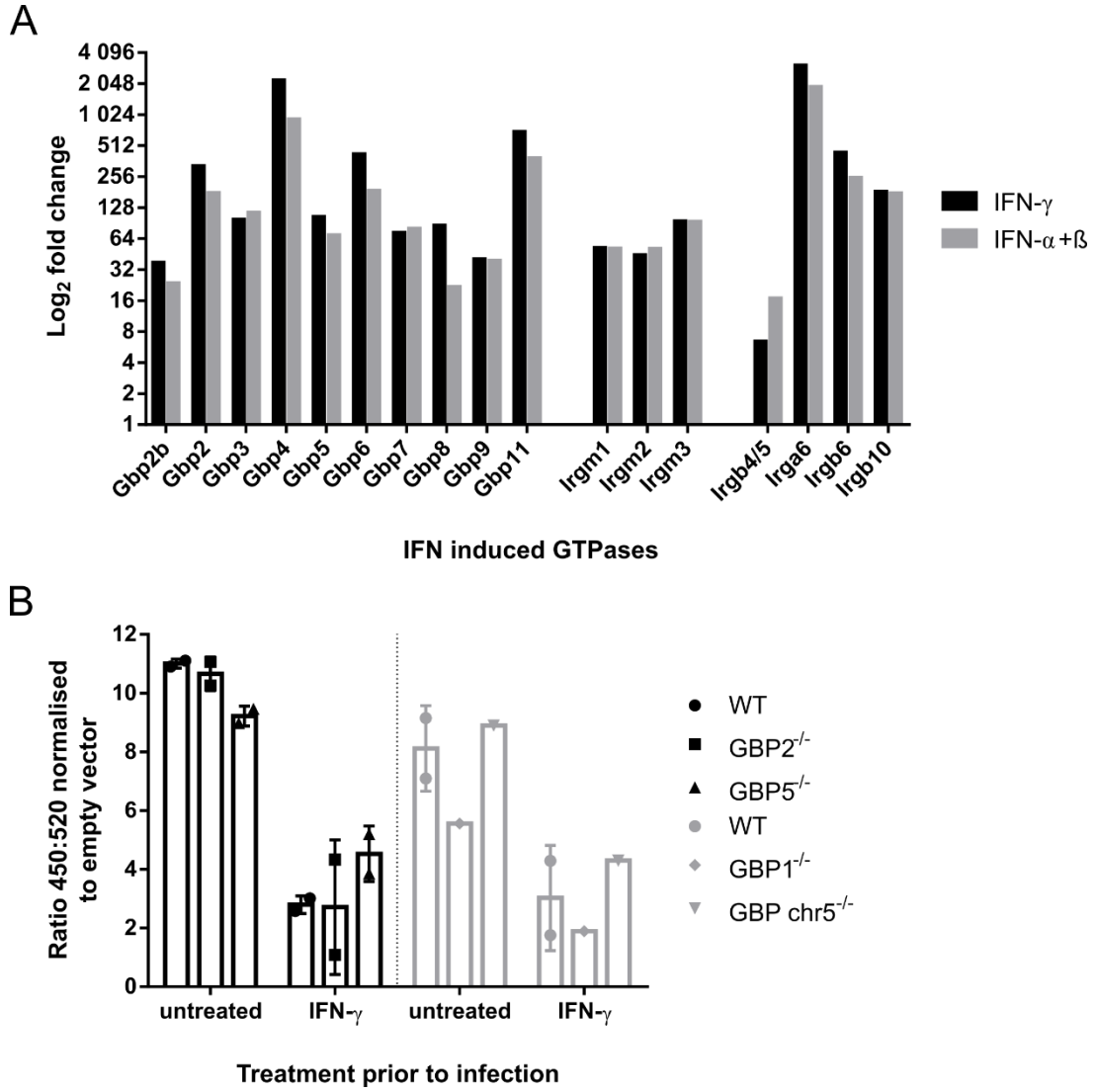


Figure 22: Interferon stimulated GTPase

A) Foldchanges of IFN stimulated GTPases (GBP and IRG) upon IFN-γ and type I interferon stimulation

For DEG identification, partek flow software was used performing the DeSeq2 algorithm with the gene count matrix. For the DEG analysis, a log2 fold-change value of $-2 \leq FC \geq 2$ as well as an adjusted P-value (corrected for multiple comparisons with the Benjamini-Hochberg procedure) of $FDR \leq 0.05$ were set as thresholds. Genes meeting both criteria were considered to be differentially expressed. GBPs and IRGs belong to the DEG induced by both types of interferon, detailed values are also listed in Table 16.

B) *L. pneumophila* effector translocation in different GBP deficient pBMDM

pBMDM from GBP deficient mice were treated with IFN-γ (50 U/ml) overnight prior to infection with *L. pneumophila* 130b Δ*flaA*, carrying pxDC61-RalF plasmid, for 1 h Subsequently, $RalF_{Lp}$ effector translocation was quantified using TEM-1 β-lactamase translocation assay. Results are shown as mean ± SD of $n \geq 1$ independent experiment carried out in technical triplicates, each dot representing a mouse.

Table 16: Interferon stimulated GBPs and IRGs: foldchange and FDR values upon IFN-γ and IFN-α+β stimulation

Gene ID	Gene name	fold change IFN-γ	fold change IFN-α+β	FDR IFN-γ	FDR IFN-α+β
ENSMUSG00000040264	Gbp2b	37.14	23.45	4.79E-008	2.06E-007
ENSMUSG00000028270	Gbp2	321.71	176.29	1.71E-180	6.18E-186
ENSMUSG00000028268	Gbp3	97.52	113.95	4.87E-150	4.24E-204
ENSMUSG00000079363	Gbp4	2,190.82	913.54	1.39E-106	2.00E-091
ENSMUSG00000105504	Gbp5	103.35	68.45	3.85E-028	2.13E-030
ENSMUSG00000104713	Gbp6	420.81	185.58	6.29E-040	1.12E-032
ENSMUSG00000040253	Gbp7	72.61	79.68	1.42E-246	0.00E+000
ENSMUSG00000034438	Gbp8	85.16	21.64	4.22E-088	8.40E-050
ENSMUSG00000029298	Gbp9	40.34	38.84	7.49E-191	1.92E-225
ENSMUSG00000105096	Gbp10	excluded due to low counts			
ENSMUSG00000092021	Gbp11	694.04	384.52	6.90E-053	5.11E-047
ENSMUSG00000046879	Irgm1	51.60	50.96	0.00E+000	0.00E+000
ENSMUSG00000069874	Irgm2	44.04	50.72	1.97E-253	0.00E+000
ENSMUSG00000078853	Irgm3	93.70	93.18	0.00E+000	0.00E+000
ENSMUSG00000062028	Irgc1	excluded due to low counts			
ENSMUSG00000069893	Irgb4/5	6.39	16.74	7.93E-007	2.14E-019
ENSMUSG00000054072	Irga6	3,055.28	1,894.02	2.39E-196	3.88E-216
ENSMUSG00000078922	Irgb6	436.54	247.14	1.27E-038	4.40E-035
ENSMUSG00000082292	Irgb10	181.45	175.87	9.75E-197	1.32E-227

Chapter 5: Characterisation of *L. longbeachae* pathogenesis

5.1 Introduction

In the previous chapters, we identified a novel mechanism of host defence against *Legionella* mediated by interferon-induced genes (ISGs). We observed that stimulation with type I interferons and IFN-γ leads to reduced Dot/Icm effector translocation into host cells. This observation substantiates the importance of interferons in host defence against *Legionella*. It has been previously demonstrated that interferon, especially IFN-γ, play a crucial role in host defence against *L. pneumophila* in vivo, as IFN-γ deficient mice [371, 377] or IFN-γ receptor-deficient mice [234, 369, 370] show severe disease progress with a higher bacteria burden in lungs compared to their WT counterparts. On the other hand, loss of type I interferon receptor did not impact the clearance of *L. pneumophila* from the lung, indicating that IFN-γ signalling is sufficient to clear the bacteria [234, 369, 370]. Although mice lacking both interferon receptors are further impaired in their anti-bacterial capacities than IFN-γ receptor-deficient animals, indicating that type I interferon signalling contributes to the bacteria's clearance [234, 370].

The importance of interferons is well documented for *L. pneumophila*, on the other hand little is known about the pathogenesis of *L. longbeachae*, the second most common causative agent of Legionnaires' Disease worldwide. During our studies, we showed that IFN-γ is able to inhibit the effector translocation of *L. longbeachae* into macrophages, thus playing an important role in host defence against this bacterium in vitro.

Previously Gobin et al. infected A/J mice with different *Legionella* species such as *L. pneumophila*, *L. micdadei*, *L. steigerwaltii* and *L. longbeachae* comparing their virulence in mouse models [510]. They observed that *L. longbeachae* serogroup 1 was able to replicate in lungs much more effectively than all the other tested *Legionella* species and caused more severe bronchopneumonia with histopathological changes [510]. Subsequently, they analysed the virulence of *L. longbeachae* in different mouse strains and observed that *L. longbeachae* is able to replicate equally well within A/J, BALB/c and C57BL/6 mice [511] and that neutrophils infiltrated the lungs of these mice [511]. In both studies, the underlying causes for the severe pneumonia or which cell types might be involved in *L. longbeachae* clearance were not analysed. Since the knowledge about the in vivo pathogenesis of *L. longbeachae* as well as any

possible impact of IFN-γ signalling in host defence against this bacterium is limited, we characterised the in vivo pathogenesis of *L. longbeachae* in WT as well as IFN-γ deficient mice. During this study we were able to show that IFN-γ is essential for the host defence against *L. longbeachae*, as IFN-γ deficient mice showed a far higher bacteria burden in the lung and also dissemination of the bacteria to other organs. This impairment in host defence is not caused by a disruption in cell migration to the lung, as no difference in cell migration was observed in IFN-γ deficient mice compared to WT mice. Furthermore, this impairment in host defence in IFN-$\gamma^{-/-}$ mice might be based on the disrupted bactericidal capacities of monocytes and neutrophils, since these cell types carried significantly higher numbers of viable bacteria than WT cells. In utilising the ß-lactamase system previously used to determine the impact of inflammatory cytokines on effector translocation, we were able to show that *L. longbeachae* is able to translocate its effectors into alveolar macrophages, monocytes as well as neutrophils. The observation that *L. longbeachae* is able to survive within and translocate its effectors into monocytes and neutrophils, which generally are capable of killing *L. pneumophila*, might explain the severe disease progression observed upon *L. longbeachae* infection.

5.2 Results

5.2.1 Survival and replication of *L. longbeachae* in mice and the role of IFN-γ in host defence against *L. longbeachae*

Since IFN-γ has such a profound effect on *L. pneumophila* replication and clearance from the host, we first analysed the impact of IFN-γ on *L. longbeachae* replication in the lung. We thus infected C57BL/6 WT and IFN-$\gamma^{-/-}$ mice intranasally with *L. longbeachae* and analysed the CFU burden in the lung after a couple of days post-infection starting from day 3 (Figure 23). We observed that *L. longbeachae* was able to replicate well in both mouse strains, starting from 2.5 x 10^5 CFU and reaching ~10^7-10^8 CFU in the lung on day 3, with IFN-$\gamma^{-/-}$ mice harbouring significantly more CFU compared to WT mice (Figure 24). In lungs of WT mice, we observed a reduction in *L. longbeachae* CFU from day 4 onwards (Figure 24). In contrast to WT mice, an increased CFU burden was observed in lungs of IFN-$\gamma^{-/-}$mice on day 4 compared to day 3, reaching close to 10^9 CFU (Figure 24). Unlike *L. pneumophila*, which rarely spread

systemically, we observed spread of *L. longbeachae* to the spleen in both mouse strains, with spleens from IFN-$\gamma^{-/-}$ mice showing a higher CFU burden compared to WT mice (Figure 24). Similar to the observations made in the lung, the bacterial burden in the spleen decreased at day 4 in WT mice but increased in IFN-$\gamma^{-/-}$ mice (Figure 24).

This indicates a severe disruption in host defence and substantiates the importance of IFN-γ in mediating the host defence against *L. longbeachae*. Due to the high weight loss, the overall sick appearance of the animals as well as adhering to animal welfare ethics regulations, we were not able to extend our observations beyond day 4 to 5 post infection (since we were only able to analyse 3 mice at day 5 we incorporated these data with the observations made at day 4 post, hence day 4/5 post infection in graphs). Overall, these observations indicate that *L. longbeachae* is able to replicate to high numbers even in WT mice and that IFN-γ is crucial to mediate the host defence against *L. longbeachae*.

5.2.2 Neutrophils are the dominant phagocytic cell type in lungs during *L. longbeachae* infection

It was previously shown that *L. pneumophila* elicits the migration of immune cells, especially monocytes and neutrophils, into the lung which are responsible for the clearance of the bacteria [349, 512]. Since *L. longbeachae* was able to replicate to high numbers in both WT and IFN-γ deficient mice, we analysed the population composition of phagocytic innate immune cells during *L. longbeachae* infections in lung tissue. Furthermore, since effective host defence is orchestrated by chemokines and cytokines, we analysed the cytokines produced during *L. longbeachae* infection. We thus analysed the immune cell populations in the lung as well as the elicited cytokines via flow cytometry.

During *L. longbeachae* infection we observed an increase of $CD45^+$ cells in lung tissue of both mouse strains and days analysed, with no major differences between WT and IFN-$\gamma^{-/-}$ mice (Figure 25). Similar observations were made for the subpopulations of neutrophils, dendritic cells and monocyte derived cells, wherein neutrophils were the most abundant cell type followed by monocyte derived cells on both days post infection (Figure 25). In addition, we observed a significant increase in neutrophils in IFN-$\gamma^{-/-}$ mice compared to WT mice on day 4/5 post infection, which might explain the increase observed in $CD45^+$ cells in IFN-$\gamma^{-/-}$ at the same timepoint (Figure 25). In contrast to all the other cell types analysed, the numbers of alveolar macrophages did not increase during the course of infection (Figure 25). Furthermore, in lungs

of IFN-$\gamma^{-/-}$ mice we observed a decrease in alveolar macrophage numbers on day 4/5 compared to uninfected IFN-$\gamma^{-/-}$ mice as well as infected WT mice. This suggests that IFN-γ might play a role in cell-autonomous defence and macrophage survival during the later stages of infection.

Upon *L. longbeachae* infection, we observed an increase in inflammatory cytokines such as IFN-γ, IL-1α, IL-6 and TNFα in the lung, while levels of GM-CSF, IL-2 and IL-10 did not differ between uninfected and infected mice (Figure 27). Furthermore, in IFN-$\gamma^{-/-}$ mice *L. longbeachae* infection triggered a significantly higher production of IL-1α and IL-6 compared to WT mice (Figure 27).

These observations suggest that the increased replication of *L. longbeachae* observed in IFN-$\gamma^{-/-}$ mice compared to WT mice, is most likely not caused by a disrupted infiltration of innate immune cells into the lung or by a lack of cytokine and chemokine production compared to WT mice.

5.2.3 *L. longbeachae* is predominantly phagocytosed by neutrophiles and monocyte derived cells during the infection

Since we observed a strong increase of neutrophils and monocyte derived cells in the lung of infected mice, we wanted to determine which of the phagocytes residing in the lung was phagocytosing *L. longbeachae* during the infection and thus possibly contributing to the clearance and host defence during infection. We therefore infected mice and processed the lung tissues as previously described in the material and methods chapter. We detected intracellular *L. longbeachae* (intact bacteria or material derived from *L. longbeachae*) by using polyclonal anti-*L. longbeachae* antibody and analysed the different cell populations and determined the numbers of *L. longbeachae*$^{+}$ phagocytes via flow cytometry. In both WT and IFN-$\gamma^{-/-}$ mice the majority of internalised *L. longbeachae* was detected in neutrophils, followed by monocyte derived cells and lastly alveolar macrophages (Figure 26). Furthermore, we observed an increase in *L. longbeachae*$^{+}$ cells in neutrophils from IFN-$\gamma^{-/-}$ mice compared to cells from WT mice at day 4 post infection (Figure 26). No significant differences were observed between alveolar macrophages from IFN-$\gamma^{-/-}$ mice compared to WT mice (Figure 26).

These results indicate that neutrophils and monocyte derived cells are the cell types which predominantly phagocytose bacterial material during infection, rather than alveolar macrophages.

5.2.4 Influence of IFN-γ on the bactericidal properties of lung phagocytes

We previously observed an increase in *L. longbeachae* CFU burden in lungs and spleen of IFN-$\gamma^{-/-}$ mice compared to WT mice and identified monocyte derived cells and neutrophils as the main cell types with internalised *L. longbeachae* material. Previously, monocyte derived cells and neutrophils had been shown to contribute to clearance of *L. pneumophila* and host defence during infection [349, 512], as well as the bactericidal activity of monocyte derived cells being dependent on IFN-γ signalling [349]. Hence, we determined if these phagocytes played a role in host defence against *L. longbeachae* and if the bactericidal properties were dependent on IFN-γ. We therefore infected WT and IFN-$\gamma^{-/-}$ mice with *L. longbeachae*, harvested the lung 3 days post-infection and purified alveolar macrophages, monocyte derived cells and neutrophils. Subsequently, these purified cells were lysed, viable bacteria cultured on BCYE plates and resulting CFU enumerated after 3 days (Figure 28). In both IFN-$\gamma^{-/-}$ and WT mice, alveolar macrophages were harbouring the highest number of viable *L. longbeachae*, followed closely by neutrophils, and monocyte derived cells harboured the least number viable of bacteria (Figure 29). Furthermore, in line with our flow cytometric data, alveolar macrophages from IFN-$\gamma^{-/-}$ mice did not harbour more viable bacteria compared to alveolar macrophages of WT mice (Figure 29). In contrast to alveolar macrophages, we observed that monocyte derived cells and neutrophils originating from IFN-$\gamma^{-/-}$ mice contained more viable bacteria than their WT counterparts (Figure 29)

These results suggest that IFN-γ is necessary for monocyte derived cells and neutrophils, but not alveolar macrophages, to control phagocytosed *L. longbeachae* effectively. Furthermore, *L. longbeachae* seems to be able to survive in all three phagocytes, even in cells originating from WT mice, although alveolar macrophages harbour the highest amount of viable bacteria.

5.2.5 Influence of IFN-γ on Dot/Icm secretion system effector translocation in vivo

In the previous chapters of this thesis, we observed that IFN-γ stimulation of macrophages resulted in a reduction of Dot/Icm effector translocation into host cells during both *L. pneumophila* and *L. longbeachae* infections. Since others previously observed a crucial role of IFN-γ in host defence against *L. pneumophila* and we too made similar observations during *L. longbeachae* infections, we wanted to analyse if IFN-γ mediates the host defence by altering the Dot/Icm effector translocation into host cells during in vivo infections of *L. pneumophila* and *L. longbeachae*. We thus infected IFN-$\gamma^{-/-}$ and WT mice with *L. pneumophila* and

L. longbeachae strains used previously for our in vitro effector translocation assays. Though, since the bacteria only express the RalF-ß-lactamase fusion protein upon IPTG stimulation, we were only able to infect the mice for max 24 h, as the fusion protein expression dropped rapidly without stimulation. As described in more detail in the material and method chapter, following infection BAL fluid was collected, harvested cells were incubated with the ß-lactamase substrate solution and lastly cells were stained with cell specific antibodies to identify the different cell populations and measure the fluorescence shift of the ß-lactamase FRET substrate CCF2 AM within these cells via flow cytometry (Figure 30).

To our surprise and in contrast to our in vitro observations, we did not detect any differences in Dot/Icm effector translocation in IFN-$\gamma^{-/-}$ cells compared to WT cells during both *L. longbeachae* and *L. pneumophila* infections (Figure 31). The highest amount of Dot/Icm effector translocation was detected in alveolar macrophages for both species (Figure 31). Although, some effector translocation was also detected in neutrophils as well as monocyte derived cells, though to differing levels between the two *Legionella* species (Figure 31). Wherein *L. longbeachae* was able to translocate effectors into monocyte derived cells and neutrophils equally well, whereas *L. pneumophila* showed the lowest effector translocation activity in monocytes (Figure 31). Furthermore, we observed a higher ratio between cleaved and uncleaved substrate fluorescence in cells infected with *L. longbeachae* (Figure 31 A right) compared to *L. pneumophila* (Figure 31 B right), suggesting *L. longbeachae* translocated more RalF-ß-lactamase fusion protein into host cells, which caused an increased cleavage of CCF2 AM and thus the observed higher fluorescence ratio.

Since we detected no difference in effector translocation between WT and IFN-$\gamma^{-/-}$ mice and all our previous in vitro data suggested a role of IFN-γ in this process, we wanted to validate our observation by analysing the amount of IFN-γ produced during this short infection period. We observed that WT mice were not producing significant amounts of IFN-γ, compared to uninfected mice during this short course of infection (Figure 32). This lack of IFN-γ production in WT mice might explain why we did not observe any impact of IFN-γ on Dot/Icm RalF effector translocation during in vivo *Legionella* infections, since in vitro the reduction in Dot/Icm effector translocation is specifically mediated by interferon. Hence, if IFN-γ mediates host defence by inhibiting the Dot/Icm effector translocation in vivo as well, remains to be investigated using *Legionella* strains which express the ß-lactamase-RalF fusion protein constitutively to allow for a longer infection period.

Since we observed a higher fluorescence ration of cleaved to uncleaved CCF2 AM substrate, in *L. longbeachae* infected cells compared to *L. pneumophila* infected cells, and we and others observed that *L. longbeachae* was able to replicate to higher numbers in mice than *L. pneumophila* [510], we wanted the determine if *L. longbeachae* might influence the host's cytokine and chemokine response differently to *L. pneumophila*. We thus measured the cytokines produced by both *Legionella* species in BAL fluid which was previously extracted from mice to study effector translocation in vivo. We observed that *L. longbeachae* triggered significantly less IL-6 and IL-10 production than *L. pneumophila* (Figure 33). For the other cytokines similar trends were observed, which may become significant if further replicates are performed.

We were able to show that *L. longbeachae* as well as *L. pneumophila* translocated Dot/Icm effectors into all phagocytes in vivo, albeit to different levels between the different cell types as well as *Legionella* species, with *L. longbeachae* showing a higher translocation activity especially in monocyte-derived cells. In addition to the different translocation activities between the two species, we observed the tendency of *L. longbeachae* to trigger a lower production of inflammatory cytokines compared to *L. pneumophila*.

5.3 Discussion

Even though pneumonia caused by *L. longbeachae* is on the rise worldwide and it is the leading causative agent in New Zealand and Australia [28, 513], knowledge about this species lifecycle in vitro and pathogenesis in vivo still remains very limited.

In the past it was observed that *L. longbeachae* is far more virulent in mouse than other species including *L. pneumophila* [25, 510]. This is in line with our observations, as *L. longbeachae* strain NSW150 was able to replicate to very high numbers within the lungs of C57BL/6 mice. Furthermore, we also observed the spread of *L. longbeachae* to other organs such as the spleen, which was also observed previously [114]. Even though mice were inoculated with a lower dose of 2.5×10^5 CFU during *L. longbeachae* infections compared to 2.5×10^6 CFU during *L. pneumophila* infections, infections with *L. longbeachae* still resulted in a much higher CFU burden in the lung ~ 10^7-10^8 CFU (Figure 24) compared to ~ 10^5-10^6 CFU in *L. pneumophila* [349]. The striking difference in virulence between the two species, might be the consequence of unique features by *L. longbeachae* which have been identified in the last couple of years. Cazalet et al. analysed the transcriptome of the *L. longbeachae* strain NSW150, indicating that the bacteria do not feature a very pronounced biphasic life cycle, switching between a replicative and transmissive form, as *L. pneumophila* does [63]. This is in line with observations, that *L. longbeachae* intracellular replication seems to be independent of the growth phase [69]. Furthermore, due to sequencing analysis of different *L. longbeachae* strains, it was revealed that *L. longbeachae* does not encode a flagellum [29, 63]. This might explain the ability of *L. longbeachae* to replicate within such a broad variety of mouse strains as it avoids triggering the Naip5-dependent caspase-1 activation, which mediates host defence against *L. pneumophila* [63, 511]. Though the lack of the flagellum does not fully explain the difference in virulence between the two species, since *L. longbeachae* still replicates better than *L. pneumophila* in A/J mouse strain as well as *L. pneumophila* Δ*flaA* mutant in C57BL/6 mice [114, 510]. Moreover, these sequencing analyses discovered that *L. longbeachae* possess a unique effector repertoire compared to *L. pneumophila*, which reflects the adaption to its soil-based environment and different host spectrum [29, 63]. This unique effector repertoire might enable the bacteria to manipulate the host differently to *L. pneumophila*. In addition to the unique effector repertoire identified by genome analysis, Cazalet et al. identified genes that might be involved in the production of a capsule and later confirmed these findings via electron microscopy [63]. These unique features of *L. longbeachae*, possibly contribute to the observed virulence of *L. longbeachae* during infections in mice.

It was previously shown that *L. pneumophila* triggers an influx of innate immune cells into the lung during infections, which are important for effective host defence against *L. pneumophila* [380, 512, 514]. Brown et al. investigated the dynamics of immune cells in the lung during *L. pneumophila* infections and showed that neutrophils and monocyte derived cell are the prominent innate immune cell types infiltrating the lung [349]. We observed a significant increase of these cells in lung tissue of infected mice, most likely caused by a robust infiltration of innate immune cells into the lungs. Similar to the observations made during *L. pneumophila* infections, neutrophils were the dominant innate immune cell type followed closely by monocyte derived cells, which infiltrated the lungs during *L. longbeachae* infection. The observations that *L. longbeachae* triggers an increase of monocyte derived cells in lungs upon infection, similar to *L. pneumophila,* is in contrast with observations made by Maasis et al. which did not detect monocytes infiltrating the lung during *L. longbeachae* infections [114]. These differences might be explained by extracting the cells from different sources, bronchoalveolar fluid (BALF) vs homogenised lung tissue, as well as different inoculation doses. Furthermore, Brown et al. [349] observed that neutrophil numbers decrease quickly from day 3 onwards during *L. pneumophila* infection, in contrast to this we did not observe such a decline during *L. longbeachae* infection, even though we observed a decline in *L. longbeachae* CFU burden in the lungs of WT mice, similar to previous observations made with *L. pneumophila* infections [349]. In addition, compared to *L. pneumophila* infection that triggered a decline in alveolar macrophages [349], *L. longbeachae* did not trigger a decrease in alveolar macrophages during the course of infection in WT mice. These differences in innate immune cell dynamics during *L. longbeachae* and *L. pneumophila* infections, may point towards different roles of these innate immune cells during *L. longbeachae* and *L. pneumophila* infections.

Further differences were observed regarding the ability of *L. longbeachae* and *L. pneumophila* to survive within innate immune cells. During *L. pneumophila* infection in WT mice, alveolar macrophages harbour the majority of viable bacteria, indicating that alveolar macrophages represent the replicative niche for *L. pneumophila* in vivo [349]. During *L. longbeachae* in vivo infections, we also observed that alveolar macrophages harbour a large portion of viable *L. longbeachae*. Though in contrast to *L. pneumophila* infection, monocyte derived cells and especially neutrophils contained considerable amounts of viable bacteria during *L. longbeachae* infection. Since monocyte derived cells as well as neutrophils infiltrate the lungs in great numbers, exceeding the numbers of alveolar macrophages by multiple orders of magnitude, and

also phagocytose the majority of bacteria during infection, neutrophils and monocyte derived cells potentially contribute to the higher CFU burden observed in lungs of *L. longbeachae* infected mice, compared to *L. pneumophila*.

In order to mount an efficient defence against various pathogens, the host produces an array of chemokines and cytokines to orchestrate the collaboration and migration of different immune cells at the site of infection. Even though *Legionella* are manipulating the host extensively, *L. pneumophila* is still triggering the production of cytokines and chemokines during infection [369]. Recently it was proposed that the high replication of *L. longbeachae* might be based on a limited cytokine production during infection caused by the poor recognition of *L. longbeachae* PAMPs in macrophages [114]. In contrast to these in vitro observations, we observed that *L. longbeachae* triggers a robust production of various inflammatory cytokines, including IFN-γ, TNFα, IL-1α and IL-6 during infections in WT and IFN-γ deficient mice. Although in line with the idea that the capsule or the unique effector repertoire expressed by *L. longbeachae* would influence the host response in favour of *L. longbeachae* survival and replication, compared to *L. pneumophila*, we observed that *L. longbeachae* induced smaller amounts of inflammatory cytokines during in vivo infection. These observations are in line with previous in vitro study comparing IL-12 cytokine production of various *Legionella* species in pBMDM, with *L. longbeachae* inducing less IL-12 compared to all other *Legionella* species [114]. Furthermore, in comparison to *L. pneumophila*, *L. longbeachae* triggered less inflammatory cytokines in infected mouse and human macrophages as well as epithelial cells in vitro [114]. However, this observed reduction in cytokine induction during *L. longbeachae* infection, compared to *L. pneumophila*, did not impair recruitment of innate immune cells in the lung which could explain the increased replication of *L. longbeachae*, as we observed a significant increase of neutrophils and monocyte-derived cells in lung tissue. Even though we did not observe migratory defects, we observed higher numbers of viable *L. longbeachae* in neutrophils and monocyte-derived cells during infection, compared to *L. pneumophila*.

However, if these differences in cytokine induction and bacteria survival in phagocytic cells are due to a restricted recognition of *L. longbeachae* PAMPs caused by the capsule or actively mediated by specific *L. longbeachae* effectors interfering with the expression or release of inflammatory cytokines, as previously observed during in vitro *L. pneumophila* infections [136, 139, 379, 383, 456], or interference with other cell-autonomous defence mechanisms and thus

supporting survival and potential replication of *L. longbeachae,* compared to *L. pneumophila,* remains to be investigated.

In previous studies, IFN-γ was identified as a crucial component in host defence against *L. pneumophila* [234, 369, 370, 377]. Furthermore, a potential role of IFN-γ in host defence against *L. longbeachae* was previously indicated in vitro, as IFN-γ treated pBMDM restricted the replication of *L. longbeachae* compared to unstimulated pBMDM [114]. During our studies we were able to substantiate the crucial role of IFN-γ in host defence against *Legionella*, since IFN-$\gamma^{-/-}$ mice were not able to restrict *L. longbeachae* replication compared to WT mice. Since IFN-$\gamma^{-/-}$ mice were not able to control the *L. longbeachae* infection, despite a normal infiltration of innate immune cells into the lung and similar cytokine and chemokine responses, we suspected that IFN-γ might have an impact on the cell-autonomous defence of the infiltrating innate immune cells. Such an impact has been previously demonstrated in vitro, with IFN-γ treatment inducing the restriction of *L. pneumophila* replication [234, 368, 370]. Furthermore, the importance of IFN-γ on bactericidal properties of phagocytes was reported during *L. pneumophila* in vivo infections previously, with varying effects on different innate immune cells of the lung [349]. However, although macrophages restrict the replication of *L. pneumophila* in vitro upon IFN-γ stimulation, they demonstrated that IFN-γ signalling does not induce the bactericidal properties in alveolar macrophages in vivo [349]. These discrepancies between in vitro and in vivo observations were later resolved by the observation that alveolar macrophages down-regulate the IFN-γ receptor and thus rendering the alveolar macrophages unresponsive to IFN-γ signalling [515]. On the other hand, neutrophils are able to restrict the replication of *L. pneumophila* independent of IFN-γ stimulation [349]. In contrast to alveolar macrophages and neutrophils which are not influenced by IFN-γ signalling in their capabilities to kill *L. pneumophila,* the bactericidal properties of monocyte derived cells are dependent on IFN-γ signalling [349]. During our *L. longbeachae* in vivo studies with WT and IFN-$\gamma^{-/-}$ mice, we observed varying impacts of IFN-γ signalling on the bactericidal properties of the different innate immune cells, distinct from *L. pneumophila* infections. Alveolar macrophages were not able to restrict replication of *L. longbeachae* upon IFN-γ signalling, which is in line with the observations made during *L. pneumophila* infection. Possibly, *L. longbeachae* infection might cause a downregulation of IFN-γ receptor in alveolar macrophages as well. Furthermore, *L. longbeachae* infected monocyte derived cells are

dependent on IFN-γ signalling to kill phagocytosed *L. longbeachae*, as they are to kill *L. pneumophila*. In contrast to *L. pneumophila* infected neutrophils, neutrophils containing *L. longbeachae* are dependent on IFN-γ stimulation to kill these bacteria. This possibly suggests that neutrophils might control *L. pneumophila* and *L. longbeachae* via different pathways or molecules.

Cell-autonomous defence mediated by IFN-γ signalling can occur via vastly different mechanisms, such as inflammasome activation [254], increased rates of autophagy [516], production of anti-pathogenic molecules [370] or rupture of pathogen containing vacuoles [268, 457]. During the previous chapters of this thesis, we discovered a new mechanism of cell-autonomous defence mediate by IFN-γ signalling, which is the disruption of *Legionella* effector translocation into host cells. Since IFN-γ was essential for the host defence against both *L. pneumophila* as well as *L. longbeachae* and was also crucial for the bactericidal properties of innate immune cells during infection, we investigate if IFN-γ mediates the host defence in vivo via the restriction of *Legionella* effector translocation. Unfortunately, we were unable to determine if IFN-γ restricts the Dot/Icm translocation in vivo, since WT mice were not producing adequate amounts of IFN-γ during our short infection period. Hence, if interferon stimulated factors mediate the novel host defence mechanism of Dot/Icm effector translocation inhibition also in vivo, remains to be investigated.

Since *L. longbeachae* was able to survive in different innate immune cells, we analysed if the survival within these host cells is linked/proportionate to the translocation of effectors into these cells. It was previously shown that *L. pneumophila* is able to translocate effectors into alveolar macrophages and neutrophils, though to a lesser degree than alveolar macrophages, but not into monocyte derived cells [512]. This was directly correlated to the amount of viable bacteria within those cells, with alveolar macrophages harbouring the highest number of viable bacteria, followed by neutrophils and monocyte derived cells, which harbour barely any viable bacteria [512]. During our in vivo translocation assay experiments with *L. pneumophila* we discovered similar translocation patterns, with alveolar macrophages displaying the highest amount of effector translocation, followed by neutrophils and the least amount of effector translocation detected in monocyte derived cells. These observations substantiate the crucial role of monocyte derived cell in host defence against *L. pneumophila* as observed by [349]. Analysing Dot/Icm effector translocation of *L. longbeachae* in vivo, also revealed the highest level of translocation activity in alveolar macrophages. In addition, *L. longbeachae* Dot/Icm effector

translocation activity was also observed in neutrophils as well as monocyte-derived cells. This is in line with the previous observations made regarding the survival of *L. longbeachae* in these innate immune cells with alveolar macrophages harbouring the highest number of viable bacteria, followed by neutrophils and monocyte derived cells. Furthermore, in comparison to *L. pneumophila*, we observed greater Dot/Icm translocation activity in *L. longbeachae* infected alveolar macrophages, neutrophils and monocyte derived cells. However, if the increased effector translocation activity of the Dot/Icm secretion system, especially into monocyte-derived cells, influences their ability to produce inflammatory cytokines, remains to be investigated. However, we did observe reduced amounts of inflammatory cytokines, including IFN-γ, in the lung during *L. longbeachae* infection compared to *L. pneumophila* infection. In addition, since monocyte-derived cells are the major source of IL-12 during *L. pneumophila* infection [349], which induces the production of IFN-γ, these observations suggest a possible disruption of IFN-γ production potentially caused by an impaired function of monocyte-derived cells.

Overall, we were able to show that *L. longbeachae* is able to replicate well in both WT and IFN-$\gamma^{-/-}$ mice and that IFN-γ is crucial for host defence against *L. longbeachae* in vivo. Furthermore, we identified some unique features of *L. longbeachae* pathogenesis compared to *L. pneumophila*, such as a reduced induction of inflammatory cytokine production, the ability to translocate Dot/Icm effectors into all innate phagocytes as well as a higher Dot/Icm effector translocation activity in these cells. However, if the ability to translocation Dot/Icm effectors into all innate immune cells investigated and the higher rate of translocation activity enables *L. longbeachae* to manipulate these host cells more effectively than *L. pneumophila* to support its survival and thus cause the high replication of *L. longbeachae* in mice, remains to be investigated.

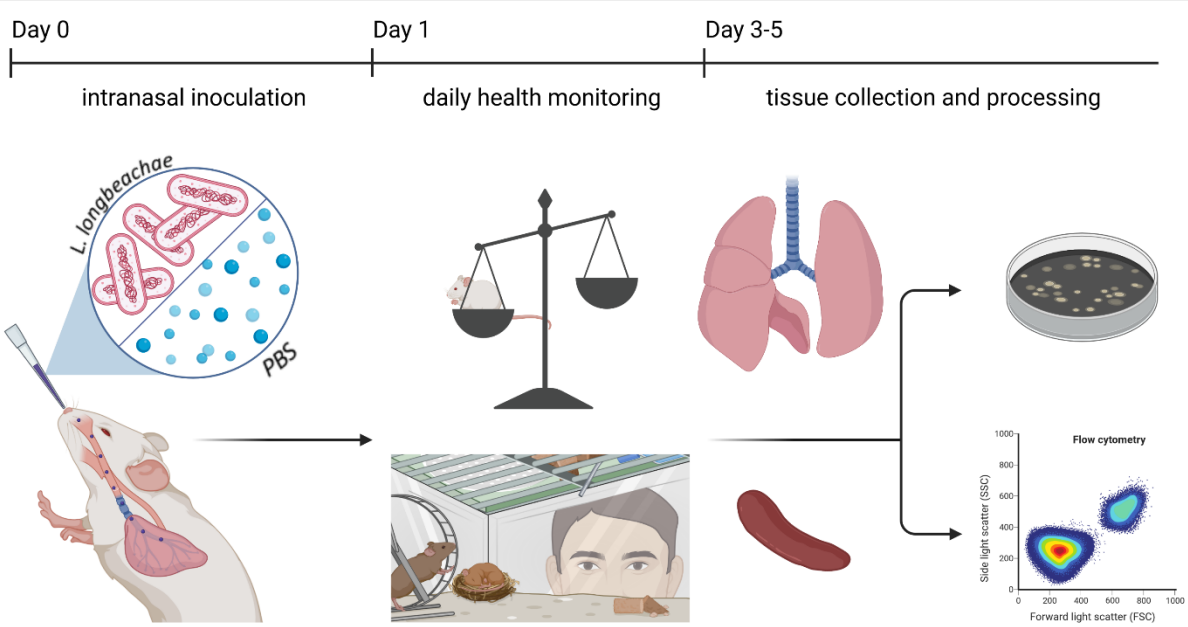


Figure 23: Work flow schematic for analysing *L. longbeachae* replication in WT and IFN-γ$^{-/-}$ mice

C57BL/6 WT and IFN-γ$^{-/-}$ mice are intranasaly infected with 2.5 x 10^5 *L. longbeachae* NSW 150 CFU or PBS and monitored for health until 3-5 days post infection. Organs (Lung and spleen) were harvested and processed, as described in Material and Methods Chapter, either for CFU enumeration or FACS analysis.

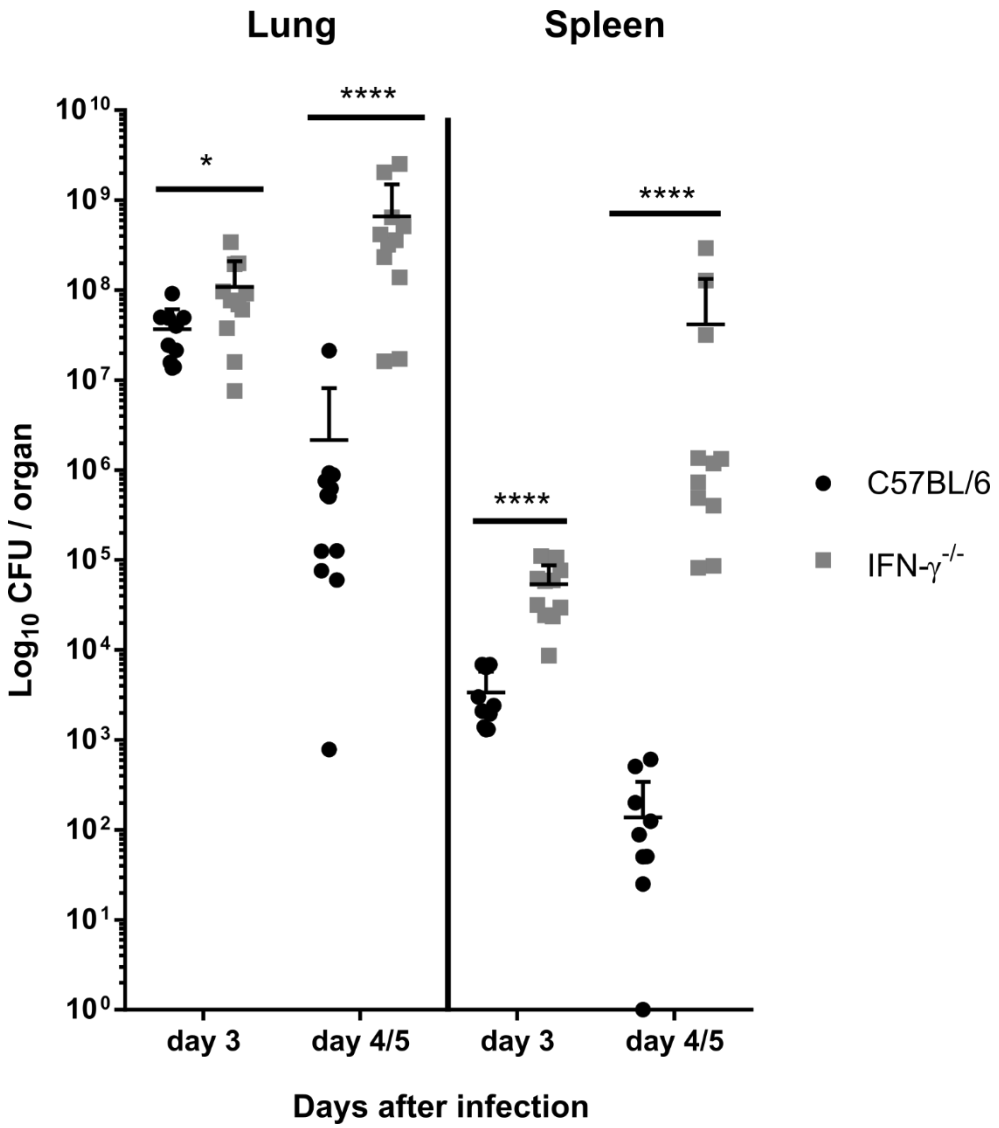


Figure 24: IFN-γ is essential for the control and clearance of *L. longbeachae* infection

C57BL/6 WT and IFN-$\gamma^{-/-}$ mice were infected with 2.5 x 10^5 *L. longbeachae* NSW 150 intranasally. 3 days and 4 to 5 days post infection lung and spleen were harvested and processed for CFU enumeration. Organ tissue was digested, cells lysed, and viable bacteria were cultured on BCYE plates for 3 days at 37 °C; subsequently CFU were enumerated. Data is shown as mean ± SD of n ≥ 3 independent experiments, each point represents 1 mouse.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

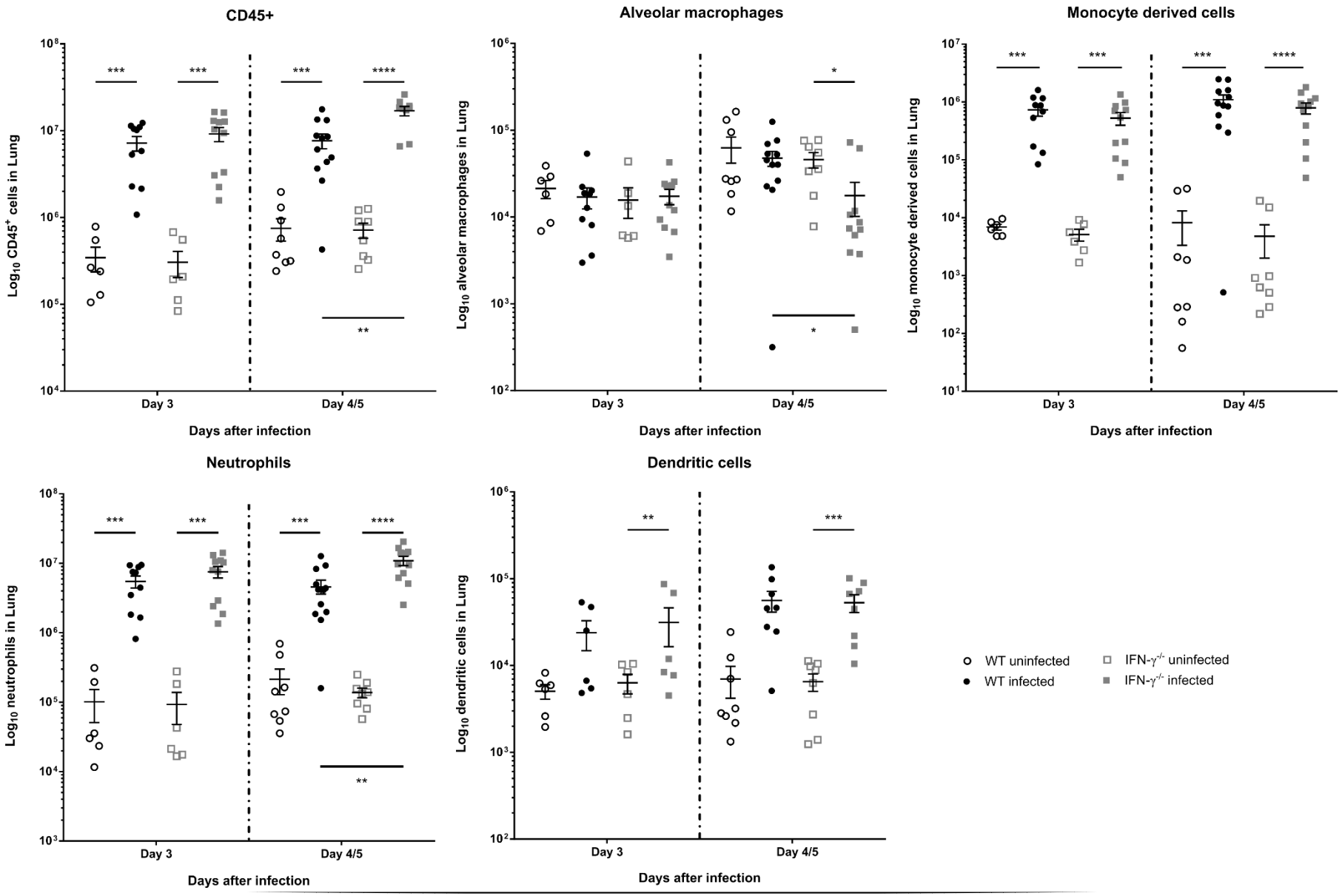

CD45+
Log10 CD45+ cells in Lung
Day 3
Day 4/5
Days after infection
Alveolar macrophages
Log10 alveolar macrophages in Lung
Monocyte derived cells
Log10 monocyte derived cells in Lung
Neutrophils
Log10 neutrophils in Lung
Dendritic cells
Log10 dendritic cells in Lung
WT uninfected
WT infected
IFN-γ-/- uninfected
IFN-γ-/- infected

Figure 25: *L. longbeachae* infection triggers a robust infiltration of phagocytes into the lung

C57BL/6 WT and IFN-$\gamma^{-/-}$ mice were infected with 2.5 x 10^5 *L. longbeachae* NSW 150 intranasally. 3 days or 4 to 5 days post infection lungs were harvested and processed for flow cytometry analysis (detailed description in method and material chapter). Lung tissue was digested and cells were stained with various antibodies to identify different cell populations during flow cytometry analysis. Data is shown as mean ± SD of n ≥ 3 independent experiments each point represents 1 mouse. (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

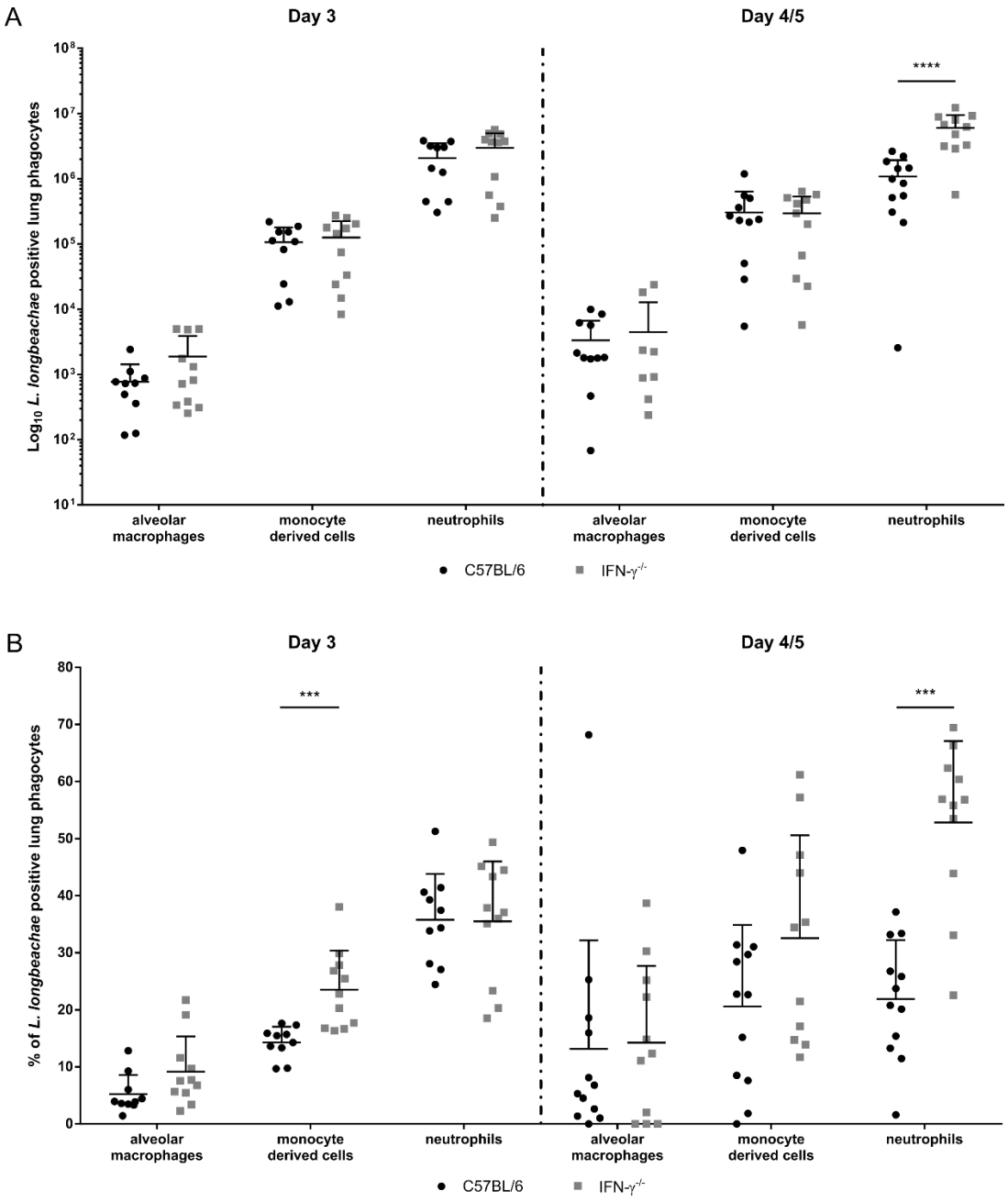


Figure 26: IFN-γ deficient pulmonary phagocytes contain more *L. longbeachae* than WT cells

C57BL/6 WT and IFN-$\gamma^{-/-}$ mice were infected with 2.5 x 10^5 *L. longbeachae* NSW 150 intranasally. 3 days or 4 to 5 days post infection lungs were harvested and processed for flow cytometry analysis. Lung tissue was digested and cells were stained with various antibodies to identify different cell populations as well as an anti *L. longbeachae* antibody to identify infected cells. A) total amount of cells stained with anti *L. longbeachae* antibody in the previously (Figure 25) gated populations. B) % of *L. longbeachae* positive cells identified in previously (Figure 25) gated population of alveolar macrophages, neutrophils and monocyte derived cells. Data shown as mean ± SD of n ≥ 3 independent experiments, each point represents 1 mouse (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

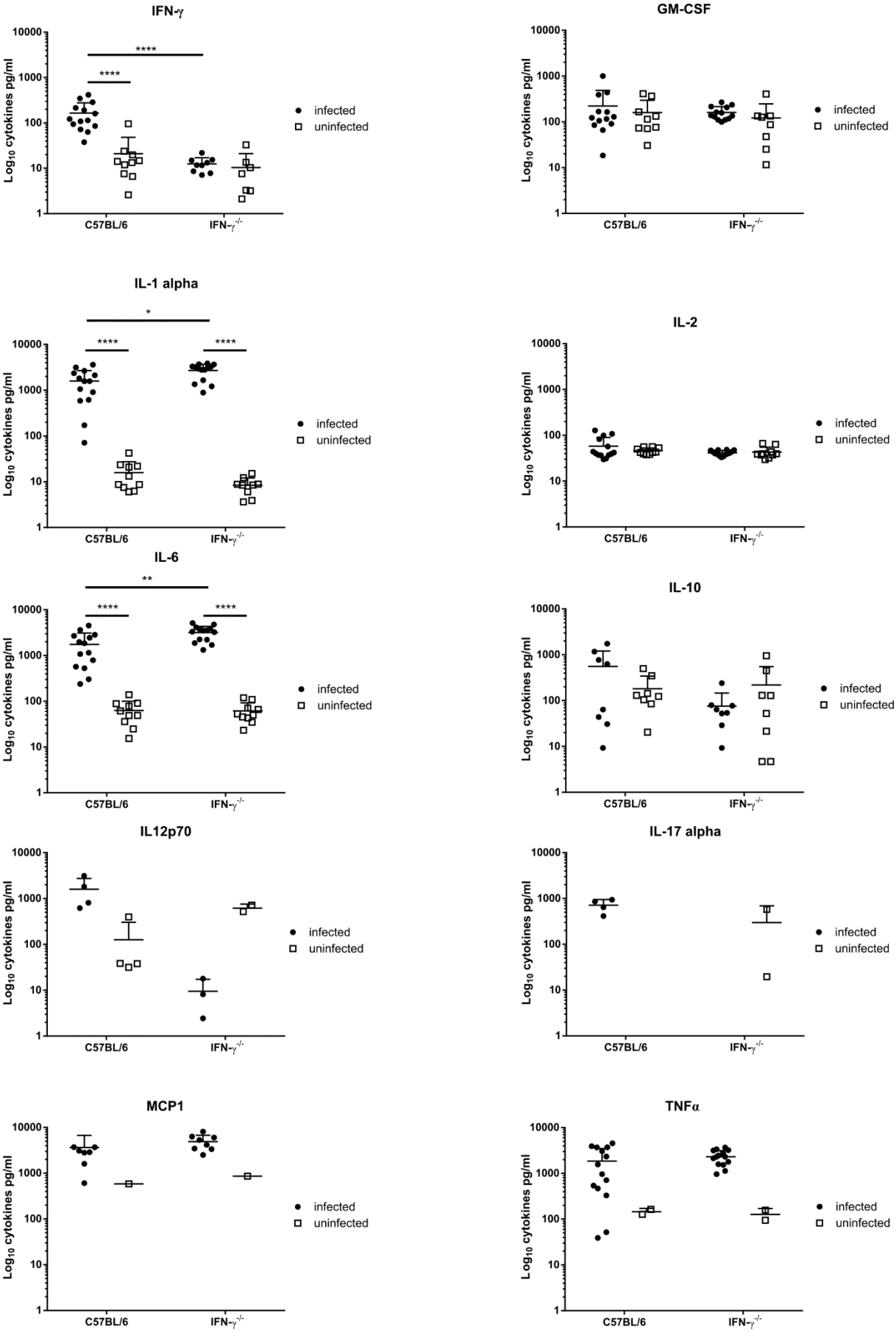

IFN-γ
GM-CSF
IL-1 alpha
IL-2
IL-6
IL-10
IL12p70
IL-17 alpha
MCP1
TNFα
Log10 cytokines pg/ml
10000
1000
100
10
1
****
*
**
infected
uninfected
C57BL/6
IFN-γ-/-

Figure 27: *L. longbeachae* infection induces IFN-γ, IL-6, TNFα and IL-1 alpha production in the lung.

C57BL/6 WT and IFN-$\gamma^{-/-}$ mice were infected with 2.5×10^5 *L. longbeachae* NSW 150 intranasally. 3 days post infection lungs were harvested and processed for flow cytometry analysis. Cytokine levels were analysed from digested lung tissue with cytokine bead array using flow cytometry. Data shown as mean ± SD of n = 5 independent experiments with n = 14 for infected WT and IFN-$\gamma^{-/-}$ mice and n = 10 for uninfected mice, each point represents 1 mouse. If fewer dots are shown, cytokine amount was below detectable range.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

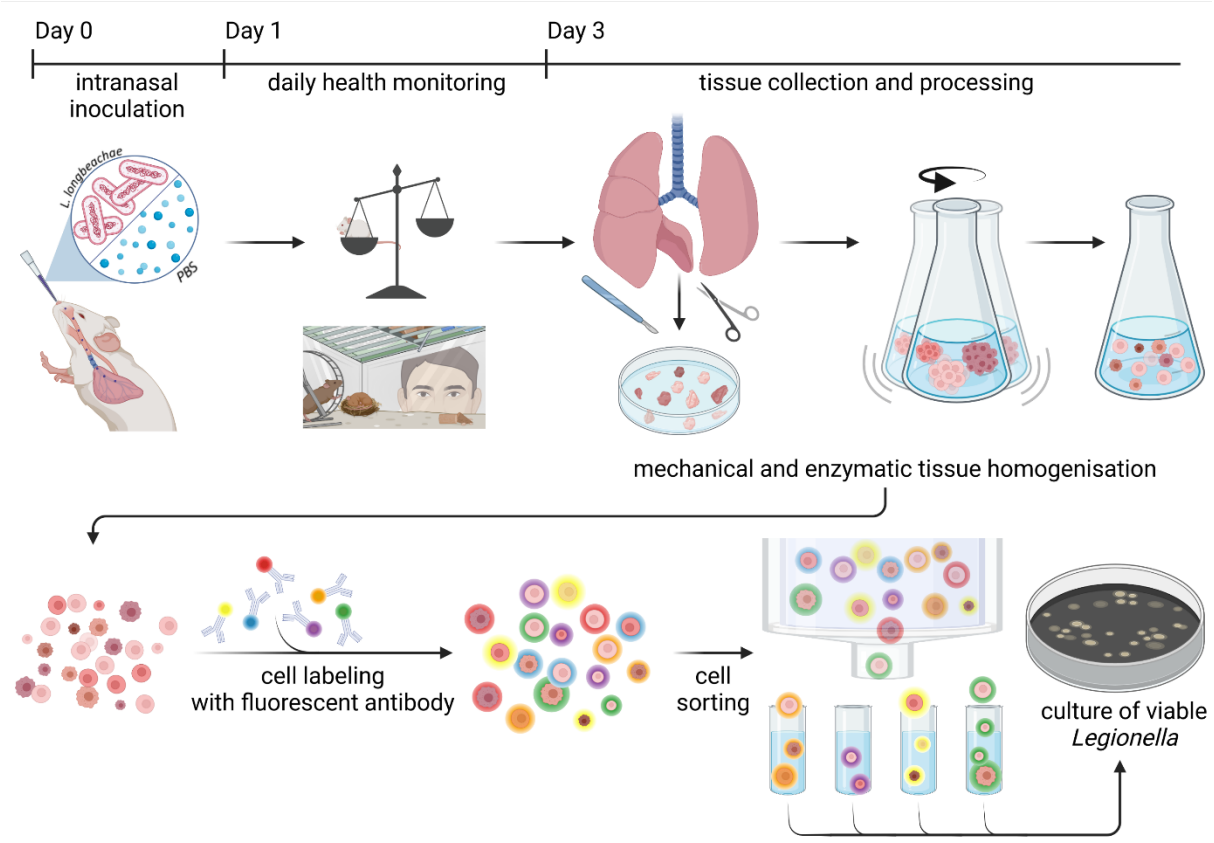


Figure 28: Work flow schematic for analysing the impact of IFN-γ on the bactericidal properties of lung phagocytes

C57BL/6 WT and IFN-$\gamma^{-/-}$ mice were infected with 2.5 x 10^5 *L. longbeachae* NSW 150 intranasally. 3 days post infection lungs were harvested and processed for fluorescence based cell sorting. Sorted cell populations were lysed and viable *L. longbeachae* were cultured on BCYE plates for 3 days at 37 °C and resulting CFU were enumerated.

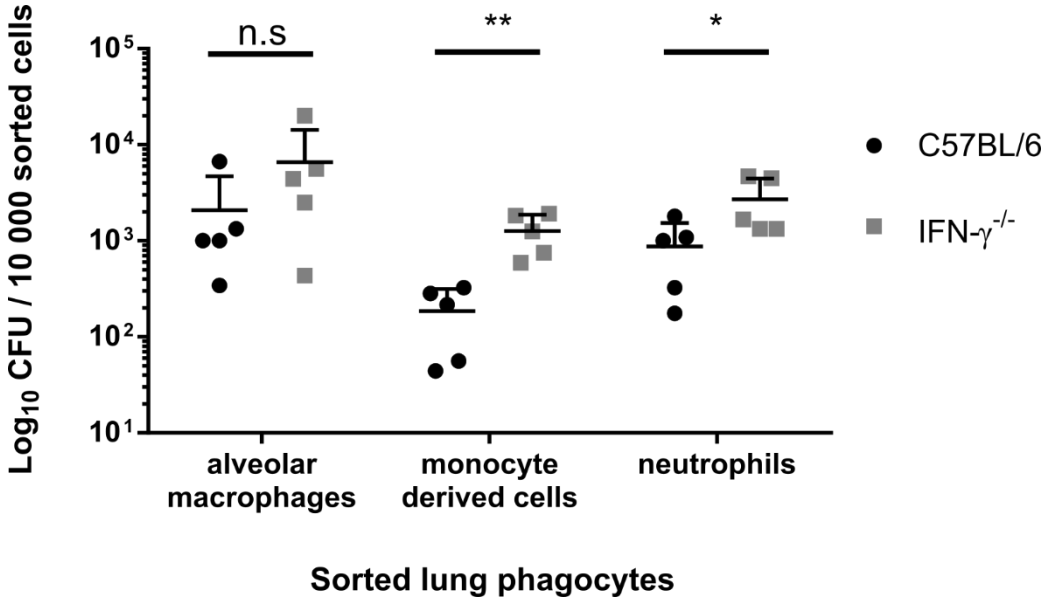


Figure 29: IFN-γ is essential for bactericidal activities of pulmonary phagocytes

C57BL/6 WT and IFN-$\gamma^{-/-}$ mice were infected with 2.5 x 10^5 *L. longbeachae* NSW 150 intranasally. 3 days post infection lungs were harvested and processed for live cell sorting and subsequent CFU enumeration. Lung tissue was digested, phagocytes were sorted and collected. Subsequently, 10 000 sorted cells of each population were lysed and viable bacteria were cultured on BCYE plates for 3 days at 37 °C for CFU enumeration. Data shown as mean ± SD of n = 4 independent infections and sorting experiments, with each point representing lungs of 2 mice pooled.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

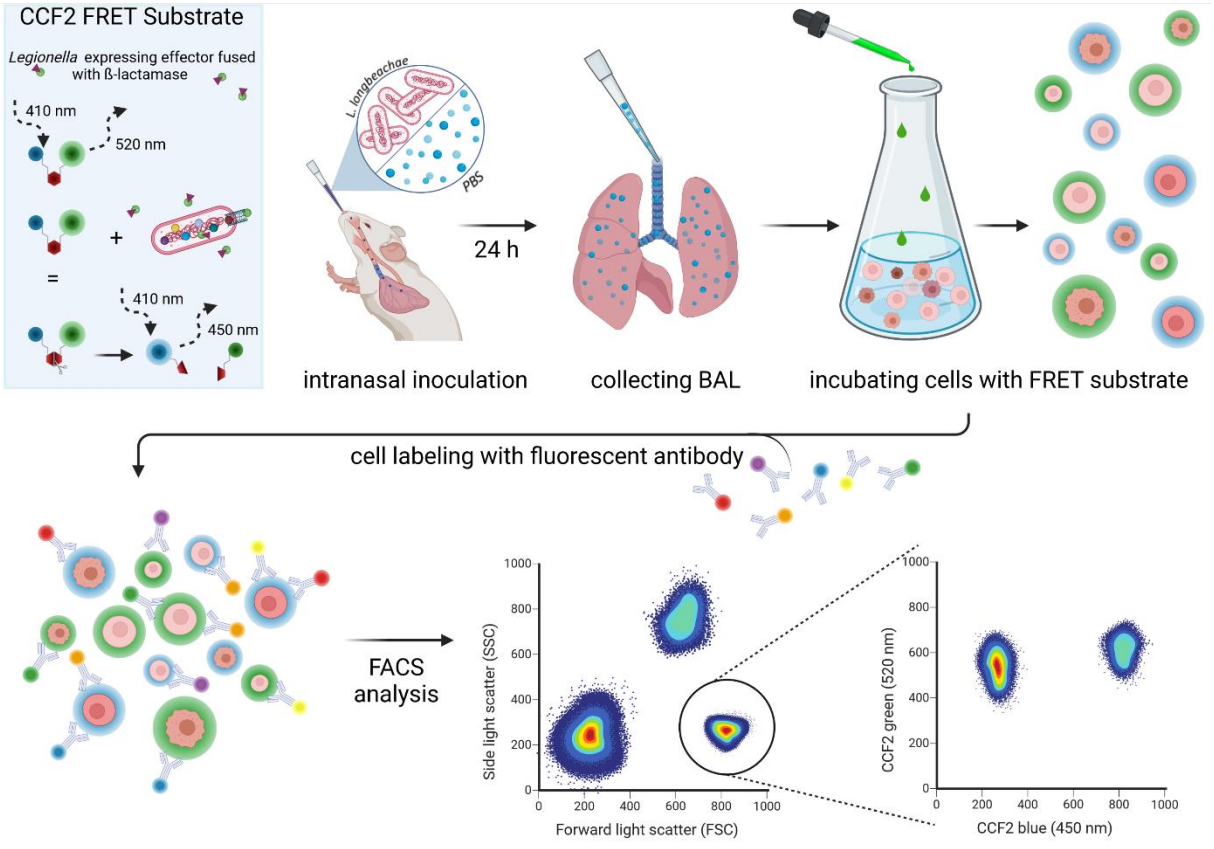
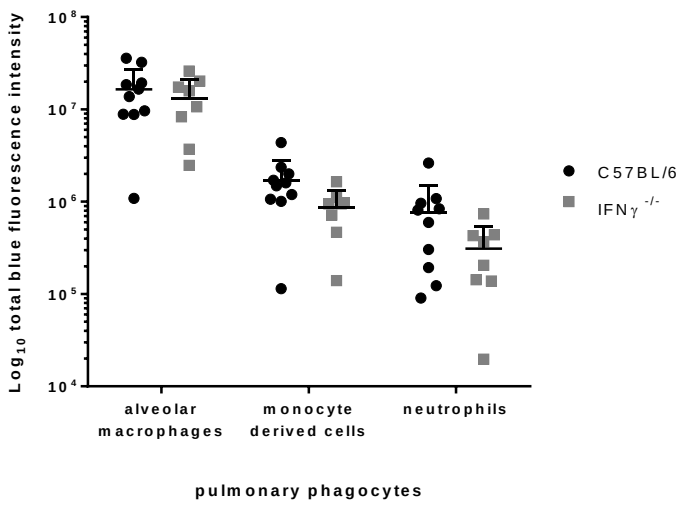
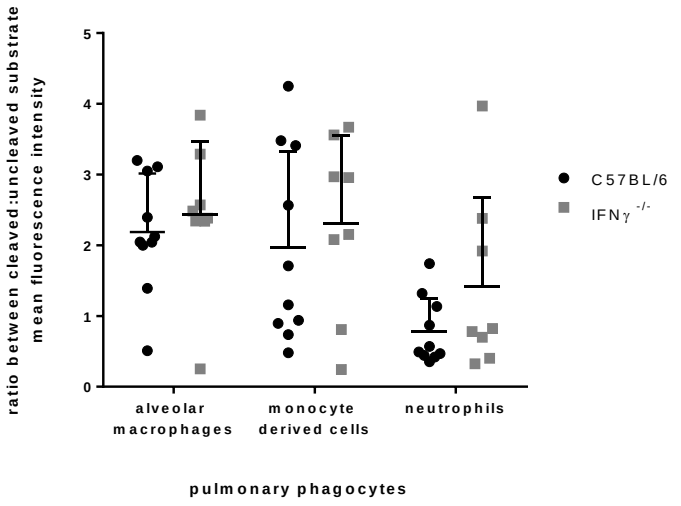


Figure 30: Work flow schematic of in vivo ß-lactamase Dot/Icm effector translocation assay

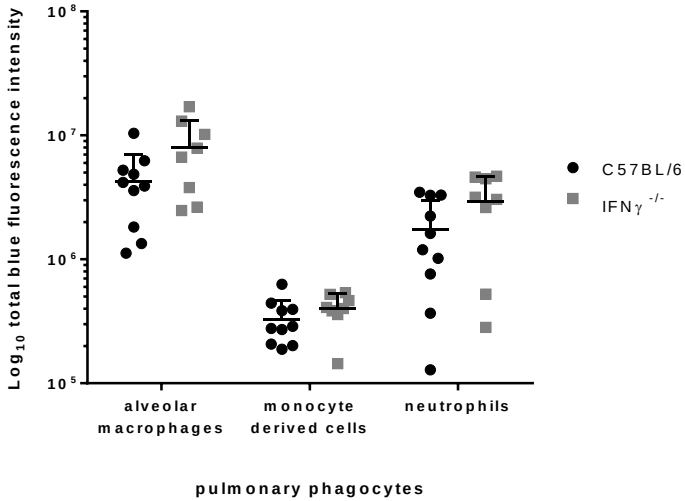
C57BL/6 WT and IFN-$\gamma^{-/-}$ mice were infected with *L. longbeachae* NSW 150 or *L. pneumophila* 130b Δ*flaA* each carrying pxDC61-RalF plasmid. 24 h post infection BALs were collected and cells harvested. Isolated cells were incubated with FRET substrate solution for 1.5 h, subsequently cells were stained with fluorescent tagged antibodies to analyse the different cell populations by flow cytometry. In each gated population, both fluorescence (450 nm and 520 nm) representing uncleaved and cleaved substrate, respectively, emitted by the FRET substrate were measured.

A


Log10 total blue fluorescence intensity
10^8
10^7
10^6
10^5
10^4
alveolar macrophages
monocyte derived cells
neutrophils
pulmonary phagocytes
C57BL/6
IFNγ -/-


ratio between cleaved:uncleaved substrate mean fluorescence intensity
5
4
3
2
1
0
alveolar macrophages
monocyte derived cells
neutrophils
pulmonary phagocytes
C57BL/6
IFNγ -/-

B


Log10 total blue fluorescence intensity
10^8
10^7
10^6
10^5
alveolar macrophages
monocyte derived cells
neutrophils
pulmonary phagocytes
C57BL/6
IFNγ -/-

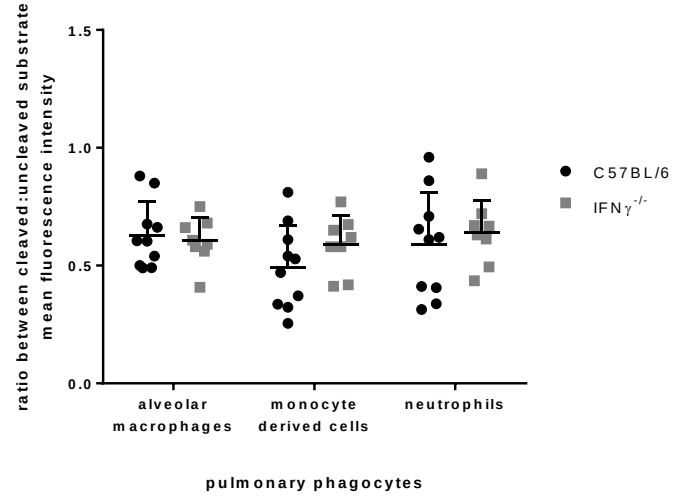

ratio between cleaved:uncleaved substrate mean fluorescence intensity
1.5
1.0
0.5
0.0
alveolar macrophages
monocyte derived cells
neutrophils
pulmonary phagocytes
C57BL/6
IFNγ -/-

Figure 31: *Legionella* spp. are able to translocate bacteria effectors in all pulmonary phagocytes

C57BL/6 WT and IFN-$\gamma^{-/-}$ mice were treated with LPS intranasally 24 h prior to intranasal infection with 2.5 x 10^5 *L. longbeachae* NSW 150 or 2.5 x 10^6 *L. pneumophila* 130b Δ*flaA*, expressing the fusion protein TEM1-RalF. 1 day post infection bronchoalveolar lavage (BAL) fluid was collected and cells harvested. Cells were incubated with the CCF2-AM substrate solution, stained with antibodies for differentiation of cell populations and subsequently fluorescence of FRET substrate was analysed with flow cytometry in different cell populations.
A) WT and IFN-$\gamma^{-/-}$ mice infected with *L. longbeachae* NSW 150 and B) WT and IFN-$\gamma^{-/-}$ mice infected with *L. pneumophila* 130b Δ*flaA*. On the left-hand side, the total fluorescence intensity of cleaved substrate (blue) in each cell population is depicted. On the right-hand side the ratio between the cleaved substrate and the uncleaved substrate fluorescence intensity is depicted. Data shown as mean ± SD of n = 4 independent infections and sorting experiments, each point represents 1 mouse.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

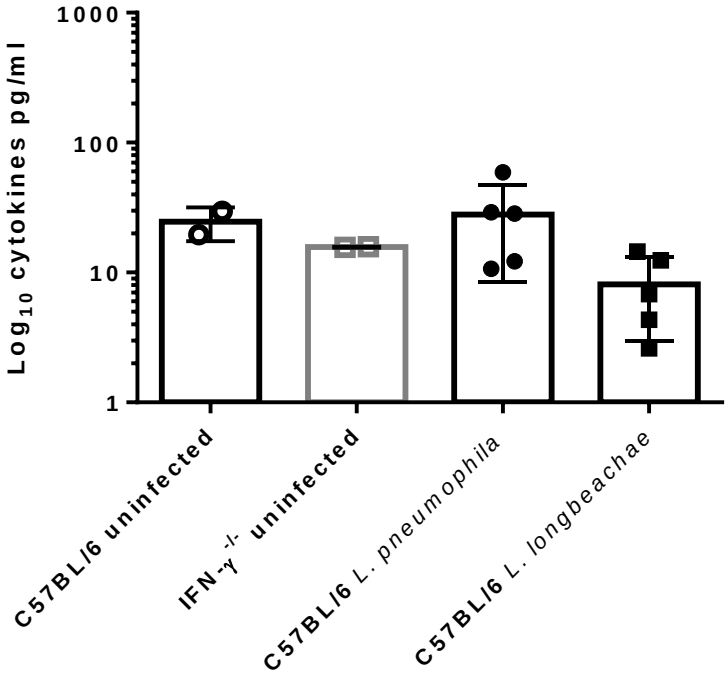


Figure 32: IFN-γ induction during in vivo ß-lactamase Dot/Icm effector translocation

C57BL/6 WT and IFN-$\gamma^{-/-}$ mice were treated with LPS intranasally 24 h prior to intranasal infection with 2.5 x 10^5 *L. longbeachae* NSW 150 or 2.5 x 10^6 *L. pneumophila* 130b Δ*flaA*, expressing the fusion protein TEM1-RalF. 1 day post infection bronchoalveolar lavage (BAL) fluid was collected and the concentration of IFN-γ in BAL fluid was analysed with cytokine bead array using flow cytometry. Data shown as mean ± SD of n = 2 independent experiments, each point represents 1 mouse.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

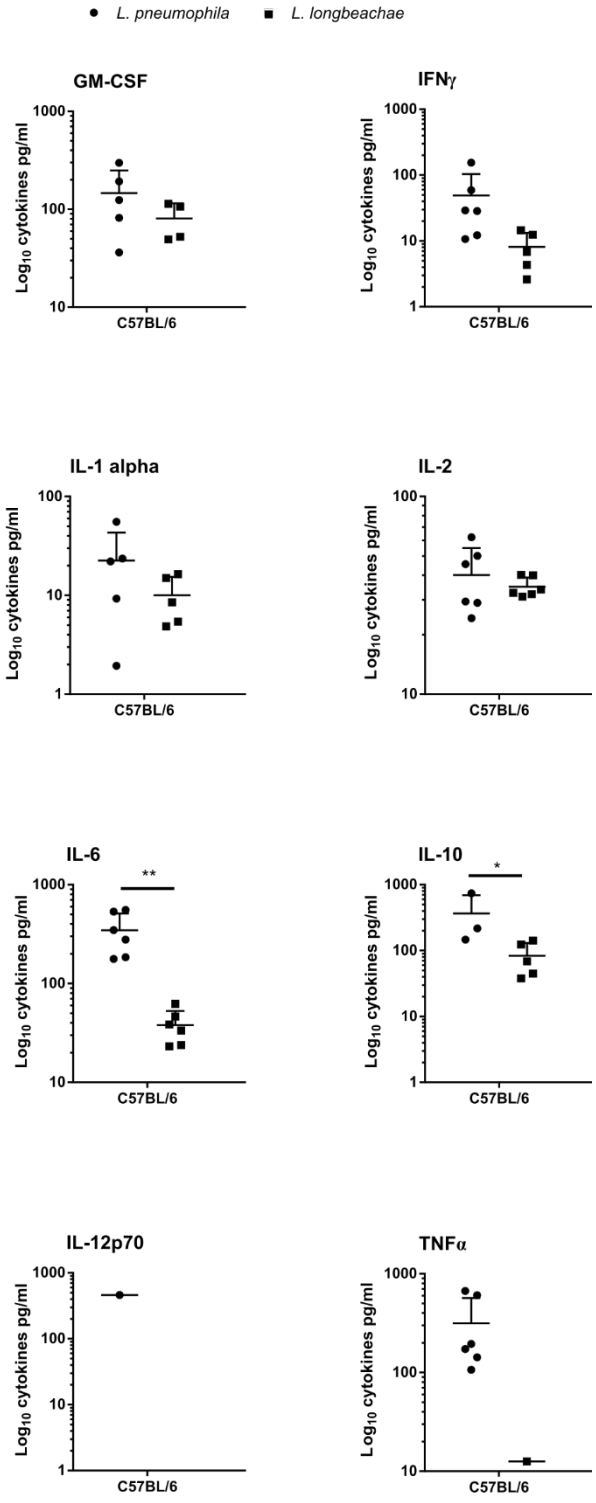


Figure 33: *L. longbeachae* seems to induce a weaker cytokine response in mice compared to a *L. pneumophila* infection

C57BL/6 WT and IFN-$\gamma^{-/-}$ mice were treated with LPS intranasally 24 h prior to intranasal infection with 2.5 x 10^5 *L. longbeachae* NSW 150 or 2.5 x 10^6 *L. pneumophila* 130b Δ*flaA*,

expressing the fusion protein TEM1-RalF. 1 day post infection bronchoalveolar lavage (BAL) fluid was collected and the concentration of cytokines in BAL fluid was analysed with cytokine bead array using flow cytometry. Data shown as mean ± SD of n = 2 independent experiments (WT 6 mice, IFN-$\gamma^{-/-}$ 5 mice), each point represents 1 mouse. If fewer dots are shown cytokine amount was below detectable range.
(* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, Mann Whitney test)

Chapter 6: Perspective

Since their discovery after the first major outbreak at the American Legion conference in Philadelphia in 1977, several species of *Legionellae* have been associated with severe pneumonia, termed Legionnaires' Disease in susceptible people, [3, 4]. Since this first documented outbreak, *L. pneumophila* regularly caused outbreaks around the world and the number of documented *L. pneumophila* infections is increasing each year in many countries [16-18]. Infection of susceptible people with *L. pneumophila* generally leads to high morbidity, with ~ 33 % of patients needing intensive care, and carries a mortality rate of 5-10 % [11, 39]. However, even with increased reporting of Legionnaires' Disease, the true burden of *Legionella* on the health system is most likely underestimated, since pneumonia caused by *Legionella* species cannot be distinguished clinically from other forms of pneumonia [14, 15] and testing for these bacteria is not done systematically upon patients presenting with pneumonia [11, 13]. In addition to these restricting factors, if patients are tested for a *Legionella* infection, it is mainly done via the standard urinary antigen test or via sputum cultivation on buffered charcoal yeast extract (BCYE). However, both techniques can lead to false-negative results due to only detecting *L. pneumophila* serogroup 1 [8, 20-22] or through inhibiting the growth of non-*L. pneumophila* species through the use of certain antibiotics [24]. This culminates in an underrated diagnosis of pneumonia caused by *L. pneumophila* and non-*L. pneumophila* species [25, 517] and thus an underestimation of pneumonia caused by *Legionella* in general. With the age average of the populations increasing in many countries worldwide, the group of people most at risk of a severe *Legionella* infection is increasing and therefore so too is the burden *Legionella* poses on the health systems.

Legionellae are foremost environmental bacteria. In order to persist in the environment as well as survive within their environmental hosts, *Legionella* creates an intracellular niche that supports its survival and replication. This is achieved through the export of effector proteins into host cells via the Dot/Icm type IV secretion system, which transports ~330 effectors into host cells [200]. The entire repertoire of effectors in the *Legionella* genus amounts to more than and 18 000 across 58 *Legionella* species [197]. The intimate relationship between *Legionella*

and environmental amoeba has equipped *Legionella* with the ability to survive and replicate within mammalian cells [47, 518], via targeting conserved eukaryotic pathways and mechanisms [203, 211]. It is believed that *Legionella* acquired the genes that allow it to survive in a mammalian host via horizontal gene transfer through its long co-evolution with protozoa [519, 520]. This is also reflected by the vast number of eukaryotic-like domains and proteins in the *Legionella* effector arsenal [79, 197, 521, 522].

Legionella acquired a large repertoire of Dot/Icm effector proteins which allow the bacteria to survive within amoebae by manipulating protozoan metabolism and cell-autonomous defence. However, mammalian hosts have the advantage of possessing a complex immune system that enables immunocompetent hosts to fight this environmental pathogen. The immune-competent host mounts a strong inflammatory response, including cytokines such as TNFα, IL-1α, IL-1β, IL-6, type 1 interferons, IL-12, GM-CSF, upon detecting *Legionella* PAMPs to orchestrate immune defence at the site of infection. One of the cytokines that is vital for host defence and survival against *Legionella* is IFN-γ [234, 349, 370]. IFN-γ restrict intracellular replication of various pathogens, ranging from viruses to bacteria to parasites. However, the detailed mechanisms by which IFN-γ inhibits the replication of such a vast range of pathogens remains elusive. IFN-γ stimulation leads to the up-regulation of thousands of genes termed interferon-stimulated genes (ISG) [224, 226]. The activities of some of these ISGs in host defence have been elucidated and these range in function from inhibiting enzymatic functions, disrupting protein complex assembly, destabilizing pathogen containing membrane compartments, stimulating the production of anti-microbial molecules, activating inflammasomes, targeting autophagy and ubiquitin machinery, to restricting the mobility and spread of invading pathogens [446]. However, precisely how interferon-stimulated proteins restrict *Legionella* replication remains elusive.

During this study, we identified a novel mechanism by which interferons are able to interfere with a key virulence attribute of *Legionella*. We discovered that interferon stimulation leads to a reduction of Dot/Icm effector translocation into the host cells. This novel host defence mechanism potentially presents a unique host defence strategy. By attacking a crucial element of infection: namely the effector translocation into host cells, this mechanism curtails the need to intervene or overcome the functions of countless effectors used to manipulate the host by reducing the amount of proteins that reach the site of action, thus making the pathogen more vulnerable to host defence mechanisms. Utilising mRNA sequencing of interferon-stimulated

macrophages, we identified candidate ISGs that possibly mediate the reduction in effector translocation into host cells and discussed two of these, ISG15 and PARPs. The role of these proteins in post-translational modifications have not yet been linked directly with host defence against *Legionella*, but have been implicated in host defence against viruses [476, 477, 503]. Thus, further studies of these proteins and the post-translational modifications they confer in the context of *Legionella* infection, represents a unique opportunity to gather new knowledge about ISG mediated host defence against *Legionella* as well as gain a greater understanding of the functions of these distinct post-translational modifications in host defence more broadly.

Although diagnostic and testing bias result in *L. pneumophila* being recorded as the predominant cause of Legionnaire's disease, other non-*L. pneumophila* species are also capable of causing severe pneumonia in susceptible people. In fact, approximately half of the known *Legionella* species have been associated with human infection [9]. Despite this knowledge the majority of research efforts have been focused primarily on *L. pneumophila*. Even though *L. longbeachae* is the second most common cause of Legionnaire's disease worldwide, knowledge about this pathogen is extremely limited, with 242 published research articles compared to 6.805 for *L. pneumophila*.

Therefore, we aimed to provide new insights into the pathogenesis of *L. longbeachae* infections during this study as well as characterising the role of IFN-γ in host defence against this pathogen. In comparing *L. longbeachae* to *L. pneumophila* pathogenesis, we were able to show some unique features of *L. longbeachae* pathogenesis. For example, *L. longbeachae* replicates to higher numbers in the lungs of mice (~ 2-3 Log_{10} higher) compared to *L. pneumophila* and spreads to other organs. These features are further increased in IFN-γ deficient mice, resulting in severe pneumonia, unrestricted replication of *L. longbeachae* and mortality. Furthermore, *L. longbeachae*, survives within alveolar macrophages and unlike *L. pneumophila*, viable bacteria could also be found in neutrophils and monocyte derived cells in considerably large numbers. In addition, the bacterial burden in these cells was increased even further in IFN-$\gamma^{-/-}$ mice, indicating an essential role for IFN-γ in cell-intrinsic pathogen control in these phagocytes. The high rate of viable *L. longbeachae* in neutrophils and monocyte-derived cells and the dependency of neutrophils on IFN-γ signalling to trigger bactericidal activities was specific to *L. longbeachae*. Moreover, *L. longbeachae* seems to be able to dampen the cytokine response of the host in comparison to *L. pneumophila*, since the amount of inflammatory

cytokines measured in lung tissue during *L. longbeachae* infections was significantly reduced compared to *L. pneumophila*.

Theses *L. longbeachae* specific features of the immune response might be triggered in part by the ability to translocate Dot/Icm effectors into all lung phagocytes tested, enabling *L. longbeachae* to manipulate a variety of host immune cells. In comparison, strains of *L. pneumophila*, including mutants lacking flagellin only appear to translocate effectors into alveolar macrophages and neutrophils.

It was previously shown that translocation of individual Dot/Icm effector proteins into host cells can either enable the bacteria to thrive in mammalian host or contribute to the recognition by the host defence and trigger effector mediated immunity (EMI). Utilising a high throughput assays, multiple Dot/Icm effectors were identified which either supported *L. pneumophila* replication or were detrimental for survival and replication during infections of different host groups such as mice, primary cells or protozoans [209]. One effector identified in this screen which triggers effector mediated immunity in mice was the *L. pneumophila* effector LegC4 [209]. LegC4 contributes to host defence against *L. pneumophila*, as *legC4* loss of function mutants showed a replicative advantage compared to WT *L. pneumophila* in mice, but not pBMDM, thus indication a role in modulating the immune response of the host in vivo [209, 523]. Moreover, it was demonstrated that *legC4* deletion mutants trigger significantly less IL-12 secretion in infected NLRC4$^{-/-}$ pBMDM compared to WT *L. pneumophila*, thus indicating that *legC4* might stimulate the production of proinflammatory cytokines in vivo and thus promote clearance of the bacteria in lungs during infections [209]. It was later demonstrated that LegC4 augments the IFN-γ and TNF mediated restriction of *Legionella* in vivo [523]. The Dot/Icm effector repertoire of *L. pneumophila* and *L. longbeachae* vary greatly [29, 63, 90, 200, 201], with only a few effectors shared between the species [63, 198, 199]. Since *L. longbeachae* does not encode a *legC4* effector homologue [63] and *L. pneumophila* Δ*legC4* mutants triggered significantly less IL-12 secretion from infected macrophages, compared to their WT counterparts [209], the lower production of proinflammatory cytokines observed during *L. longbeachae* might be based on the lack of LegC4 triggered EMI. Furthermore, it was recently identified how EMI contributes to host defence against *L. pneumophila* in vivo. EMI triggered by *L. pneumophila* induced inhibition of translation, causes selective upregulation and secretion of IL-1α in infected cells [429, 524]. IL-1α in turn triggers GM-CSF secretion by alveolar epithelial cells and subsequently GM-CSF stimulates production of pro-inflammatory

cytokines in monocytes by upregulation of aerobic glycolysis [525]. Since *L. longbeachae* does not seem to trigger GM-CSF during infection (Figure 27) and we observed a reduction in pro inflammatory cytokine levels compared to *L. pneumophila*, *L. longbeachae* might avoid or interfere with EMI induced crosstalk between infected alveolar macrophages, alveolar epithelial cells and monocytes, which induces the robust production of pro-inflammatory cytokines and thus aides in clearance of *L. pneumophila*. However, if and how *L. longbeachae* might avoid effector mediated immunity during infections, remains to be investigated.

Another possible explanation for the lower cytokine profile of *L. longbeachae* compared to *L. pneumophila* could arise from a differential regulation of mTOR activity. It was previously demonstrated the host cells supress mTOR activity upon detection of virulent *L. pneumophila* by ubiquitination of activated Akt, triggering the subsequent proteasome degradation, which promotes biased production of proinflammatory cytokines (e.g. IL-6) by favouring these highly abundant transcripts via suppression of cap-dependent translation [526]. The ubiquitination of Akt is a host response upon detection of pathogenic *Legionella* PAMPs [526], since *L. longbeachae* expresses a capsule the detection of virulent PAMPs might be reduced or inhibited in *L. longbeachae* infected cells compared to *L. pneumophila*. This potential reduced detection of virulent *L. longbeachae* traits could possibly result in different ubiquitination level of Akt, and thus reduced degradation, which might lead to a higher mTOR activity which results in lower IL-6 production. Apart from the capsule which might interfere with the detection of *L. longbeachae* PAMPs, *L. longbeachae* might translocate effectors which are able to remove ubiquitin from activated Akt, and thus inhibit the proteasomal degradation of Akt, which would inhibit the suppression of mTOR activity or interact directly with targets downstream of mTOR and thus lead to a reduced production of pro-inflammatory cytokines. Moreover, differential regulation of mTOR activity by Dot/Icm effectors between *L. pneumophila* and *L. longbeachae* has been previously observed [527]. However, if *L. longbeachae* infection causes different ubiquitylation levels or patterns of Akt and mTOR during infection, either mediated by the capsule or by specific Dot/Icm effectors, compared *L. pneumophila* remains to be investigated.

Our observations corroborate the importance of IFN-γ in host defence against *Legionella* infection in vitro and in vivo and indicate the need to characterise the pathogenesis of non-*L. pneumophila* species, since their unique effector repertoire potentially enables them to manipulate the host in distinct ways. Therefore, we would advocate developing a greater understanding of the full breadth of host manipulation and pathogenesis characteristics caused

by non-*L. pneumophila* species, to inform treatment regimens against pneumonia caused by *Legionella*.

The manipulation of host cell biology through injected pathogen effector proteins is not exclusive to *Legionella* but utilized by a variety of bacterial and parasite pathogens to ensure their intracellular survival. These include but are not limited to *Burkholderia thailandensis, Coxiella burnetii*, *Chlamydia trachomatis*, enteropathogenic *Escherichia coli, Mycobacterium tuberculosis*, *Plasmodium falciparum*, *Salmonella enterica* serovar Typhimurium, *Shigella flexneri* and *Toxoplasma gondii*. The ß-lactamase reporter system used during this thesis to track the Dot/Icm effector translocation into host cells can be used in various experimental conditions and analyses, including for high throughput screens. This makes it an ideal tool to observe the dynamics of pathogen protein transport into host cells by various secretion systems and transporters as well as different pathogen species. IFN-γ is also involved in the host defence against multiple pathogens [446], thus raising the possibility that the potential to disrupt effector transport into the host cell is not limited to *Legionella*, but may represent a mechanism applicable to a range of pathogens.

In light of rapidly increasing antibiotic resistance, even within *Legionella* [41, 528], we urgently need to develop alternative treatments for various pathogens of public health concern. Since the host immune system is in an arms race against a myriad of pathogens, it has evolved to fight various pathogens successfully through innate and adaptive immunity. However, it is crucial to understand the mechanisms of host defence mediated by IFN-γ and other inflammatory cytokines in greater detail at the cell-intrinsic level as well as the interplay between these cytokines and mechanisms, to exploit the full potential of the innate and adaptive immune system during infection. This would enable us to achieve a comprehensive understanding of host defence against particular pathogens as well as the mechanisms employed by pathogens to subvert host defence, thus enabling the development of treatments and drugs supporting immune defence mechanisms. This immune centred approach has huge potential for drug development against various pathogens, as it undermines the capacity of pathogens to cause disease through injecting effector proteins into the host cytosol that manipulate host cell metabolism and cell-autonomous defence.

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Appendix 1 Complete list of common differentially expressed genes upon IFN-γ and IFN-α+β stimulation

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000078853	Igtp	0.00E+00	0.00E+00	93.70	93.18	0.00E+00	93.44
ENSMUSG00000046879	Irgm1	0.00E+00	0.00E+00	51.60	50.96	0.00E+00	51.28
ENSMUSG00000074151	Nlrc5	1.04E-270	0.00E+00	18.32	22.63	5.19E-271	20.48
ENSMUSG00000078920	Ifi47	1.31E-262	0.00E+00	105.15	120.64	6.53E-263	112.89
ENSMUSG00000069874	Irgm2	1.97E-253	0.00E+00	44.04	50.72	9.85E-254	47.38
ENSMUSG00000040253	Gbp7	1.42E-246	0.00E+00	72.61	79.68	7.08E-247	76.14
ENSMUSG00000045932	Ifit2	3.78E-204	0.00E+00	121.61	592.12	1.89E-204	356.87
ENSMUSG00000027639	Samhd1	6.59E-199	1.83E-282	14.89	17.12	3.29E-199	16.00
ENSMUSG00000082292	Gm12250	9.75E-197	1.32E-227	181.45	175.87	4.87E-197	178.66
ENSMUSG00000054072	Iigp1	2.39E-196	3.88E-216	3,055.28	1,894.02	1.19E-196	2,474.65
ENSMUSG00000029298	Gbp9	7.49E-191	1.92E-225	40.34	38.84	3.75E-191	39.59
ENSMUSG00000073555	Gm4951	1.09E-185	7.34E-192	899.42	726.22	5.44E-186	812.82
ENSMUSG00000028270	Gbp2	1.71E-180	6.18E-186	321.71	176.29	8.54E-181	249.00
ENSMUSG00000090272	Mndal	8.41E-174	0.00E+00	12.71	27.72	4.21E-174	20.22
ENSMUSG00000033355	Rtp4	2.55E-154	0.00E+00	15.62	38.48	1.28E-154	27.05
ENSMUSG00000037321	Tap1	1.41E-153	1.68E-213	18.92	21.31	7.05E-154	20.11
ENSMUSG00000028268	Gbp3	4.87E-150	4.24E-204	97.52	113.95	2.44E-150	105.73
ENSMUSG00000030921	Trim30a	5.91E-150	0.00E+00	8.38	18.27	2.95E-150	13.33
ENSMUSG00000059089	Fcgr4	4.79E-149	1.24E-173	13.90	12.33	2.39E-149	13.11
ENSMUSG00000063268	Parp10	1.64E-146	0.00E+00	6.68	15.24	8.22E-147	10.96
ENSMUSG00000049502	Dtx3l	1.32E-141	4.55E-225	12.03	16.00	6.61E-142	14.01

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000039699	Batf2	8.83E-181	4.26E-136	196.91	64.02	2.13E-136	130.46
ENSMUSG00000027514	Zbp1	3.88E-129	1.59E-186	71.77	97.17	1.94E-129	84.47
ENSMUSG00000029561	Oasl2	2.25E-120	5.78E-240	23.57	52.31	1.13E-120	37.94
ENSMUSG00000054404	Slfn5	1.14E-115	1.22E-243	14.32	30.29	5.71E-116	22.31
ENSMUSG00000070327	Rnf213	2.43E-113	6.86E-231	13.31	26.17	1.22E-113	19.74
ENSMUSG00000042726	Trafd1	2.32E-111	1.90E-241	6.74	11.93	1.16E-111	9.33
ENSMUSG00000070730	Rmdn3	1.82E-110	5.56E-159	5.56	6.16	9.11E-111	5.86
ENSMUSG00000058163	Gm5431	2.54E-108	1.94E-225	15.96	37.40	1.27E-108	26.68
ENSMUSG00000020572	Nampt	1.29E-149	1.04E-106	14.23	7.21	5.21E-107	10.72
ENSMUSG00000024349	Sting1	3.66E-128	1.90E-102	8.01	5.20	9.52E-103	6.60
ENSMUSG00000004040	Stat3	6.41E-112	2.75E-101	4.41	3.47	1.38E-101	3.94
ENSMUSG00000041481	Serpina3g	1.01E-135	3.74E-101	351.06	107.86	1.87E-101	229.46
ENSMUSG00000040328	Olfr56	3.71E-99	3.31E-125	145.05	227.05	1.85E-99	186.05
ENSMUSG00000073489	Ifi204	2.43E-97	5.78E-205	7.85	13.99	1.22E-97	10.92
ENSMUSG00000074896	Ifit3	7.58E-97	0.00E+00	31.27	378.05	3.79E-97	204.66
ENSMUSG00000039899	Fgl2	3.00E-94	2.28E-135	81.47	105.13	1.50E-94	93.30
ENSMUSG00000034422	Parp14	3.00E-94	3.65E-137	17.54	21.02	1.50E-94	19.28
ENSMUSG00000022906	Parp9	6.57E-94	2.24E-155	10.22	14.00	3.28E-94	12.11
ENSMUSG00000009585	Apobec3	5.16E-93	2.05E-135	6.73	7.63	2.58E-93	7.18
ENSMUSG00000079363	Gbp4	1.39E-106	2.00E-91	2,190.82	913.54	9.98E-92	1,552.18
ENSMUSG00000028894	Inpp5b	1.25E-199	3.51E-91	7.12	3.30	1.75E-91	5.21
ENSMUSG00000017830	Dhx58	7.98E-91	4.29E-255	6.99	17.81	3.99E-91	12.40
ENSMUSG00000090222	Ifi203-ps	3.06E-90	9.63E-178	15.65	32.52	1.53E-90	24.09
ENSMUSG00000033213	AA467197	7.24E-90	1.79E-126	75.88	94.60	3.62E-90	85.24
ENSMUSG00000027669	Gnb4	1.20E-86	2.21E-166	9.69	16.20	6.02E-87	12.95

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000029798	Herc6	2.97E-85	1.46E-204	12.60	32.22	1.49E-85	22.41
ENSMUSG00000024079	Eif2ak2	7.78E-84	9.19E-215	5.32	10.58	3.89E-84	7.95
ENSMUSG00000020638	Cmpk2	3.11E-82	0.00E+00	41.04	821.02	1.55E-82	431.03
ENSMUSG00000043263	Ifi209	3.70E-82	4.89E-244	33.41	218.26	1.85E-82	125.83
ENSMUSG00000009185	Ccl8	3.16E-79	3.80E-134	220.89	796.99	1.58E-79	508.94
ENSMUSG00000063286	Gvin-ps7	2.16E-78	1.03E-110	19.49	22.42	1.08E-78	20.96
ENSMUSG00000034459	Ifit1	8.82E-77	2.66E-262	55.26	713.73	4.41E-77	384.50
ENSMUSG00000027951	Adar	2.28E-76	5.14E-203	4.01	7.31	1.14E-76	5.66
ENSMUSG00000069892	9930111J21Rik2	5.94E-76	4.28E-173	6.38	11.84	2.97E-76	9.11
ENSMUSG00000035692	Isg15	1.61E-75	2.07E-195	43.76	216.09	8.06E-76	129.92
ENSMUSG00000036986	Pml	2.21E-75	2.23E-204	5.83	12.92	1.11E-75	9.38
ENSMUSG00000046031	Calhm6	1.53E-88	3.95E-75	152.40	59.81	1.98E-75	106.11
ENSMUSG00000050029	Rap2c	7.49E-75	1.47E-142	3.53	4.64	3.75E-75	4.09
ENSMUSG00000078616	Trim30c	1.21E-74	2.65E-176	46.66	207.78	6.04E-75	127.22
ENSMUSG00000031712	Il15	2.22E-74	1.09E-179	8.36	18.47	1.11E-74	13.42
ENSMUSG00000030275	Etnk1	3.12E-74	4.66E-291	2.98	6.62	1.56E-74	4.80
ENSMUSG00000053318	Slamf8	5.49E-107	9.36E-74	126.12	34.91	4.68E-74	80.51
ENSMUSG00000066363	Serpina3f	7.14E-92	4.15E-73	3,194.99	1,130.73	2.08E-73	2,162.86
ENSMUSG00000036381	P2ry14	1.64E-72	4.70E-148	7.02	11.71	8.19E-73	9.37
ENSMUSG00000025498	Irf7	7.13E-72	3.06E-272	19.64	169.52	3.56E-72	94.58
ENSMUSG00000040033	Stat2	2.74E-71	4.66E-190	9.80	26.90	1.37E-71	18.35
ENSMUSG00000035208	Slfn8	2.42E-70	2.05E-172	12.67	33.53	1.21E-70	23.10
ENSMUSG00000002307	Daxx	1.62E-69	1.29E-211	6.72	18.78	8.12E-70	12.75
ENSMUSG00000030341	Tnfrsf1a	9.85E-69	5.90E-73	3.96	3.49	4.92E-69	3.73
ENSMUSG00000038507	Parp12	2.06E-68	6.65E-189	6.20	14.52	1.03E-68	10.36

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000078921	Tgtp2	3.47E-66	2.48E-67	780.50	730.59	1.86E-66	755.55
ENSMUSG00000016496	Cd274	7.04E-66	1.37E-80	29.48	26.97	3.52E-66	28.22
ENSMUSG00000026104	Stat1	9.69E-66	1.53E-97	14.58	17.76	4.84E-66	16.17
ENSMUSG00000021266	Wars	4.80E-94	1.45E-64	10.04	5.41	7.24E-65	7.73
ENSMUSG00000031792	Usb1	1.23E-63	1.23E-241	3.00	6.53	6.17E-64	4.76
ENSMUSG00000030966	Trim21	3.06E-63	1.07E-144	6.59	12.45	1.53E-63	9.52
ENSMUSG00000017057	Il13ra1	3.99E-63	3.82E-114	7.22	10.57	2.00E-63	8.90
ENSMUSG00000037816	Fbxw17	7.40E-63	1.77E-128	4.28	6.24	3.70E-63	5.26
ENSMUSG00000057596	Trim30d	1.86E-62	8.44E-162	9.74	25.42	9.30E-63	17.58
ENSMUSG00000060519	Tor3a	4.22E-62	1.53E-193	6.40	18.00	2.11E-62	12.20
ENSMUSG00000038058	Nod1	8.34E-61	4.04E-85	15.08	17.10	4.17E-61	16.09
ENSMUSG00000070034	Sp110	9.72E-61	9.66E-144	7.42	15.22	4.86E-61	11.32
ENSMUSG00000026088	Mitd1	7.50E-60	2.12E-269	3.44	9.83	3.75E-60	6.63
ENSMUSG00000070031	Sp140	8.56E-60	1.57E-189	6.85	20.55	4.28E-60	13.70
ENSMUSG00000023307	Marchf5	8.99E-60	1.09E-179	3.74	7.49	4.49E-60	5.62
ENSMUSG00000040483	Xaf1	9.78E-60	5.81E-143	10.96	27.14	4.89E-60	19.05
ENSMUSG00000026222	Sp100	2.18E-59	4.38E-214	4.71	13.40	1.09E-59	9.06
ENSMUSG00000090942	F830016B08Rik	4.45E-73	2.22E-58	1,260.43	517.37	1.11E-58	888.90
ENSMUSG00000090125	Pou3f1	2.82E-58	1.13E-148	26.70	108.31	1.41E-58	67.50
ENSMUSG00000063236	1110038F14Rik	4.59E-67	6.87E-58	4.58	3.49	3.44E-58	4.04
ENSMUSG00000034118	Tpst1	7.47E-58	7.86E-179	5.74	14.91	3.74E-58	10.32
ENSMUSG00000029860	Zyx	1.56E-60	2.11E-54	11.27	7.54	1.05E-54	9.41
ENSMUSG00000073902	Gvin3	8.30E-58	1.38E-53	38.13	23.60	6.92E-54	30.86
ENSMUSG00000040296	Ddx58	5.39E-53	2.40E-276	5.68	33.01	2.70E-53	19.34
ENSMUSG00000029780	Nt5c3	6.90E-53	9.72E-205	5.60	19.90	3.45E-53	12.75

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000030107	Usp18	7.27E-53	1.43E-191	21.06	172.02	3.63E-53	96.54
ENSMUSG00000035352	Ccl12	2.09E-52	2.84E-107	69.33	217.19	1.04E-52	143.26
ENSMUSG00000068606	Gm4841	2.56E-67	2.15E-51	1,242.46	424.89	1.07E-51	833.68
ENSMUSG00000029502	Golga3	3.96E-51	1.06E-118	3.29	4.93	1.98E-51	4.11
ENSMUSG00000037849	Ifi206	8.27E-51	4.32E-109	96.05	446.47	4.13E-51	271.26
ENSMUSG00000000386	Mx1	2.64E-50	1.30E-150	77.70	821.82	1.32E-50	449.76
ENSMUSG00000029771	Irf5	6.26E-50	7.15E-90	3.32	4.13	3.13E-50	3.72
ENSMUSG00000034438	Gbp8	4.22E-88	8.40E-50	85.16	21.64	4.20E-50	53.40
ENSMUSG00000057137	Tmem140	6.07E-49	7.01E-54	4.33	3.87	3.04E-49	4.10
ENSMUSG00000059436	Max	6.85E-49	7.22E-120	2.90	4.34	3.42E-49	3.62
ENSMUSG00000037731	Themis2	7.88E-49	6.18E-114	10.27	23.08	3.94E-49	16.68
ENSMUSG00000032690	Oas2	1.46E-48	1.35E-163	5.90	17.63	7.29E-49	11.77
ENSMUSG00000039997	Ifi203	2.05E-48	2.98E-81	14.29	20.80	1.03E-48	17.55
ENSMUSG00000035725	Prkx	4.75E-48	3.48E-101	3.18	4.38	2.38E-48	3.78
ENSMUSG00000025165	Sectm1a	5.00E-48	8.07E-54	496.04	564.76	2.50E-48	530.40
ENSMUSG00000037685	Atp8a1	3.82E-50	1.27E-47	2.90	2.49	6.35E-48	2.70
ENSMUSG00000026946	Nmi	1.54E-47	1.72E-155	4.60	11.36	7.70E-48	7.98
ENSMUSG00000091649	Phf11b	2.65E-47	2.44E-154	19.56	115.29	1.33E-47	67.43
ENSMUSG00000015947	Fcgr1	2.66E-47	2.81E-143	8.75	27.97	1.33E-47	18.36
ENSMUSG00000092021	Gbp11	6.90E-53	5.11E-47	694.04	384.52	2.56E-47	539.28
ENSMUSG00000097194	9330175E14Rik	1.45E-46	9.77E-53	12.62	11.32	7.27E-47	11.97
ENSMUSG00000022035	Ccdc25	6.94E-46	1.89E-96	4.53	6.89	3.47E-46	5.71
ENSMUSG00000056692	Ilrun	7.07E-46	3.36E-85	2.29	2.70	3.53E-46	2.50
ENSMUSG00000047735	Samd9l	1.65E-45	7.86E-165	5.18	15.81	8.25E-46	10.49
ENSMUSG00000074342	I830077J02Rik	2.41E-45	2.06E-144	6.87	20.79	1.21E-45	13.83

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000025888	Casp1	6.87E-45	3.33E-132	3.51	6.68	3.44E-45	5.10
ENSMUSG00000029417	Cxcl9	4.89E-108	1.08E-44	3,479.08	108.39	5.40E-45	1,793.74
ENSMUSG00000023206	Il15ra	1.60E-44	2.64E-76	22.99	38.77	8.01E-45	30.88
ENSMUSG00000037400	Atp11b	1.72E-44	2.89E-75	3.07	3.61	8.60E-45	3.34
ENSMUSG00000022186	Oxct1	7.53E-44	3.33E-100	2.25	2.94	3.76E-44	2.60
ENSMUSG00000026896	Ifih1	1.27E-43	1.47E-172	7.59	35.13	6.37E-44	21.36
ENSMUSG00000037921	Ddx60	1.92E-43	1.23E-277	6.39	62.22	9.59E-44	34.30
ENSMUSG00000010358	Ifi35	3.17E-42	1.29E-131	5.37	13.67	1.59E-42	9.52
ENSMUSG00000059498	Fcgr3	2.16E-74	4.05E-42	3.14	2.13	2.03E-42	2.64
ENSMUSG00000034855	Cxcl10	5.62E-42	1.61E-57	180.62	211.44	2.81E-42	196.03
ENSMUSG00000041827	Oasl1	1.23E-41	3.05E-91	94.96	406.65	6.15E-42	250.80
ENSMUSG00000020641	Rsad2	1.50E-41	1.43E-147	39.88	460.90	7.51E-42	250.39
ENSMUSG00000026536	Ifi211	2.67E-41	2.44E-80	14.49	26.84	1.34E-41	20.67
ENSMUSG00000049401	Ogfr	3.42E-41	1.08E-118	3.33	6.04	1.71E-41	4.69
ENSMUSG00000034320	Slc26a2	4.81E-53	6.04E-41	3.20	2.47	3.02E-41	2.83
ENSMUSG00000029279	Brdt	4.10E-43	6.02E-41	5.59	4.55	3.03E-41	5.07
ENSMUSG00000053931	Cnn3	3.62E-67	1.19E-40	20.19	7.91	5.93E-41	14.05
ENSMUSG00000039982	Dtx4	6.40E-49	1.20E-40	-4.48	-3.24	5.99E-41	-3.86
ENSMUSG00000020407	Upp1	4.78E-61	2.87E-40	265.89	58.40	1.43E-40	162.14
ENSMUSG00000023961	Enpp4	3.61E-40	1.47E-114	12.30	44.15	1.81E-40	28.23
ENSMUSG00000029474	Rnf34	4.51E-40	1.76E-117	3.49	6.56	2.25E-40	5.03
ENSMUSG00000032661	Oas3	9.98E-40	7.42E-82	7.34	12.52	4.99E-40	9.93
ENSMUSG00000060183	Cxcl11	2.15E-42	1.04E-39	1,783.34	847.84	5.23E-40	1,315.59
ENSMUSG00000048852	Gm12185	2.29E-39	4.50E-43	234.00	247.91	1.14E-39	240.95
ENSMUSG00000022901	Cd86	2.56E-39	1.07E-59	9.54	11.60	1.28E-39	10.57

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000038213	Tapbpl	3.99E-41	3.68E-39	8.84	6.50	1.86E-39	7.67
ENSMUSG00000068245	Phf11d	4.75E-39	3.90E-117	21.13	109.29	2.38E-39	65.21
ENSMUSG00000012519	Mlkl	7.61E-39	1.63E-101	5.30	10.78	3.80E-39	8.04
ENSMUSG00000115338	Pnp	5.27E-38	9.65E-115	6.61	18.07	2.63E-38	12.34
ENSMUSG00000007036	Abhd16a	1.62E-47	6.89E-38	4.06	3.01	3.45E-38	3.53
ENSMUSG00000039304	Tnfsf10	8.33E-38	8.26E-85	102.29	555.87	4.16E-38	329.08
ENSMUSG00000053007	Creb5	1.01E-37	9.02E-76	4.11	5.85	5.05E-38	4.98
ENSMUSG00000066677	Ifi208	1.52E-37	7.95E-76	215.45	1,610.23	7.59E-38	912.84
ENSMUSG00000049488	Tmem67	1.82E-37	1.70E-87	6.06	11.37	9.12E-38	8.71
ENSMUSG00000006418	Rnf114	4.05E-37	2.03E-116	2.85	5.12	2.03E-37	3.99
ENSMUSG00000096727	Psmb9	5.69E-37	7.56E-63	8.10	11.05	2.84E-37	9.58
ENSMUSG00000054203	Ifi205	1.37E-36	2.75E-65	68.87	150.13	6.84E-37	109.50
ENSMUSG00000019794	Katna1	8.02E-36	5.75E-53	3.56	3.89	4.01E-36	3.72
ENSMUSG00000112627	4933412E12Rik	8.07E-36	2.94E-66	9.87	16.15	4.04E-36	13.01
ENSMUSG00000025790	Slco3a1	3.68E-35	1.36E-52	22.17	28.26	1.84E-35	25.22
ENSMUSG00000020089	Ppa1	3.77E-35	2.26E-56	3.83	4.47	1.89E-35	4.15
ENSMUSG00000023959	Clic5	3.89E-35	4.46E-43	96.54	98.37	1.94E-35	97.46
ENSMUSG00000075010	AW112010	4.39E-35	1.52E-66	50.43	117.40	2.19E-35	83.91
ENSMUSG00000050565	Tor1aip2	4.39E-35	1.94E-123	2.86	5.69	2.19E-35	4.28
ENSMUSG00000078922	Tgtp1	1.27E-38	4.40E-35	436.54	247.14	2.20E-35	341.84
ENSMUSG00000028037	Ifi44	8.20E-35	3.38E-94	93.81	774.44	4.10E-35	434.13
ENSMUSG00000031897	Psmb10	3.54E-34	6.44E-68	6.41	10.05	1.77E-34	8.23
ENSMUSG00000024308	Tapbp	1.20E-33	8.04E-55	3.73	4.39	5.99E-34	4.06
ENSMUSG00000004952	Rasa4	3.77E-33	6.42E-76	2.66	3.68	1.89E-33	3.17
ENSMUSG00000066258	Trim12a	4.46E-33	5.13E-69	4.04	5.92	2.23E-33	4.98

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000045210	Vcpip1	4.60E-33	1.09E-118	2.35	4.13	2.30E-33	3.24
ENSMUSG00000104713	Gbp6	6.29E-40	1.12E-32	420.81	185.58	5.60E-33	303.20
ENSMUSG00000021725	Parp8	1.19E-32	2.06E-36	5.30	4.75	5.94E-33	5.03
ENSMUSG00000037997	Parp11	1.24E-32	1.77E-87	5.83	12.75	6.20E-33	9.29
ENSMUSG00000025887	Casp12	3.87E-32	1.88E-46	13.99	17.74	1.94E-32	15.86
ENSMUSG00000035392	Dennd1a	6.55E-32	2.06E-66	2.63	3.42	3.28E-32	3.03
ENSMUSG00000039531	Zup1	2.00E-31	9.95E-85	4.68	9.34	1.00E-31	7.01
ENSMUSG00000028796	Phc2	8.92E-31	1.54E-91	2.48	3.96	4.46E-31	3.22
ENSMUSG00000026110	Mgat4a	3.35E-30	7.11E-33	2.69	2.48	1.68E-30	2.59
ENSMUSG00000050549	Fam241a	3.40E-30	2.88E-71	4.13	6.83	1.70E-30	5.48
ENSMUSG00000052749	Trim30b	5.29E-30	8.45E-85	22.20	115.35	2.64E-30	68.78
ENSMUSG00000045092	S1pr1	1.18E-37	7.95E-30	-7.65	-4.67	3.98E-30	-6.16
ENSMUSG00000000247	Lhx2	9.06E-30	1.29E-82	19.64	84.26	4.53E-30	51.95
ENSMUSG00000022765	Snap29	5.11E-47	1.09E-29	2.76	2.04	5.44E-30	2.40
ENSMUSG00000025492	Ifitm3	1.27E-29	1.30E-112	3.73	9.65	6.35E-30	6.69
ENSMUSG00000024338	Psmb8	1.79E-29	7.30E-54	4.62	6.18	8.96E-30	5.40
ENSMUSG00000042228	Lyn	2.52E-29	1.66E-111	2.39	4.49	1.26E-29	3.44
ENSMUSG00000047798	Cd300lf	3.10E-29	2.06E-86	3.44	6.52	1.55E-29	4.98
ENSMUSG00000073491	Ifi213	3.71E-29	2.78E-63	136.87	767.55	1.86E-29	452.21
ENSMUSG00000078153	Psme2b	4.07E-29	1.16E-56	6.92	11.16	2.03E-29	9.04
ENSMUSG00000019866	Crybg1	5.66E-29	2.29E-96	3.18	6.42	2.83E-29	4.80
ENSMUSG00000002325	Irf9	1.13E-28	1.07E-78	2.30	3.36	5.67E-29	2.83
ENSMUSG00000019806	Aig1	2.13E-39	1.37E-28	4.37	3.03	6.86E-29	3.70
ENSMUSG00000033581	Igf2bp2	1.75E-28	9.74E-32	4.45	3.99	8.77E-29	4.22
ENSMUSG00000027835	Pdcd10	3.40E-28	1.31E-37	2.09	2.11	1.70E-28	2.10

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000105504	Gbp5	3.85E-28	2.13E-30	103.35	68.45	1.93E-28	85.90
ENSMUSG00000021196	Pfkp	2.70E-33	5.24E-28	3.44	2.70	2.62E-28	3.07
ENSMUSG00000038301	Snx10	1.39E-33	7.86E-28	3.60	2.78	3.93E-28	3.19
ENSMUSG00000026395	Ptprc	1.11E-27	6.75E-36	2.13	2.13	5.56E-28	2.13
ENSMUSG00000056144	Trim34a	2.80E-27	2.36E-96	3.62	8.32	1.40E-27	5.97
ENSMUSG00000062488	Ifit3b	3.82E-27	3.29E-194	14.21	560.34	1.91E-27	287.28
ENSMUSG00000052336	Cx3cr1	9.71E-34	4.91E-27	-12.58	-6.84	2.45E-27	-9.71
ENSMUSG00000039501	Znfx1	1.02E-26	1.07E-106	4.12	12.17	5.10E-27	8.15
ENSMUSG00000106734	Gm20559	2.14E-26	1.99E-81	3.52	6.95	1.07E-26	5.24
ENSMUSG00000052512	Nav2	2.23E-26	1.52E-35	-3.69	-3.76	1.12E-26	-3.73
ENSMUSG00000053338	Tarm1	5.39E-26	1.91E-40	10.27	13.19	2.69E-26	11.73
ENSMUSG00000030199	Etv6	6.26E-26	6.05E-33	2.88	2.85	3.13E-26	2.86
ENSMUSG00000060675	Plaat3	7.10E-26	9.15E-28	11.08	8.89	3.60E-26	9.98
ENSMUSG00000028233	Tgs1	7.62E-26	3.33E-31	2.60	2.51	3.81E-26	2.56
ENSMUSG00000031627	Irf2	1.16E-25	1.14E-85	2.32	3.88	5.82E-26	3.10
ENSMUSG00000032508	Myd88	1.37E-25	6.13E-46	3.47	4.34	6.87E-26	3.91
ENSMUSG00000036362	P2ry13	2.15E-25	2.01E-59	4.98	8.73	1.07E-25	6.86
ENSMUSG00000019966	Kitl	4.72E-25	4.86E-33	4.13	4.19	2.36E-25	4.16
ENSMUSG00000071068	Treml2	7.67E-25	2.08E-101	4.72	15.66	3.84E-25	10.19
ENSMUSG00000057143	Trim12c	8.09E-25	7.74E-63	3.45	5.67	4.04E-25	4.56
ENSMUSG00000027035	Cers6	4.44E-29	1.05E-24	5.63	4.03	5.26E-25	4.83
ENSMUSG00000024805	Pcgf5	2.57E-24	1.77E-80	3.51	7.44	1.29E-24	5.47
ENSMUSG00000060802	B2m	2.75E-24	3.22E-41	2.52	2.88	1.38E-24	2.70
ENSMUSG00000037752	Xkr8	5.81E-24	2.04E-41	5.33	6.98	2.90E-24	6.15
ENSMUSG00000087477	Gm13822	9.04E-24	1.67E-48	36.98	127.09	4.52E-24	82.03

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000046157	Tmem229b	9.51E-24	1.93E-94	2.91	6.51	4.76E-24	4.71
ENSMUSG00000029605	Oas1b	1.35E-23	8.92E-98	5.74	22.45	6.73E-24	14.09
ENSMUSG00000030149	Klrk1	1.40E-23	1.42E-41	133.32	444.46	6.98E-24	288.89
ENSMUSG00000091144	Phf11c	1.77E-23	1.24E-102	5.80	25.13	8.85E-24	15.47
ENSMUSG00000028019	Pdgfc	1.26E-33	2.49E-23	4.28	2.94	1.25E-23	3.61
ENSMUSG00000039936	Pik3cd	2.60E-23	5.51E-24	2.97	2.63	1.58E-23	2.80
ENSMUSG00000023341	Mx2	3.18E-23	8.82E-75	33.51	271.31	1.59E-23	152.41
ENSMUSG00000027078	Ube2l6	3.36E-23	5.44E-59	4.93	9.42	1.68E-23	7.18
ENSMUSG00000037242	Clic4	4.70E-23	8.41E-50	3.30	4.70	2.35E-23	4.00
ENSMUSG00000033088	Triobp	6.89E-23	4.09E-79	2.19	3.59	3.44E-23	2.89
ENSMUSG00000027219	Slc28a2	8.35E-23	3.87E-88	6.18	23.63	4.17E-23	14.90
ENSMUSG00000027199	Gatm	1.05E-22	1.53E-32	2.25	2.35	5.23E-23	2.30
ENSMUSG00000044468	Tent5c	1.06E-22	4.85E-25	2.75	2.54	5.31E-23	2.64
ENSMUSG00000079659	Tmem243	3.20E-22	2.94E-50	3.29	4.84	1.60E-22	4.07
ENSMUSG00000025877	Hk3	4.01E-22	1.13E-25	3.62	3.37	2.01E-22	3.49
ENSMUSG00000093661	Eif4e3	4.58E-22	1.94E-44	2.08	2.49	2.29E-22	2.28
ENSMUSG00000002227	Mov10	6.26E-22	3.24E-107	4.28	16.95	3.13E-22	10.61
ENSMUSG00000000791	Il12rb1	7.82E-22	4.70E-27	53.20	52.16	3.91E-22	52.68
ENSMUSG00000020134	Peli1	1.03E-21	1.48E-53	4.01	6.86	5.15E-22	5.43
ENSMUSG00000032265	Tent5a	1.16E-21	2.76E-100	2.95	7.79	5.81E-22	5.37
ENSMUSG00000038179	Slamf7	1.56E-21	1.46E-33	6.08	7.25	7.82E-22	6.67
ENSMUSG00000019768	Esr1	1.71E-21	3.82E-34	4.96	5.99	8.56E-22	5.48
ENSMUSG00000028466	Creb3	1.86E-21	1.23E-26	2.55	2.50	9.32E-22	2.53
ENSMUSG00000078606	Gvin2	2.35E-21	1.25E-24	69.02	76.31	1.18E-21	72.66
ENSMUSG00000037820	Tgm2	2.42E-21	1.46E-36	2.77	3.24	1.21E-21	3.01

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000041238	Rbbp8	1.17E-26	3.13E-21	3.17	2.46	1.57E-21	2.81
ENSMUSG00000027340	Slc23a2	4.04E-21	4.54E-25	2.60	2.49	2.02E-21	2.54
ENSMUSG00000081769	Gm12216	4.53E-21	2.62E-42	7.95	13.71	2.27E-21	10.83
ENSMUSG00000044703	Phf11a	6.21E-21	2.44E-69	48.78	612.88	3.10E-21	330.83
ENSMUSG00000078763	Slfn1	7.62E-21	5.71E-54	98.15	1,023.58	3.81E-21	560.87
ENSMUSG00000033487	Fndc3a	8.83E-21	1.67E-151	2.38	7.86	4.41E-21	5.12
ENSMUSG00000071714	Csf2rb2	8.90E-21	6.37E-31	2.12	2.24	4.45E-21	2.18
ENSMUSG00000050075	Gpr171	3.00E-21	9.02E-21	12.03	8.82	6.01E-21	10.42
ENSMUSG00000085977	Gm5970	1.83E-28	1.20E-20	162.20	63.67	6.02E-21	112.93
ENSMUSG00000002797	Ggct	5.36E-45	1.28E-20	9.36	3.81	6.42E-21	6.58
ENSMUSG00000048118	Arid4a	1.35E-20	5.96E-30	2.46	2.60	6.74E-21	2.53
ENSMUSG00000075602	Ly6a	2.48E-22	1.47E-20	27.16	15.92	7.48E-21	21.54
ENSMUSG00000024789	Jak2	1.69E-20	1.28E-55	3.92	7.29	8.44E-21	5.60
ENSMUSG00000032883	Acsl3	2.15E-20	5.20E-34	-3.25	-3.82	1.07E-20	-3.53
ENSMUSG00000030102	Itpr1	2.19E-20	9.15E-67	5.29	14.30	1.09E-20	9.79
ENSMUSG00000024472	Dcp2	2.66E-20	5.77E-114	2.20	5.12	1.33E-20	3.66
ENSMUSG00000037926	Ssh2	2.72E-20	5.77E-35	-3.12	-3.72	1.36E-20	-3.42
ENSMUSG00000039285	Azi2	2.77E-20	1.03E-105	2.23	4.94	1.38E-20	3.58
ENSMUSG00000050957	Insl6	3.22E-20	1.30E-39	3.53	4.73	1.61E-20	4.13
ENSMUSG00000022564	Grina	5.25E-20	1.02E-34	2.13	2.40	2.63E-20	2.27
ENSMUSG00000017756	Slc12a7	6.28E-20	3.74E-38	2.39	2.89	3.14E-20	2.64
ENSMUSG00000053101	Gpr141	2.72E-23	1.02E-19	3.98	3.04	5.12E-20	3.51
ENSMUSG00000026814	Eng	1.03E-19	4.89E-58	2.48	3.94	5.14E-20	3.21
ENSMUSG00000071042	Rasgrp3	1.07E-19	8.74E-27	-4.62	-4.70	5.36E-20	-4.66
ENSMUSG00000038910	Plcl2	1.11E-19	2.79E-41	2.72	3.58	5.54E-20	3.15

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000032596	Uba7	1.13E-19	4.08E-92	3.25	9.51	5.63E-20	6.38
ENSMUSG00000052776	Oas1a	1.32E-19	3.97E-83	4.34	14.05	6.58E-20	9.19
ENSMUSG00000063800	Prpf38a	1.58E-19	6.47E-105	2.64	7.18	7.92E-20	4.91
ENSMUSG00000053846	Lipg	1.97E-19	9.47E-50	104.18	1,009.31	9.87E-20	556.74
ENSMUSG00000024030	Abcg1	2.22E-19	2.75E-56	3.07	5.42	1.11E-19	4.24
ENSMUSG00000050002	Idnk	2.39E-19	2.75E-26	2.64	2.70	1.19E-19	2.67
ENSMUSG00000054676	1600014C10Rik	2.90E-19	1.33E-75	4.60	14.51	1.45E-19	9.55
ENSMUSG00000024074	Crim1	2.91E-19	1.68E-48	3.22	5.14	1.46E-19	4.18
ENSMUSG00000004846	Plod3	2.95E-19	2.83E-61	2.09	3.19	1.48E-19	2.64
ENSMUSG00000079339	Ifit1bl1	2.96E-19	8.82E-227	12.55	2,323.05	1.48E-19	1,167.80
ENSMUSG00000042901	Aida	4.44E-19	8.81E-64	2.62	4.73	2.22E-19	3.68
ENSMUSG00000049657	Zbtb5	4.76E-19	8.43E-24	2.83	2.79	2.38E-19	2.81
ENSMUSG00000029428	Stx2	5.40E-25	6.94E-19	3.72	2.71	3.47E-19	3.22
ENSMUSG00000037965	Zc3h7a	7.17E-19	5.35E-48	2.40	3.43	3.58E-19	2.92
ENSMUSG00000022501	Prm1	7.47E-19	3.47E-38	79.75	334.02	3.74E-19	206.88
ENSMUSG00000093507	Gm20627	8.73E-25	8.30E-19	22.76	13.66	4.15E-19	18.21
ENSMUSG00000070427	Il18bp	8.84E-19	7.81E-41	8.33	15.82	4.42E-19	12.07
ENSMUSG00000025279	Dnase1l3	6.32E-19	3.87E-19	97.68	72.51	5.09E-19	85.10
ENSMUSG00000021895	Arhgef3	1.05E-18	4.56E-21	4.93	4.41	5.26E-19	4.67
ENSMUSG00000029826	Zc3hav1	1.31E-18	1.68E-69	2.10	3.55	6.55E-19	2.83
ENSMUSG00000029156	Sgcb	1.63E-18	1.79E-59	2.62	4.59	8.17E-19	3.61
ENSMUSG00000036469	Marchf1	2.02E-18	2.89E-40	2.94	4.08	1.01E-18	3.51
ENSMUSG00000104955	1700016F12Rik	4.09E-27	2.04E-18	226.41	68.50	1.02E-18	147.45
ENSMUSG00000055013	Agap1	2.24E-18	4.11E-28	-3.00	-3.30	1.12E-18	-3.15
ENSMUSG00000017652	Cd40	1.37E-21	2.50E-18	46.41	21.84	1.25E-18	34.12

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000038037	Socs1	1.22E-31	3.03E-18	60.84	15.30	1.51E-18	38.07
ENSMUSG00000063388	BC023105	1.58E-18	1.46E-18	58.64	48.05	1.52E-18	53.35
ENSMUSG00000020564	Atxn7l1	3.15E-18	1.27E-22	2.46	2.41	1.57E-18	2.44
ENSMUSG00000034111	Tmed8	3.26E-18	3.86E-21	2.32	2.22	1.63E-18	2.27
ENSMUSG00000029862	Clcn1	3.37E-18	3.53E-71	10.46	65.04	1.68E-18	37.75
ENSMUSG00000023249	Parp3	3.38E-18	2.00E-37	4.35	6.42	1.69E-18	5.38
ENSMUSG00000022216	Psme1	4.80E-18	1.16E-37	2.94	3.95	2.40E-18	3.44
ENSMUSG00000030852	Tacc2	4.91E-18	1.37E-30	-5.38	-7.23	2.46E-18	-6.30
ENSMUSG00000094796	BC147527	5.49E-18	1.75E-42	44.04	232.77	2.74E-18	138.40
ENSMUSG00000026482	Rgl1	5.86E-18	9.04E-42	4.44	7.46	2.93E-18	5.95
ENSMUSG00000026764	Kif5c	6.22E-18	1.91E-58	3.83	8.38	3.11E-18	6.11
ENSMUSG00000022814	Umps	7.51E-18	5.30E-26	-3.42	-3.65	3.76E-18	-3.54
ENSMUSG00000028480	Glipr2	7.68E-18	5.82E-75	3.92	11.88	3.84E-18	7.90
ENSMUSG00000032232	Cgnl1	8.30E-22	9.30E-18	-4.86	-3.27	4.65E-18	-4.07
ENSMUSG00000033538	Casp4	1.06E-17	8.48E-25	4.79	5.10	5.28E-18	4.95
ENSMUSG00000026466	Tor1aip1	1.15E-17	3.65E-97	2.36	5.96	5.75E-18	4.16
ENSMUSG00000054520	Sh3bp2	1.22E-17	2.42E-33	2.02	2.34	6.09E-18	2.18
ENSMUSG00000020128	Vps54	1.36E-17	1.14E-41	2.22	2.94	6.79E-18	2.58
ENSMUSG00000032724	Abtb2	1.36E-17	1.36E-32	9.44	14.94	6.79E-18	12.19
ENSMUSG00000030530	Furin	2.76E-18	1.40E-17	2.49	2.18	8.37E-18	2.33
ENSMUSG00000027360	Hdc	2.48E-17	7.01E-54	22.20	152.91	1.24E-17	87.56
ENSMUSG00000037434	Slc30a1	2.74E-17	1.44E-45	3.28	5.51	1.37E-17	4.39
ENSMUSG00000001156	Mxd1	2.80E-17	2.91E-42	5.47	10.48	1.40E-17	7.97
ENSMUSG00000031824	6430548M08Rik	4.38E-17	1.58E-23	-4.31	-4.46	2.19E-17	-4.39
ENSMUSG00000027580	Helz2	4.41E-17	4.18E-33	9.97	16.85	2.20E-17	13.41

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000034987	Hrh2	5.69E-17	1.13E-25	13.92	18.40	2.85E-17	16.16
ENSMUSG00000070501	Ifi214	5.70E-17	1.52E-52	51.14	655.51	2.85E-17	353.32
ENSMUSG00000026981	Il1rn	6.80E-17	3.82E-27	6.62	8.23	3.40E-17	7.43
ENSMUSG00000026068	Il18rap	1.63E-20	8.07E-17	12.88	7.69	4.04E-17	10.29
ENSMUSG00000026797	Stxbp1	8.63E-17	3.75E-32	2.95	3.74	4.32E-17	3.34
ENSMUSG00000005580	Adcy9	1.18E-16	1.82E-22	-3.27	-3.29	5.89E-17	-3.28
ENSMUSG00000046062	Ppp1r15b	1.44E-16	7.26E-41	2.08	2.76	7.19E-17	2.42
ENSMUSG00000007617	Homer1	2.48E-16	3.25E-56	2.58	4.71	1.24E-16	3.65
ENSMUSG00000085501	Gm11772	2.63E-16	2.26E-54	5.85	17.24	1.32E-16	11.55
ENSMUSG00000068015	Lrch1	2.64E-16	1.53E-38	3.32	5.10	1.32E-16	4.21
ENSMUSG00000023903	Mmp25	3.21E-18	2.66E-16	49.85	27.27	1.35E-16	38.56
ENSMUSG00000042719	Naa25	3.04E-16	6.43E-40	2.54	3.62	1.52E-16	3.08
ENSMUSG00000020057	Dram1	7.79E-24	3.73E-16	6.60	3.87	1.86E-16	5.24
ENSMUSG00000032333	Stoml1	4.36E-16	5.21E-45	2.35	3.51	2.18E-16	2.93
ENSMUSG00000047534	Mis18bp1	4.36E-16	2.30E-23	-2.62	-2.76	2.18E-16	-2.69
ENSMUSG00000030560	Ctsc	3.54E-24	4.70E-16	6.81	3.88	2.35E-16	5.34
ENSMUSG00000097457	#NV	5.26E-16	8.36E-51	26.32	221.22	2.63E-16	123.77
ENSMUSG00000027882	Stxbp3	1.00E-15	1.26E-44	2.68	4.33	5.00E-16	3.50
ENSMUSG00000041649	Klf8	1.04E-15	5.08E-35	3.49	5.16	5.21E-16	4.32
ENSMUSG00000022587	Ly6e	1.10E-15	3.05E-36	4.55	7.65	5.48E-16	6.10
ENSMUSG00000079470	Utp14b	1.24E-15	3.53E-17	-4.09	-3.48	6.37E-16	-3.79
ENSMUSG00000032434	Cmtm6	1.48E-15	3.43E-43	2.27	3.33	7.38E-16	2.80
ENSMUSG00000027366	Sppl2a	1.64E-15	1.57E-31	2.53	3.21	8.22E-16	2.87
ENSMUSG00000021583	Erap1	1.72E-21	1.67E-15	2.87	2.19	8.34E-16	2.53
ENSMUSG00000024539	Ptpn2	1.87E-20	1.96E-15	2.76	2.16	9.81E-16	2.46

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000036712	Cyld	2.00E-15	2.62E-23	2.00	2.12	9.99E-16	2.06
ENSMUSG00000041483	Zfp281	2.72E-15	2.08E-19	2.82	2.79	1.36E-15	2.81
ENSMUSG00000029313	Aff1	3.37E-15	1.22E-31	2.44	3.11	1.69E-15	2.77
ENSMUSG00000029204	Rhoh	4.11E-15	1.08E-16	5.96	5.18	2.11E-15	5.57
ENSMUSG00000024660	Incenp	3.51E-15	7.48E-16	-2.28	-2.07	2.13E-15	-2.17
ENSMUSG00000039682	Lap3	2.21E-19	4.41E-15	3.37	2.55	2.20E-15	2.96
ENSMUSG00000021067	Sav1	5.51E-15	1.99E-30	2.14	2.60	2.76E-15	2.37
ENSMUSG00000020707	Rnf135	5.71E-15	1.88E-97	2.13	5.42	2.86E-15	3.78
ENSMUSG00000054976	Nyap2	5.11E-16	5.83E-15	10.25	7.39	3.17E-15	8.82
ENSMUSG00000026112	Coa5	7.23E-15	2.53E-22	2.17	2.31	3.61E-15	2.24
ENSMUSG00000049091	Sephs2	8.14E-15	1.94E-39	-2.66	-4.16	4.07E-15	-3.41
ENSMUSG00000026580	Selp	4.28E-29	8.97E-15	103.85	22.98	4.49E-15	63.42
ENSMUSG00000041707	Tmem273	9.32E-15	3.85E-17	-2.26	-2.15	4.68E-15	-2.21
ENSMUSG00000068749	Psma5	9.77E-15	9.08E-29	2.24	2.70	4.89E-15	2.47
ENSMUSG00000041736	Tspo	1.04E-14	4.82E-42	2.51	3.97	5.22E-15	3.24
ENSMUSG00000071350	Setdb2	1.06E-14	9.96E-66	4.43	15.94	5.31E-15	10.18
ENSMUSG00000064181	Rab3ip	1.21E-14	1.60E-20	2.69	2.82	6.04E-15	2.76
ENSMUSG00000020611	Gna13	1.84E-19	1.22E-14	2.76	2.15	6.11E-15	2.45
ENSMUSG00000100975	Gm28875	9.95E-15	2.38E-15	-2.41	-2.16	6.16E-15	-2.29
ENSMUSG00000022575	Gsdmd	1.47E-14	5.54E-27	2.97	3.70	7.34E-15	3.34
ENSMUSG00000051339	2900026A02Rik	3.00E-16	1.45E-14	-3.47	-2.67	7.38E-15	-3.07
ENSMUSG00000021880	Rnase6	2.18E-35	2.21E-14	10.65	3.75	1.11E-14	7.20
ENSMUSG00000040774	Cept1	2.63E-14	4.49E-38	2.70	4.19	1.32E-14	3.45
ENSMUSG00000053835	H2-T24	4.23E-14	6.12E-42	8.19	25.18	2.11E-14	16.68
ENSMUSG00000106990	Gm42547	4.63E-14	1.28E-15	8.03	6.87	2.38E-14	7.45

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000044340	Phlpp1	5.32E-14	2.06E-21	3.96	4.48	2.66E-14	4.22
ENSMUSG00000021384	Susd3	5.50E-14	2.08E-22	-3.58	-4.14	2.75E-14	-3.86
ENSMUSG00000034297	Med13	2.51E-20	5.80E-14	2.93	2.17	2.90E-14	2.55
ENSMUSG00000068129	Cst7	7.75E-14	3.72E-17	5.54	5.34	3.88E-14	5.44
ENSMUSG00000079197	Psme2	8.62E-14	4.21E-16	4.19	3.90	4.33E-14	4.04
ENSMUSG00000044701	Il27	9.01E-14	5.39E-18	37.59	38.82	4.51E-14	38.21
ENSMUSG00000112843	Gm46224	8.82E-14	3.41E-15	2.35	2.20	4.58E-14	2.27
ENSMUSG00000116549	Gm49728	9.21E-14	2.07E-19	26.01	38.89	4.61E-14	32.45
ENSMUSG00000029009	Mthfr	1.29E-13	2.50E-92	2.65	9.36	6.45E-14	6.01
ENSMUSG00000038256	Bcl9	1.33E-13	2.70E-54	2.78	6.09	6.67E-14	4.43
ENSMUSG00000048534	Jaml	1.44E-13	4.46E-43	10.76	45.70	7.19E-14	28.23
ENSMUSG00000087175	Gm15133	1.44E-13	1.66E-29	5.14	8.51	7.19E-14	6.82
ENSMUSG00000001741	Il16	1.44E-13	1.06E-16	-3.78	-3.55	7.23E-14	-3.67
ENSMUSG00000025997	Ikzf2	4.07E-14	1.07E-13	5.09	4.07	7.41E-14	4.58
ENSMUSG00000045795	Whamm	1.51E-13	3.00E-30	2.88	4.03	7.55E-14	3.46
ENSMUSG00000030157	Clec2d	1.60E-13	2.57E-22	4.16	5.04	8.01E-14	4.60
ENSMUSG00000045827	Serpinb9	1.60E-13	3.49E-19	5.89	6.42	8.02E-14	6.16
ENSMUSG00000035042	Ccl5	1.82E-13	1.55E-18	41.75	46.82	9.10E-14	44.28
ENSMUSG00000043279	Trim56	2.30E-13	3.04E-27	2.25	2.79	1.15E-13	2.52
ENSMUSG00000020272	Stk10	2.50E-13	4.12E-34	-2.53	-3.83	1.25E-13	-3.18
ENSMUSG00000021614	Vcan	2.95E-13	3.63E-78	4.71	28.11	1.47E-13	16.41
ENSMUSG00000067212	H2-T23	3.95E-13	3.39E-21	8.67	11.41	1.97E-13	10.04
ENSMUSG00000058624	Gda	5.26E-27	4.14E-13	4.47	2.47	2.07E-13	3.47
ENSMUSG00000032841	Prr5l	1.55E-19	4.28E-13	5.59	3.39	2.14E-13	4.49
ENSMUSG00000026893	Gca	4.55E-13	6.31E-39	4.54	10.06	2.28E-13	7.30

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000025764	Jade1	4.72E-13	2.43E-20	-2.91	-3.22	2.36E-13	-3.07
ENSMUSG00000059970	Hspa2	5.06E-13	7.03E-14	2.83	2.57	2.88E-13	2.70
ENSMUSG00000022014	Epsti1	6.22E-13	5.62E-118	2.69	14.30	3.11E-13	8.50
ENSMUSG00000024245	Tmem178	7.38E-13	5.11E-21	9.36	12.60	3.69E-13	10.98
ENSMUSG00000024675	Ms4a4c	7.63E-13	1.36E-78	14.65	379.87	3.81E-13	197.26
ENSMUSG00000024339	Tap2	8.25E-13	4.56E-19	7.10	8.20	4.12E-13	7.65
ENSMUSG00000042167	Tent2	8.28E-13	1.44E-37	2.26	3.40	4.14E-13	2.83
ENSMUSG00000029366	Dck	9.23E-13	2.70E-62	2.79	7.48	4.62E-13	5.13
ENSMUSG00000066152	Slc31a2	9.59E-13	1.18E-16	2.89	2.90	4.79E-13	2.90
ENSMUSG00000037826	Ppm1k	1.00E-12	1.62E-91	3.13	14.83	5.02E-13	8.98
ENSMUSG00000006411	Nectin4	1.05E-12	6.49E-65	3.08	9.43	5.24E-13	6.26
ENSMUSG00000042350	Arel1	1.21E-12	6.45E-92	2.30	7.30	6.03E-13	4.80
ENSMUSG00000001123	Lgals9	1.50E-12	8.27E-83	2.33	6.94	7.50E-13	4.64
ENSMUSG00000105283	Gm33370	1.51E-12	3.27E-23	3.93	5.19	7.57E-13	4.56
ENSMUSG00000033576	Apol6	4.26E-14	1.54E-12	43.55	28.33	7.89E-13	35.94
ENSMUSG00000031639	Tlr3	1.92E-12	1.28E-133	2.94	22.51	9.62E-13	12.73
ENSMUSG00000016206	H2-M3	2.02E-12	1.08E-22	2.76	3.35	1.01E-12	3.05
ENSMUSG00000035232	Pdk3	2.45E-12	4.11E-42	2.26	3.78	1.23E-12	3.02
ENSMUSG00000003283	Hck	2.49E-12	1.30E-21	2.86	3.42	1.24E-12	3.14
ENSMUSG00000020092	Pald1	2.55E-12	2.26E-29	-4.11	-8.03	1.28E-12	-6.07
ENSMUSG00000087700	Gm15283	2.72E-12	2.14E-19	30.74	55.30	1.36E-12	43.02
ENSMUSG00000024451	Arap3	2.73E-12	6.56E-17	-2.75	-2.80	1.37E-12	-2.78
ENSMUSG00000020826	Nos2	3.06E-19	2.78E-12	369.43	63.07	1.39E-12	216.25
ENSMUSG00000030745	Il21r	2.79E-12	1.42E-42	2.34	4.08	1.40E-12	3.21
ENSMUSG00000005973	Rcn1	2.80E-12	5.10E-18	2.38	2.52	1.40E-12	2.45

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000039841	Zfp800	3.32E-12	7.03E-15	4.05	3.87	1.66E-12	3.96
ENSMUSG00000035929	H2-Q4	3.44E-12	1.56E-22	6.38	9.35	1.72E-12	7.86
ENSMUSG00000061232	H2-K1	4.06E-12	5.19E-17	2.25	2.33	2.03E-12	2.29
ENSMUSG00000022867	Usp25	4.07E-12	2.31E-60	2.19	4.74	2.04E-12	3.47
ENSMUSG00000039934	Gsap	2.40E-19	4.74E-12	3.97	2.58	2.37E-12	3.27
ENSMUSG00000020023	Tmcc3	7.17E-12	6.66E-28	2.99	4.42	3.58E-12	3.70
ENSMUSG00000025612	Bach1	7.40E-12	7.10E-26	2.42	3.17	3.70E-12	2.79
ENSMUSG00000021877	Arf4	7.41E-12	4.40E-29	2.19	2.97	3.70E-12	2.58
ENSMUSG00000050394	Armcx6	7.71E-12	1.94E-56	4.33	16.01	3.86E-12	10.17
ENSMUSG00000004266	Ptpn6	3.66E-13	8.12E-12	2.91	2.41	4.24E-12	2.66
ENSMUSG00000031785	Adgrg1	1.06E-11	7.39E-15	-3.75	-3.56	5.30E-12	-3.65
ENSMUSG00000021624	Cd180	1.13E-11	1.88E-51	2.08	3.93	5.67E-12	3.00
ENSMUSG00000052477	C130026I21Rik	1.16E-11	1.04E-42	6.04	20.88	5.80E-12	13.46
ENSMUSG00000022504	Ciita	1.41E-64	1.19E-11	44.63	4.10	5.93E-12	24.37
ENSMUSG00000023147	Get1	1.42E-11	1.31E-19	-2.57	-2.95	7.09E-12	-2.76
ENSMUSG00000032750	Gab3	1.89E-11	2.46E-17	-3.31	-3.65	9.47E-12	-3.48
ENSMUSG00000023953	Polh	2.02E-11	3.00E-15	-2.38	-2.36	1.01E-11	-2.37
ENSMUSG00000017412	Cacnb4	2.04E-11	1.40E-18	6.18	8.04	1.02E-11	7.11
ENSMUSG00000039116	Adgrg6	3.99E-14	2.38E-11	3.07	2.41	1.19E-11	2.74
ENSMUSG00000079293	Clec7a	2.50E-11	5.60E-20	2.79	3.34	1.25E-11	3.07
ENSMUSG00000024601	Isoc1	2.60E-11	5.17E-46	2.09	3.73	1.30E-11	2.91
ENSMUSG00000047098	Rnf31	2.93E-11	6.63E-32	2.67	4.22	1.47E-11	3.45
ENSMUSG00000046908	Ltb4r1	5.58E-36	2.97E-11	21.56	4.75	1.49E-11	13.16
ENSMUSG00000049130	C5ar1	3.79E-23	2.97E-11	-3.61	-2.14	1.49E-11	-2.88
ENSMUSG00000034575	Tent4a	3.49E-11	1.19E-38	3.09	6.42	1.74E-11	4.76

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000025089	Gfra1	3.59E-11	4.52E-36	6.78	21.17	1.80E-11	13.97
ENSMUSG00000090231	Cfb	3.50E-11	1.27E-12	76.12	66.71	1.81E-11	71.41
ENSMUSG00000025076	Casp7	3.69E-11	3.56E-27	2.35	3.26	1.85E-11	2.81
ENSMUSG00000020357	Flt4	3.72E-11	2.00E-30	17.53	75.28	1.86E-11	46.40
ENSMUSG00000096954	#NV	9.08E-25	4.16E-11	10.91	3.98	2.08E-11	7.44
ENSMUSG00000052760	A630001G21Rik	5.03E-11	8.14E-27	2.27	3.09	2.51E-11	2.68
ENSMUSG00000051065	Mb21d2	1.04E-36	6.02E-11	12.87	3.63	3.01E-11	8.25
ENSMUSG00000046718	Bst2	6.63E-11	5.08E-44	3.02	7.24	3.31E-11	5.13
ENSMUSG00000029648	Flt1	7.14E-11	8.54E-55	6.25	39.34	3.57E-11	22.80
ENSMUSG00000019699	Akt3	7.46E-11	1.54E-41	2.42	4.66	3.73E-11	3.54
ENSMUSG00000034265	Zdhhc14	7.83E-13	7.64E-11	-3.50	-2.67	3.86E-11	-3.08
ENSMUSG00000038774	Ascc3	7.82E-11	4.31E-43	2.06	3.58	3.91E-11	2.82
ENSMUSG00000031596	Slc7a2	8.73E-12	7.06E-11	8.09	5.72	3.97E-11	6.91
ENSMUSG00000035125	Gcfc2	7.12E-11	9.37E-12	-2.27	-2.04	4.03E-11	-2.16
ENSMUSG00000033880	Lgals3bp	8.70E-11	6.00E-40	2.13	3.67	4.35E-11	2.90
ENSMUSG00000057135	Scimp	9.59E-11	7.72E-71	6.34	66.49	4.79E-11	36.42
ENSMUSG00000031304	Il2rg	9.52E-11	3.86E-12	2.80	2.60	4.95E-11	2.70
ENSMUSG00000042489	Clspn	1.29E-11	8.93E-11	-4.90	-3.70	5.11E-11	-4.30
ENSMUSG00000024732	Ccdc86	1.05E-10	5.89E-40	2.15	3.74	5.27E-11	2.95
ENSMUSG00000022364	Tbc1d31	1.09E-10	5.96E-16	-2.98	-3.20	5.45E-11	-3.09
ENSMUSG00000044350	Lacc1	1.14E-10	2.77E-30	2.72	4.49	5.68E-11	3.60
ENSMUSG00000044700	Tmem201	1.24E-10	2.66E-17	-3.11	-3.59	6.20E-11	-3.35
ENSMUSG00000037860	Aim2	1.29E-10	4.15E-69	2.09	5.37	6.44E-11	3.73
ENSMUSG00000030269	Mtmr14	1.53E-10	1.31E-15	2.59	2.78	7.63E-11	2.68
ENSMUSG00000021758	Ddx4	1.62E-10	1.26E-44	7.82	43.78	8.10E-11	25.80

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000023952	Gtpbp2	1.67E-10	6.35E-28	2.13	3.00	8.35E-11	2.57
ENSMUSG00000054728	Phactr1	1.87E-10	1.45E-21	8.07	15.02	9.34E-11	11.54
ENSMUSG00000073490	Ifi207	2.24E-10	4.05E-33	2.73	4.94	1.12E-10	3.83
ENSMUSG00000057367	Birc2	2.28E-10	2.04E-17	2.02	2.23	1.14E-10	2.12
ENSMUSG00000027009	Itga4	1.48E-23	2.57E-10	4.34	2.30	1.28E-10	3.32
ENSMUSG00000020476	Dbnl	2.59E-10	1.31E-47	2.22	4.63	1.29E-10	3.43
ENSMUSG00000046688	Tifa	2.67E-10	1.30E-13	2.41	2.43	1.33E-10	2.42
ENSMUSG00000024754	Cemip2	2.88E-10	2.49E-15	3.32	3.64	1.44E-10	3.48
ENSMUSG00000026770	Il2ra	2.95E-10	2.02E-32	15.51	89.93	1.47E-10	52.72
ENSMUSG00000047409	Ctdspl	3.19E-10	5.73E-22	-2.75	-3.82	1.60E-10	-3.28
ENSMUSG00000004446	Bid	3.43E-10	2.28E-34	2.08	3.33	1.72E-10	2.71
ENSMUSG00000040276	Pacsin1	3.55E-10	1.23E-18	15.91	30.41	1.77E-10	23.16
ENSMUSG00000009575	Cbx5	3.11E-10	4.81E-11	-2.43	-2.23	1.80E-10	-2.33
ENSMUSG00000000184	Ccnd2	3.71E-10	2.10E-46	3.05	8.45	1.86E-10	5.75
ENSMUSG00000017715	Pgs1	6.56E-23	3.73E-10	3.90	2.18	1.87E-10	3.04
ENSMUSG00000106959	Gm42548	9.63E-15	3.84E-10	8.36	4.82	1.92E-10	6.59
ENSMUSG00000025591	Tma16	1.39E-15	4.30E-10	3.94	2.58	2.15E-10	3.26
ENSMUSG00000061607	Mdc1	4.23E-10	3.13E-11	-2.30	-2.13	2.27E-10	-2.21
ENSMUSG00000071713	Csf2rb	4.56E-10	2.84E-12	2.21	2.16	2.29E-10	2.18
ENSMUSG00000039217	Il18	4.67E-10	1.15E-72	2.32	7.50	2.34E-10	4.91
ENSMUSG00000018909	Arrb1	5.07E-10	1.31E-31	-2.29	-3.78	2.54E-10	-3.04
ENSMUSG00000014846	Tppp3	1.22E-10	3.91E-10	6.56	4.99	2.57E-10	5.77
ENSMUSG00000024786	Majin	1.62E-10	3.70E-10	33.32	24.54	2.66E-10	28.93
ENSMUSG00000029438	Bcl7a	5.45E-10	8.82E-24	-4.03	-8.81	2.73E-10	-6.42
ENSMUSG00000107320	Gm42549	2.57E-11	5.41E-10	6.03	4.38	2.83E-10	5.20

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000092564	BC051226	6.39E-10	4.29E-58	2.00	4.39	3.19E-10	3.20
ENSMUSG00000020694	Tlk2	6.59E-10	6.91E-40	2.04	3.59	3.30E-10	2.82
ENSMUSG00000068417	Pnp2	6.80E-10	2.67E-32	6.15	18.41	3.40E-10	12.28
ENSMUSG00000028793	Rnf19b	2.26E-12	6.83E-10	4.84	3.37	3.43E-10	4.10
ENSMUSG00000031647	Mfap3l	7.57E-10	1.62E-18	-2.54	-3.14	3.78E-10	-2.84
ENSMUSG00000026131	Dst	5.78E-14	8.38E-10	3.29	2.36	4.19E-10	2.83
ENSMUSG00000000409	Lck	9.37E-10	1.42E-22	4.89	8.55	4.69E-10	6.72
ENSMUSG00000031403	Dkc1	9.97E-10	6.53E-31	-3.02	-6.01	4.98E-10	-4.51
ENSMUSG00000038658	Ric1	1.00E-09	3.94E-15	2.05	2.21	5.00E-10	2.13
ENSMUSG00000079442	St6galnac4	4.21E-27	1.10E-09	5.28	2.34	5.52E-10	3.81
ENSMUSG00000018983	E2f2	1.93E-10	9.59E-10	-2.87	-2.40	5.76E-10	-2.64
ENSMUSG00000055884	Fancm	2.51E-10	9.32E-10	-3.47	-2.69	5.91E-10	-3.08
ENSMUSG00000041633	Kctd12b	7.08E-11	1.15E-09	-3.76	-2.85	6.12E-10	-3.31
ENSMUSG00000026974	Zmynd19	1.25E-09	3.03E-21	-2.29	-3.06	6.25E-10	-2.68
ENSMUSG00000046096	Mosmo	1.25E-09	4.24E-24	2.07	2.76	6.27E-10	2.41
ENSMUSG00000038332	Sesn1	1.26E-09	3.53E-13	-5.43	-5.69	6.31E-10	-5.56
ENSMUSG00000037406	Htra4	1.36E-09	4.98E-30	6.37	18.63	6.78E-10	12.50
ENSMUSG00000022684	Bfar	1.38E-09	3.15E-22	2.20	2.90	6.88E-10	2.55
ENSMUSG00000022126	Acod1	5.98E-10	7.87E-10	23.70	15.31	6.93E-10	19.50
ENSMUSG00000031971	Ccsap	1.39E-09	3.05E-11	-5.22	-4.62	7.10E-10	-4.92
ENSMUSG00000026581	Sell	1.66E-09	2.50E-24	10.71	32.40	8.32E-10	21.55
ENSMUSG00000007570	Fance	1.79E-09	5.11E-12	-2.33	-2.29	8.98E-10	-2.31
ENSMUSG00000048922	Cdca2	1.80E-09	1.11E-22	-3.34	-5.44	9.02E-10	-4.39
ENSMUSG00000024164	C3	4.15E-12	1.89E-09	15.47	8.01	9.45E-10	11.74
ENSMUSG00000038866	Zcchc2	1.91E-09	5.38E-42	2.51	5.66	9.56E-10	4.08

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000020464	Pnpt1	1.92E-09	1.05E-42	2.47	5.51	9.62E-10	3.99
ENSMUSG00000047446	Arl4a	1.93E-09	1.12E-27	2.22	3.37	9.64E-10	2.80
ENSMUSG00000020593	Lpin1	2.09E-09	6.56E-29	-2.91	-5.52	1.05E-09	-4.21
ENSMUSG00000076441	Ass1	2.18E-09	1.75E-17	3.36	4.33	1.09E-09	3.84
ENSMUSG00000055322	Tns1	2.25E-09	1.74E-10	-2.80	-2.58	1.21E-09	-2.69
ENSMUSG00000031788	Kifc3	2.43E-09	9.64E-12	-2.31	-2.25	1.22E-09	-2.28
ENSMUSG00000041515	Irf8	2.88E-50	2.44E-09	10.02	2.32	1.22E-09	6.17
ENSMUSG00000056116	H2-T22	2.82E-09	3.01E-73	3.03	16.32	1.41E-09	9.67
ENSMUSG00000033470	Cysltr2	3.06E-09	3.05E-37	5.21	19.15	1.53E-09	12.18
ENSMUSG00000107355	AI839979	3.07E-09	9.57E-11	-2.49	-2.31	1.58E-09	-2.40
ENSMUSG00000000318	Clec10a	3.10E-16	3.18E-09	3.81	2.38	1.59E-09	3.10
ENSMUSG00000049969	Plekhf2	3.95E-09	7.20E-55	2.07	4.94	1.97E-09	3.51
ENSMUSG00000032184	Lysmd2	4.04E-09	3.96E-11	2.92	2.86	2.04E-09	2.89
ENSMUSG00000025582	Nptx1	8.63E-16	4.61E-09	-6.24	-3.18	2.31E-09	-4.71
ENSMUSG00000032350	Gclc	4.81E-09	2.52E-35	-2.36	-4.66	2.41E-09	-3.51
ENSMUSG00000042182	Bend6	1.38E-23	5.27E-09	3.51	2.06	2.64E-09	2.78
ENSMUSG00000029640	Usp12	5.37E-09	1.10E-29	2.93	5.63	2.69E-09	4.28
ENSMUSG00000048186	Bend7	5.62E-09	8.56E-23	6.50	14.44	2.81E-09	10.47
ENSMUSG00000040987	Mill2	5.62E-09	1.56E-23	2.99	4.83	2.81E-09	3.91
ENSMUSG00000025153	Fasn	5.96E-09	7.94E-30	-2.25	-3.87	2.98E-09	-3.06
ENSMUSG00000035842	Ddx11	5.86E-09	2.45E-10	-4.09	-3.48	3.05E-09	-3.78
ENSMUSG00000035852	Misp	6.54E-09	1.13E-32	14.62	112.01	3.27E-09	63.31
ENSMUSG00000026566	Mpzl1	7.66E-09	7.46E-11	-2.51	-2.40	3.86E-09	-2.45
ENSMUSG00000063760	Rnf217	1.99E-10	7.57E-09	2.45	2.05	3.88E-09	2.25
ENSMUSG00000089940	Gm4117	8.33E-09	2.93E-30	3.21	6.55	4.16E-09	4.88

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000031595	Pdgfrl	4.81E-13	8.82E-09	17.41	8.96	4.41E-09	13.18
ENSMUSG00000109715	Gm45606	9.62E-09	4.21E-13	-2.95	-3.16	4.81E-09	-3.06
ENSMUSG00000021838	Samd4	4.95E-11	9.66E-09	-3.23	-2.38	4.85E-09	-2.81
ENSMUSG00000111118	Gm6545	9.76E-09	3.47E-52	18.85	716.48	4.88E-09	367.67
ENSMUSG00000029082	Bst1	4.80E-40	9.81E-09	7.06	2.21	4.91E-09	4.63
ENSMUSG00000018537	Pcgf2	9.97E-09	2.59E-13	-2.09	-2.21	4.98E-09	-2.15
ENSMUSG00000097113	Gm19705	1.20E-08	4.56E-25	2.37	3.64	6.01E-09	3.01
ENSMUSG00000032397	Tipin	9.47E-11	1.21E-08	-2.82	-2.19	6.12E-09	-2.51
ENSMUSG00000034731	Dgkh	1.84E-14	1.28E-08	2.92	2.03	6.38E-09	2.47
ENSMUSG00000059851	Kmt5c	1.40E-08	2.19E-10	-2.34	-2.24	7.11E-09	-2.29
ENSMUSG00000018796	Acsl1	4.42E-15	1.68E-08	5.48	2.97	8.42E-09	4.22
ENSMUSG00000040229	Gpr34	1.77E-08	8.67E-17	-2.95	-3.95	8.83E-09	-3.45
ENSMUSG00000047649	Cd3eap	1.75E-08	1.25E-10	-2.10	-2.06	8.83E-09	-2.08
ENSMUSG00000039908	Slc26a11	1.64E-08	3.37E-09	-3.24	-2.87	9.87E-09	-3.05
ENSMUSG00000037972	Snn	5.87E-10	2.13E-08	3.46	2.68	1.09E-08	3.07
ENSMUSG00000000811	Txnrd3	2.26E-08	2.20E-17	-2.09	-2.59	1.13E-08	-2.34
ENSMUSG00000049939	Lrrc4	2.29E-08	1.49E-17	12.81	29.01	1.15E-08	20.91
ENSMUSG00000041147	Brca2	2.33E-08	1.15E-10	-4.08	-3.91	1.17E-08	-3.99
ENSMUSG00000029322	Plac8	2.76E-08	6.43E-28	5.47	16.10	1.38E-08	10.78
ENSMUSG00000051212	Gpr183	2.36E-17	2.82E-08	-4.72	-2.30	1.41E-08	-3.51
ENSMUSG00000097567	#NV	2.89E-08	1.31E-27	2.85	5.28	1.45E-08	4.07
ENSMUSG00000019823	Mical1	3.36E-08	2.03E-11	-2.11	-2.17	1.68E-08	-2.14
ENSMUSG00000021322	Aoah	3.49E-08	1.39E-10	2.30	2.30	1.75E-08	2.30
ENSMUSG00000037151	Lrrc20	3.63E-08	1.08E-12	-2.41	-2.63	1.82E-08	-2.52
ENSMUSG00000053617	Sh3pxd2a	3.87E-08	3.14E-21	-2.36	-3.57	1.94E-08	-2.96

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000023067	Cdkn1a	1.12E-09	3.96E-08	3.08	2.42	2.03E-08	2.75
ENSMUSG00000093726	Gm20667	4.29E-08	9.50E-13	-6.69	-9.47	2.14E-08	-8.08
ENSMUSG00000055782	Abcd2	1.94E-09	4.76E-08	-7.11	-4.34	2.48E-08	-5.72
ENSMUSG00000027315	Spint1	2.04E-10	4.98E-08	4.95	3.41	2.50E-08	4.18
ENSMUSG00000064090	Vrk2	5.17E-08	4.12E-18	2.57	3.55	2.59E-08	3.06
ENSMUSG00000022360	Atad2	5.17E-08	1.10E-10	-2.28	-2.30	2.59E-08	-2.29
ENSMUSG00000015846	Rxra	5.26E-08	6.87E-13	-2.32	-2.57	2.63E-08	-2.44
ENSMUSG00000019082	Slc25a22	5.53E-08	8.70E-49	3.09	12.32	2.76E-08	7.71
ENSMUSG00000038485	Socs7	5.53E-08	4.99E-20	2.19	3.03	2.76E-08	2.61
ENSMUSG00000092627	D130058E05Rik	5.81E-08	2.82E-11	-5.27	-5.51	2.91E-08	-5.39
ENSMUSG00000033781	Asb13	5.96E-08	3.36E-52	2.46	7.80	2.98E-08	5.13
ENSMUSG00000039842	Mcph1	6.22E-08	3.57E-16	-2.13	-2.65	3.11E-08	-2.39
ENSMUSG00000079505	Gm11131	6.30E-08	2.16E-19	5.51	10.90	3.15E-08	8.21
ENSMUSG00000039232	Stx11	6.36E-08	1.44E-09	3.81	3.62	3.25E-08	3.72
ENSMUSG00000027676	Ccdc39	6.79E-08	2.38E-26	5.26	14.72	3.40E-08	9.99
ENSMUSG00000020077	Srgn	5.55E-08	1.49E-08	2.63	2.39	3.52E-08	2.51
ENSMUSG00000041406	BC055324	6.40E-08	9.13E-09	-3.67	-3.17	3.66E-08	-3.42
ENSMUSG00000097534	Gm16675	8.05E-08	1.48E-19	6.16	13.22	4.03E-08	9.69
ENSMUSG00000041075	Fzd7	8.96E-20	8.91E-08	4.15	2.13	4.45E-08	3.14
ENSMUSG00000039236	Isg20	8.99E-08	2.75E-89	5.36	169.24	4.50E-08	87.30
ENSMUSG00000078349	AW011738	1.02E-07	1.21E-33	5.86	26.21	5.08E-08	16.03
ENSMUSG00000067297	Ifit1bl2	1.02E-07	2.17E-37	10.55	116.78	5.12E-08	63.66
ENSMUSG00000027351	Spred1	1.07E-07	9.70E-20	2.75	4.27	5.37E-08	3.51
ENSMUSG00000000686	Abhd15	3.78E-08	7.02E-08	-4.21	-3.08	5.40E-08	-3.65
ENSMUSG00000022070	Bora	1.13E-07	3.48E-15	-3.34	-4.78	5.66E-08	-4.06

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000005370	Msh6	6.57E-14	1.18E-07	-3.63	-2.20	5.89E-08	-2.91
ENSMUSG00000089844	A530032D15Rik	1.33E-07	1.40E-23	13.10	65.99	6.64E-08	39.54
ENSMUSG00000110141	Gm45684	8.43E-10	1.42E-07	18.93	10.94	7.12E-08	14.94
ENSMUSG00000021366	Hivep1	4.22E-08	1.03E-07	2.85	2.42	7.26E-08	2.64
ENSMUSG00000116961	Gm49662	1.48E-07	9.74E-15	13.49	29.54	7.41E-08	21.52
ENSMUSG00000034522	Zfp395	1.49E-07	2.09E-15	-3.56	-5.34	7.43E-08	-4.45
ENSMUSG00000019487	Trip10	3.41E-11	1.52E-07	3.27	2.30	7.58E-08	2.78
ENSMUSG00000115855	Gm34643	1.52E-07	8.24E-10	4.58	4.69	7.66E-08	4.63
ENSMUSG00000030156	Cd69	1.58E-07	7.20E-17	16.03	41.29	7.92E-08	28.66
ENSMUSG00000056220	Pla2g4a	4.23E-19	1.61E-07	6.21	2.64	8.04E-08	4.43
ENSMUSG00000002289	Angptl4	8.23E-08	8.12E-08	-4.50	-3.43	8.17E-08	-3.97
ENSMUSG00000053957	Gm12474	1.66E-07	1.61E-12	5.97	8.10	8.30E-08	7.03
ENSMUSG00000058392	Rrp1b	1.68E-07	1.84E-15	-2.60	-3.43	8.41E-08	-3.02
ENSMUSG00000043872	Zmym1	1.81E-07	8.29E-14	-2.47	-3.02	9.03E-08	-2.75
ENSMUSG00000029992	Gfpt1	1.85E-07	3.07E-12	2.01	2.21	9.27E-08	2.11
ENSMUSG00000069844	Sco1	1.93E-07	3.40E-44	2.22	5.70	9.66E-08	3.96
ENSMUSG00000021338	Carmil1	1.93E-07	2.80E-09	3.10	3.03	9.79E-08	3.07
ENSMUSG00000095609	Gm21188	1.98E-07	4.38E-16	3.22	4.64	9.90E-08	3.93
ENSMUSG00000027203	Dut	1.55E-07	4.30E-08	-2.67	-2.41	9.92E-08	-2.54
ENSMUSG00000066861	Oas1g	2.15E-07	1.30E-40	4.15	18.76	1.07E-07	11.46
ENSMUSG00000045751	Mms22l	1.90E-09	2.28E-07	-2.87	-2.16	1.15E-07	-2.52
ENSMUSG00000039748	Exo1	7.77E-09	2.28E-07	-7.16	-3.96	1.18E-07	-5.56
ENSMUSG00000027347	Rasgrp1	2.64E-11	2.51E-07	27.82	11.51	1.26E-07	19.67
ENSMUSG00000040264	Gbp2b	4.79E-08	2.06E-07	37.14	23.45	1.27E-07	30.29
ENSMUSG00000033857	Engase	1.94E-07	6.22E-08	-3.66	-3.12	1.28E-07	-3.39

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000050370	Ch25h	2.68E-07	1.31E-16	12.91	32.65	1.34E-07	22.78
ENSMUSG00000055200	Sertad3	2.71E-07	1.33E-35	2.32	5.38	1.36E-07	3.85
ENSMUSG00000032089	Il10ra	3.96E-08	2.35E-07	2.65	2.22	1.37E-07	2.43
ENSMUSG00000079014	Serpina3i	4.37E-11	2.86E-07	46.96	18.03	1.43E-07	32.50
ENSMUSG00000062082	Cd200r4	2.87E-07	3.05E-51	2.00	5.34	1.44E-07	3.67
ENSMUSG00000069793	Slfn9	2.88E-07	2.22E-56	2.65	11.59	1.44E-07	7.12
ENSMUSG00000034110	Kctd7	2.99E-07	5.31E-17	-2.22	-3.18	1.50E-07	-2.70
ENSMUSG00000021287	Xrcc3	2.53E-08	2.90E-07	-4.96	-3.10	1.58E-07	-4.03
ENSMUSG00000033610	Pank1	3.16E-07	1.45E-22	-2.95	-6.08	1.58E-07	-4.52
ENSMUSG00000072109	A530040E14Rik	3.21E-07	5.51E-21	15.67	70.10	1.60E-07	42.89
ENSMUSG00000090812	Samd15	3.71E-07	1.30E-14	2.97	3.98	1.86E-07	3.48
ENSMUSG00000073705	Cenps	1.47E-07	2.41E-07	-3.13	-2.56	1.94E-07	-2.84
ENSMUSG00000026773	Pfkfb3	3.99E-07	6.88E-23	2.39	4.10	2.00E-07	3.25
ENSMUSG00000022184	Fbxo4	4.06E-07	3.84E-20	2.17	3.22	2.03E-07	2.70
ENSMUSG00000047067	Dusp28	4.36E-07	2.76E-46	2.22	6.21	2.18E-07	4.22
ENSMUSG00000020649	Rrm2	4.84E-07	7.28E-09	-3.16	-3.09	2.46E-07	-3.13
ENSMUSG00000020185	E2f7	2.50E-07	2.92E-07	-4.04	-3.19	2.71E-07	-3.61
ENSMUSG00000040329	Il7	5.69E-07	7.40E-17	3.90	6.56	2.84E-07	5.23
ENSMUSG00000002602	Axl	6.18E-07	1.86E-15	2.78	3.94	3.09E-07	3.36
ENSMUSG00000025574	Tk1	4.11E-07	2.42E-07	-3.05	-2.66	3.26E-07	-2.86
ENSMUSG00000023940	Sgo1	6.64E-07	4.54E-12	-2.76	-3.32	3.32E-07	-3.04
ENSMUSG00000041859	Mcm3	7.22E-09	7.56E-07	-3.16	-2.36	3.81E-07	-2.76
ENSMUSG00000047473	Zfp30	7.60E-07	4.79E-09	-3.45	-3.35	3.82E-07	-3.40
ENSMUSG00000025195	Dnmbp	7.83E-07	1.22E-11	-2.59	-3.02	3.91E-07	-2.80
ENSMUSG00000069893	9930111J21Rik1	7.93E-07	2.14E-19	6.39	16.74	3.96E-07	11.56

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000024151	Msh2	8.09E-07	3.10E-11	-2.64	-3.03	4.04E-07	-2.84
ENSMUSG00000028633	Ctps	8.14E-07	4.15E-11	-2.92	-3.37	4.07E-07	-3.14
ENSMUSG00000037509	Arhgef4	9.32E-07	4.60E-09	-3.59	-3.51	4.68E-07	-3.55
ENSMUSG00000045045	Lrfn4	9.96E-07	9.92E-13	-3.30	-4.64	4.98E-07	-3.97
ENSMUSG00000086513	Gvin-ps1	4.85E-09	1.03E-06	15.26	8.73	5.16E-07	11.99
ENSMUSG00000053801	Grwd1	1.04E-06	5.06E-15	-2.71	-3.91	5.18E-07	-3.31
ENSMUSG00000029923	Rab19	1.06E-06	3.14E-42	2.28	6.25	5.31E-07	4.27
ENSMUSG00000001228	Uhrf1	9.29E-07	1.34E-07	-3.47	-3.12	5.32E-07	-3.30
ENSMUSG00000021929	Kpna3	1.13E-06	7.06E-13	2.36	2.91	5.66E-07	2.64
ENSMUSG00000085184	4933439K11Rik	7.42E-16	1.14E-06	6.80	3.13	5.70E-07	4.97
ENSMUSG00000044066	Cep68	1.02E-06	1.55E-07	-2.42	-2.20	5.89E-07	-2.31
ENSMUSG00000054008	Ndst1	1.15E-06	3.09E-08	-2.09	-2.04	5.92E-07	-2.06
ENSMUSG00000038644	Pold1	1.17E-06	4.72E-08	-3.06	-2.91	6.09E-07	-2.99
ENSMUSG00000020739	Nup85	1.24E-06	4.17E-09	-2.16	-2.21	6.20E-07	-2.19
ENSMUSG00000038379	Ttk	1.24E-06	3.00E-09	-2.51	-2.59	6.22E-07	-2.55
ENSMUSG00000089715	Cbx6	1.29E-06	1.05E-09	-2.39	-2.54	6.48E-07	-2.47
ENSMUSG00000009654	Oit3	1.33E-06	9.37E-10	-2.21	-2.33	6.67E-07	-2.27
ENSMUSG00000002997	Prkar2b	1.47E-06	9.91E-12	-2.19	-2.54	7.33E-07	-2.37
ENSMUSG00000025491	Ifitm1	1.20E-11	1.52E-06	5.53	2.99	7.59E-07	4.26
ENSMUSG00000021565	Slc6a19	5.63E-08	1.46E-06	6.86	4.68	7.60E-07	5.77
ENSMUSG00000024791	Cdca5	1.52E-06	2.87E-08	-2.65	-2.57	7.76E-07	-2.61
ENSMUSG00000055172	C1ra	3.45E-18	1.61E-06	9.86	3.35	8.07E-07	6.60
ENSMUSG00000021575	Ahrr	1.29E-08	1.60E-06	2.82	2.17	8.09E-07	2.50
ENSMUSG00000025921	Rdh10	1.63E-06	5.73E-11	-2.25	-2.55	8.15E-07	-2.40
ENSMUSG00000007827	Ankrd26	1.67E-06	6.41E-10	-2.12	-2.27	8.34E-07	-2.20

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000038668	Lpar1	1.68E-06	1.45E-08	5.83	5.96	8.47E-07	5.89
ENSMUSG00000028687	Mutyh	1.69E-06	1.05E-08	-3.87	-3.80	8.51E-07	-3.84
ENSMUSG00000018986	Slfn3	1.76E-06	7.67E-34	3.36	11.75	8.78E-07	7.55
ENSMUSG00000074217	Misp3	1.52E-06	5.07E-07	-2.82	-2.48	1.01E-06	-2.65
ENSMUSG00000073144	4930599N23Rik	2.11E-06	3.97E-24	3.31	7.86	1.05E-06	5.58
ENSMUSG00000018899	Irf1	3.59E-13	2.19E-06	11.77	4.20	1.09E-06	7.98
ENSMUSG00000041774	Ydjc	2.45E-06	8.34E-10	-2.32	-2.52	1.23E-06	-2.42
ENSMUSG00000061143	Maml3	2.60E-06	1.66E-10	-2.90	-3.40	1.30E-06	-3.15
ENSMUSG00000034906	Ncaph	2.69E-06	1.55E-09	-2.46	-2.66	1.35E-06	-2.56
ENSMUSG00000005470	Asf1b	1.74E-08	2.88E-06	-2.67	-2.03	1.45E-06	-2.35
ENSMUSG00000046295	Ankle1	3.08E-06	4.17E-08	-5.62	-5.15	1.56E-06	-5.38
ENSMUSG00000037235	Mxd4	3.08E-06	5.49E-08	-2.56	-2.54	1.57E-06	-2.55
ENSMUSG00000030737	Slco2b1	2.21E-06	1.04E-06	-4.80	-3.56	1.63E-06	-4.18
ENSMUSG00000032411	Tfdp2	3.47E-06	2.78E-10	-2.04	-2.26	1.74E-06	-2.15
ENSMUSG00000018654	Ikzf1	3.50E-06	3.90E-18	2.42	3.94	1.75E-06	3.18
ENSMUSG00000020806	Rhbdf2	3.70E-06	4.69E-08	2.33	2.34	1.87E-06	2.34
ENSMUSG00000050410	Tcf19	7.67E-07	2.98E-06	-3.19	-2.54	1.87E-06	-2.86
ENSMUSG00000052485	Tmem171	3.89E-06	4.76E-47	2.64	11.79	1.94E-06	7.22
ENSMUSG00000041135	Ripk2	3.90E-06	1.05E-08	3.68	3.94	1.96E-06	3.81
ENSMUSG00000022034	Esco2	3.92E-06	3.96E-11	-3.48	-4.59	1.96E-06	-4.03
ENSMUSG00000029730	Mcm7	1.34E-08	3.97E-06	-3.51	-2.44	1.99E-06	-2.98
ENSMUSG00000035024	Ncapd3	3.16E-06	9.49E-07	-2.18	-2.01	2.05E-06	-2.09
ENSMUSG00000023224	Serping1	2.65E-13	4.17E-06	5.70	2.82	2.08E-06	4.26
ENSMUSG00000027171	Prrg4	1.35E-07	4.06E-06	4.55	3.25	2.10E-06	3.90
ENSMUSG00000112226	Gm48786	1.93E-15	4.22E-06	9.23	3.44	2.11E-06	6.34

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000107761	2010008C14Rik	4.47E-06	5.29E-12	-2.95	-3.99	2.24E-06	-3.47
ENSMUSG00000059323	Tonsl	4.86E-07	4.00E-06	-4.13	-2.98	2.24E-06	-3.56
ENSMUSG00000019773	Fbxo5	4.49E-06	5.57E-10	-2.91	-3.39	2.24E-06	-3.15
ENSMUSG00000025577	Cbx2	5.69E-07	4.25E-06	-5.22	-3.35	2.41E-06	-4.29
ENSMUSG00000048142	Nat8l	2.48E-06	2.42E-06	-4.58	-3.58	2.45E-06	-4.08
ENSMUSG00000040321	Zfp770	3.29E-06	1.63E-06	-2.27	-2.01	2.46E-06	-2.14
ENSMUSG00000024397	Aif1	4.98E-06	1.92E-09	2.57	2.86	2.49E-06	2.71
ENSMUSG00000002699	Lcp2	1.29E-13	5.13E-06	4.32	2.25	2.57E-06	3.28
ENSMUSG00000074578	Zfas1	5.13E-06	7.36E-28	2.03	4.03	2.57E-06	3.03
ENSMUSG00000019813	Cep57l1	5.05E-06	1.12E-07	-2.28	-2.22	2.58E-06	-2.25
ENSMUSG00000034773	Hrob	1.59E-06	3.59E-06	-3.23	-2.57	2.59E-06	-2.90
ENSMUSG00000020781	Tsen54	5.20E-06	8.74E-14	-2.04	-2.74	2.60E-06	-2.39
ENSMUSG00000033450	Tagap	1.14E-09	5.21E-06	8.37	4.09	2.60E-06	6.23
ENSMUSG00000004100	Ppan	5.22E-06	3.52E-14	-2.59	-3.90	2.61E-06	-3.24
ENSMUSG00000035834	Polr3g	5.30E-06	1.33E-17	-3.19	-6.44	2.65E-06	-4.81
ENSMUSG00000039713	Plekhg5	1.29E-08	5.50E-06	-3.07	-2.05	2.76E-06	-2.56
ENSMUSG00000079109	Pms2	5.59E-06	1.28E-08	-2.27	-2.36	2.80E-06	-2.32
ENSMUSG00000061186	Sfmbt2	6.34E-06	7.01E-14	2.68	3.85	3.17E-06	3.27
ENSMUSG00000025203	Scd2	6.41E-06	2.53E-12	-2.78	-3.80	3.21E-06	-3.29
ENSMUSG00000042606	Hirip3	6.48E-06	2.21E-12	-2.67	-3.64	3.24E-06	-3.16
ENSMUSG00000053541	Gvin-ps6	3.08E-06	4.27E-06	19.11	14.26	3.68E-06	16.68
ENSMUSG00000062960	Kdr	7.40E-06	1.22E-58	2.91	22.32	3.70E-06	12.62
ENSMUSG00000039396	Neil3	7.68E-06	9.69E-10	-3.25	-3.90	3.84E-06	-3.57
ENSMUSG00000028362	Tnfsf8	8.23E-06	2.99E-59	3.10	26.68	4.11E-06	14.89
ENSMUSG00000027832	Ptx3	1.70E-07	8.60E-06	5.24	3.55	4.38E-06	4.39

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000027641	Rbl1	9.33E-06	1.07E-26	2.06	4.12	4.67E-06	3.09
ENSMUSG00000116380	Gm39556	9.87E-06	8.51E-20	5.42	16.89	4.93E-06	11.15
ENSMUSG00000073739	Gm16287	1.04E-05	1.09E-09	-2.16	-2.44	5.18E-06	-2.30
ENSMUSG00000030505	Prmt3	1.06E-05	8.56E-18	-2.16	-3.54	5.32E-06	-2.85
ENSMUSG00000037224	Zfyve28	1.06E-05	4.89E-08	-4.31	-4.55	5.34E-06	-4.43
ENSMUSG00000029516	Cit	1.04E-05	4.13E-07	-2.19	-2.14	5.40E-06	-2.17
ENSMUSG00000022471	Xrcc6	1.07E-05	1.95E-07	-2.21	-2.19	5.45E-06	-2.20
ENSMUSG00000015340	Cybb	1.11E-05	6.38E-10	2.08	2.37	5.57E-06	2.23
ENSMUSG00000068246	Apol9b	1.13E-05	7.67E-34	16.48	510.66	5.63E-06	263.57
ENSMUSG00000020228	Helb	1.15E-05	1.65E-08	-2.01	-2.13	5.76E-06	-2.07
ENSMUSG00000033985	Tesk2	1.03E-06	1.06E-05	-4.34	-2.75	5.83E-06	-3.55
ENSMUSG00000032666	1700025G04Rik	1.11E-05	7.56E-07	-2.08	-2.01	5.93E-06	-2.04
ENSMUSG00000027242	Wdr76	8.25E-08	1.18E-05	-3.80	-2.54	5.93E-06	-3.17
ENSMUSG00000034959	Rubcnl	1.20E-05	5.11E-22	3.33	8.60	5.99E-06	5.97
ENSMUSG00000107041	Gm42735	1.06E-05	1.74E-06	3.69	3.41	6.18E-06	3.55
ENSMUSG00000086291	Gm15513	1.25E-05	2.20E-08	-6.61	-7.71	6.26E-06	-7.16
ENSMUSG00000037649	H2-DMa	7.83E-32	1.25E-05	8.35	2.08	6.26E-06	5.21
ENSMUSG00000021965	Ska3	1.27E-05	1.64E-08	-2.97	-3.25	6.35E-06	-3.11
ENSMUSG00000024795	Kif20b	1.28E-05	1.05E-09	-2.36	-2.75	6.40E-06	-2.56
ENSMUSG00000112093	Gm47941	1.89E-07	1.31E-05	17.52	9.94	6.62E-06	13.73
ENSMUSG00000046591	Ticrr	1.33E-05	1.52E-11	-2.84	-4.07	6.67E-06	-3.45
ENSMUSG00000028944	Prkag2	1.39E-05	2.22E-17	-2.41	-4.22	6.95E-06	-3.32
ENSMUSG00000004996	Mri1	1.39E-05	7.80E-09	-2.23	-2.44	6.96E-06	-2.33
ENSMUSG00000018143	Mafk	1.39E-05	3.29E-11	2.33	2.94	6.97E-06	2.63
ENSMUSG00000039270	Megf9	1.40E-05	7.21E-10	-2.78	-3.39	6.99E-06	-3.08

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000037447	Arid5a	1.41E-05	2.60E-07	4.54	4.60	7.20E-06	4.57
ENSMUSG00000056394	Lig1	1.21E-10	1.48E-05	-3.26	-2.03	7.39E-06	-2.64
ENSMUSG00000046080	Clec9a	8.12E-08	1.52E-05	34.50	13.13	7.65E-06	23.81
ENSMUSG00000108004	Gm44080	1.52E-05	1.07E-07	3.90	4.18	7.66E-06	4.04
ENSMUSG00000022583	Ly6f	3.09E-07	1.55E-05	25.30	13.13	7.90E-06	19.22
ENSMUSG00000047747	Rnf150	1.17E-05	4.40E-06	-3.09	-2.74	8.03E-06	-2.91
ENSMUSG00000050947	Amigo1	1.17E-05	4.78E-06	-3.90	-3.05	8.23E-06	-3.48
ENSMUSG00000043140	Tmem186	1.72E-05	1.00E-15	-2.08	-3.33	8.58E-06	-2.71
ENSMUSG00000030930	Chst15	1.75E-05	2.83E-35	2.55	7.81	8.77E-06	5.18
ENSMUSG00000020573	Pik3cg	1.80E-05	8.53E-14	-2.25	-3.25	9.00E-06	-2.75
ENSMUSG00000040978	Gm11992	4.13E-07	1.77E-05	10.21	6.13	9.04E-06	8.17
ENSMUSG00000072620	Slfn2	1.86E-05	1.56E-12	2.70	3.92	9.28E-06	3.31
ENSMUSG00000062232	Rapgef2	2.02E-05	4.42E-08	2.50	2.70	1.01E-05	2.60
ENSMUSG00000031442	Mcf2l	2.82E-13	2.10E-05	5.21	2.51	1.05E-05	3.86
ENSMUSG00000035561	Aldh1b1	2.14E-05	9.89E-81	2.17	15.76	1.07E-05	8.97
ENSMUSG00000027115	Kif18a	2.28E-05	3.40E-10	-3.09	-4.19	1.14E-05	-3.64
ENSMUSG00000030929	Eri2	2.25E-05	4.05E-07	-2.09	-2.08	1.15E-05	-2.08
ENSMUSG00000031480	Thsd1	2.36E-05	1.29E-09	-3.25	-4.35	1.18E-05	-3.80
ENSMUSG00000086782	E130102H24Rik	2.39E-05	5.67E-09	2.79	3.28	1.20E-05	3.03
ENSMUSG00000029189	Sel1l3	4.54E-06	2.05E-05	-3.42	-2.56	1.25E-05	-2.99
ENSMUSG00000035186	Ubd	2.47E-31	2.58E-05	602.97	11.57	1.29E-05	307.27
ENSMUSG00000025395	Prim1	2.83E-06	2.31E-05	-2.63	-2.10	1.29E-05	-2.36
ENSMUSG00000025950	Idh1	4.04E-06	2.19E-05	-2.40	-2.01	1.30E-05	-2.21
ENSMUSG00000023832	Acat2	2.86E-05	2.47E-09	-2.14	-2.48	1.43E-05	-2.31
ENSMUSG00000024891	Slc29a2	2.97E-05	8.16E-10	-2.90	-4.01	1.49E-05	-3.45

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000022033	Pbk	2.68E-05	2.92E-06	-2.74	-2.57	1.49E-05	-2.65
ENSMUSG00000022554	Hgh1	3.25E-05	1.34E-11	-2.04	-2.73	1.63E-05	-2.39
ENSMUSG00000039865	Slc44a3	3.25E-05	1.17E-07	12.53	16.39	1.63E-05	14.46
ENSMUSG00000038807	Rap1gap2	2.47E-07	3.59E-05	3.75	2.63	1.81E-05	3.19
ENSMUSG00000072082	Ccnf	1.95E-06	3.55E-05	-2.61	-2.03	1.87E-05	-2.32
ENSMUSG00000020032	Nuak1	3.79E-05	1.09E-07	-2.79	-3.04	1.90E-05	-2.92
ENSMUSG00000061414	Cracr2a	4.08E-05	2.34E-07	-2.29	-2.39	2.05E-05	-2.34
ENSMUSG00000024118	Tedc2	3.31E-05	8.74E-06	-2.62	-2.32	2.09E-05	-2.47
ENSMUSG00000022718	Dgcr8	4.30E-05	5.32E-07	-2.17	-2.22	2.18E-05	-2.20
ENSMUSG00000045287	Rtn4rl1	4.40E-05	4.01E-13	-2.66	-4.50	2.20E-05	-3.58
ENSMUSG00000042978	Sbk1	4.43E-05	3.43E-09	-3.15	-4.15	2.21E-05	-3.65
ENSMUSG00000015316	Slamf1	4.60E-05	1.48E-08	10.28	16.36	2.30E-05	13.32
ENSMUSG00000038295	Atg9b	4.79E-05	1.34E-07	-3.66	-4.08	2.40E-05	-3.87
ENSMUSG00000072066	6720489N17Rik	4.81E-05	5.18E-08	-4.36	-5.38	2.41E-05	-4.87
ENSMUSG00000036067	Slc2a6	1.05E-07	4.85E-05	5.57	3.18	2.43E-05	4.37
ENSMUSG00000038126	Mphosph9	4.92E-05	1.27E-13	-2.22	-3.59	2.46E-05	-2.91
ENSMUSG00000030748	Il4ra	1.21E-11	4.93E-05	4.30	2.19	2.46E-05	3.25
ENSMUSG00000030717	Nupr1	4.91E-05	1.68E-07	2.60	2.83	2.47E-05	2.72
ENSMUSG00000041642	Kif21b	4.84E-05	1.42E-06	-2.25	-2.26	2.49E-05	-2.26
ENSMUSG00000022177	Haus4	7.65E-08	5.04E-05	-2.93	-2.01	2.52E-05	-2.47
ENSMUSG00000107586	Gm44283	5.21E-05	4.19E-07	2.52	2.66	2.63E-05	2.59
ENSMUSG00000015880	Ncapg	5.26E-05	1.17E-07	-2.32	-2.52	2.64E-05	-2.42
ENSMUSG00000050751	Pgbd5	5.34E-05	3.35E-10	-5.29	-14.58	2.67E-05	-9.94
ENSMUSG00000111133	Gm5831	5.52E-05	2.44E-16	7.25	26.87	2.76E-05	17.06
ENSMUSG00000030882	Dnhd1	5.60E-05	7.87E-09	3.33	4.22	2.80E-05	3.77

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000030871	Ears2	5.64E-05	7.29E-08	-2.16	-2.36	2.82E-05	-2.26
ENSMUSG00000039783	Kmo	5.70E-05	4.75E-20	4.37	14.98	2.85E-05	9.67
ENSMUSG00000044469	Tnfaip8l1	6.06E-05	5.06E-11	-2.08	-2.82	3.03E-05	-2.45
ENSMUSG00000053749	Gm9920	1.99E-05	4.17E-05	-5.94	-3.53	3.08E-05	-4.73
ENSMUSG00000014164	Klhl3	6.43E-05	5.45E-12	-4.01	-10.86	3.21E-05	-7.43
ENSMUSG00000007379	Dennd2c	6.94E-05	6.40E-09	-3.18	-4.38	3.47E-05	-3.78
ENSMUSG00000001053	N4bp3	3.51E-05	3.51E-05	-2.61	-2.16	3.51E-05	-2.39
ENSMUSG00000045411	2410002F23Rik	7.33E-05	2.26E-12	-2.06	-2.97	3.67E-05	-2.52
ENSMUSG00000018920	Cxcl16	1.87E-10	7.46E-05	3.91	2.14	3.73E-05	3.03
ENSMUSG00000008734	Gprc5b	7.96E-05	8.06E-07	-2.32	2.34	4.02E-05	0.01
ENSMUSG00000116673	A630089N07Rik	8.22E-05	7.87E-09	-2.47	-3.08	4.11E-05	-2.77
ENSMUSG00000064289	Tank	8.40E-05	4.32E-08	2.29	2.63	4.20E-05	2.46
ENSMUSG00000057346	Apol9a	8.55E-05	1.40E-22	10.14	104.11	4.27E-05	57.12
ENSMUSG00000085327	Gm16104	9.05E-05	4.03E-07	-3.03	-3.30	4.54E-05	-3.17
ENSMUSG00000030671	Pde3b	6.65E-06	8.46E-05	-2.64	-2.07	4.56E-05	-2.35
ENSMUSG00000002870	Mcm2	1.53E-06	9.04E-05	-3.07	-2.21	4.59E-05	-2.64
ENSMUSG00000097166	9330179D12Rik	1.81E-05	7.48E-05	6.20	4.59	4.65E-05	5.40
ENSMUSG00000058290	Espl1	9.36E-05	5.52E-12	-2.08	-2.97	4.68E-05	-2.52
ENSMUSG00000022686	B3gnt5	5.71E-06	9.24E-05	3.63	2.66	4.90E-05	3.15
ENSMUSG00000001630	Stk38l	8.88E-05	9.80E-06	2.31	2.24	4.93E-05	2.27
ENSMUSG00000029591	Ung	1.00E-04	7.83E-11	-2.94	-4.55	5.01E-05	-3.74
ENSMUSG00000024235	Map3k8	1.03E-04	1.64E-06	2.29	2.38	5.22E-05	2.34
ENSMUSG00000026077	Npas2	8.34E-05	2.11E-05	-3.22	-2.77	5.22E-05	-2.99
ENSMUSG00000024975	Pdcd4	1.06E-04	3.96E-08	-2.39	-2.81	5.29E-05	-2.60
ENSMUSG00000025804	Ccr1	1.06E-04	6.16E-08	3.08	3.72	5.31E-05	3.40

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000007080	Pole	5.95E-05	4.84E-05	-2.40	-2.11	5.40E-05	-2.26
ENSMUSG00000002835	Chaf1a	2.92E-06	1.07E-04	-2.99	-2.19	5.47E-05	-2.59
ENSMUSG00000086247	Gm15787	1.13E-04	4.39E-08	4.36	5.80	5.64E-05	5.08
ENSMUSG00000026866	Kynu	7.45E-12	1.13E-04	24.26	5.27	5.65E-05	14.77
ENSMUSG00000031756	Cenpn	1.13E-04	8.36E-07	-2.13	-2.24	5.68E-05	-2.18
ENSMUSG00000117239	Gpr31c	1.13E-04	1.86E-07	3.30	3.87	5.68E-05	3.59
ENSMUSG00000072572	Slc39a2	5.18E-05	6.29E-05	4.66	3.89	5.74E-05	4.28
ENSMUSG00000061603	Akap6	2.15E-07	1.17E-04	4.31	2.66	5.87E-05	3.48
ENSMUSG00000032593	Amigo3	1.23E-04	7.33E-25	2.44	6.19	6.17E-05	4.31
ENSMUSG00000026473	Glul	1.32E-04	2.66E-10	-2.00	-2.59	6.60E-05	-2.29
ENSMUSG00000052125	F730043M19Rik	1.95E-13	1.32E-04	5.01	2.24	6.62E-05	3.62
ENSMUSG00000109244	Gm44751	1.58E-13	1.33E-04	8.69	2.95	6.64E-05	5.82
ENSMUSG00000005410	Mcm5	6.19E-08	1.37E-04	-3.33	-2.11	6.86E-05	-2.72
ENSMUSG00000052609	Plekhg3	1.38E-04	7.95E-09	-2.27	-2.81	6.89E-05	-2.54
ENSMUSG00000015217	Hmgb3	1.35E-04	6.23E-06	-2.51	-2.49	7.05E-05	-2.50
ENSMUSG00000020381	Mrnip	1.19E-04	2.76E-05	-2.92	-2.63	7.35E-05	-2.78
ENSMUSG00000108238	Gm43984	6.44E-05	8.80E-05	3.41	2.88	7.62E-05	3.14
ENSMUSG00000019214	Chtf18	1.06E-04	5.12E-05	-2.77	-2.41	7.83E-05	-2.59
ENSMUSG00000055994	Nod2	1.18E-04	4.24E-05	4.43	3.86	8.02E-05	4.15
ENSMUSG00000036995	Asap3	1.64E-04	2.00E-12	5.07	11.83	8.18E-05	8.45
ENSMUSG00000006930	Hap1	1.64E-04	5.89E-32	8.02	172.07	8.21E-05	90.05
ENSMUSG00000034883	Lrr1	1.65E-04	5.28E-08	-3.09	-3.98	8.25E-05	-3.53
ENSMUSG00000071324	Armc2	1.51E-04	1.44E-05	-2.41	-2.30	8.28E-05	-2.36
ENSMUSG00000104272	Gm38297	1.40E-04	2.61E-05	7.33	6.79	8.30E-05	7.06
ENSMUSG00000040204	Pclaf	1.53E-05	1.53E-04	-2.62	-2.08	8.40E-05	-2.35

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000013089	Etv5	1.75E-05	1.52E-04	-2.96	-2.27	8.48E-05	-2.62
ENSMUSG00000036206	Sh3bp4	8.05E-08	1.77E-04	3.19	2.08	8.84E-05	2.63
ENSMUSG00000025429	Pstpip2	8.93E-14	1.80E-04	14.86	3.77	9.02E-05	9.32
ENSMUSG00000035064	Eef2k	1.86E-04	4.74E-12	-2.55	-4.23	9.32E-05	-3.39
ENSMUSG00000042389	Tsen2	1.88E-04	1.74E-10	-2.29	-3.33	9.41E-05	-2.81
ENSMUSG00000055809	Dnaaf3	1.20E-07	1.88E-04	3.23	2.13	9.43E-05	2.68
ENSMUSG00000025934	Gsta3	1.97E-04	6.54E-06	-2.07	-2.08	1.02E-04	-2.08
ENSMUSG00000063889	Crem	1.10E-07	2.04E-04	3.53	2.19	1.02E-04	2.86
ENSMUSG00000066191	Anks6	3.76E-05	1.73E-04	-2.68	-2.04	1.05E-04	-2.36
ENSMUSG00000033316	Galnt9	1.61E-04	5.00E-05	-5.57	-4.33	1.06E-04	-4.95
ENSMUSG00000090319	Gm4462	2.12E-04	2.05E-12	9.48	30.34	1.06E-04	19.91
ENSMUSG00000061878	Sphk1	4.86E-08	2.14E-04	6.26	3.08	1.07E-04	4.67
ENSMUSG00000064338	mt-Tv	2.17E-04	1.53E-11	2.11	3.05	1.08E-04	2.58
ENSMUSG00000031896	Ctrl	2.18E-04	1.20E-12	4.99	12.14	1.09E-04	8.57
ENSMUSG00000042842	Serpinb6b	2.20E-04	1.13E-13	2.48	4.44	1.10E-04	3.46
ENSMUSG00000026039	Sgo2a	2.20E-04	5.05E-09	-2.25	-2.90	1.10E-04	-2.57
ENSMUSG00000052270	Fpr2	2.22E-04	2.70E-07	6.22	8.40	1.11E-04	7.31
ENSMUSG00000036223	Ska1	2.28E-04	9.78E-09	-2.61	-3.47	1.14E-04	-3.04
ENSMUSG00000086564	Cd101	4.51E-05	1.84E-04	-3.64	-2.50	1.14E-04	-3.07
ENSMUSG00000022900	Ildr1	1.04E-04	1.25E-04	16.37	12.02	1.15E-04	14.20
ENSMUSG00000032392	Parp16	2.31E-04	6.42E-08	-2.84	-3.72	1.16E-04	-3.28
ENSMUSG00000032221	Mns1	2.01E-04	4.12E-05	-2.70	-2.49	1.21E-04	-2.59
ENSMUSG00000040829	Zmynd15	2.20E-04	3.58E-05	2.36	2.26	1.28E-04	2.31
ENSMUSG00000029246	Ppat	2.58E-04	2.47E-08	-2.06	-2.50	1.29E-04	-2.28
ENSMUSG00000047003	Zfp41	2.10E-04	5.88E-05	-2.44	-2.22	1.34E-04	-2.33

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000031652	N4bp1	2.69E-04	5.03E-11	2.01	2.82	1.35E-04	2.41
ENSMUSG00000035735	Dagla	6.27E-05	2.07E-04	-2.74	-2.18	1.35E-04	-2.46
ENSMUSG00000003992	Ssbp2	3.79E-06	2.72E-04	2.81	2.10	1.38E-04	2.45
ENSMUSG00000100018	Gm7776	2.25E-04	6.12E-05	3.30	3.09	1.43E-04	3.20
ENSMUSG00000076431	Sox4	3.20E-11	2.92E-04	-4.76	-2.15	1.46E-04	-3.46
ENSMUSG00000066687	Zbtb16	2.94E-04	1.61E-08	-4.18	-11.69	1.47E-04	-7.93
ENSMUSG00000017861	Mybl2	2.77E-04	1.95E-05	-4.00	-3.83	1.48E-04	-3.92
ENSMUSG00000041220	Elovl6	2.99E-04	1.48E-12	-2.40	-4.27	1.50E-04	-3.34
ENSMUSG00000000028	Cdc45	9.91E-06	2.96E-04	-2.91	-2.10	1.53E-04	-2.51
ENSMUSG00000034023	Fancd2	1.24E-05	2.95E-04	-2.96	-2.12	1.54E-04	-2.54
ENSMUSG00000099974	Bcl2a1d	2.99E-04	1.25E-05	7.16	7.59	1.56E-04	7.37
ENSMUSG00000045502	Hcar2	8.67E-10	3.15E-04	25.56	5.57	1.58E-04	15.56
ENSMUSG00000105008	Gm43652	3.13E-04	6.64E-06	2.72	2.87	1.60E-04	2.80
ENSMUSG00000020300	Cpeb4	3.18E-04	7.46E-07	2.12	2.37	1.60E-04	2.24
ENSMUSG00000104524	Gm37333	1.66E-05	3.04E-04	-3.15	-2.18	1.60E-04	-2.67
ENSMUSG00000026134	Prim2	3.02E-04	2.16E-05	-2.05	-2.02	1.62E-04	-2.04
ENSMUSG00000054675	Tmem119	3.21E-04	6.06E-06	-3.05	-3.19	1.63E-04	-3.12
ENSMUSG00000104867	Gm43728	3.30E-04	1.34E-07	2.67	3.31	1.65E-04	2.99
ENSMUSG00000062510	Nsl1	1.22E-05	3.20E-04	-3.01	-2.10	1.66E-04	-2.56
ENSMUSG00000114980	4933432I03Rik	9.92E-08	3.40E-04	6.17	3.19	1.70E-04	4.68
ENSMUSG00000020589	Cyria	3.42E-04	7.40E-07	2.17	2.45	1.71E-04	2.31
ENSMUSG00000027254	Map1a	2.55E-04	1.01E-04	-2.44	-2.14	1.78E-04	-2.29
ENSMUSG00000042213	Zfand4	1.77E-04	1.84E-04	-3.07	-2.45	1.81E-04	-2.76
ENSMUSG00000027962	Vcam1	9.14E-07	3.61E-04	3.54	2.26	1.81E-04	2.90
ENSMUSG00000025050	Pcgf6	3.63E-04	3.24E-11	-2.39	-4.00	1.82E-04	-3.19

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000022802	Lmln	3.60E-04	3.43E-06	-2.36	-2.52	1.82E-04	-2.44
ENSMUSG00000040034	Nup43	3.88E-04	4.10E-07	-2.37	-2.80	1.94E-04	-2.58
ENSMUSG00000021572	Cep72	9.93E-05	2.95E-04	-2.97	-2.24	1.97E-04	-2.60
ENSMUSG00000045382	Cxcr4	4.37E-05	3.61E-04	-3.10	-2.35	2.02E-04	-2.73
ENSMUSG00000042066	Tmcc2	2.53E-04	1.61E-04	-2.61	-2.26	2.07E-04	-2.44
ENSMUSG00000051235	Gen1	4.06E-04	2.45E-05	-2.11	-2.10	2.15E-04	-2.10
ENSMUSG00000032113	Chek1	3.31E-04	1.13E-04	-3.16	-2.82	2.22E-04	-2.99
ENSMUSG00000042155	Klhl23	4.43E-04	3.40E-06	-4.37	-5.10	2.23E-04	-4.74
ENSMUSG00000031555	Adam9	4.15E-04	3.34E-05	2.10	2.09	2.24E-04	2.09
ENSMUSG00000097006	9530082P21Rik	4.54E-04	2.57E-22	2.82	9.31	2.27E-04	6.07
ENSMUSG00000050350	Gpr18	1.36E-23	4.64E-04	22.62	2.92	2.32E-04	12.77
ENSMUSG00000002055	Spag5	4.63E-04	4.82E-06	-2.28	-2.46	2.34E-04	-2.37
ENSMUSG00000030207	Fam234b	4.67E-04	9.91E-07	-2.39	-2.76	2.34E-04	-2.58
ENSMUSG00000074345	Tnfaip8l3	4.75E-04	1.99E-24	4.17	24.75	2.38E-04	14.46
ENSMUSG00000112571	Gm48207	1.30E-05	4.65E-04	13.92	7.42	2.39E-04	10.67
ENSMUSG00000034872	Gipc3	2.60E-04	2.21E-04	9.09	7.57	2.40E-04	8.33
ENSMUSG00000038173	Enpp6	4.84E-04	2.09E-08	3.80	5.79	2.42E-04	4.80
ENSMUSG00000072949	Acot1	5.02E-04	3.06E-07	-5.06	-9.08	2.51E-04	-7.07
ENSMUSG00000062007	Hsh2d	5.20E-04	6.42E-19	7.83	58.77	2.60E-04	33.30
ENSMUSG00000025026	Add3	5.58E-04	4.93E-09	-2.04	-2.71	2.79E-04	-2.38
ENSMUSG00000029406	Pitpnm2	5.18E-05	5.42E-04	-3.53	-2.31	2.97E-04	-2.92
ENSMUSG00000036862	Dchs1	5.96E-04	2.94E-08	-3.06	-5.74	2.98E-04	-4.40
ENSMUSG00000035458	Tnni3	5.52E-05	5.44E-04	3.20	2.45	3.00E-04	2.82
ENSMUSG00000098176	Ccdc166	4.20E-05	5.80E-04	-4.35	-2.55	3.11E-04	-3.45
ENSMUSG00000108732	2310043P16Rik	6.39E-04	7.86E-43	2.42	13.02	3.20E-04	7.72

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000103291	Gm38235	6.37E-04	3.15E-06	3.49	4.16	3.20E-04	3.82
ENSMUSG00000020717	Pecam1	6.65E-04	2.03E-20	2.66	7.52	3.33E-04	5.09
ENSMUSG00000054115	Skp2	5.91E-04	8.36E-05	-2.41	-2.32	3.37E-04	-2.37
ENSMUSG00000045868	Gvin1	4.28E-04	2.49E-04	24.05	18.24	3.39E-04	21.15
ENSMUSG00000052934	Fbxo31	4.82E-05	6.34E-04	-2.92	-2.17	3.41E-04	-2.54
ENSMUSG00000085882	2610507I01Rik	3.98E-04	2.88E-04	-3.57	-2.77	3.43E-04	-3.17
ENSMUSG00000022146	Osmr	5.95E-04	1.04E-04	3.28	3.16	3.50E-04	3.22
ENSMUSG00000018925	Heatr9	6.90E-04	1.34E-05	12.72	16.10	3.51E-04	14.41
ENSMUSG00000025001	Hells	1.19E-06	7.10E-04	-3.82	-2.27	3.55E-04	-3.04
ENSMUSG00000026031	Cflar	6.65E-04	5.23E-05	3.21	3.21	3.59E-04	3.21
ENSMUSG00000043740	B430306N03Rik	7.19E-04	3.97E-24	-2.08	5.46	3.60E-04	1.69
ENSMUSG00000043487	Acot6	1.52E-04	5.68E-04	-4.15	-2.72	3.60E-04	-3.44
ENSMUSG00000027692	Tnik	6.72E-04	8.76E-05	3.36	3.28	3.80E-04	3.32
ENSMUSG00000103688	Gm6321	7.60E-04	4.60E-07	8.28	13.80	3.80E-04	11.04
ENSMUSG00000073700	Klhl21	7.72E-04	1.16E-10	-2.11	-3.22	3.86E-04	-2.66
ENSMUSG00000049823	Zbtb12	7.54E-04	2.69E-05	-2.13	-2.18	3.91E-04	-2.15
ENSMUSG00000032035	Ets1	5.58E-04	2.30E-04	-2.61	-2.31	3.94E-04	-2.46
ENSMUSG00000023473	Celsr3	8.00E-04	1.43E-07	-2.03	-2.56	4.00E-04	-2.30
ENSMUSG00000038252	Ncapd2	7.92E-04	1.41E-05	-2.09	-2.22	4.03E-04	-2.16
ENSMUSG00000104088	Gm38275	8.15E-04	2.78E-07	3.37	4.62	4.07E-04	4.00
ENSMUSG00000102964	9430034N14Rik	8.18E-04	8.79E-08	2.17	2.75	4.09E-04	2.46
ENSMUSG00000058470	Gm8369	8.31E-04	2.39E-22	2.24	6.04	4.16E-04	4.14
ENSMUSG00000051969	Tlr11	8.75E-04	3.04E-07	10.17	19.06	4.38E-04	14.61
ENSMUSG00000090556	Olfr753-ps1	5.03E-04	3.80E-04	13.02	10.35	4.41E-04	11.68
ENSMUSG00000048058	Ldlrad3	8.86E-04	1.56E-06	-2.30	-2.72	4.44E-04	-2.51

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000027324	Rpusd2	8.92E-04	4.87E-06	-2.98	-3.53	4.48E-04	-3.26
ENSMUSG00000036777	Anln	8.99E-04	1.99E-11	-2.10	-3.47	4.49E-04	-2.78
ENSMUSG00000042498	Radx	8.95E-04	4.66E-06	-3.95	-4.99	4.50E-04	-4.47
ENSMUSG00000086527	Gm15856	9.08E-04	4.72E-13	5.42	18.80	4.54E-04	12.11
ENSMUSG00000026821	Ralgds	1.96E-14	9.52E-04	5.82	2.02	4.76E-04	3.92
ENSMUSG00000073434	Wdr90	3.36E-05	9.38E-04	-5.42	-2.62	4.86E-04	-4.02
ENSMUSG00000072889	Nfxl1	9.95E-04	4.73E-28	2.14	7.32	4.97E-04	4.73
ENSMUSG00000029490	Mfsd7a	9.87E-04	8.34E-06	2.54	2.86	4.98E-04	2.70
ENSMUSG00000022586	Ly6i	2.21E-10	1.01E-03	51.36	7.64	5.04E-04	29.50
ENSMUSG00000043939	A530064D06Rik	1.02E-03	9.52E-15	-2.67	5.32	5.08E-04	1.33
ENSMUSG00000021846	Peli2	9.09E-04	1.23E-04	-2.25	-2.20	5.16E-04	-2.22
ENSMUSG00000027326	Knl1	9.50E-04	8.28E-05	-2.02	-2.01	5.16E-04	-2.02
ENSMUSG00000063851	Rnf183	3.34E-04	7.23E-04	-12.16	-6.95	5.28E-04	-9.56
ENSMUSG00000097128	#NV	4.99E-07	1.06E-03	14.11	5.57	5.29E-04	9.84
ENSMUSG00000032815	Fanca	4.57E-04	6.31E-04	-2.62	2.04	5.44E-04	-0.29
ENSMUSG00000027387	Zc3h8	1.09E-03	3.00E-13	-2.17	-4.81	5.45E-04	-3.49
ENSMUSG00000021367	Edn1	1.08E-03	1.02E-05	10.16	13.60	5.46E-04	11.88
ENSMUSG00000074863	Platr25	8.00E-04	2.94E-04	-2.42	-2.20	5.47E-04	-2.31
ENSMUSG00000074796	Slc4a11	1.11E-03	2.16E-32	3.07	20.66	5.56E-04	11.86
ENSMUSG00000029283	Cdc7	3.52E-05	1.08E-03	-3.26	-2.15	5.60E-04	-2.70
ENSMUSG00000048924	Ccdc125	1.10E-03	3.86E-05	-3.37	-3.56	5.68E-04	-3.47
ENSMUSG00000024121	Atp6v0c	1.20E-04	1.02E-03	2.66	2.12	5.72E-04	2.39
ENSMUSG00000026955	Sapcd2	1.15E-03	8.51E-09	-3.58	-9.74	5.73E-04	-6.66
ENSMUSG00000020648	Dus4l	1.16E-03	2.03E-06	-2.70	-3.41	5.81E-04	-3.05
ENSMUSG00000100235	Gm28557	9.72E-04	1.96E-04	-4.85	-3.84	5.84E-04	-4.34

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000108291	Gm44292	1.19E-03	1.85E-05	3.39	3.84	6.03E-04	3.61
ENSMUSG00000060301	2610008E11Rik	1.18E-03	3.07E-05	-2.02	-2.11	6.05E-04	-2.07
ENSMUSG00000038046	Mrm3	1.26E-03	7.33E-10	-2.25	-3.89	6.32E-04	-3.07
ENSMUSG00000026622	Nek2	1.25E-03	2.25E-05	-2.28	-2.46	6.37E-04	-2.37
ENSMUSG00000060923	Acyp2	1.00E-03	2.84E-04	3.69	3.47	6.44E-04	3.58
ENSMUSG00000047604	Frat2	1.29E-03	3.39E-08	-2.26	-3.17	6.46E-04	-2.71
ENSMUSG00000056749	Nfil3	2.07E-04	1.11E-03	3.25	2.46	6.58E-04	2.85
ENSMUSG00000006362	Cbfa2t3	1.32E-03	2.35E-10	-2.05	-3.20	6.61E-04	-2.62
ENSMUSG00000031548	Sfrp1	1.36E-03	4.26E-06	6.30	9.21	6.82E-04	7.75
ENSMUSG00000034842	Art3	1.37E-03	2.89E-07	12.24	26.57	6.86E-04	19.40
ENSMUSG00000055240	Zfp101	1.20E-03	1.79E-04	-2.50	-2.40	6.89E-04	-2.45
ENSMUSG00000045231	BC106179	7.98E-04	6.01E-04	-11.24	-7.60	6.99E-04	-9.42
ENSMUSG00000039384	Dusp10	1.22E-03	2.07E-04	3.14	3.03	7.11E-04	3.09
ENSMUSG00000093765	Gm20658	1.47E-03	6.02E-07	-2.67	-3.73	7.35E-04	-3.20
ENSMUSG00000046159	Chrm3	5.05E-12	1.47E-03	81.34	7.03	7.37E-04	44.18
ENSMUSG00000041396	Mettl18	1.48E-03	8.98E-07	-2.53	-3.37	7.39E-04	-2.95
ENSMUSG00000105541	Gm43136	1.46E-03	4.83E-05	3.90	4.38	7.52E-04	4.14
ENSMUSG00000036882	Arhgap33	1.49E-03	1.76E-05	-3.90	-4.67	7.52E-04	-4.28
ENSMUSG00000042351	Grap2	1.57E-03	1.91E-09	2.31	3.57	7.84E-04	2.94
ENSMUSG00000031549	Ido2	1.26E-05	1.57E-03	20.17	8.17	7.90E-04	14.17
ENSMUSG00000106951	5930430L01Rik	1.43E-03	1.70E-04	-4.78	-4.26	8.02E-04	-4.52
ENSMUSG00000023066	Rttn	1.60E-03	5.42E-06	-2.22	-2.60	8.03E-04	-2.41
ENSMUSG00000037640	Zfp60	1.61E-03	2.42E-05	-2.00	-2.15	8.18E-04	-2.08
ENSMUSG00000097804	Gm16685	1.58E-05	1.64E-03	9.01	4.35	8.28E-04	6.68
ENSMUSG00000022584	Ly6c2	1.04E-03	6.22E-04	3.26	2.91	8.29E-04	3.09

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000049811	Fam161a	4.66E-05	1.66E-03	-4.72	-2.52	8.53E-04	-3.62
ENSMUSG00000025324	Atp10a	1.71E-03	5.53E-41	2.25	13.79	8.57E-04	8.02
ENSMUSG00000112892	Gm8613	1.83E-03	4.61E-12	9.66	45.77	9.15E-04	27.72
ENSMUSG00000052632	Asap2	1.83E-03	2.79E-08	-2.33	-3.55	9.17E-04	-2.94
ENSMUSG00000028678	Kif2c	1.67E-03	1.81E-04	-2.54	-2.53	9.24E-04	-2.53
ENSMUSG00000000730	Dnmt3l	8.00E-04	1.09E-03	-4.35	-2.94	9.46E-04	-3.65
ENSMUSG00000055546	Timd4	1.83E-03	1.00E-04	7.70	9.00	9.67E-04	8.35
ENSMUSG00000113918	Gm6566	1.89E-03	6.32E-05	2.99	3.27	9.78E-04	3.13
ENSMUSG00000053411	Cbx7	1.97E-03	3.58E-10	-2.21	-3.98	9.86E-04	-3.10
ENSMUSG00000049555	Tmie	5.65E-04	1.43E-03	3.38	2.70	9.98E-04	3.04
ENSMUSG00000022419	Deptor	2.06E-03	3.52E-06	-2.40	-2.96	1.03E-03	-2.68
ENSMUSG00000109685	Gvin-ps1	1.71E-03	4.44E-04	8.77	8.43	1.08E-03	8.60
ENSMUSG00000001036	Epn2	4.06E-04	1.79E-03	-2.93	-2.11	1.10E-03	-2.52
ENSMUSG00000022661	Cd200	1.95E-03	2.58E-04	3.34	3.31	1.10E-03	3.32
ENSMUSG00000093622	Gm20703	2.12E-03	9.87E-05	-2.04	-2.10	1.11E-03	-2.07
ENSMUSG00000092118	Fancf	2.24E-03	4.03E-08	-2.34	-3.85	1.12E-03	-3.09
ENSMUSG00000054580	Pla2r1	2.24E-03	1.58E-12	2.37	4.69	1.12E-03	3.53
ENSMUSG00000064336	mt-Tf	2.22E-03	3.77E-05	3.34	3.88	1.13E-03	3.61
ENSMUSG00000078954	Arhgap8	2.16E-03	1.04E-04	6.70	7.96	1.13E-03	7.33
ENSMUSG00000048911	Rnf24	4.22E-08	2.27E-03	4.00	2.04	1.13E-03	3.02
ENSMUSG00000092626	9130230N09Rik	2.12E-03	1.54E-04	2.28	2.35	1.13E-03	2.31
ENSMUSG00000097705	Gm26740	2.29E-03	6.70E-07	-2.27	-3.03	1.14E-03	-2.65
ENSMUSG00000104436	Gm37423	2.29E-03	2.54E-07	2.08	2.73	1.14E-03	2.41
ENSMUSG00000072844	G530011O06Rik	2.35E-03	2.27E-10	6.10	20.86	1.18E-03	13.48
ENSMUSG00000026274	Pask	2.36E-03	1.25E-06	-2.93	-4.32	1.18E-03	-3.63

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000112067	Gm48015	2.37E-03	3.57E-10	3.12	6.36	1.18E-03	4.74
ENSMUSG00000020897	Aurkb	2.09E-03	2.90E-04	-2.08	-2.05	1.19E-03	-2.07
ENSMUSG00000104654	Gm43814	2.23E-03	2.57E-04	5.33	5.36	1.24E-03	5.35
ENSMUSG00000060550	H2-Q7	2.50E-03	4.14E-08	3.76	6.93	1.25E-03	5.34
ENSMUSG00000089643	Gm16301	2.53E-03	1.95E-06	10.73	20.56	1.27E-03	15.65
ENSMUSG00000027715	Ccna2	2.76E-03	1.54E-05	-2.04	-2.33	1.39E-03	-2.19
ENSMUSG00000051378	Kif18b	2.84E-03	2.32E-05	-2.30	-2.66	1.43E-03	-2.48
ENSMUSG00000020988	L2hgdh	2.84E-03	5.08E-05	-3.14	-3.63	1.44E-03	-3.39
ENSMUSG00000033083	Tbc1d4	2.61E-03	2.99E-04	-2.06	-2.06	1.45E-03	-2.06
ENSMUSG00000024301	Kifc5b	3.03E-03	6.16E-07	-2.37	-3.47	1.51E-03	-2.92
ENSMUSG00000109861	4930458B22Rik	6.69E-04	2.44E-03	18.56	10.62	1.55E-03	14.59
ENSMUSG00000000562	Adora3	3.13E-03	2.22E-06	4.21	6.56	1.56E-03	5.39
ENSMUSG00000028031	Dkk2	1.79E-03	1.35E-03	-8.84	-5.33	1.57E-03	-7.08
ENSMUSG00000097000	Gm17435	3.15E-03	6.17E-10	3.04	6.23	1.58E-03	4.64
ENSMUSG00000083822	Hmgb1-ps5	3.15E-03	4.03E-08	2.14	3.09	1.58E-03	2.61
ENSMUSG00000079737	3110001I22Rik	3.18E-03	6.44E-08	2.09	2.97	1.59E-03	2.53
ENSMUSG00000003617	Cp	3.20E-03	4.04E-18	2.27	6.47	1.60E-03	4.37
ENSMUSG00000028957	Per3	3.31E-03	2.90E-07	-2.04	-2.82	1.66E-03	-2.43
ENSMUSG00000042784	Muc1	2.70E-03	6.40E-04	7.73	7.66	1.67E-03	7.70
ENSMUSG00000091906	1700099I09Rik	3.36E-03	9.19E-10	2.31	3.89	1.68E-03	3.10
ENSMUSG00000049608	Gpr55	3.35E-03	1.26E-04	7.05	8.77	1.74E-03	7.91
ENSMUSG00000116927	Gm30881	3.63E-03	8.97E-17	2.37	6.21	1.81E-03	4.29
ENSMUSG00000006398	Cdc20	3.77E-03	1.01E-09	-2.18	-3.80	1.88E-03	-2.99
ENSMUSG00000074738	Fndc10	3.79E-03	7.63E-06	-2.38	-3.06	1.90E-03	-2.72
ENSMUSG00000106962	Gm43633	3.81E-03	2.22E-07	4.21	7.87	1.90E-03	6.04

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000000884	Gnb1l	3.77E-03	4.06E-05	-2.23	-2.55	1.90E-03	-2.39
ENSMUSG00000041429	Nthl1	3.89E-03	4.67E-09	-2.16	-3.99	1.94E-03	-3.08
ENSMUSG00000025255	Zfhx4	3.89E-03	2.66E-09	2.81	5.32	1.95E-03	4.07
ENSMUSG00000024462	Gabbr1	3.77E-03	1.33E-04	2.49	2.72	1.95E-03	2.60
ENSMUSG00000109560	Gm8463	3.99E-03	2.29E-07	3.45	5.90	1.99E-03	4.67
ENSMUSG00000039410	Prdm16	3.81E-03	3.28E-04	-2.36	-2.41	2.07E-03	-2.38
ENSMUSG00000079018	Ly6c1	4.26E-07	4.16E-03	10.78	3.97	2.08E-03	7.38
ENSMUSG00000097023	Mir9-3hg	3.76E-03	4.04E-04	11.47	12.68	2.08E-03	12.08
ENSMUSG00000045381	Olfr433	4.06E-03	1.82E-04	4.89	5.70	2.12E-03	5.29
ENSMUSG00000039781	Cep131	4.31E-03	1.91E-07	-2.00	-2.88	2.15E-03	-2.44
ENSMUSG00000044854	1700056E22Rik	1.80E-03	2.59E-03	2.79	2.40	2.20E-03	2.60
ENSMUSG00000026646	Suv39h2	4.01E-03	4.13E-04	-2.15	-2.16	2.21E-03	-2.16
ENSMUSG00000108030	9530062K07Rik	4.15E-03	2.88E-04	-3.57	-3.61	2.22E-03	-3.59
ENSMUSG00000114835	Gm48194	4.52E-03	1.73E-06	2.53	3.51	2.26E-03	3.02
ENSMUSG00000020974	Pole2	4.58E-03	1.60E-06	-2.55	-3.73	2.29E-03	-3.14
ENSMUSG00000020808	Pimreg	4.64E-03	1.49E-06	-2.23	-3.05	2.32E-03	-2.64
ENSMUSG00000044551	9930012K11Rik	2.43E-04	4.44E-03	-4.41	-2.35	2.34E-03	-3.38
ENSMUSG00000019845	Tube1	1.72E-03	2.98E-03	-2.68	-2.16	2.35E-03	-2.42
ENSMUSG00000036053	Fmnl2	4.64E-03	6.61E-05	2.35	2.70	2.35E-03	2.53
ENSMUSG00000030677	Kif22	4.54E-03	2.58E-04	-2.09	-2.20	2.40E-03	-2.14
ENSMUSG00000018427	Ypel2	7.40E-07	4.85E-03	-4.10	-2.03	2.43E-03	-3.06
ENSMUSG00000113587	Gm36287	2.37E-03	2.52E-03	5.38	4.36	2.44E-03	4.87
ENSMUSG00000105950	Gm43679	4.88E-03	2.41E-06	2.71	3.82	2.44E-03	3.27
ENSMUSG00000035279	Ssc5d	4.93E-03	2.40E-13	2.36	5.50	2.46E-03	3.93
ENSMUSG00000028773	Fabp3	4.94E-03	1.65E-16	2.07	5.37	2.47E-03	3.72

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000050578	Mmp13	5.04E-03	2.91E-35	2.72	30.74	2.52E-03	16.73
ENSMUSG00000102437	#NV	5.08E-03	9.02E-19	3.15	14.22	2.54E-03	8.68
ENSMUSG00000020656	Grhl1	3.28E-05	5.05E-03	3.43	2.16	2.54E-03	2.79
ENSMUSG00000097636	Mirt1	4.10E-03	1.00E-03	-3.21	-2.98	2.55E-03	-3.09
ENSMUSG00000026429	Ube2t	5.25E-03	1.45E-08	-2.22	-3.92	2.62E-03	-3.07
ENSMUSG00000107792	Gm43914	2.29E-03	3.02E-03	17.58	11.84	2.65E-03	14.71
ENSMUSG00000055210	Foxd2	5.63E-03	6.39E-06	-2.32	-3.17	2.82E-03	-2.75
ENSMUSG00000037474	Dtl	1.34E-08	5.84E-03	-5.20	-2.03	2.92E-03	-3.62
ENSMUSG00000002100	Mybpc3	5.58E-03	2.88E-04	2.13	2.27	2.94E-03	2.20
ENSMUSG00000082088	Gm15753	5.91E-03	8.38E-09	4.86	13.41	2.96E-03	9.14
ENSMUSG00000114070	Gm47727	4.57E-04	5.62E-03	4.09	2.70	3.04E-03	3.39
ENSMUSG00000032826	Ank2	9.29E-08	6.34E-03	5.31	2.25	3.17E-03	3.78
ENSMUSG00000024421	Lama3	5.76E-03	6.94E-04	-2.84	-2.86	3.23E-03	-2.85
ENSMUSG00000016498	Pdcd1lg2	6.50E-03	3.08E-10	4.70	15.89	3.25E-03	10.30
ENSMUSG00000036898	Zfp157	6.55E-03	9.84E-06	-2.07	-2.65	3.28E-03	-2.36
ENSMUSG00000048445	Ccdc57	5.89E-03	6.85E-04	-2.52	-2.53	3.29E-03	-2.53
ENSMUSG00000043953	Ccrl2	6.31E-03	4.98E-04	3.83	4.15	3.40E-03	3.99
ENSMUSG00000107529	Gm44291	4.53E-03	2.34E-03	2.17	2.02	3.44E-03	2.10
ENSMUSG00000084846	A730011C13Rik	7.00E-03	1.52E-11	2.98	7.85	3.50E-03	5.42
ENSMUSG00000106209	Gm42918	7.00E-03	1.58E-05	2.61	3.45	3.51E-03	3.03
ENSMUSG00000030725	Lipt2	7.08E-03	1.88E-07	-2.09	-3.47	3.54E-03	-2.78
ENSMUSG00000014773	Dll1	7.26E-03	3.78E-12	6.81	39.53	3.63E-03	23.17
ENSMUSG00000020546	Stxbp4	5.92E-03	1.38E-03	-2.15	-2.07	3.65E-03	-2.11
ENSMUSG00000029861	Fam131b	1.06E-03	6.30E-03	11.95	6.88	3.68E-03	9.42
ENSMUSG00000027456	Sdcbp2	7.37E-03	4.68E-07	2.69	4.38	3.69E-03	3.54

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000027811	4930579G24Rik	7.38E-03	3.94E-06	-2.31	-3.36	3.69E-03	-2.83
ENSMUSG00000035121	Neil2	7.45E-03	1.58E-06	-2.02	-2.89	3.72E-03	-2.46
ENSMUSG00000074892	B3galt5	7.48E-03	2.97E-04	-3.58	-4.16	3.89E-03	-3.87
ENSMUSG00000044231	Nhlrc1	8.15E-03	1.07E-04	-2.84	-3.53	4.13E-03	-3.19
ENSMUSG00000037568	Vash2	8.21E-03	1.70E-04	-2.20	-2.51	4.19E-03	-2.36
ENSMUSG00000074607	Tox2	4.83E-03	3.79E-03	-2.67	-2.35	4.31E-03	-2.51
ENSMUSG00000033762	Recql4	8.65E-03	1.00E-05	-2.43	-3.69	4.33E-03	-3.06
ENSMUSG00000028128	F3	2.80E-07	8.74E-03	37.48	5.66	4.37E-03	21.57
ENSMUSG00000053062	Jam2	8.11E-03	6.34E-04	3.67	4.06	4.37E-03	3.86
ENSMUSG00000005718	Tfap4	8.75E-03	1.86E-10	-2.65	-7.50	4.38E-03	-5.07
ENSMUSG00000114169	Gm47075	4.10E-03	4.73E-03	11.54	8.50	4.41E-03	10.02
ENSMUSG00000099843	Gm7160	9.11E-03	3.17E-11	2.16	4.47	4.55E-03	3.32
ENSMUSG00000102059	Gm20257	8.40E-03	7.45E-04	2.27	2.40	4.57E-03	2.33
ENSMUSG00000017499	Cdc6	1.64E-04	8.99E-03	-3.56	-2.14	4.57E-03	-2.85
ENSMUSG00000114784	Gm47754	9.18E-03	5.36E-11	2.04	3.82	4.59E-03	2.93
ENSMUSG00000066000	Zfp979	8.99E-03	4.86E-04	-2.46	-2.67	4.74E-03	-2.57
ENSMUSG00000048806	Ifnb1	2.75E-03	6.87E-03	21.63	11.55	4.81E-03	16.59
ENSMUSG00000035165	Kcne3	3.62E-04	9.31E-03	-11.94	-3.23	4.84E-03	-7.58
ENSMUSG00000083678	Gm12989	2.29E-03	7.41E-03	4.32	3.22	4.85E-03	3.77
ENSMUSG00000039648	Kyat1	9.52E-03	3.84E-04	-2.10	-2.30	4.95E-03	-2.20
ENSMUSG00000043419	Rnf227	8.74E-03	1.26E-03	-3.06	-3.08	5.00E-03	-3.07
ENSMUSG00000041907	Gpr45	7.58E-03	2.54E-03	2.91	2.82	5.06E-03	2.86
ENSMUSG00000038456	Dennd2a	1.01E-02	1.71E-04	-2.19	2.26	5.11E-03	0.04
ENSMUSG00000030393	Zik1	4.60E-03	6.28E-03	-5.93	-3.51	5.44E-03	-4.72
ENSMUSG00000034957	Cebpa	7.06E-03	3.95E-03	-2.18	-2.03	5.51E-03	-2.10

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000115116	Gm46496	5.36E-03	5.68E-03	5.34	4.46	5.52E-03	4.90
ENSMUSG00000097287	D130017N08Rik	1.10E-02	1.03E-04	-2.17	-2.68	5.58E-03	-2.43
ENSMUSG00000022218	Tgm1	2.34E-03	8.81E-03	9.62	6.05	5.58E-03	7.83
ENSMUSG00000042010	Acacb	8.38E-03	3.33E-03	3.17	3.02	5.85E-03	3.10
ENSMUSG00000106115	Gm43420	5.17E-03	6.88E-03	2.54	2.19	6.02E-03	2.37
ENSMUSG00000026303	Mlph	9.43E-03	2.84E-03	-8.58	-7.44	6.13E-03	-8.01
ENSMUSG00000102672	Gm37105	1.04E-02	1.90E-03	-2.27	-2.23	6.14E-03	-2.25
ENSMUSG00000050592	Fam78a	1.25E-02	4.40E-06	-2.47	-3.94	6.24E-03	-3.20
ENSMUSG00000101823	Gm29438	4.07E-07	1.27E-02	4.49	2.07	6.33E-03	3.28
ENSMUSG00000101903	Gm29291	1.23E-02	4.38E-04	-9.54	-12.56	6.36E-03	-11.05
ENSMUSG00000039131	Gipc2	1.28E-02	1.70E-06	-2.23	-3.99	6.41E-03	-3.11
ENSMUSG00000073409	H2-Q6	8.05E-03	5.14E-03	5.13	4.52	6.59E-03	4.82
ENSMUSG00000028933	Xrcc2	1.32E-02	2.89E-05	-2.22	-3.05	6.63E-03	-2.63
ENSMUSG00000084883	Ccdc85c	1.04E-03	1.25E-02	-9.89	-4.06	6.77E-03	-6.98
ENSMUSG00000101462	Gm3052	1.35E-02	4.10E-04	-2.70	-3.23	6.93E-03	-2.97
ENSMUSG00000110388	Gm30329	1.32E-02	6.47E-04	-2.11	-2.32	6.93E-03	-2.22
ENSMUSG00000027654	Fam83d	1.42E-02	6.19E-07	-2.29	-3.98	7.12E-03	-3.13
ENSMUSG00000109428	Gm45698	1.38E-02	4.71E-04	3.57	4.40	7.12E-03	3.99
ENSMUSG00000085295	4930430E12Rik	1.45E-02	2.99E-05	2.04	2.67	7.24E-03	2.35
ENSMUSG00000000078	Klf6	7.01E-03	7.52E-03	2.66	2.29	7.27E-03	2.47
ENSMUSG00000034800	Zfp661	1.45E-02	1.48E-05	-2.07	-2.97	7.27E-03	-2.52
ENSMUSG00000023947	Nfkbie	2.95E-03	1.22E-02	3.67	2.60	7.56E-03	3.13
ENSMUSG00000099746	Ppnr	2.05E-03	1.43E-02	3.31	2.41	8.18E-03	2.86
ENSMUSG00000116796	Gm49784	1.08E-02	5.55E-03	2.45	2.29	8.18E-03	2.37
ENSMUSG00000103284	3110080O07Rik	1.60E-02	3.97E-04	-4.10	-6.32	8.22E-03	-5.21

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000072919	Noxred1	1.67E-02	5.58E-06	2.42	3.75	8.35E-03	3.08
ENSMUSG00000070997	1700055D18Rik	1.70E-02	1.21E-05	2.35	3.42	8.50E-03	2.89
ENSMUSG00000040270	Bach2	1.69E-02	1.55E-04	-2.80	-3.81	8.52E-03	-3.30
ENSMUSG00000097295	Hmgb1-ps8	1.70E-02	4.20E-05	-2.01	-2.65	8.53E-03	-2.33
ENSMUSG00000025746	Il6	1.70E-02	3.31E-04	8.53	13.82	8.67E-03	11.17
ENSMUSG00000090290	Tarbp1	1.73E-02	7.59E-05	-2.77	-4.55	8.68E-03	-3.66
ENSMUSG00000022790	Igsf11	4.00E-10	1.77E-02	8.45	2.29	8.84E-03	5.37
ENSMUSG00000097558	Gm26902	1.77E-02	1.10E-04	4.67	7.60	8.88E-03	6.14
ENSMUSG00000027317	Ppp1r14d	1.83E-02	6.82E-07	6.53	18.81	9.16E-03	12.67
ENSMUSG00000024575	Pde6a	1.84E-02	4.17E-05	4.71	8.60	9.21E-03	6.65
ENSMUSG00000024014	Pim1	1.19E-02	6.60E-03	2.22	2.07	9.24E-03	2.14
ENSMUSG00000025010	Ccnj	1.87E-02	4.06E-13	2.05	5.13	9.33E-03	3.59
ENSMUSG00000109408	A930037H05Rik	1.77E-02	1.13E-03	-5.73	-6.87	9.39E-03	-6.30
ENSMUSG00000105270	Gm42863	1.32E-02	5.90E-03	4.39	4.18	9.54E-03	4.28
ENSMUSG00000046169	Adamts6	1.92E-02	9.66E-15	2.22	6.86	9.59E-03	4.54
ENSMUSG00000097572	Gm26797	1.97E-02	8.29E-26	2.33	14.04	9.86E-03	8.19
ENSMUSG00000022885	St6gal1	1.60E-02	3.74E-03	-2.22	-2.22	9.89E-03	-2.22
ENSMUSG00000037725	Ckap2	1.93E-02	5.76E-04	-2.11	-2.45	9.96E-03	-2.28
ENSMUSG00000031906	Smpd3	3.29E-03	1.70E-02	-5.86	-2.93	1.01E-02	-4.40
ENSMUSG00000089687	Rab42	1.18E-02	8.53E-03	-2.56	-2.17	1.02E-02	-2.36
ENSMUSG00000033900	Map9	1.06E-02	9.80E-03	-2.94	-2.40	1.02E-02	-2.67
ENSMUSG00000104897	Gm43203	5.00E-03	1.55E-02	4.63	3.33	1.03E-02	3.98
ENSMUSG00000094595	Fsbp	2.50E-04	2.05E-02	-7.02	-2.37	1.04E-02	-4.69
ENSMUSG00000100121	1700025N23Rik	1.83E-02	2.54E-03	9.77	11.38	1.04E-02	10.57
ENSMUSG00000070691	Runx3	1.79E-02	3.31E-03	2.14	2.19	1.06E-02	2.17

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000050605	Zfp61	2.01E-02	1.25E-03	-2.22	-2.47	1.07E-02	-2.34
ENSMUSG00000043415	Otud1	2.14E-02	1.01E-04	2.81	4.08	1.07E-02	3.44
ENSMUSG00000073415	Gm10501	3.86E-03	1.80E-02	-5.64	-2.50	1.09E-02	-4.07
ENSMUSG00000067928	Zfp760	8.92E-03	1.31E-02	-2.60	-2.05	1.10E-02	-2.32
ENSMUSG00000015709	Arnt2	1.16E-03	2.09E-02	4.50	2.67	1.10E-02	3.59
ENSMUSG00000044702	Palb2	2.22E-02	2.12E-05	-2.10	-3.10	1.11E-02	-2.60
ENSMUSG00000032281	Acsbg1	2.12E-02	1.26E-03	-3.35	-4.03	1.12E-02	-3.69
ENSMUSG00000020623	Map2k6	1.41E-02	8.45E-03	-2.57	-2.28	1.13E-02	-2.42
ENSMUSG00000115543	B230362B09Rik	8.00E-04	2.23E-02	-3.84	-2.02	1.16E-02	-2.93
ENSMUSG00000102423	Gm37465	2.18E-02	1.39E-03	-6.31	-7.64	1.16E-02	-6.98
ENSMUSG00000010021	Kif19a	8.11E-03	1.53E-02	4.15	3.18	1.17E-02	3.66
ENSMUSG00000032515	Csrnp1	5.51E-03	1.83E-02	4.87	3.22	1.19E-02	4.05
ENSMUSG00000084964	Gm15503	2.38E-02	3.10E-05	-2.01	-2.86	1.19E-02	-2.44
ENSMUSG00000059395	Nkapl	2.17E-02	2.22E-03	-6.41	-7.14	1.19E-02	-6.77
ENSMUSG00000020332	Meikin	2.40E-02	5.77E-10	6.42	35.72	1.20E-02	21.07
ENSMUSG00000032487	Ptgs2	1.72E-04	2.40E-02	11.90	3.85	1.21E-02	7.87
ENSMUSG00000022519	Srl	2.26E-02	1.88E-03	-2.66	-2.96	1.23E-02	-2.81
ENSMUSG00000047143	Dmrta2	1.79E-02	6.70E-03	-2.84	-2.57	1.23E-02	-2.71
ENSMUSG00000035373	Ccl7	2.64E-02	1.58E-08	3.32	10.82	1.32E-02	7.07
ENSMUSG00000026778	Prkcq	2.63E-02	3.26E-04	5.60	9.08	1.33E-02	7.34
ENSMUSG00000097754	Ptgs2os2	2.11E-06	2.67E-02	8.07	2.50	1.33E-02	5.28
ENSMUSG00000037995	Igsf9	2.68E-02	5.82E-28	2.15	16.10	1.34E-02	9.12
ENSMUSG00000017639	Rab11fip4	2.69E-02	1.31E-04	-2.51	-4.17	1.35E-02	-3.34
ENSMUSG00000024530	Prelid3a	2.52E-02	2.75E-03	-2.10	-2.24	1.40E-02	-2.17
ENSMUSG00000086150	Bach2os	2.75E-02	5.85E-04	-3.75	-5.89	1.40E-02	-4.82

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000096959	4930509G22Rik	2.74E-02	8.18E-04	6.13	9.42	1.41E-02	7.78
ENSMUSG00000051920	Rspo2	2.62E-02	2.12E-03	-2.56	2.28	1.42E-02	-0.14
ENSMUSG00000050395	Tnfsf15	2.88E-02	3.11E-04	3.87	5.99	1.46E-02	4.93
ENSMUSG00000044026	Slc35g1	2.89E-02	3.70E-04	-2.08	-2.65	1.46E-02	-2.36
ENSMUSG00000025738	Fbxl16	2.62E-02	3.18E-03	-2.43	-2.60	1.47E-02	-2.51
ENSMUSG00000115355	4930445E18Rik	3.71E-03	2.60E-02	8.79	4.88	1.48E-02	6.84
ENSMUSG00000030283	St8sia1	2.98E-02	2.22E-06	4.61	12.51	1.49E-02	8.56
ENSMUSG00000107604	Gm44041	1.45E-02	1.59E-02	-8.59	-5.81	1.52E-02	-7.20
ENSMUSG00000006435	Neurl1a	2.43E-02	6.53E-03	-4.31	-3.96	1.54E-02	-4.14
ENSMUSG00000031613	Hpgd	1.70E-03	2.96E-02	-3.69	-2.10	1.56E-02	-2.90
ENSMUSG00000098789	Jmjd7	2.38E-02	8.23E-03	-2.34	-2.23	1.60E-02	-2.28
ENSMUSG00000041064	Pif1	2.06E-02	1.14E-02	-2.55	-2.33	1.60E-02	-2.44
ENSMUSG00000047115	Fam221a	2.60E-02	6.43E-03	-2.54	-2.50	1.62E-02	-2.52
ENSMUSG00000032578	Cish	2.00E-04	3.23E-02	6.01	2.57	1.62E-02	4.29
ENSMUSG00000078773	Rad54b	2.26E-02	9.89E-03	-2.15	-2.05	1.62E-02	-2.10
ENSMUSG00000067199	Frat1	3.37E-02	7.22E-04	-2.34	-2.99	1.72E-02	-2.66
ENSMUSG00000034538	Zfp418	3.15E-02	3.74E-03	-2.88	-3.17	1.76E-02	-3.03
ENSMUSG00000043833	2900005J15Rik	3.52E-02	6.75E-05	-2.50	-4.34	1.76E-02	-3.42
ENSMUSG00000073590	3222401L13Rik	2.94E-02	6.28E-03	-2.62	-2.66	1.78E-02	-2.64
ENSMUSG00000020953	Coch	3.57E-02	3.85E-31	4.64	119.10	1.79E-02	61.87
ENSMUSG00000026700	Tnfsf4	3.62E-02	1.13E-10	2.75	10.53	1.81E-02	6.64
ENSMUSG00000097325	Gm16897	3.30E-02	3.30E-03	4.82	6.02	1.81E-02	5.42
ENSMUSG00000031327	Chic1	3.63E-02	9.73E-07	3.87	10.62	1.82E-02	7.24
ENSMUSG00000110500	Gm32568	3.51E-05	3.75E-02	22.52	5.18	1.88E-02	13.85
ENSMUSG00000072618	Gm10384	3.76E-02	1.31E-07	-2.96	-17.23	1.88E-02	-10.09

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000065494	Mir28a	1.27E-02	2.51E-02	5.79	4.11	1.89E-02	4.95
ENSMUSG00000104018	4833412K13Rik	3.82E-02	1.40E-04	-2.27	-3.42	1.92E-02	-2.84
ENSMUSG00000058979	Hdhd5	3.10E-02	7.48E-03	-2.27	-2.26	1.92E-02	-2.26
ENSMUSG00000021364	Elovl2	3.85E-02	9.53E-05	4.89	10.12	1.93E-02	7.51
ENSMUSG00000049872	Calhm5	1.73E-06	3.86E-02	5.50	2.15	1.93E-02	3.82
ENSMUSG00000030747	Dgat2	3.65E-02	2.08E-03	2.23	2.60	1.93E-02	2.41
ENSMUSG00000000320	Alox12	3.35E-03	3.55E-02	12.02	5.56	1.94E-02	8.79
ENSMUSG00000035594	Chrna5	3.91E-02	9.28E-10	5.83	42.47	1.95E-02	24.15
ENSMUSG00000024402	Lta	3.98E-02	3.65E-04	4.08	6.89	2.01E-02	5.49
ENSMUSG00000032420	Nt5e	1.41E-02	2.63E-02	-6.38	-3.97	2.02E-02	-5.17
ENSMUSG00000022240	Ctnnd2	4.07E-02	1.13E-10	2.04	5.43	2.04E-02	3.74
ENSMUSG00000068957	4930589L23Rik	3.55E-02	5.29E-03	2.98	3.30	2.04E-02	3.14
ENSMUSG00000087252	Gm14379	4.11E-02	3.00E-04	2.13	2.84	2.07E-02	2.49
ENSMUSG00000081650	Gm16181	8.69E-04	4.12E-02	7.26	3.21	2.10E-02	5.24
ENSMUSG00000098292	Gm27194	5.08E-05	4.26E-02	15.85	4.16	2.13E-02	10.01
ENSMUSG00000031382	Asb11	4.19E-02	1.09E-03	7.62	13.12	2.15E-02	10.37
ENSMUSG00000009614	Sardh	1.00E-02	3.31E-02	-3.00	-2.07	2.15E-02	-2.53
ENSMUSG00000052565	H1f3	4.12E-02	2.17E-03	-2.21	-2.62	2.17E-02	-2.41
ENSMUSG00000037279	Ovol2	4.11E-03	3.93E-02	23.57	8.32	2.17E-02	15.94
ENSMUSG00000034336	Ina	4.32E-02	6.76E-04	-2.29	-3.17	2.19E-02	-2.73
ENSMUSG00000055866	Per2	3.51E-02	9.06E-03	-2.31	-2.34	2.21E-02	-2.33
ENSMUSG00000112767	Gm47532	4.37E-02	3.95E-04	7.74	16.08	2.21E-02	11.91
ENSMUSG00000019437	Tlcd1	3.70E-02	7.82E-03	-2.29	-2.36	2.24E-02	-2.32
ENSMUSG00000003585	Sec14l2	3.92E-02	5.67E-03	-5.60	-6.24	2.24E-02	-5.92
ENSMUSG00000024486	Hbegf	3.22E-02	1.37E-02	2.94	2.82	2.30E-02	2.88

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000051727	Kctd14	3.58E-02	1.03E-02	3.83	3.98	2.30E-02	3.90
ENSMUSG00000035000	Dpp4	3.10E-02	1.63E-02	4.89	4.63	2.36E-02	4.76
ENSMUSG00000018849	Wwc1	1.75E-02	3.05E-02	-2.78	2.00	2.40E-02	-0.39
ENSMUSG00000101662	Gm28499	4.30E-02	5.98E-03	-4.81	-5.36	2.45E-02	-5.08
ENSMUSG00000109708	Gm45809	3.68E-02	1.24E-02	-6.29	-5.93	2.46E-02	-6.11
ENSMUSG00000110393	Gm36445	3.77E-02	1.32E-02	-2.82	-2.68	2.55E-02	-2.75
ENSMUSG00000085129	5031425F14Rik	4.63E-02	4.97E-03	-2.83	-3.31	2.57E-02	-3.07
ENSMUSG00000102662	Gm38377	9.06E-03	4.26E-02	2.82	2.05	2.58E-02	2.43
ENSMUSG00000065808	#NV	3.85E-02	1.33E-02	4.62	4.66	2.59E-02	4.64
ENSMUSG00000115384	Gm49205	1.29E-02	3.98E-02	8.63	5.15	2.64E-02	6.89
ENSMUSG00000112883	Gm48023	1.08E-02	4.20E-02	6.98	4.29	2.64E-02	5.63
ENSMUSG00000085030	2810455O05Rik	1.75E-02	3.74E-02	-2.75	-2.05	2.75E-02	-2.40
ENSMUSG00000105607	Gm43513	4.70E-02	7.94E-03	-5.91	-6.58	2.75E-02	-6.24
ENSMUSG00000021485	Mxd3	3.51E-02	2.02E-02	-2.59	-2.32	2.76E-02	-2.45
ENSMUSG00000115480	Gm49249	1.99E-02	3.71E-02	-3.25	-2.26	2.85E-02	-2.76
ENSMUSG00000035283	Adrb1	1.46E-02	4.43E-02	-4.16	-2.37	2.94E-02	-3.27
ENSMUSG00000015665	Awat1	3.93E-02	2.00E-02	2.13	2.06	2.97E-02	2.09
ENSMUSG00000027977	Ndst3	1.66E-02	4.31E-02	10.01	5.91	2.99E-02	7.96
ENSMUSG00000036136	Fam110c	4.16E-02	1.99E-02	-2.73	2.25	3.07E-02	-0.24
ENSMUSG00000102863	Gm37639	4.96E-02	1.21E-02	2.12	2.20	3.09E-02	2.16
ENSMUSG00000046323	Dppa3	4.18E-02	2.00E-02	-3.30	2.05	3.09E-02	-0.62
ENSMUSG00000006586	Runx1t1	2.50E-02	3.84E-02	2.50	2.11	3.17E-02	2.31
ENSMUSG00000026875	Traf1	3.95E-02	2.60E-02	3.28	2.94	3.27E-02	3.11
ENSMUSG00000038180	Spag4	4.60E-02	1.95E-02	-2.98	-2.74	3.27E-02	-2.86
ENSMUSG00000022178	Ajuba	2.62E-02	4.19E-02	-2.71	-2.09	3.41E-02	-2.40

Gene ID	Gene name	FDR IFN-γ	FDR IFN-α+β	Foldchange IFN-γ	Foldchange IFN-α+β	FDR average	Foldchange average
ENSMUSG00000047945	Marcksl1	2.84E-02	4.03E-02	2.84	2.31	3.43E-02	2.57
ENSMUSG00000045662	Henmt1	4.63E-02	2.29E-02	5.09	4.90	3.46E-02	4.99
ENSMUSG00000039814	Xkr5	2.49E-02	4.46E-02	-2.56	-2.03	3.48E-02	-2.29
ENSMUSG00000055413	H2-Q5	4.82E-02	2.13E-02	3.18	3.11	3.48E-02	3.14
ENSMUSG00000025141	Myadml2	2.77E-02	4.79E-02	-5.90	-3.76	3.78E-02	-4.83

Appendix 2 Complete list of differentially expressed genes upon IFN-α+β stimulation

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000020638	Cmpk2	0.00E+00	0.00E+00	821.02	2.49E+04	3.03E+01
ENSMUSG00000045932	Ifit2	0.00E+00	0.00E+00	592.12	1.21E+04	2.05E+01
ENSMUSG00000074896	Ifit3	0.00E+00	0.00E+00	378.05	1.28E+04	3.38E+01
ENSMUSG00000078920	Ifi47	0.00E+00	0.00E+00	120.64	8.89E+03	7.37E+01
ENSMUSG00000078853	Igtp	0.00E+00	0.00E+00	93.18	4.82E+03	5.17E+01
ENSMUSG00000040253	Gbp7	0.00E+00	0.00E+00	79.68	7.25E+03	9.10E+01
ENSMUSG00000046879	Irgm1	0.00E+00	0.00E+00	50.96	2.92E+03	5.73E+01
ENSMUSG00000069874	Irgm2	0.00E+00	0.00E+00	50.72	1.34E+03	2.64E+01
ENSMUSG00000033355	Rtp4	0.00E+00	0.00E+00	38.48	4.89E+03	1.27E+02
ENSMUSG00000090272	Mndal	0.00E+00	0.00E+00	27.72	1.97E+04	7.11E+02
ENSMUSG00000074151	Nlrc5	0.00E+00	0.00E+00	22.63	1.01E+03	4.44E+01
ENSMUSG00000030921	Trim30a	0.00E+00	0.00E+00	18.27	8.53E+03	4.67E+02
ENSMUSG00000063268	Parp10	0.00E+00	0.00E+00	15.24	1.06E+03	6.97E+01
ENSMUSG00000030275	Etnk1	3.73E-294	4.66E-291	6.62	1.45E+03	2.19E+02
ENSMUSG00000027639	Samhd1	1.57E-285	1.83E-282	17.12	1.55E+04	9.04E+02
ENSMUSG00000037921	Ddx60	1.13E-280	1.23E-277	62.22	2.80E+03	4.50E+01
ENSMUSG00000040296	Ddx58	2.33E-279	2.40E-276	33.01	3.66E+03	1.11E+02
ENSMUSG00000025498	Irf7	3.15E-275	3.06E-272	169.52	9.55E+03	5.63E+01
ENSMUSG00000026088	Mitd1	2.30E-272	2.12E-269	9.83	1.04E+03	1.06E+02
ENSMUSG00000034459	Ifit1	3.05E-265	2.66E-262	713.73	2.70E+04	3.79E+01
ENSMUSG00000017830	Dhx58	5.16E-258	4.29E-255	17.81	8.43E+02	4.73E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000043263	Ifi209	6.16E-247	4.89E-244	218.26	4.19E+03	1.92E+01
ENSMUSG00000054404	Slfn5	1.60E-246	1.22E-243	30.29	1.09E+04	3.61E+02
ENSMUSG00000031792	Usb1	1.69E-244	1.23E-241	6.53	1.63E+03	2.49E+02
ENSMUSG00000042726	Trafd1	2.73E-244	1.90E-241	11.93	4.59E+03	3.85E+02
ENSMUSG00000029561	Oasl2	8.61E-243	5.78E-240	52.31	2.81E+03	5.38E+01
ENSMUSG00000070327	Rnf213	1.06E-233	6.86E-231	26.17	4.36E+03	1.67E+02
ENSMUSG00000082292	Gm12250	2.12E-230	1.32E-227	175.87	8.74E+02	4.97E+00
ENSMUSG00000079339	Ifit1bl1	1.46E-229	8.82E-227	2,323.05	1.19E+04	5.12E+00
ENSMUSG00000029298	Gbp9	3.30E-228	1.92E-225	38.84	5.31E+02	1.37E+01
ENSMUSG00000058163	Gm5431	3.44E-228	1.94E-225	37.40	3.91E+02	1.05E+01
ENSMUSG00000049502	Dtx3l	8.33E-228	4.55E-225	16.00	3.26E+03	2.04E+02
ENSMUSG00000054072	Iigp1	7.32E-219	3.88E-216	1,894.02	1.14E+04	6.00E+00
ENSMUSG00000024079	Eif2ak2	1.79E-217	9.19E-215	10.58	1.34E+03	1.27E+02
ENSMUSG00000026222	Sp100	8.77E-217	4.38E-214	13.40	4.03E+03	3.01E+02
ENSMUSG00000037321	Tap1	3.47E-216	1.68E-213	21.31	8.47E+03	3.98E+02
ENSMUSG00000002307	Daxx	2.73E-214	1.29E-211	18.78	4.71E+03	2.51E+02
ENSMUSG00000073489	Ifi204	1.26E-207	5.78E-205	13.99	6.74E+03	4.82E+02
ENSMUSG00000029780	Nt5c3	2.17E-207	9.72E-205	19.90	4.99E+03	2.51E+02
ENSMUSG00000029798	Herc6	3.34E-207	1.46E-204	32.22	2.33E+03	7.24E+01
ENSMUSG00000036986	Pml	5.23E-207	2.23E-204	12.92	1.90E+03	1.47E+02
ENSMUSG00000028268	Gbp3	1.02E-206	4.24E-204	113.95	4.41E+03	3.87E+01
ENSMUSG00000027951	Adar	1.26E-205	5.14E-203	7.31	9.53E+02	1.30E+02
ENSMUSG00000035692	Isg15	5.23E-198	2.07E-195	216.09	1.16E+04	5.37E+01
ENSMUSG00000062488	Ifit3b	8.46E-197	3.29E-194	560.34	3.34E+03	5.95E+00
ENSMUSG00000060519	Tor3a	4.02E-196	1.53E-193	18.00	6.57E+03	3.65E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000073555	Gm4951	1.97E-194	7.34E-192	726.22	1.18E+03	1.62E+00
ENSMUSG00000030107	Usp18	3.92E-194	1.43E-191	172.02	3.68E+03	2.14E+01
ENSMUSG00000040033	Stat2	1.31E-192	4.66E-190	26.90	2.84E+03	1.06E+02
ENSMUSG00000070031	Sp140	4.49E-192	1.57E-189	20.55	1.01E+03	4.91E+01
ENSMUSG00000038507	Parp12	1.94E-191	6.65E-189	14.52	1.67E+03	1.15E+02
ENSMUSG00000027514	Zbp1	4.73E-189	1.59E-186	97.17	1.97E+03	2.03E+01
ENSMUSG00000028270	Gbp2	1.88E-188	6.18E-186	176.29	1.53E+04	8.67E+01
ENSMUSG00000031712	Il15	3.43E-182	1.09E-179	18.47	1.51E+03	8.17E+01
ENSMUSG00000023307	Marchf5	3.38E-182	1.09E-179	7.49	2.60E+03	3.47E+02
ENSMUSG00000034118	Tpst1	2.52E-181	7.86E-179	14.91	5.33E+02	3.57E+01
ENSMUSG00000090222	Ifi203-ps	3.14E-180	9.63E-178	32.52	3.52E+02	1.08E+01
ENSMUSG00000078616	Trim30c	8.80E-179	2.65E-176	207.78	1.19E+03	5.73E+00
ENSMUSG00000059089	Fcgr4	4.18E-176	1.24E-173	12.33	2.20E+03	1.78E+02
ENSMUSG00000069892	9930111J21Rik2	1.47E-175	4.28E-173	11.84	5.68E+02	4.80E+01
ENSMUSG00000026896	Ifih1	5.14E-175	1.47E-172	35.13	3.33E+03	9.49E+01
ENSMUSG00000035208	Slfn8	7.26E-175	2.05E-172	33.53	2.89E+03	8.61E+01
ENSMUSG00000027669	Gnb4	7.95E-169	2.21E-166	16.20	1.18E+03	7.28E+01
ENSMUSG00000047735	Samd9l	2.88E-167	7.86E-165	15.81	2.78E+03	1.76E+02
ENSMUSG00000032690	Oas2	5.04E-166	1.35E-163	17.63	9.65E+02	5.47E+01
ENSMUSG00000057596	Trim30d	3.19E-164	8.44E-162	25.42	2.32E+03	9.11E+01
ENSMUSG00000070730	Rmdn3	2.13E-161	5.56E-159	6.16	1.54E+03	2.50E+02
ENSMUSG00000026946	Nmi	6.69E-158	1.72E-155	11.36	1.22E+03	1.07E+02
ENSMUSG00000022906	Parp9	8.83E-158	2.24E-155	14.00	2.95E+03	2.11E+02
ENSMUSG00000091649	Phf11b	9.78E-157	2.44E-154	115.29	7.03E+03	6.10E+01
ENSMUSG00000033487	Fndc3a	6.77E-154	1.67E-151	7.86	3.25E+03	4.14E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000000386	Mx1	5.34E-153	1.30E-150	821.82	6.41E+03	7.80E+00
ENSMUSG00000090125	Pou3f1	4.73E-151	1.13E-148	108.31	1.13E+03	1.04E+01
ENSMUSG00000036381	P2ry14	1.99E-150	4.70E-148	11.71	9.60E+02	8.20E+01
ENSMUSG00000020641	Rsad2	6.14E-150	1.43E-147	460.90	1.56E+05	3.39E+02
ENSMUSG00000030966	Trim21	4.65E-147	1.07E-144	12.45	4.59E+02	3.69E+01
ENSMUSG00000074342	I830077J02Rik	9.08E-147	2.06E-144	20.79	5.96E+02	2.87E+01
ENSMUSG00000070034	Sp110	4.31E-146	9.66E-144	15.22	1.03E+03	6.80E+01
ENSMUSG00000015947	Fcgr1	1.27E-145	2.81E-143	27.97	6.51E+03	2.33E+02
ENSMUSG00000040483	Xaf1	2.66E-145	5.81E-143	27.14	3.68E+02	1.36E+01
ENSMUSG00000050029	Rap2c	6.84E-145	1.47E-142	4.64	2.44E+03	5.25E+02
ENSMUSG00000054823	Nsd3	9.74E-143	2.07E-140	3.74	1.94E+03	5.19E+02
ENSMUSG00000034422	Parp14	1.74E-139	3.65E-137	21.02	9.20E+03	4.37E+02
ENSMUSG00000039699	Batf2	2.05E-138	4.26E-136	64.02	4.85E+02	7.57E+00
ENSMUSG00000009585	Apobec3	9.98E-138	2.05E-135	7.63	1.32E+03	1.73E+02
ENSMUSG00000039899	Fgl2	1.12E-137	2.28E-135	105.13	6.68E+03	6.35E+01
ENSMUSG00000009185	Ccl8	1.89E-136	3.80E-134	796.99	8.66E+02	1.09E+00
ENSMUSG00000031639	Tlr3	6.47E-136	1.28E-133	22.51	1.02E+03	4.52E+01
ENSMUSG00000057554	Lgals8	1.24E-135	2.43E-133	3.08	1.91E+03	6.20E+02
ENSMUSG00000024679	Ms4a6d	7.23E-135	1.40E-132	4.94	5.69E+03	1.15E+03
ENSMUSG00000025888	Casp1	1.73E-134	3.33E-132	6.68	3.98E+03	5.95E+02
ENSMUSG00000010358	Ifi35	6.77E-134	1.29E-131	13.67	1.19E+03	8.73E+01
ENSMUSG00000037816	Fbxw17	9.41E-131	1.77E-128	6.24	6.34E+02	1.02E+02
ENSMUSG00000033213	AA467197	9.63E-129	1.79E-126	94.60	2.51E+03	2.66E+01
ENSMUSG00000040328	Olfr56	1.80E-127	3.31E-125	227.05	2.82E+02	1.24E+00
ENSMUSG00000050565	Tor1aip2	1.07E-125	1.94E-123	5.69	2.82E+03	4.96E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000059436	Max	4.01E-122	7.22E-120	4.34	2.97E+03	6.85E+02
ENSMUSG00000029502	Golga3	5.97E-121	1.06E-118	4.93	7.19E+02	1.46E+02
ENSMUSG00000049401	Ogfr	6.14E-121	1.08E-118	6.04	1.51E+03	2.50E+02
ENSMUSG00000045210	Vcpip1	6.22E-121	1.09E-118	4.13	1.30E+03	3.15E+02
ENSMUSG00000022014	Epsti1	3.25E-120	5.62E-118	14.30	3.63E+03	2.54E+02
ENSMUSG00000029474	Rnf34	1.03E-119	1.76E-117	6.56	8.80E+02	1.34E+02
ENSMUSG00000068245	Phf11d	2.30E-119	3.90E-117	109.29	1.40E+03	1.28E+01
ENSMUSG00000006418	Rnf114	1.21E-118	2.03E-116	5.12	1.36E+03	2.66E+02
ENSMUSG00000115338	Pnp	5.80E-117	9.65E-115	18.07	3.28E+03	1.82E+02
ENSMUSG00000023961	Enpp4	8.93E-117	1.47E-114	44.15	2.86E+02	6.48E+00
ENSMUSG00000026425	Srgap2	1.42E-116	2.32E-114	3.17	1.62E+03	5.11E+02
ENSMUSG00000017057	Il13ra1	2.36E-116	3.82E-114	10.57	3.44E+02	3.25E+01
ENSMUSG00000024472	Dcp2	3.60E-116	5.77E-114	5.12	6.57E+02	1.28E+02
ENSMUSG00000037731	Themis2	3.89E-116	6.18E-114	23.08	3.88E+03	1.68E+02
ENSMUSG00000025492	Ifitm3	8.24E-115	1.30E-112	9.65	1.56E+04	1.62E+03
ENSMUSG00000008393	Carhsp1	4.37E-114	6.82E-112	5.33	7.61E+02	1.43E+02
ENSMUSG00000042228	Lyn	1.07E-113	1.66E-111	4.49	6.57E+03	1.46E+03
ENSMUSG00000063286	Gvin-ps7	6.73E-113	1.03E-110	22.42	6.21E+03	2.77E+02
ENSMUSG00000037849	Ifi206	2.84E-111	4.32E-109	446.47	9.57E+02	2.14E+00
ENSMUSG00000049659	Aftph	1.18E-109	1.78E-107	5.67	4.02E+03	7.09E+02
ENSMUSG00000035352	Ccl12	1.90E-109	2.84E-107	217.19	2.83E+03	1.30E+01
ENSMUSG00000002227	Mov10	2.19E-109	3.24E-107	16.95	1.02E+03	6.02E+01
ENSMUSG00000020572	Nampt	7.10E-109	1.04E-106	7.21	5.51E+03	7.65E+02
ENSMUSG00000039501	Znfx1	7.32E-109	1.07E-106	12.17	5.41E+03	4.45E+02
ENSMUSG00000039285	Azi2	7.14E-108	1.03E-105	4.94	7.42E+02	1.50E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000063800	Prpf38a	4.52E-107	6.47E-105	7.18	7.94E+02	1.11E+02
ENSMUSG00000091144	Phf11c	8.75E-105	1.24E-102	25.13	2.82E+02	1.12E+01
ENSMUSG00000024349	Sting1	1.35E-104	1.90E-102	5.20	1.01E+03	1.94E+02
ENSMUSG00000012519	Mlkl	1.17E-103	1.63E-101	10.78	6.21E+02	5.76E+01
ENSMUSG00000071068	Treml2	1.50E-103	2.08E-101	15.66	4.05E+02	2.59E+01
ENSMUSG00000004040	Stat3	2.00E-103	2.75E-101	3.47	3.51E+03	1.01E+03
ENSMUSG00000035725	Prkx	2.55E-103	3.48E-101	4.38	2.25E+03	5.13E+02
ENSMUSG00000041481	Serpina3g	2.76E-103	3.74E-101	107.86	2.89E+02	2.68E+00
ENSMUSG00000032265	Tent5a	2.06E-102	2.76E-100	7.79	2.46E+03	3.15E+02
ENSMUSG00000024066	Xdh	2.49E-102	3.32E-100	4.05	5.27E+03	1.30E+03
ENSMUSG00000022186	Oxct1	2.52E-102	3.33E-100	2.94	7.27E+03	2.47E+03
ENSMUSG00000056268	Dennd1b	2.06E-100	2.71E-98	4.69	1.17E+03	2.49E+02
ENSMUSG00000029605	Oas1b	6.84E-100	8.92E-98	22.45	1.82E+02	8.10E+00
ENSMUSG00000026104	Stat1	1.18E-99	1.53E-97	17.76	5.30E+03	2.99E+02
ENSMUSG00000020707	Rnf135	1.46E-99	1.88E-97	5.42	6.26E+02	1.15E+02
ENSMUSG00000026466	Tor1aip1	2.87E-99	3.65E-97	5.96	4.36E+03	7.31E+02
ENSMUSG00000016831	Tox4	6.10E-99	7.73E-97	2.53	7.70E+02	3.04E+02
ENSMUSG00000018167	Stard3	1.45E-98	1.82E-96	4.15	1.18E+03	2.85E+02
ENSMUSG00000022035	Ccdc25	1.51E-98	1.89E-96	6.89	3.19E+03	4.63E+02
ENSMUSG00000019866	Crybg1	1.85E-98	2.29E-96	6.42	1.42E+03	2.22E+02
ENSMUSG00000056144	Trim34a	1.92E-98	2.36E-96	8.32	4.48E+02	5.38E+01
ENSMUSG00000000708	Kat2b	3.77E-98	4.61E-96	4.11	6.62E+02	1.61E+02
ENSMUSG00000046157	Tmem229b	1.59E-96	1.93E-94	6.51	9.82E+02	1.51E+02
ENSMUSG00000028037	Ifi44	2.81E-96	3.38E-94	774.44	4.31E+03	5.57E+00
ENSMUSG00000029009	Mthfr	2.09E-94	2.50E-92	9.36	7.53E+02	8.04E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000032596	Uba7	3.43E-94	4.08E-92	9.51	2.12E+03	2.23E+02
ENSMUSG00000042350	Arel1	5.50E-94	6.45E-92	7.30	1.41E+03	1.94E+02
ENSMUSG00000031557	Plekha2	5.47E-94	6.45E-92	3.48	3.06E+03	8.79E+02
ENSMUSG00000028796	Phc2	1.33E-93	1.54E-91	3.96	1.15E+03	2.91E+02
ENSMUSG00000037826	Ppm1k	1.40E-93	1.62E-91	14.83	5.73E+02	3.86E+01
ENSMUSG00000079363	Gbp4	1.74E-93	2.00E-91	913.54	6.18E+02	6.76E-01
ENSMUSG00000041827	Oasl1	2.67E-93	3.05E-91	406.65	2.26E+03	5.55E+00
ENSMUSG00000028894	Inpp5b	3.09E-93	3.51E-91	3.30	4.88E+02	1.48E+02
ENSMUSG00000029771	Irf5	6.35E-92	7.15E-90	4.13	3.66E+03	8.87E+02
ENSMUSG00000039236	Isg20	2.45E-91	2.75E-89	169.24	1.49E+03	8.83E+00
ENSMUSG00000027219	Slc28a2	3.48E-90	3.87E-88	23.63	8.97E+02	3.79E+01
ENSMUSG00000049488	Tmem67	1.53E-89	1.70E-87	11.37	2.85E+02	2.51E+01
ENSMUSG00000037997	Parp11	1.61E-89	1.77E-87	12.75	9.73E+02	7.63E+01
ENSMUSG00000027678	Ncoa3	5.56E-89	6.07E-87	2.38	1.03E+03	4.34E+02
ENSMUSG00000047798	Cd300lf	1.90E-88	2.06E-86	6.52	6.54E+03	1.00E+03
ENSMUSG00000031627	Irf2	1.06E-87	1.14E-85	3.88	2.11E+03	5.44E+02
ENSMUSG00000056692	Ilrun	3.13E-87	3.36E-85	2.70	2.95E+03	1.09E+03
ENSMUSG00000038058	Nod1	3.80E-87	4.04E-85	17.10	8.34E+02	4.88E+01
ENSMUSG00000039304	Tnfsf10	7.80E-87	8.26E-85	555.87	8.81E+02	1.58E+00
ENSMUSG00000052749	Trim30b	8.03E-87	8.45E-85	115.35	2.34E+02	2.03E+00
ENSMUSG00000039531	Zup1	9.51E-87	9.95E-85	9.34	8.34E+02	8.93E+01
ENSMUSG00000052776	Oas1a	3.82E-85	3.97E-83	14.05	2.34E+02	1.66E+01
ENSMUSG00000001123	Lgals9	8.00E-85	8.27E-83	6.94	8.14E+03	1.17E+03
ENSMUSG00000034485	Uaca	1.09E-84	1.12E-82	10.37	6.07E+02	5.85E+01
ENSMUSG00000000247	Lhx2	1.26E-84	1.29E-82	84.26	4.36E+02	5.17E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000021036	Sptlc2	6.40E-84	6.50E-82	2.68	1.73E+03	6.45E+02
ENSMUSG00000032661	Oas3	7.35E-84	7.42E-82	12.52	5.30E+02	4.24E+01
ENSMUSG00000044583	Tlr7	1.74E-83	1.75E-81	4.41	1.18E+03	2.67E+02
ENSMUSG00000106734	Gm20559	1.99E-83	1.99E-81	6.95	3.92E+02	5.64E+01
ENSMUSG00000039997	Ifi203	3.00E-83	2.98E-81	20.80	9.94E+03	4.78E+02
ENSMUSG00000030654	Arl6ip1	3.68E-83	3.63E-81	2.51	8.92E+03	3.55E+03
ENSMUSG00000035561	Aldh1b1	1.01E-82	9.89E-81	15.76	1.39E+03	8.82E+01
ENSMUSG00000016496	Cd274	1.40E-82	1.37E-80	26.97	8.80E+03	3.26E+02
ENSMUSG00000024805	Pcgf5	1.82E-82	1.77E-80	7.44	6.42E+02	8.63E+01
ENSMUSG00000026536	Ifi211	2.53E-82	2.44E-80	26.84	2.16E+03	8.05E+01
ENSMUSG00000033088	Triobp	4.26E-81	4.09E-79	3.59	7.31E+02	2.04E+02
ENSMUSG00000002325	Irf9	1.12E-80	1.07E-78	3.36	9.78E+02	2.91E+02
ENSMUSG00000024675	Ms4a4c	1.43E-80	1.36E-78	379.87	2.60E+03	6.84E+00
ENSMUSG00000021614	Vcan	3.85E-80	3.63E-78	28.11	7.61E+02	2.71E+01
ENSMUSG00000035248	Tut7	2.16E-79	2.03E-77	3.07	2.16E+03	7.03E+02
ENSMUSG00000023206	Il15ra	2.83E-78	2.64E-76	38.77	3.93E+02	1.01E+01
ENSMUSG00000004952	Rasa4	6.91E-78	6.42E-76	3.68	1.57E+03	4.27E+02
ENSMUSG00000066677	Ifi208	8.60E-78	7.95E-76	1,610.23	5.91E+02	3.67E-01
ENSMUSG00000053007	Creb5	9.81E-78	9.02E-76	5.85	2.97E+03	5.07E+02
ENSMUSG00000054676	1600014C10Rik	1.45E-77	1.33E-75	14.51	1.69E+03	1.17E+02
ENSMUSG00000037400	Atp11b	3.17E-77	2.89E-75	3.61	1.07E+03	2.96E+02
ENSMUSG00000046031	Calhm6	4.37E-77	3.95E-75	59.81	1.52E+03	2.54E+01
ENSMUSG00000028480	Glipr2	6.46E-77	5.82E-75	11.88	1.03E+03	8.69E+01
ENSMUSG00000023341	Mx2	9.84E-77	8.82E-75	271.31	1.99E+03	7.35E+00
ENSMUSG00000053318	Slamf8	1.05E-75	9.36E-74	34.91	9.52E+02	2.73E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000006782	Cnp	2.43E-75	2.15E-73	7.68	1.31E+03	1.71E+02
ENSMUSG00000056116	H2-T22	3.41E-75	3.01E-73	16.32	1.51E+03	9.26E+01
ENSMUSG00000066363	Serpina3f	4.73E-75	4.15E-73	1,130.73	3.23E+02	2.86E-01
ENSMUSG00000030341	Tnfrsf1a	6.75E-75	5.90E-73	3.49	1.86E+03	5.32E+02
ENSMUSG00000085492	Trmt61b	7.89E-75	6.86E-73	4.91	3.97E+02	8.07E+01
ENSMUSG00000039217	Il18	1.33E-74	1.15E-72	7.50	7.76E+02	1.03E+02
ENSMUSG00000050549	Fam241a	3.35E-73	2.88E-71	6.83	1.06E+03	1.55E+02
ENSMUSG00000056121	Fez2	3.45E-73	2.95E-71	3.28	8.80E+02	2.68E+02
ENSMUSG00000029862	Clcn1	4.14E-73	3.53E-71	65.04	9.48E+01	1.46E+00
ENSMUSG00000057135	Scimp	9.10E-73	7.72E-71	66.49	2.39E+02	3.59E+00
ENSMUSG00000025915	Sgk3	4.44E-72	3.74E-70	3.26	7.34E+02	2.25E+02
ENSMUSG00000027012	Dync1i2	1.68E-71	1.41E-69	3.04	1.43E+04	4.69E+03
ENSMUSG00000034947	Tmem106a	1.95E-71	1.63E-69	2.16	4.17E+03	1.93E+03
ENSMUSG00000029826	Zc3hav1	2.03E-71	1.68E-69	3.55	2.51E+03	7.07E+02
ENSMUSG00000044703	Phf11a	2.94E-71	2.44E-69	612.88	8.92E+02	1.46E+00
ENSMUSG00000037860	Aim2	5.04E-71	4.15E-69	5.37	1.26E+03	2.35E+02
ENSMUSG00000066258	Trim12a	6.25E-71	5.13E-69	5.92	3.16E+02	5.33E+01
ENSMUSG00000031897	Psmb10	7.89E-70	6.44E-68	10.05	3.75E+03	3.74E+02
ENSMUSG00000078921	Tgtp2	3.05E-69	2.48E-67	730.59	2.37E+02	3.24E-01
ENSMUSG00000030102	Itpr1	1.13E-68	9.15E-67	14.30	5.02E+02	3.51E+01
ENSMUSG00000075010	AW112010	1.89E-68	1.52E-66	117.40	4.77E+03	4.06E+01
ENSMUSG00000035392	Dennd1a	2.56E-68	2.06E-66	3.42	8.77E+02	2.57E+02
ENSMUSG00000112627	4933412E12Rik	3.69E-68	2.94E-66	16.15	1.37E+02	8.49E+00
ENSMUSG00000071350	Setdb2	1.25E-67	9.96E-66	15.94	2.54E+02	1.59E+01
ENSMUSG00000061288	Taok3	1.41E-67	1.12E-65	2.58	7.62E+03	2.96E+03

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000054203	Ifi205	3.50E-67	2.75E-65	150.13	1.49E+03	9.93E+00
ENSMUSG00000006411	Nectin4	8.29E-67	6.49E-65	9.43	4.29E+02	4.55E+01
ENSMUSG00000029291	Rufy3	9.65E-67	7.52E-65	2.78	1.71E+03	6.15E+02
ENSMUSG00000021266	Wars	1.87E-66	1.45E-64	5.41	1.00E+03	1.85E+02
ENSMUSG00000027293	Ehd4	8.70E-66	6.70E-64	2.90	7.51E+03	2.59E+03
ENSMUSG00000042901	Aida	1.15E-65	8.81E-64	4.73	7.35E+02	1.55E+02
ENSMUSG00000060538	Tmem219	1.43E-65	1.09E-63	2.67	8.45E+02	3.17E+02
ENSMUSG00000073491	Ifi213	3.65E-65	2.78E-63	767.55	7.28E+02	9.48E-01
ENSMUSG00000053477	Tcf4	3.86E-65	2.92E-63	3.47	4.18E+03	1.21E+03
ENSMUSG00000096727	Psmb9	1.00E-64	7.56E-63	11.05	3.35E+03	3.03E+02
ENSMUSG00000057143	Trim12c	1.03E-64	7.74E-63	5.67	9.83E+02	1.73E+02
ENSMUSG00000020415	Pttg1	1.30E-64	9.69E-63	6.43	1.88E+03	2.92E+02
ENSMUSG00000029330	Cds1	1.30E-64	9.69E-63	3.57	4.18E+02	1.17E+02
ENSMUSG00000029366	Dck	3.65E-64	2.70E-62	7.48	7.85E+02	1.05E+02
ENSMUSG00000026433	Rab29	2.84E-63	2.09E-61	3.38	5.40E+02	1.60E+02
ENSMUSG00000004846	Plod3	3.86E-63	2.83E-61	3.19	1.42E+03	4.45E+02
ENSMUSG00000022867	Usp25	3.16E-62	2.31E-60	4.74	2.48E+03	5.22E+02
ENSMUSG00000028496	Mllt3	6.72E-62	4.89E-60	3.77	3.79E+02	1.00E+02
ENSMUSG00000040351	Ankib1	1.20E-61	8.68E-60	2.92	3.22E+02	1.10E+02
ENSMUSG00000022901	Cd86	1.48E-61	1.07E-59	11.60	1.09E+03	9.36E+01
ENSMUSG00000029156	Sgcb	2.49E-61	1.79E-59	4.59	6.17E+02	1.34E+02
ENSMUSG00000036362	P2ry13	2.81E-61	2.01E-59	8.73	2.70E+02	3.09E+01
ENSMUSG00000028362	Tnfsf8	4.19E-61	2.99E-59	26.68	3.91E+02	1.47E+01
ENSMUSG00000027078	Ube2l6	7.67E-61	5.44E-59	9.42	1.81E+02	1.92E+01
ENSMUSG00000062960	Kdr	1.73E-60	1.22E-58	22.32	1.08E+03	4.82E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000026764	Kif5c	2.71E-60	1.91E-58	8.38	1.61E+02	1.92E+01
ENSMUSG00000090942	F830016B08Rik	3.17E-60	2.22E-58	517.37	7.91E+01	1.53E-01
ENSMUSG00000092564	BC051226	6.14E-60	4.29E-58	4.39	2.76E+02	6.28E+01
ENSMUSG00000078771	Evi2a	6.53E-60	4.54E-58	3.47	2.75E+03	7.92E+02
ENSMUSG00000026814	Eng	7.05E-60	4.89E-58	3.94	9.79E+02	2.48E+02
ENSMUSG00000020315	Sptbn1	7.48E-60	5.17E-58	2.09	1.98E+03	9.49E+02
ENSMUSG00000019818	Cd164	8.88E-60	6.11E-58	4.29	2.37E+03	5.53E+02
ENSMUSG00000063236	1110038F14Rik	1.00E-59	6.87E-58	3.49	5.61E+02	1.61E+02
ENSMUSG00000022973	Synj1	2.07E-59	1.41E-57	2.75	2.24E+03	8.13E+02
ENSMUSG00000034855	Cxcl10	2.36E-59	1.61E-57	211.44	2.66E+04	1.26E+02
ENSMUSG00000024644	Cndp2	3.85E-59	2.61E-57	2.06	3.06E+03	1.49E+03
ENSMUSG00000069539	Scyl2	8.25E-59	5.56E-57	2.94	5.69E+02	1.94E+02
ENSMUSG00000078153	Psme2b	1.72E-58	1.16E-56	11.16	6.37E+01	5.70E+00
ENSMUSG00000058587	Tmod3	2.50E-58	1.67E-56	2.39	1.43E+03	5.99E+02
ENSMUSG00000050394	Armcx6	2.91E-58	1.94E-56	16.01	7.83E+01	4.89E+00
ENSMUSG00000069793	Slfn9	3.34E-58	2.22E-56	11.59	6.45E+02	5.56E+01
ENSMUSG00000020089	Ppa1	3.41E-58	2.26E-56	4.47	5.13E+02	1.15E+02
ENSMUSG00000024030	Abcg1	4.18E-58	2.75E-56	5.42	1.47E+03	2.72E+02
ENSMUSG00000055204	Ankrd17	4.18E-58	2.75E-56	2.70	3.07E+03	1.14E+03
ENSMUSG00000007617	Homer1	4.97E-58	3.25E-56	4.71	5.64E+02	1.20E+02
ENSMUSG00000024789	Jak2	1.96E-57	1.28E-55	7.29	9.96E+02	1.37E+02
ENSMUSG00000031402	Mpp1	3.44E-57	2.24E-55	2.39	4.93E+03	2.06E+03
ENSMUSG00000049969	Plekhf2	1.11E-56	7.20E-55	4.94	1.14E+03	2.31E+02
ENSMUSG00000024308	Tapbp	1.25E-56	8.04E-55	4.39	1.31E+04	2.98E+03
ENSMUSG00000029648	Flt1	1.33E-56	8.54E-55	39.34	8.67E+02	2.20E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000038467	Chmp4b	1.58E-56	1.01E-54	3.49	1.70E+04	4.86E+03
ENSMUSG00000021371	Mcur1	2.58E-56	1.64E-54	2.59	1.63E+03	6.28E+02
ENSMUSG00000029860	Zyx	3.31E-56	2.11E-54	7.54	2.88E+03	3.82E+02
ENSMUSG00000085501	Gm11772	3.56E-56	2.26E-54	17.24	1.57E+02	9.09E+00
ENSMUSG00000038256	Bcl9	4.28E-56	2.70E-54	6.09	5.04E+02	8.27E+01
ENSMUSG00000021039	Snw1	4.40E-56	2.77E-54	2.15	2.72E+03	1.27E+03
ENSMUSG00000078763	Slfn1	9.13E-56	5.71E-54	1,023.58	2.01E+02	1.96E-01
ENSMUSG00000027360	Hdc	1.13E-55	7.01E-54	152.91	1.43E+02	9.33E-01
ENSMUSG00000057137	Tmem140	1.12E-55	7.01E-54	3.87	2.69E+03	6.94E+02
ENSMUSG00000024338	Psmb8	1.18E-55	7.30E-54	6.18	5.09E+03	8.25E+02
ENSMUSG00000025165	Sectm1a	1.31E-55	8.07E-54	564.76	1.26E+02	2.23E-01
ENSMUSG00000032560	Dnajc13	1.57E-55	9.66E-54	2.52	8.52E+02	3.38E+02
ENSMUSG00000073902	Gvin3	2.27E-55	1.38E-53	23.60	1.44E+02	6.11E+00
ENSMUSG00000028854	Slc9a1	2.26E-55	1.38E-53	2.73	4.02E+02	1.47E+02
ENSMUSG00000020134	Peli1	2.43E-55	1.48E-53	6.86	3.19E+03	4.65E+02
ENSMUSG00000059920	4930453N24Rik	2.65E-55	1.60E-53	2.91	2.78E+02	9.54E+01
ENSMUSG00000032698	Lmo2	2.64E-55	1.60E-53	2.25	1.36E+03	6.05E+02
ENSMUSG00000040850	Psme4	4.21E-55	2.53E-53	2.06	9.42E+02	4.57E+02
ENSMUSG00000019794	Katna1	9.58E-55	5.75E-53	3.89	9.42E+02	2.42E+02
ENSMUSG00000097194	9330175E14Rik	1.63E-54	9.77E-53	11.32	1.13E+02	9.98E+00
ENSMUSG00000047423	AI837181	1.78E-54	1.06E-52	2.81	9.66E+02	3.43E+02
ENSMUSG00000024431	Nr3c1	2.24E-54	1.33E-52	2.28	7.85E+02	3.45E+02
ENSMUSG00000025790	Slco3a1	2.29E-54	1.36E-52	28.26	1.46E+03	5.17E+01
ENSMUSG00000070501	Ifi214	2.58E-54	1.52E-52	655.51	1.46E+02	2.23E-01
ENSMUSG00000033781	Asb13	5.71E-54	3.36E-52	7.80	2.49E+02	3.19E+01

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ENSMUSG00000111118	Gm6545	5.92E-54	3.47E-52	716.48	7.26E+02	1.01E+00
ENSMUSG00000021114	Atp6v1d	7.70E-54	4.50E-52	3.00	6.05E+03	2.01E+03
ENSMUSG00000019916	P4ha1	9.38E-54	5.46E-52	4.27	1.19E+03	2.79E+02
ENSMUSG00000021624	Cd180	3.25E-53	1.88E-51	3.93	4.53E+03	1.15E+03
ENSMUSG00000034484	Snx2	3.41E-53	1.97E-51	3.62	1.78E+03	4.91E+02
ENSMUSG00000068606	Gm4841	3.72E-53	2.15E-51	424.89	6.50E+01	1.53E-01
ENSMUSG00000062082	Cd200r4	5.30E-53	3.05E-51	5.34	2.31E+03	4.33E+02
ENSMUSG00000038518	Jarid2	5.45E-53	3.12E-51	3.94	6.67E+02	1.69E+02
ENSMUSG00000003226	Ranbp2	8.48E-53	4.84E-51	3.40	1.41E+03	4.16E+02
ENSMUSG00000024696	Lpxn	9.44E-53	5.37E-51	3.60	2.45E+03	6.82E+02
ENSMUSG00000030452	Nipa2	9.68E-53	5.49E-51	2.08	5.47E+02	2.63E+02
ENSMUSG00000079419	Ms4a6c	1.00E-52	5.66E-51	6.04	7.04E+03	1.16E+03
ENSMUSG00000021774	Ube2e1	1.19E-52	6.70E-51	2.92	1.05E+03	3.60E+02
ENSMUSG00000097457	nan	1.49E-52	8.36E-51	221.22	1.59E+02	7.18E-01
ENSMUSG00000079659	Tmem243	5.25E-52	2.94E-50	4.84	4.20E+02	8.67E+01
ENSMUSG00000040584	Abcb1a	1.45E-51	8.12E-50	7.84	4.94E+02	6.30E+01
ENSMUSG00000034438	Gbp8	1.51E-51	8.40E-50	21.64	8.40E+01	3.88E+00
ENSMUSG00000037242	Clic4	1.52E-51	8.41E-50	4.70	9.97E+03	2.12E+03
ENSMUSG00000053846	Lipg	1.71E-51	9.47E-50	1,009.31	5.16E+02	5.12E-01
ENSMUSG00000022667	Cd200r1	2.62E-51	1.44E-49	3.27	1.15E+03	3.51E+02
ENSMUSG00000054604	Cggbp1	4.12E-51	2.26E-49	2.27	1.69E+03	7.45E+02
ENSMUSG00000037075	Rnf139	4.33E-51	2.37E-49	3.24	3.97E+02	1.23E+02
ENSMUSG00000021038	Vipas39	1.04E-50	5.68E-49	2.60	2.39E+03	9.19E+02
ENSMUSG00000041390	Mdfic	1.07E-50	5.81E-49	2.30	2.25E+03	9.77E+02
ENSMUSG00000109901	Chmp1b	1.29E-50	6.99E-49	3.26	1.39E+03	4.26E+02

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ENSMUSG00000019082	Slc25a22	1.61E-50	8.70E-49	12.32	6.48E+02	5.26E+01
ENSMUSG00000087477	Gm13822	3.10E-50	1.67E-48	127.09	9.25E+01	7.28E-01
ENSMUSG00000024074	Crim1	3.12E-50	1.68E-48	5.14	4.11E+02	8.01E+01
ENSMUSG00000039536	Stau1	8.50E-50	4.55E-48	2.46	5.59E+02	2.27E+02
ENSMUSG00000037965	Zc3h7a	1.00E-49	5.35E-48	3.43	9.58E+02	2.79E+02
ENSMUSG00000027433	Xrn2	1.03E-49	5.48E-48	2.02	1.96E+03	9.72E+02
ENSMUSG00000055447	Cd47	1.56E-49	8.29E-48	3.59	7.92E+03	2.21E+03
ENSMUSG00000036249	Rbm43	2.26E-49	1.20E-47	4.17	3.65E+02	8.75E+01
ENSMUSG00000037685	Atp8a1	2.40E-49	1.27E-47	2.49	6.78E+02	2.72E+02
ENSMUSG00000020476	Dbnl	2.50E-49	1.31E-47	4.63	2.59E+03	5.60E+02
ENSMUSG00000028228	Cpne3	7.64E-49	4.01E-47	2.55	2.03E+03	7.98E+02
ENSMUSG00000052485	Tmem171	9.10E-49	4.76E-47	11.79	1.72E+03	1.46E+02
ENSMUSG00000092021	Gbp11	9.84E-49	5.11E-47	384.52	5.88E+01	1.53E-01
ENSMUSG00000031540	Kat6a	9.82E-49	5.11E-47	2.22	5.22E+02	2.35E+02
ENSMUSG00000039456	Morc3	2.63E-48	1.36E-46	3.55	6.66E+02	1.88E+02
ENSMUSG00000025887	Casp12	3.64E-48	1.88E-46	17.74	6.79E+01	3.83E+00
ENSMUSG00000000184	Ccnd2	4.09E-48	2.10E-46	8.45	6.65E+03	7.86E+02
ENSMUSG00000047067	Dusp28	5.40E-48	2.76E-46	6.21	2.40E+02	3.86E+01
ENSMUSG00000066036	Ubr4	7.85E-48	4.00E-46	2.59	2.80E+03	1.08E+03
ENSMUSG00000036180	Gatad2a	8.86E-48	4.50E-46	2.05	1.65E+03	8.06E+02
ENSMUSG00000024601	Isoc1	1.02E-47	5.17E-46	3.73	5.07E+02	1.36E+02
ENSMUSG00000032508	Myd88	1.21E-47	6.13E-46	4.34	2.30E+03	5.29E+02
ENSMUSG00000037434	Slc30a1	2.87E-47	1.44E-45	5.51	2.13E+03	3.86E+02
ENSMUSG00000026421	Csrp1	4.21E-47	2.11E-45	3.02	1.91E+03	6.34E+02
ENSMUSG00000026571	Dcaf6	5.28E-47	2.64E-45	2.82	6.54E+02	2.32E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000032410	Xrn1	5.40E-47	2.69E-45	2.82	7.85E+02	2.79E+02
ENSMUSG00000032333	Stoml1	1.05E-46	5.21E-45	3.51	2.75E+02	7.83E+01
ENSMUSG00000029417	Cxcl9	2.17E-46	1.08E-44	108.39	3.33E+02	3.07E+00
ENSMUSG00000024457	Trim26	2.33E-46	1.15E-44	3.47	6.14E+02	1.77E+02
ENSMUSG00000021758	Ddx4	2.57E-46	1.26E-44	43.78	7.45E+01	1.70E+00
ENSMUSG00000027882	Stxbp3	2.57E-46	1.26E-44	4.33	1.04E+03	2.41E+02
ENSMUSG00000025178	Pi4k2a	2.58E-46	1.26E-44	2.80	1.75E+03	6.26E+02
ENSMUSG00000026029	Casp8	2.86E-46	1.40E-44	3.71	1.94E+03	5.21E+02
ENSMUSG00000021377	Dek	3.80E-46	1.85E-44	2.87	4.89E+03	1.70E+03
ENSMUSG00000093661	Eif4e3	3.99E-46	1.94E-44	2.49	6.91E+02	2.78E+02
ENSMUSG00000069844	Sco1	7.01E-46	3.40E-44	5.70	3.03E+02	5.31E+01
ENSMUSG00000046718	Bst2	1.05E-45	5.08E-44	7.24	6.75E+03	9.32E+02
ENSMUSG00000026341	Actr3	1.42E-45	6.86E-44	2.36	3.24E+03	1.37E+03
ENSMUSG00000020132	Rab21	2.30E-45	1.11E-43	2.26	1.66E+03	7.33E+02
ENSMUSG00000026158	Ogfrl1	3.22E-45	1.54E-43	3.74	2.26E+03	6.04E+02
ENSMUSG00000032434	Cmtm6	7.17E-45	3.43E-43	3.33	9.45E+02	2.84E+02
ENSMUSG00000037933	Bicd2	7.98E-45	3.81E-43	-2.13	1.83E+02	3.90E+02
ENSMUSG00000038774	Ascc3	9.06E-45	4.31E-43	3.58	5.72E+02	1.60E+02
ENSMUSG00000023959	Clic5	9.42E-45	4.46E-43	98.37	1.71E+02	1.74E+00
ENSMUSG00000048534	Jaml	9.43E-45	4.46E-43	45.70	5.97E+01	1.31E+00
ENSMUSG00000048852	Gm12185	9.52E-45	4.50E-43	247.91	1.03E+02	4.15E-01
ENSMUSG00000038848	Ythdf1	1.30E-44	6.12E-43	2.79	8.35E+02	2.99E+02
ENSMUSG00000038884	Shfl	1.37E-44	6.42E-43	6.31	6.73E+01	1.07E+01
ENSMUSG00000041571	Selenow	1.60E-44	7.49E-43	3.18	1.33E+03	4.18E+02
ENSMUSG00000108732	2310043P16Rik	1.69E-44	7.86E-43	13.02	5.49E+01	4.21E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000052477	C130026I21Rik	2.25E-44	1.04E-42	20.88	6.51E+01	3.12E+00
ENSMUSG00000020464	Pnpt1	2.26E-44	1.05E-42	5.51	2.58E+02	4.69E+01
ENSMUSG00000066456	Hmgn3	2.57E-44	1.19E-42	7.58	1.27E+03	1.67E+02
ENSMUSG00000030745	Il21r	3.08E-44	1.42E-42	4.08	1.57E+03	3.85E+02
ENSMUSG00000094796	BC147527	3.81E-44	1.75E-42	232.77	4.57E+01	1.96E-01
ENSMUSG00000081769	Gm12216	5.72E-44	2.62E-42	13.71	7.46E+01	5.44E+00
ENSMUSG00000003308	Keap1	5.78E-44	2.64E-42	3.10	1.19E+03	3.85E+02
ENSMUSG00000001156	Mxd1	6.38E-44	2.91E-42	10.48	4.10E+03	3.91E+02
ENSMUSG00000029923	Rab19	6.91E-44	3.14E-42	6.25	1.26E+02	2.01E+01
ENSMUSG00000059498	Fcgr3	8.93E-44	4.05E-42	2.13	7.52E+03	3.53E+03
ENSMUSG00000035232	Pdk3	9.08E-44	4.11E-42	3.78	3.37E+02	8.90E+01
ENSMUSG00000041736	Tspo	1.07E-43	4.82E-42	3.97	3.13E+03	7.90E+02
ENSMUSG00000038866	Zcchc2	1.19E-43	5.38E-42	5.66	6.77E+02	1.20E+02
ENSMUSG00000001768	Rin2	1.32E-43	5.94E-42	6.44	1.43E+03	2.22E+02
ENSMUSG00000053835	H2-T24	1.37E-43	6.12E-42	25.18	1.20E+02	4.77E+00
ENSMUSG00000000204	Slfn4	1.44E-43	6.44E-42	144.25	1.21E+02	8.38E-01
ENSMUSG00000026482	Rgl1	2.03E-43	9.04E-42	7.46	1.23E+03	1.65E+02
ENSMUSG00000020128	Vps54	2.56E-43	1.14E-41	2.94	3.58E+02	1.22E+02
ENSMUSG00000030149	Klrk1	3.21E-43	1.42E-41	444.46	2.06E+02	4.63E-01
ENSMUSG00000019699	Akt3	3.49E-43	1.54E-41	4.66	7.54E+02	1.62E+02
ENSMUSG00000035151	Elmod2	3.65E-43	1.61E-41	2.32	2.31E+02	9.93E+01
ENSMUSG00000037752	Xkr8	4.65E-43	2.04E-41	6.98	2.12E+02	3.04E+01
ENSMUSG00000032253	Phip	5.83E-43	2.56E-41	3.38	2.39E+03	7.07E+02
ENSMUSG00000025017	Pik3ap1	5.86E-43	2.57E-41	3.75	6.72E+02	1.79E+02
ENSMUSG00000038910	Plcl2	6.40E-43	2.79E-41	3.58	9.75E+02	2.72E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000060802	B2m	7.38E-43	3.22E-41	2.88	1.09E+05	3.79E+04
ENSMUSG00000030990	Pgap2	7.71E-43	3.35E-41	3.85	1.23E+03	3.18E+02
ENSMUSG00000028245	Nsmaf	9.72E-43	4.21E-41	3.67	3.19E+02	8.70E+01
ENSMUSG00000019820	Utrn	1.04E-42	4.49E-41	2.66	6.63E+02	2.49E+02
ENSMUSG00000025324	Atp10a	1.28E-42	5.53E-41	13.79	1.64E+02	1.19E+01
ENSMUSG00000029279	Brdt	1.40E-42	6.02E-41	4.55	7.84E+01	1.72E+01
ENSMUSG00000034320	Slc26a2	1.41E-42	6.04E-41	2.47	6.60E+02	2.68E+02
ENSMUSG00000024677	Ms4a6b	1.51E-42	6.48E-41	7.81	3.22E+03	4.12E+02
ENSMUSG00000030760	Acer3	1.53E-42	6.54E-41	2.82	9.14E+02	3.24E+02
ENSMUSG00000046062	Ppp1r15b	1.70E-42	7.26E-41	2.76	1.16E+03	4.21E+02
ENSMUSG00000070427	Il18bp	1.84E-42	7.81E-41	15.82	7.67E+02	4.85E+01
ENSMUSG00000053931	Cnn3	2.80E-42	1.19E-40	7.91	3.38E+02	4.28E+01
ENSMUSG00000039982	Dtx4	2.83E-42	1.20E-40	-3.24	2.10E+02	6.82E+02
ENSMUSG00000066861	Oas1g	3.09E-42	1.30E-40	18.76	6.48E+01	3.45E+00
ENSMUSG00000029505	Ep400	3.74E-42	1.58E-40	2.08	6.88E+02	3.31E+02
ENSMUSG00000015536	Mocs2	4.08E-42	1.71E-40	2.22	5.76E+02	2.59E+02
ENSMUSG00000053338	Tarm1	4.55E-42	1.91E-40	13.19	1.49E+02	1.13E+01
ENSMUSG00000020407	Upp1	6.86E-42	2.87E-40	58.40	1.84E+02	3.15E+00
ENSMUSG00000036469	Marchf1	6.92E-42	2.89E-40	4.08	7.56E+02	1.85E+02
ENSMUSG00000080717	B230307C23Rik	6.95E-42	2.89E-40	3.53	1.95E+02	5.53E+01
ENSMUSG00000024732	Ccdc86	1.42E-41	5.89E-40	3.74	1.13E+03	3.02E+02
ENSMUSG00000033880	Lgals3bp	1.45E-41	6.00E-40	3.67	6.88E+03	1.88E+03
ENSMUSG00000042719	Naa25	1.56E-41	6.43E-40	3.62	7.67E+02	2.12E+02
ENSMUSG00000020694	Tlk2	1.68E-41	6.91E-40	3.59	9.05E+02	2.52E+02
ENSMUSG00000015377	Dennd6b	2.00E-41	8.18E-40	6.92	9.88E+01	1.43E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000020790	Ankfy1	2.53E-41	1.03E-39	2.01	8.37E+02	4.17E+02
ENSMUSG00000060183	Cxcl11	2.56E-41	1.04E-39	847.84	3.11E+02	3.67E-01
ENSMUSG00000050957	Insl6	3.19E-41	1.30E-39	4.73	2.83E+02	5.97E+01
ENSMUSG00000029405	G3bp2	3.36E-41	1.36E-39	2.71	2.23E+03	8.23E+02
ENSMUSG00000049091	Sephs2	4.81E-41	1.94E-39	-4.16	1.12E+02	4.68E+02
ENSMUSG00000038213	Tapbpl	9.11E-41	3.68E-39	6.50	6.43E+02	9.90E+01
ENSMUSG00000042772	Smg7	9.17E-41	3.69E-39	2.77	2.03E+03	7.31E+02
ENSMUSG00000071537	Klrg2	1.08E-40	4.33E-39	10.01	5.76E+01	5.76E+00
ENSMUSG00000045636	Mtus1	1.28E-40	5.13E-39	4.59	7.95E+02	1.73E+02
ENSMUSG00000026893	Gca	1.58E-40	6.31E-39	10.06	1.35E+02	1.34E+01
ENSMUSG00000026102	Inpp1	2.88E-40	1.15E-38	4.61	3.91E+02	8.49E+01
ENSMUSG00000034575	Tent4a	3.01E-40	1.19E-38	6.42	3.10E+02	4.83E+01
ENSMUSG00000068015	Lrch1	3.85E-40	1.53E-38	5.10	5.18E+02	1.02E+02
ENSMUSG00000031729	Ist1	4.48E-40	1.77E-38	2.26	1.76E+03	7.80E+02
ENSMUSG00000023353	Agap3	7.32E-40	2.89E-38	-2.08	2.45E+02	5.10E+02
ENSMUSG00000022501	Prm1	8.82E-40	3.47E-38	334.02	5.11E+01	1.53E-01
ENSMUSG00000017756	Slc12a7	9.53E-40	3.74E-38	2.89	3.74E+02	1.29E+02
ENSMUSG00000035505	Cox18	1.05E-39	4.12E-38	2.83	1.60E+02	5.66E+01
ENSMUSG00000025246	Tbl1x	1.06E-39	4.15E-38	2.22	9.80E+02	4.42E+02
ENSMUSG00000044768	Macir	1.13E-39	4.40E-38	3.17	6.93E+02	2.19E+02
ENSMUSG00000040774	Cept1	1.15E-39	4.49E-38	4.19	2.06E+03	4.91E+02
ENSMUSG00000007036	Abhd16a	1.78E-39	6.89E-38	3.01	9.97E+02	3.32E+02
ENSMUSG00000064128	Cenpj	1.89E-39	7.30E-38	3.29	1.86E+02	5.65E+01
ENSMUSG00000022216	Psme1	3.00E-39	1.16E-37	3.95	4.41E+03	1.12E+03
ENSMUSG00000027835	Pdcd10	3.41E-39	1.31E-37	2.11	4.35E+02	2.06E+02

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ENSMUSG00000042167	Tent2	3.74E-39	1.44E-37	3.40	1.46E+02	4.30E+01
ENSMUSG00000027522	Stx16	5.10E-39	1.95E-37	2.53	6.42E+02	2.53E+02
ENSMUSG00000023249	Parp3	5.24E-39	2.00E-37	6.42	9.17E+02	1.43E+02
ENSMUSG00000067297	Ifit1bl2	5.70E-39	2.17E-37	116.78	4.85E+01	4.15E-01
ENSMUSG00000001089	Luzp1	5.99E-39	2.27E-37	2.03	6.78E+02	3.33E+02
ENSMUSG00000000838	Fmr1	6.84E-39	2.59E-37	2.21	3.55E+02	1.60E+02
ENSMUSG00000033470	Cysltr2	8.06E-39	3.05E-37	19.15	1.43E+02	7.45E+00
ENSMUSG00000004070	Hmox2	1.21E-38	4.58E-37	2.67	2.78E+03	1.04E+03
ENSMUSG00000037062	Sh3glb1	1.42E-38	5.35E-37	2.15	5.02E+03	2.34E+03
ENSMUSG00000001166	Oas1c	1.76E-38	6.61E-37	5.58	1.44E+02	2.57E+01
ENSMUSG00000020737	Jpt1	2.26E-38	8.46E-37	2.42	1.08E+03	4.45E+02
ENSMUSG00000011114	Tbrg1	2.89E-38	1.08E-36	2.19	6.00E+02	2.75E+02
ENSMUSG00000028643	Svbp	3.54E-38	1.32E-36	3.45	4.01E+02	1.16E+02
ENSMUSG00000037820	Tgm2	3.93E-38	1.46E-36	3.24	7.88E+03	2.43E+03
ENSMUSG00000021725	Parp8	5.58E-38	2.06E-36	4.75	2.02E+02	4.26E+01
ENSMUSG00000014547	Wdfy2	5.99E-38	2.21E-36	2.16	1.29E+03	5.95E+02
ENSMUSG00000034135	Sik3	7.55E-38	2.78E-36	3.02	4.23E+02	1.40E+02
ENSMUSG00000031539	Ap3m2	7.57E-38	2.78E-36	3.11	4.90E+02	1.57E+02
ENSMUSG00000022587	Ly6e	8.33E-38	3.05E-36	7.65	7.80E+03	1.02E+03
ENSMUSG00000023186	Vwa5a	8.32E-38	3.05E-36	2.14	2.21E+03	1.03E+03
ENSMUSG00000022801	Lrch3	9.25E-38	3.38E-36	2.72	3.73E+02	1.37E+02
ENSMUSG00000034300	Fam53c	1.02E-37	3.71E-36	3.21	1.05E+03	3.29E+02
ENSMUSG00000025089	Gfra1	1.24E-37	4.52E-36	21.17	3.18E+01	1.50E+00
ENSMUSG00000042790	Rnf214	1.33E-37	4.83E-36	2.44	2.28E+02	9.32E+01
ENSMUSG00000024642	Tle4	1.68E-37	6.07E-36	2.20	7.17E+02	3.27E+02

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ENSMUSG00000041115	Iqsec2	1.77E-37	6.40E-36	2.47	4.74E+02	1.92E+02
ENSMUSG00000026395	Ptprc	1.87E-37	6.75E-36	2.13	4.78E+03	2.24E+03
ENSMUSG00000040528	Milr1	1.96E-37	7.08E-36	2.70	2.20E+03	8.17E+02
ENSMUSG00000000275	Trim25	2.21E-37	7.93E-36	2.82	2.81E+03	9.95E+02
ENSMUSG00000028098	Rnf115	2.64E-37	9.46E-36	2.04	7.70E+02	3.77E+02
ENSMUSG00000028954	Nub1	3.28E-37	1.17E-35	2.41	2.40E+03	9.96E+02
ENSMUSG00000023845	Lnpep	3.46E-37	1.23E-35	2.97	1.67E+03	5.63E+02
ENSMUSG00000055200	Sertad3	3.75E-37	1.33E-35	5.38	1.06E+03	1.97E+02
ENSMUSG00000027519	Rab22a	4.27E-37	1.52E-35	2.31	1.13E+03	4.87E+02
ENSMUSG00000052512	Nav2	4.28E-37	1.52E-35	-3.76	1.38E+02	5.20E+02
ENSMUSG00000032120	C2cd2l	5.42E-37	1.92E-35	-2.22	1.31E+02	2.90E+02
ENSMUSG00000079017	Ifi27l2a	6.50E-37	2.29E-35	2.77	1.95E+03	7.06E+02
ENSMUSG00000032350	Gclc	7.15E-37	2.52E-35	-4.66	1.38E+02	6.43E+02
ENSMUSG00000030930	Chst15	8.06E-37	2.83E-35	7.81	4.29E+01	5.50E+00
ENSMUSG00000021809	Nudt13	8.14E-37	2.86E-35	2.44	2.50E+02	1.02E+02
ENSMUSG00000050578	Mmp13	8.30E-37	2.91E-35	30.74	1.08E+04	3.53E+02
ENSMUSG00000062310	Glrp1	1.10E-36	3.86E-35	3.53	1.59E+02	4.50E+01
ENSMUSG00000078922	Tgtp1	1.26E-36	4.40E-35	247.14	3.78E+01	1.53E-01
ENSMUSG00000041649	Klf8	1.46E-36	5.08E-35	5.16	1.06E+02	2.06E+01
ENSMUSG00000031536	Polb	1.61E-36	5.59E-35	2.25	3.64E+02	1.62E+02
ENSMUSG00000037926	Ssh2	1.67E-36	5.77E-35	-3.72	7.60E+01	2.83E+02
ENSMUSG00000038855	Itpkb	1.87E-36	6.47E-35	3.10	2.47E+03	7.97E+02
ENSMUSG00000022564	Grina	2.95E-36	1.02E-34	2.40	2.78E+03	1.16E+03
ENSMUSG00000032727	Mier3	3.44E-36	1.19E-34	4.57	4.73E+02	1.03E+02
ENSMUSG00000061665	Cd2ap	4.63E-36	1.59E-34	2.43	5.36E+02	2.21E+02

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ENSMUSG00000004446	Bid	6.67E-36	2.28E-34	3.33	1.14E+03	3.43E+02
ENSMUSG00000020346	Mgat1	1.07E-35	3.66E-34	3.99	2.26E+03	5.67E+02
ENSMUSG00000039308	Ndst2	1.08E-35	3.67E-34	2.91	4.90E+02	1.68E+02
ENSMUSG00000019768	Esr1	1.12E-35	3.82E-34	5.99	7.78E+01	1.30E+01
ENSMUSG00000020272	Stk10	1.21E-35	4.12E-34	-3.83	4.59E+01	1.76E+02
ENSMUSG00000096472	Cdkn2d	1.43E-35	4.85E-34	2.83	5.23E+02	1.85E+02
ENSMUSG00000032883	Acsl3	1.54E-35	5.20E-34	-3.82	7.38E+01	2.82E+02
ENSMUSG00000027555	Car13	1.81E-35	6.11E-34	4.40	4.04E+02	9.18E+01
ENSMUSG00000018986	Slfn3	2.27E-35	7.67E-34	11.75	7.74E+01	6.59E+00
ENSMUSG00000068246	Apol9b	2.28E-35	7.67E-34	510.66	1.00E+02	1.96E-01
ENSMUSG00000078349	AW011738	3.61E-35	1.21E-33	26.21	3.39E+01	1.30E+00
ENSMUSG00000005804	Bloc1s6	3.80E-35	1.28E-33	2.56	3.89E+02	1.52E+02
ENSMUSG00000038179	Slamf7	4.36E-35	1.46E-33	7.25	7.14E+03	9.84E+02
ENSMUSG00000054520	Sh3bp2	7.24E-35	2.42E-33	2.34	2.02E+03	8.65E+02
ENSMUSG00000073490	Ifi207	1.22E-34	4.05E-33	4.94	3.68E+03	7.45E+02
ENSMUSG00000027580	Helz2	1.26E-34	4.18E-33	16.85	2.13E+03	1.27E+02
ENSMUSG00000001786	Fbxo7	1.29E-34	4.28E-33	2.26	3.30E+02	1.46E+02
ENSMUSG00000032322	Pstpip1	1.39E-34	4.60E-33	2.79	1.29E+03	4.61E+02
ENSMUSG00000019966	Kitl	1.47E-34	4.86E-33	4.19	3.18E+02	7.57E+01
ENSMUSG00000030199	Etv6	1.84E-34	6.05E-33	2.85	1.12E+03	3.94E+02
ENSMUSG00000026110	Mgat4a	2.16E-34	7.11E-33	2.48	3.50E+02	1.41E+02
ENSMUSG00000104713	Gbp6	3.42E-34	1.12E-32	185.58	2.84E+01	1.53E-01
ENSMUSG00000035852	Misp	3.45E-34	1.13E-32	112.01	3.63E+01	3.24E-01
ENSMUSG00000024985	Tcf7l2	3.79E-34	1.24E-32	2.53	1.35E+03	5.33E+02
ENSMUSG00000032724	Abtb2	4.16E-34	1.36E-32	14.94	2.32E+02	1.55E+01

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ENSMUSG00000009035	Tmem184b	4.62E-34	1.50E-32	3.46	1.20E+03	3.48E+02
ENSMUSG00000032312	Csk	4.64E-34	1.51E-32	2.28	1.46E+03	6.38E+02
ENSMUSG00000027199	Gatm	4.74E-34	1.53E-32	2.35	3.75E+02	1.59E+02
ENSMUSG00000026770	Il2ra	6.23E-34	2.02E-32	89.93	2.91E+01	3.24E-01
ENSMUSG00000074796	Slc4a11	6.69E-34	2.16E-32	20.66	5.09E+01	2.46E+00
ENSMUSG00000068417	Pnp2	8.30E-34	2.67E-32	18.41	3.42E+01	1.86E+00
ENSMUSG00000020100	Slc29a3	9.37E-34	3.01E-32	4.00	4.60E+03	1.15E+03
ENSMUSG00000029036	Atad3a	9.48E-34	3.05E-32	-4.49	2.86E+01	1.28E+02
ENSMUSG00000026657	Frmd4a	1.03E-33	3.29E-32	4.19	6.47E+02	1.54E+02
ENSMUSG00000026797	Stxbp1	1.17E-33	3.75E-32	3.74	4.64E+02	1.24E+02
ENSMUSG00000013662	Atad1	1.32E-33	4.21E-32	2.29	1.06E+03	4.62E+02
ENSMUSG00000025193	Cutc	1.53E-33	4.87E-32	2.83	2.44E+02	8.64E+01
ENSMUSG00000031985	Gnpat	1.67E-33	5.30E-32	-2.26	6.69E+01	1.51E+02
ENSMUSG00000006930	Hap1	1.86E-33	5.89E-32	172.07	7.10E+01	4.13E-01
ENSMUSG00000046556	Zfp319	1.88E-33	5.93E-32	2.89	2.26E+02	7.84E+01
ENSMUSG00000079227	Ccr5	2.06E-33	6.49E-32	4.40	4.85E+02	1.10E+02
ENSMUSG00000047098	Rnf31	2.10E-33	6.63E-32	4.22	6.12E+01	1.45E+01
ENSMUSG00000033581	Igf2bp2	3.10E-33	9.74E-32	3.99	1.00E+03	2.51E+02
ENSMUSG00000027883	Gpsm2	3.40E-33	1.07E-31	4.52	1.72E+02	3.82E+01
ENSMUSG00000031154	Otud5	3.66E-33	1.15E-31	2.30	6.52E+02	2.84E+02
ENSMUSG00000029313	Aff1	3.90E-33	1.22E-31	3.11	1.02E+03	3.29E+02
ENSMUSG00000018909	Arrb1	4.20E-33	1.31E-31	-3.78	1.25E+02	4.72E+02
ENSMUSG00000027366	Sppl2a	5.02E-33	1.57E-31	3.21	3.44E+03	1.07E+03
ENSMUSG00000061039	Olfr920	9.31E-33	2.90E-31	2.67	1.26E+02	4.72E+01
ENSMUSG00000031701	Dnaja2	9.39E-33	2.92E-31	2.35	2.64E+03	1.12E+03

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000028233	Tgs1	1.07E-32	3.33E-31	2.51	7.07E+02	2.81E+02
ENSMUSG00000020953	Coch	1.24E-32	3.85E-31	119.10	1.82E+01	1.53E-01
ENSMUSG00000027010	Slc25a12	1.26E-32	3.89E-31	3.18	7.11E+02	2.23E+02
ENSMUSG00000025743	Sdc3	1.61E-32	4.98E-31	2.67	2.10E+03	7.85E+02
ENSMUSG00000033004	Mycbp2	1.75E-32	5.39E-31	2.05	1.15E+03	5.61E+02
ENSMUSG00000071714	Csf2rb2	2.07E-32	6.37E-31	2.24	3.00E+03	1.34E+03
ENSMUSG00000031403	Dkc1	2.13E-32	6.53E-31	-6.01	4.51E+01	2.71E+02
ENSMUSG00000020709	Adap2	3.35E-32	1.03E-30	4.88	7.98E+02	1.63E+02
ENSMUSG00000029110	Rnf4	3.43E-32	1.05E-30	2.23	7.44E+02	3.33E+02
ENSMUSG00000030852	Tacc2	4.49E-32	1.37E-30	-7.23	8.71E+00	6.30E+01
ENSMUSG00000072568	Lratd2	4.53E-32	1.38E-30	3.22	2.73E+02	8.47E+01
ENSMUSG00000021067	Sav1	6.58E-32	1.99E-30	2.60	4.26E+02	1.64E+02
ENSMUSG00000020357	Flt4	6.62E-32	2.00E-30	75.28	6.64E+01	8.82E-01
ENSMUSG00000105504	Gbp5	7.06E-32	2.13E-30	68.45	1.33E+04	1.94E+02
ENSMUSG00000044350	Lacc1	9.19E-32	2.77E-30	4.49	1.41E+03	3.15E+02
ENSMUSG00000089940	Gm4117	9.72E-32	2.93E-30	6.55	3.40E+01	5.19E+00
ENSMUSG00000045795	Whamm	9.99E-32	3.00E-30	4.03	1.70E+02	4.21E+01
ENSMUSG00000037406	Htra4	1.66E-31	4.98E-30	18.63	1.17E+02	6.26E+00
ENSMUSG00000021693	Kif2a	1.99E-31	5.95E-30	-2.30	1.49E+02	3.44E+02
ENSMUSG00000048118	Arid4a	1.99E-31	5.96E-30	2.60	1.78E+03	6.84E+02
ENSMUSG00000039678	Tbc1d13	2.41E-31	7.21E-30	3.01	1.98E+03	6.59E+02
ENSMUSG00000033400	Agl	2.52E-31	7.50E-30	-2.42	1.07E+02	2.60E+02
ENSMUSG00000025153	Fasn	2.67E-31	7.94E-30	-3.87	6.43E+01	2.48E+02
ENSMUSG00000045092	S1pr1	2.68E-31	7.95E-30	-4.67	8.68E+01	4.05E+02
ENSMUSG00000078485	Plekhn1	3.29E-31	9.77E-30	2.62	3.84E+02	1.47E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000022765	Snap29	3.68E-31	1.09E-29	2.04	4.50E+02	2.21E+02
ENSMUSG00000024737	Slc15a3	3.70E-31	1.09E-29	3.26	7.12E+03	2.18E+03
ENSMUSG00000029640	Usp12	3.74E-31	1.10E-29	5.63	9.61E+01	1.71E+01
ENSMUSG00000004936	Map2k1	4.63E-31	1.36E-29	2.95	9.54E+02	3.23E+02
ENSMUSG00000087175	Gm15133	5.65E-31	1.66E-29	8.51	2.85E+01	3.36E+00
ENSMUSG00000030223	Ptpro	6.82E-31	2.00E-29	2.76	8.08E+02	2.93E+02
ENSMUSG00000003123	Lipe	6.95E-31	2.04E-29	3.18	2.72E+02	8.55E+01
ENSMUSG00000020092	Pald1	7.72E-31	2.26E-29	-8.03	8.39E+00	6.74E+01
ENSMUSG00000035517	Tdrd7	9.01E-31	2.62E-29	5.73	6.52E+02	1.14E+02
ENSMUSG00000001911	Nfix	9.98E-31	2.90E-29	2.83	5.42E+02	1.91E+02
ENSMUSG00000097354	2310001H17Rik	1.17E-30	3.38E-29	2.55	1.67E+02	6.53E+01
ENSMUSG00000091780	Sco2	1.27E-30	3.67E-29	-3.44	3.13E+01	1.08E+02
ENSMUSG00000020271	Fbxw11	1.27E-30	3.68E-29	2.19	8.96E+02	4.09E+02
ENSMUSG00000043895	S1pr2	1.33E-30	3.84E-29	2.83	1.65E+03	5.83E+02
ENSMUSG00000021877	Arf4	1.53E-30	4.40E-29	2.97	2.37E+03	7.97E+02
ENSMUSG00000020593	Lpin1	2.28E-30	6.56E-29	-5.52	4.16E+01	2.29E+02
ENSMUSG00000054509	Parp4	2.68E-30	7.70E-29	2.08	4.12E+02	1.98E+02
ENSMUSG00000068749	Psma5	3.16E-30	9.08E-29	2.70	6.02E+02	2.23E+02
ENSMUSG00000079184	Mphosph8	3.26E-30	9.35E-29	-2.08	2.81E+02	5.86E+02
ENSMUSG00000037270	4932438A13Rik	3.91E-30	1.12E-28	2.36	7.32E+02	3.11E+02
ENSMUSG00000100615	Gm5511	4.05E-30	1.16E-28	10.59	3.42E+01	3.23E+00
ENSMUSG00000062526	Mppe1	4.23E-30	1.20E-28	5.72	8.72E+01	1.52E+01
ENSMUSG00000019806	Aig1	4.82E-30	1.37E-28	3.03	2.55E+02	8.41E+01
ENSMUSG00000036461	Elf1	5.18E-30	1.47E-28	2.17	2.00E+03	9.20E+02
ENSMUSG00000017929	B4galt5	5.49E-30	1.56E-28	2.82	1.77E+03	6.29E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000045038	Prkce	5.59E-30	1.58E-28	4.08	9.68E+01	2.37E+01
ENSMUSG00000038740	Mvb12b	6.33E-30	1.79E-28	-2.27	1.47E+02	3.34E+02
ENSMUSG00000019528	Gyg	6.45E-30	1.82E-28	2.09	2.04E+03	9.78E+02
ENSMUSG00000026019	Wdr12	7.74E-30	2.18E-28	-4.19	3.08E+01	1.29E+02
ENSMUSG00000032412	Atp1b3	1.39E-29	3.90E-28	2.19	3.85E+03	1.75E+03
ENSMUSG00000055013	Agap1	1.47E-29	4.11E-28	-3.30	1.06E+02	3.49E+02
ENSMUSG00000072889	Nfxl1	1.69E-29	4.73E-28	7.32	3.83E+02	5.23E+01
ENSMUSG00000079316	Rab9	1.73E-29	4.84E-28	2.60	6.45E+02	2.48E+02
ENSMUSG00000021196	Pfkp	1.88E-29	5.24E-28	2.70	1.48E+03	5.48E+02
ENSMUSG00000037995	Igsf9	2.09E-29	5.82E-28	16.10	1.61E+02	9.98E+00
ENSMUSG00000023952	Gtpbp2	2.29E-29	6.35E-28	3.00	9.53E+02	3.18E+02
ENSMUSG00000029322	Plac8	2.32E-29	6.43E-28	16.10	4.96E+01	3.08E+00
ENSMUSG00000029152	Ociad1	2.37E-29	6.57E-28	2.04	2.47E+03	1.21E+03
ENSMUSG00000020023	Tmcc3	2.41E-29	6.66E-28	4.42	8.53E+02	1.93E+02
ENSMUSG00000074578	Zfas1	2.67E-29	7.36E-28	4.03	1.10E+03	2.72E+02
ENSMUSG00000038301	Snx10	2.85E-29	7.86E-28	2.78	1.47E+03	5.30E+02
ENSMUSG00000060675	Plaat3	3.33E-29	9.15E-28	8.89	1.15E+03	1.29E+02
ENSMUSG00000001909	Trmt1	3.90E-29	1.07E-27	-2.08	1.32E+02	2.75E+02
ENSMUSG00000047446	Arl4a	4.07E-29	1.12E-27	3.37	3.10E+02	9.21E+01
ENSMUSG00000097567	nan	4.80E-29	1.31E-27	5.28	3.43E+01	6.48E+00
ENSMUSG00000071660	Ttc9c	5.09E-29	1.39E-27	2.84	2.73E+02	9.60E+01
ENSMUSG00000031012	Cask	5.89E-29	1.61E-27	2.75	2.47E+02	8.97E+01
ENSMUSG00000005846	Rsl1d1	8.85E-29	2.40E-27	-2.13	3.72E+02	7.95E+02
ENSMUSG00000056290	Ms4a4b	9.36E-29	2.53E-27	12.03	4.20E+01	3.49E+00
ENSMUSG00000043279	Trim56	1.12E-28	3.04E-27	2.79	7.91E+02	2.84E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000025076	Casp7	1.32E-28	3.56E-27	3.26	2.72E+02	8.36E+01
ENSMUSG00000031862	Atp13a1	1.38E-28	3.72E-27	2.12	4.97E+02	2.35E+02
ENSMUSG00000026970	Rbms1	1.41E-28	3.78E-27	2.23	8.20E+03	3.67E+03
ENSMUSG00000026981	Il1rn	1.42E-28	3.82E-27	8.23	4.58E+03	5.57E+02
ENSMUSG00000021981	Cab39l	1.57E-28	4.20E-27	2.37	3.47E+02	1.47E+02
ENSMUSG00000027900	Dram2	1.68E-28	4.50E-27	2.13	8.70E+02	4.09E+02
ENSMUSG00000000791	Il12rb1	1.77E-28	4.70E-27	52.16	1.23E+02	2.36E+00
ENSMUSG00000052336	Cx3cr1	1.85E-28	4.91E-27	-6.84	5.95E+01	4.07E+02
ENSMUSG00000022575	Gsdmd	2.09E-28	5.54E-27	3.70	5.64E+02	1.52E+02
ENSMUSG00000017837	Nkiras2	2.94E-28	7.79E-27	2.42	8.93E+02	3.69E+02
ENSMUSG00000052760	A630001G21Rik	3.08E-28	8.14E-27	3.09	1.96E+02	6.35E+01
ENSMUSG00000033885	Pxk	3.13E-28	8.26E-27	2.30	4.82E+02	2.09E+02
ENSMUSG00000071042	Rasgrp3	3.32E-28	8.74E-27	-4.70	2.97E+01	1.40E+02
ENSMUSG00000027641	Rbl1	4.08E-28	1.07E-26	4.12	3.73E+02	9.05E+01
ENSMUSG00000028337	Coro2a	4.17E-28	1.10E-26	2.13	1.03E+03	4.84E+02
ENSMUSG00000030681	Mvp	4.63E-28	1.21E-26	2.12	8.59E+02	4.05E+02
ENSMUSG00000028466	Creb3	4.68E-28	1.23E-26	2.50	9.16E+02	3.66E+02
ENSMUSG00000042354	Gnl3	5.66E-28	1.48E-26	-2.93	1.26E+02	3.70E+02
ENSMUSG00000078942	Naip6	7.48E-28	1.95E-26	2.29	1.71E+02	7.46E+01
ENSMUSG00000057110	Cntrl	8.06E-28	2.09E-26	2.15	4.07E+02	1.89E+02
ENSMUSG00000115219	Eef1akmt4	9.14E-28	2.37E-26	3.08	3.14E+02	1.02E+02
ENSMUSG00000027676	Ccdc39	9.17E-28	2.38E-26	14.72	2.66E+01	1.81E+00
ENSMUSG00000048163	Selplg	9.79E-28	2.53E-26	2.38	2.07E+03	8.69E+02
ENSMUSG00000050002	Idnk	1.06E-27	2.75E-26	2.70	2.63E+02	9.72E+01
ENSMUSG00000026917	Wdr5	1.26E-27	3.25E-26	-2.07	1.43E+02	2.96E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000020124	Usp15	1.65E-27	4.26E-26	2.04	5.25E+02	2.57E+02
ENSMUSG00000018707	Dync1h1	1.72E-27	4.41E-26	2.01	2.65E+03	1.32E+03
ENSMUSG00000022814	Umps	2.07E-27	5.30E-26	-3.65	3.84E+01	1.40E+02
ENSMUSG00000051390	Zbtb22	2.42E-27	6.20E-26	-2.05	1.16E+02	2.38E+02
ENSMUSG00000025612	Bach1	2.78E-27	7.10E-26	3.17	1.88E+03	5.91E+02
ENSMUSG00000043445	Pgp	3.25E-27	8.27E-26	-2.34	8.74E+01	2.04E+02
ENSMUSG00000097572	Gm26797	3.26E-27	8.29E-26	14.04	3.47E+01	2.47E+00
ENSMUSG00000022309	Angpt1	3.44E-27	8.74E-26	86.65	1.33E+02	1.53E+00
ENSMUSG00000034987	Hrh2	4.45E-27	1.13E-25	18.40	5.00E+01	2.72E+00
ENSMUSG00000025877	Hk3	4.48E-27	1.13E-25	3.37	3.64E+03	1.08E+03
ENSMUSG00000000149	Gna12	6.13E-27	1.55E-25	-2.31	1.52E+02	3.51E+02
ENSMUSG00000028790	Khdrbs1	8.32E-27	2.09E-25	2.06	5.39E+02	2.61E+02
ENSMUSG00000024513	Mbd2	9.19E-27	2.30E-25	2.44	7.93E+02	3.24E+02
ENSMUSG00000049047	Armcx3	1.20E-26	3.00E-25	2.17	1.32E+02	6.10E+01
ENSMUSG00000040522	Tlr8	1.28E-26	3.18E-25	4.10	8.00E+01	1.95E+01
ENSMUSG00000099398	Ms4a14	1.35E-26	3.36E-25	2.93	5.42E+02	1.85E+02
ENSMUSG00000032305	Fam219b	1.68E-26	4.16E-25	-2.26	5.09E+01	1.15E+02
ENSMUSG00000059518	Znhit1	1.73E-26	4.28E-25	2.13	8.31E+02	3.90E+02
ENSMUSG00000027340	Slc23a2	1.84E-26	4.54E-25	2.49	7.48E+02	3.00E+02
ENSMUSG00000097113	Gm19705	1.85E-26	4.56E-25	3.64	6.50E+01	1.79E+01
ENSMUSG00000044468	Tent5c	1.97E-26	4.85E-25	2.54	1.64E+03	6.46E+02
ENSMUSG00000097119	B230354K17Rik	1.99E-26	4.89E-25	-2.73	3.36E+01	9.16E+01
ENSMUSG00000024378	Stard4	2.17E-26	5.33E-25	-3.25	8.96E+01	2.91E+02
ENSMUSG00000032593	Amigo3	3.00E-26	7.33E-25	6.19	3.30E+01	5.33E+00
ENSMUSG00000041607	Mbp	3.22E-26	7.83E-25	-2.02	1.35E+02	2.73E+02

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ENSMUSG00000033767	Tmem131l	3.38E-26	8.23E-25	-2.27	6.88E+01	1.56E+02
ENSMUSG00000033538	Casp4	3.49E-26	8.48E-25	5.10	1.69E+03	3.31E+02
ENSMUSG00000027035	Cers6	4.34E-26	1.05E-24	4.03	1.06E+03	2.62E+02
ENSMUSG00000078606	Gvin2	5.16E-26	1.25E-24	76.31	1.92E+01	2.52E-01
ENSMUSG00000031311	Nono	6.02E-26	1.46E-24	2.30	6.23E+02	2.71E+02
ENSMUSG00000019990	Pde7b	6.09E-26	1.47E-24	4.43	9.67E+01	2.18E+01
ENSMUSG00000075700	Selenot	6.78E-26	1.63E-24	2.24	9.49E+02	4.24E+02
ENSMUSG00000074345	Tnfaip8l3	8.25E-26	1.99E-24	24.75	3.79E+01	1.53E+00
ENSMUSG00000052087	Rgs14	8.55E-26	2.05E-24	3.32	4.35E+02	1.31E+02
ENSMUSG00000026581	Sell	1.04E-25	2.50E-24	32.40	2.18E+01	6.73E-01
ENSMUSG00000037012	Hk1	1.05E-25	2.52E-24	2.27	7.98E+02	3.52E+02
ENSMUSG00000070284	Gmppb	1.33E-25	3.17E-24	3.39	3.62E+02	1.07E+02
ENSMUSG00000073144	4930599N23Rik	1.67E-25	3.97E-24	7.86	4.14E+01	5.26E+00
ENSMUSG00000043740	B430306N03Rik	1.67E-25	3.97E-24	5.46	6.49E+02	1.19E+02
ENSMUSG00000037580	Gch1	1.74E-25	4.13E-24	5.13	1.55E+03	3.02E+02
ENSMUSG00000046096	Mosmo	1.79E-25	4.24E-24	2.76	1.88E+02	6.79E+01
ENSMUSG00000039936	Pik3cd	2.33E-25	5.51E-24	2.63	8.19E+02	3.11E+02
ENSMUSG00000001750	Tcirg1	3.28E-25	7.75E-24	2.30	3.38E+03	1.47E+03
ENSMUSG00000041438	Utp4	3.50E-25	8.27E-24	-2.53	3.55E+01	8.98E+01
ENSMUSG00000049657	Zbtb5	3.58E-25	8.43E-24	2.79	1.47E+02	5.25E+01
ENSMUSG00000029438	Bcl7a	3.75E-25	8.82E-24	-8.81	4.38E+00	3.86E+01
ENSMUSG00000031709	Tbc1d9	3.76E-25	8.83E-24	2.08	5.94E+02	2.86E+02
ENSMUSG00000027429	Sec23b	3.85E-25	9.02E-24	2.02	3.42E+02	1.70E+02
ENSMUSG00000035382	Pcsk7	4.24E-25	9.93E-24	2.79	1.54E+02	5.51E+01
ENSMUSG00000024887	Asah2	4.47E-25	1.05E-23	2.96	1.63E+02	5.51E+01

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ENSMUSG00000089844	A530032D15Rik	6.00E-25	1.40E-23	65.99	2.42E+01	3.67E-01
ENSMUSG00000040987	Mill2	6.70E-25	1.56E-23	4.83	9.89E+01	2.05E+01
ENSMUSG00000031824	6430548M08Rik	6.81E-25	1.58E-23	-4.46	3.83E+01	1.71E+02
ENSMUSG00000039005	Tlr4	6.84E-25	1.59E-23	2.34	3.80E+02	1.62E+02
ENSMUSG00000066148	Prpf4	7.95E-25	1.84E-23	2.85	4.42E+02	1.55E+02
ENSMUSG00000002489	Tiam1	7.99E-25	1.85E-23	3.83	3.93E+02	1.03E+02
ENSMUSG00000047534	Mis18bp1	9.98E-25	2.30E-23	-2.76	8.22E+01	2.27E+02
ENSMUSG00000031103	Elf4	1.04E-24	2.39E-23	2.07	3.90E+02	1.88E+02
ENSMUSG00000028019	Pdgfc	1.08E-24	2.49E-23	2.94	1.20E+02	4.08E+01
ENSMUSG00000036712	Cyld	1.14E-24	2.62E-23	2.12	5.69E+02	2.69E+02
ENSMUSG00000035941	Ibtk	1.18E-24	2.70E-23	-2.25	7.48E+01	1.68E+02
ENSMUSG00000027422	Rrbp1	1.25E-24	2.88E-23	2.29	7.04E+03	3.07E+03
ENSMUSG00000105283	Gm33370	1.43E-24	3.27E-23	5.19	5.34E+01	1.03E+01
ENSMUSG00000043059	Zfp513	1.57E-24	3.58E-23	2.28	3.16E+02	1.38E+02
ENSMUSG00000015733	Capza2	1.83E-24	4.18E-23	2.38	3.16E+03	1.33E+03
ENSMUSG00000027907	S100a11	1.89E-24	4.31E-23	2.15	6.95E+03	3.23E+03
ENSMUSG00000038121	Fam210a	1.93E-24	4.39E-23	-2.29	4.66E+01	1.07E+02
ENSMUSG00000018651	Tada2a	2.29E-24	5.20E-23	-3.59	2.36E+01	8.46E+01
ENSMUSG00000025171	Ubtd1	2.46E-24	5.56E-23	2.37	4.59E+02	1.93E+02
ENSMUSG00000003948	Mmd	2.88E-24	6.51E-23	-2.71	9.40E+01	2.55E+02
ENSMUSG00000020642	Rnf144a	3.00E-24	6.78E-23	8.33	6.48E+01	7.78E+00
ENSMUSG00000026773	Pfkfb3	3.05E-24	6.88E-23	4.10	7.11E+02	1.73E+02
ENSMUSG00000052713	Zfp608	3.08E-24	6.93E-23	-3.41	2.09E+01	7.11E+01
ENSMUSG00000031093	Dock11	3.61E-24	8.11E-23	2.83	5.67E+02	2.00E+02
ENSMUSG00000048186	Bend7	3.82E-24	8.56E-23	14.44	2.78E+01	1.93E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000047412	Zbtb44	4.29E-24	9.60E-23	-2.27	8.53E+01	1.93E+02
ENSMUSG00000016206	H2-M3	4.85E-24	1.08E-22	3.35	2.66E+02	7.93E+01
ENSMUSG00000048922	Cdca2	4.98E-24	1.11E-22	-5.44	2.62E+01	1.42E+02
ENSMUSG00000020564	Atxn7l1	5.69E-24	1.27E-22	2.41	2.78E+02	1.15E+02
ENSMUSG00000057346	Apol9a	6.28E-24	1.40E-22	104.11	3.37E+01	3.24E-01
ENSMUSG00000000409	Lck	6.39E-24	1.42E-22	8.55	1.69E+01	1.98E+00
ENSMUSG00000033610	Pank1	6.51E-24	1.45E-22	-6.08	1.52E+01	9.25E+01
ENSMUSG00000035929	H2-Q4	7.01E-24	1.56E-22	9.35	8.98E+01	9.60E+00
ENSMUSG00000005580	Adcy9	8.19E-24	1.82E-22	-3.29	3.92E+01	1.29E+02
ENSMUSG00000021384	Susd3	9.40E-24	2.08E-22	-4.14	8.20E+01	3.40E+02
ENSMUSG00000097062	nan	9.84E-24	2.17E-22	-3.39	2.41E+01	8.19E+01
ENSMUSG00000058470	Gm8369	1.09E-23	2.39E-22	6.04	5.20E+01	8.61E+00
ENSMUSG00000026112	Coa5	1.15E-23	2.53E-22	2.31	1.41E+03	6.11E+02
ENSMUSG00000030157	Clec2d	1.17E-23	2.57E-22	5.04	2.24E+02	4.45E+01
ENSMUSG00000097006	9530082P21Rik	1.17E-23	2.57E-22	9.31	4.84E+01	5.20E+00
ENSMUSG00000020392	Cdkn2aipnl	1.19E-23	2.60E-22	-2.18	1.51E+02	3.28E+02
ENSMUSG00000028459	Cd72	1.20E-23	2.63E-22	4.77	1.80E+03	3.77E+02
ENSMUSG00000029344	Tpst2	1.23E-23	2.68E-22	2.54	6.56E+02	2.58E+02
ENSMUSG00000022684	Bfar	1.45E-23	3.15E-22	2.90	9.36E+02	3.22E+02
ENSMUSG00000066278	Vps37b	2.06E-23	4.49E-22	2.39	6.17E+02	2.58E+02
ENSMUSG00000034959	Rubcnl	2.35E-23	5.11E-22	8.60	7.57E+01	8.81E+00
ENSMUSG00000041215	Yeats2	2.45E-23	5.31E-22	-2.87	2.21E+01	6.32E+01
ENSMUSG00000047409	Ctdspl	2.65E-23	5.73E-22	-3.82	2.59E+01	9.86E+01
ENSMUSG00000047414	Flrt2	2.67E-23	5.78E-22	5.69	8.41E+02	1.48E+02
ENSMUSG00000059108	Ifitm6	2.71E-23	5.86E-22	4.50	5.57E+01	1.24E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000023010	Tmbim6	2.74E-23	5.91E-22	2.13	4.39E+03	2.06E+03
ENSMUSG00000032009	Sesn3	3.21E-23	6.92E-22	2.96	1.71E+02	5.76E+01
ENSMUSG00000032425	Zfp949	4.47E-23	9.61E-22	3.23	8.76E+01	2.71E+01
ENSMUSG00000078851	H2aw	5.28E-23	1.13E-21	3.45	1.69E+03	4.89E+02
ENSMUSG00000058006	Mdn1	5.76E-23	1.23E-21	-3.52	4.79E+01	1.69E+02
ENSMUSG00000003283	Hck	6.12E-23	1.30E-21	3.42	1.34E+03	3.92E+02
ENSMUSG00000029190	D5Ertd579e	6.27E-23	1.33E-21	2.13	4.14E+02	1.94E+02
ENSMUSG00000041926	Rnpep	6.46E-23	1.37E-21	2.02	1.90E+03	9.42E+02
ENSMUSG00000004535	Tax1bp1	6.81E-23	1.44E-21	2.04	5.05E+03	2.47E+03
ENSMUSG00000054728	Phactr1	6.86E-23	1.45E-21	15.02	2.09E+01	1.39E+00
ENSMUSG00000039096	Rsad1	7.13E-23	1.50E-21	-4.09	1.07E+01	4.36E+01
ENSMUSG00000019857	Asf1a	7.72E-23	1.63E-21	2.06	1.90E+02	9.25E+01
ENSMUSG00000021143	Pacs2	7.98E-23	1.68E-21	2.29	8.78E+02	3.83E+02
ENSMUSG00000044340	Phlpp1	9.78E-23	2.06E-21	4.48	2.69E+02	6.00E+01
ENSMUSG00000029501	Ankle2	1.13E-22	2.36E-21	2.17	3.27E+02	1.51E+02
ENSMUSG00000042599	Kdm7a	1.16E-22	2.43E-21	2.30	4.90E+02	2.13E+02
ENSMUSG00000029310	Nudt9	1.18E-22	2.48E-21	2.00	3.42E+02	1.70E+02
ENSMUSG00000043008	Klhl6	1.26E-22	2.64E-21	-3.31	6.43E+01	2.13E+02
ENSMUSG00000027367	Stard7	1.32E-22	2.76E-21	-2.52	7.07E+01	1.78E+02
ENSMUSG00000035967	Ints6l	1.32E-22	2.76E-21	-2.96	3.60E+01	1.06E+02
ENSMUSG00000025283	Sat1	1.46E-22	3.03E-21	3.49	1.86E+03	5.34E+02
ENSMUSG00000026974	Zmynd19	1.46E-22	3.03E-21	-3.06	2.61E+01	7.98E+01
ENSMUSG00000002058	Unc119	1.48E-22	3.06E-21	-2.20	1.13E+02	2.48E+02
ENSMUSG00000039640	Mrpl12	1.48E-22	3.07E-21	-2.12	1.97E+02	4.18E+02
ENSMUSG00000041238	Rbbp8	1.52E-22	3.13E-21	2.46	5.89E+02	2.39E+02

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ENSMUSG00000053617	Sh3pxd2a	1.52E-22	3.14E-21	-3.57	3.12E+01	1.11E+02
ENSMUSG00000067212	H2-T23	1.65E-22	3.39E-21	11.41	8.55E+01	7.49E+00
ENSMUSG00000060450	Rnf14	1.68E-22	3.45E-21	2.12	1.00E+03	4.72E+02
ENSMUSG00000020027	Socs2	1.70E-22	3.50E-21	3.69	1.28E+02	3.47E+01
ENSMUSG00000032215	Rsl24d1	1.70E-22	3.50E-21	2.12	2.54E+02	1.20E+02
ENSMUSG00000020741	Cluh	1.71E-22	3.50E-21	-2.89	1.63E+02	4.71E+02
ENSMUSG00000034111	Tmed8	1.89E-22	3.86E-21	2.22	1.56E+02	7.03E+01
ENSMUSG00000043067	Dpy19l1	2.10E-22	4.29E-21	2.65	6.39E+02	2.41E+02
ENSMUSG00000021895	Arhgef3	2.24E-22	4.56E-21	4.41	1.03E+03	2.34E+02
ENSMUSG00000031628	Casp3	2.37E-22	4.82E-21	3.46	7.39E+02	2.13E+02
ENSMUSG00000024245	Tmem178	2.51E-22	5.11E-21	12.60	1.14E+02	9.03E+00
ENSMUSG00000055720	Ubl7	2.52E-22	5.11E-21	2.46	1.88E+02	7.62E+01
ENSMUSG00000037419	Endod1	2.66E-22	5.39E-21	2.91	7.38E+02	2.53E+02
ENSMUSG00000072109	A530040E14Rik	2.72E-22	5.51E-21	70.10	1.56E+01	2.23E-01
ENSMUSG00000026269	Rnpepl1	3.14E-22	6.35E-21	2.03	4.82E+02	2.38E+02
ENSMUSG00000048279	Sacs	3.31E-22	6.68E-21	-2.89	3.64E+01	1.05E+02
ENSMUSG00000025287	Acot9	4.09E-22	8.25E-21	2.09	4.37E+02	2.09E+02
ENSMUSG00000033799	Tasor2	4.15E-22	8.36E-21	4.24	1.22E+02	2.88E+01
ENSMUSG00000050075	Gpr171	4.48E-22	9.02E-21	8.82	8.53E+01	9.67E+00
ENSMUSG00000040552	C3ar1	4.63E-22	9.31E-21	2.23	2.66E+04	1.19E+04
ENSMUSG00000028207	Asph	4.97E-22	9.96E-21	2.19	1.28E+03	5.86E+02
ENSMUSG00000024081	Cebpz	5.49E-22	1.10E-20	-2.30	1.62E+02	3.73E+02
ENSMUSG00000030126	Tmcc1	5.77E-22	1.15E-20	-2.07	9.37E+01	1.94E+02
ENSMUSG00000026548	Slamf9	5.99E-22	1.19E-20	6.92	6.98E+02	1.01E+02
ENSMUSG00000085977	Gm5970	6.05E-22	1.20E-20	63.67	1.10E+01	1.73E-01

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ENSMUSG00000021037	Ahsa1	6.27E-22	1.25E-20	2.61	4.63E+02	1.77E+02
ENSMUSG00000026005	Rpe	6.46E-22	1.28E-20	2.28	3.13E+02	1.38E+02
ENSMUSG00000002797	Ggct	6.46E-22	1.28E-20	3.81	1.51E+02	3.95E+01
ENSMUSG00000072621	Slfn10-ps	6.56E-22	1.30E-20	2.65	6.54E+02	2.46E+02
ENSMUSG00000075602	Ly6a	7.43E-22	1.47E-20	15.92	1.50E+03	9.44E+01
ENSMUSG00000064181	Rab3ip	8.07E-22	1.60E-20	2.82	6.53E+01	2.32E+01
ENSMUSG00000046982	Tshz1	8.24E-22	1.63E-20	-2.37	1.59E+02	3.76E+02
ENSMUSG00000028896	Rcc1	9.57E-22	1.89E-20	-3.50	4.56E+01	1.60E+02
ENSMUSG00000040414	Slc25a28	9.98E-22	1.97E-20	2.52	3.90E+02	1.55E+02
ENSMUSG00000020717	Pecam1	1.03E-21	2.03E-20	7.52	2.62E+01	3.49E+00
ENSMUSG00000039048	Foxred1	1.14E-21	2.25E-20	2.11	1.97E+02	9.35E+01
ENSMUSG00000034574	Daam1	1.22E-21	2.39E-20	2.78	4.23E+02	1.52E+02
ENSMUSG00000025764	Jade1	1.24E-21	2.43E-20	-3.22	6.90E+01	2.22E+02
ENSMUSG00000029491	Pde6b	1.25E-21	2.45E-20	32.46	2.02E+01	6.21E-01
ENSMUSG00000021392	Nol8	1.31E-21	2.55E-20	-2.35	9.19E+01	2.16E+02
ENSMUSG00000022184	Fbxo4	1.97E-21	3.84E-20	3.22	4.04E+02	1.25E+02
ENSMUSG00000021840	Mapk1ip1l	2.11E-21	4.10E-20	2.10	2.69E+02	1.28E+02
ENSMUSG00000039783	Kmo	2.45E-21	4.75E-20	14.98	5.53E+01	3.69E+00
ENSMUSG00000026664	Phyh	2.56E-21	4.95E-20	2.53	4.35E+02	1.72E+02
ENSMUSG00000038485	Socs7	2.58E-21	4.99E-20	3.03	7.24E+02	2.39E+02
ENSMUSG00000029392	Rilpl1	2.72E-21	5.25E-20	3.20	1.52E+02	4.74E+01
ENSMUSG00000039853	Trim14	2.89E-21	5.57E-20	3.55	4.49E+01	1.26E+01
ENSMUSG00000079293	Clec7a	2.91E-21	5.60E-20	3.34	3.86E+03	1.16E+03
ENSMUSG00000116380	Gm39556	4.45E-21	8.51E-20	16.89	2.10E+01	1.25E+00
ENSMUSG00000030766	Arhgap17	4.96E-21	9.45E-20	2.41	8.67E+02	3.60E+02

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ENSMUSG00000027351	Spred1	5.10E-21	9.70E-20	4.27	2.38E+03	5.57E+02
ENSMUSG00000053101	Gpr141	5.40E-21	1.02E-19	3.04	3.92E+02	1.29E+02
ENSMUSG00000026289	Atg16l1	6.52E-21	1.24E-19	2.04	2.16E+02	1.06E+02
ENSMUSG00000023147	Get1	6.93E-21	1.31E-19	-2.95	4.15E+01	1.22E+02
ENSMUSG00000097534	Gm16675	7.85E-21	1.48E-19	13.22	1.99E+01	1.51E+00
ENSMUSG00000032288	Imp3	9.89E-21	1.87E-19	-2.32	1.29E+02	2.98E+02
ENSMUSG00000034792	Gna15	9.91E-21	1.87E-19	3.00	3.25E+02	1.09E+02
ENSMUSG00000116549	Gm49728	1.10E-20	2.07E-19	38.89	1.11E+01	2.86E-01
ENSMUSG00000041483	Zfp281	1.11E-20	2.08E-19	2.79	6.10E+02	2.19E+02
ENSMUSG00000087700	Gm15283	1.14E-20	2.14E-19	55.30	1.39E+01	2.52E-01
ENSMUSG00000069893	9930111J21Rik1	1.14E-20	2.14E-19	16.74	1.65E+01	9.84E-01
ENSMUSG00000079505	Gm11131	1.15E-20	2.16E-19	10.90	1.94E+01	1.78E+00
ENSMUSG00000031216	Stard8	1.63E-20	3.05E-19	2.01	5.17E+02	2.57E+02
ENSMUSG00000029703	Lrwd1	1.79E-20	3.35E-19	-2.30	5.97E+01	1.37E+02
ENSMUSG00000045827	Serpinb9	1.87E-20	3.49E-19	6.42	3.95E+02	6.16E+01
ENSMUSG00000025279	Dnase1l3	2.07E-20	3.87E-19	72.51	3.37E+01	4.65E-01
ENSMUSG00000034312	Iqsec1	2.30E-20	4.28E-19	-2.38	1.91E+02	4.55E+02
ENSMUSG00000024339	Tap2	2.45E-20	4.56E-19	8.20	4.80E+03	5.86E+02
ENSMUSG00000057789	Bak1	3.39E-20	6.28E-19	2.14	1.35E+03	6.30E+02
ENSMUSG00000062007	Hsh2d	3.47E-20	6.42E-19	58.77	1.68E+01	2.86E-01
ENSMUSG00000029428	Stx2	3.75E-20	6.94E-19	2.71	7.04E+02	2.60E+02
ENSMUSG00000061759	Armt1	3.95E-20	7.29E-19	-2.43	2.98E+01	7.23E+01
ENSMUSG00000093507	Gm20627	4.50E-20	8.30E-19	13.66	1.27E+01	9.31E-01
ENSMUSG00000051147	Nat2	4.83E-20	8.89E-19	3.28	7.75E+01	2.36E+01
ENSMUSG00000102437	nan	4.91E-20	9.02E-19	14.22	1.98E+01	1.39E+00

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ENSMUSG00000026202	Tuba4a	5.06E-20	9.30E-19	-2.89	9.55E+01	2.76E+02
ENSMUSG00000035273	Hpse	5.22E-20	9.59E-19	2.42	1.88E+03	7.80E+02
ENSMUSG00000037331	Larp1	6.53E-20	1.20E-18	2.20	7.34E+02	3.34E+02
ENSMUSG00000040276	Pacsin1	6.72E-20	1.23E-18	30.41	2.86E+01	9.39E-01
ENSMUSG00000017412	Cacnb4	7.69E-20	1.40E-18	8.04	2.17E+01	2.69E+00
ENSMUSG00000063388	BC023105	7.99E-20	1.46E-18	48.05	7.35E+00	1.53E-01
ENSMUSG00000035042	Ccl5	8.49E-20	1.55E-18	46.82	3.30E+03	7.05E+01
ENSMUSG00000031647	Mfap3l	8.89E-20	1.62E-18	-3.14	1.98E+01	6.22E+01
ENSMUSG00000028261	Ndufaf4	9.84E-20	1.79E-18	-2.31	6.53E+01	1.51E+02
ENSMUSG00000104955	1700016F12Rik	1.13E-19	2.04E-18	68.50	1.05E+01	1.53E-01
ENSMUSG00000008384	Sertad1	1.35E-19	2.45E-18	2.49	7.22E+02	2.90E+02
ENSMUSG00000033813	Tcea1	1.36E-19	2.46E-18	2.34	1.08E+02	4.62E+01
ENSMUSG00000017652	Cd40	1.39E-19	2.50E-18	21.84	1.84E+03	8.42E+01
ENSMUSG00000050619	Zscan29	1.66E-19	3.00E-18	2.12	1.91E+02	9.04E+01
ENSMUSG00000038037	Socs1	1.68E-19	3.03E-18	15.30	2.19E+02	1.43E+01
ENSMUSG00000022721	Trmt2a	1.68E-19	3.03E-18	-2.06	7.29E+01	1.50E+02
ENSMUSG00000006732	Mettl1	1.82E-19	3.27E-18	-3.45	3.71E+01	1.28E+02
ENSMUSG00000018654	Ikzf1	2.17E-19	3.90E-18	3.94	8.30E+02	2.10E+02
ENSMUSG00000023150	Ivns1abp	2.19E-19	3.93E-18	-2.85	1.78E+02	5.06E+02
ENSMUSG00000003617	Cp	2.26E-19	4.04E-18	6.47	8.67E+01	1.34E+01
ENSMUSG00000064090	Vrk2	2.31E-19	4.12E-18	3.55	6.44E+02	1.81E+02
ENSMUSG00000024238	Zeb1	2.44E-19	4.35E-18	4.79	9.76E+01	2.04E+01
ENSMUSG00000021115	Vrk1	2.60E-19	4.62E-18	2.09	4.46E+02	2.13E+02
ENSMUSG00000028800	Hdac1	2.66E-19	4.73E-18	2.29	1.71E+02	7.47E+01
ENSMUSG00000005973	Rcn1	2.87E-19	5.10E-18	2.52	1.34E+02	5.32E+01

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ENSMUSG00000101264	Gm28347	2.98E-19	5.28E-18	61.80	9.45E+00	1.53E-01
ENSMUSG00000044701	Il27	3.04E-19	5.39E-18	38.82	2.10E+02	5.42E+00
ENSMUSG00000048720	Tbc1d12	3.23E-19	5.72E-18	-2.50	3.50E+01	8.76E+01
ENSMUSG00000025626	Phf6	3.44E-19	6.08E-18	2.13	1.68E+02	7.92E+01
ENSMUSG00000036281	Snapc4	3.96E-19	6.97E-18	-2.91	1.61E+01	4.69E+01
ENSMUSG00000024897	Apba1	3.98E-19	7.01E-18	2.30	2.65E+02	1.15E+02
ENSMUSG00000026037	Orc2	3.99E-19	7.02E-18	-2.19	9.01E+01	1.97E+02
ENSMUSG00000056069	Otulinl	4.02E-19	7.07E-18	-2.06	2.36E+02	4.87E+02
ENSMUSG00000030505	Prmt3	4.89E-19	8.56E-18	-3.54	4.32E+01	1.53E+02
ENSMUSG00000032232	Cgnl1	5.32E-19	9.30E-18	-3.27	4.00E+01	1.31E+02
ENSMUSG00000006442	Srm	5.36E-19	9.35E-18	-3.84	5.67E+01	2.17E+02
ENSMUSG00000049553	Polr1a	5.68E-19	9.90E-18	-2.68	5.90E+01	1.58E+02
ENSMUSG00000052296	Ppp6r1	5.99E-19	1.04E-17	2.07	1.45E+03	7.00E+02
ENSMUSG00000046207	Pik3r6	6.12E-19	1.06E-17	2.78	2.94E+02	1.06E+02
ENSMUSG00000021375	Kif13a	6.28E-19	1.09E-17	-2.03	8.26E+01	1.68E+02
ENSMUSG00000020366	Mapk9	6.65E-19	1.15E-17	2.27	4.12E+02	1.82E+02
ENSMUSG00000024037	Wdr4	6.85E-19	1.19E-17	-2.24	3.49E+01	7.83E+01
ENSMUSG00000051306	Usp42	7.14E-19	1.24E-17	2.73	2.18E+02	7.99E+01
ENSMUSG00000026784	Pdss1	7.33E-19	1.27E-17	3.28	5.24E+01	1.60E+01
ENSMUSG00000035834	Polr3g	7.72E-19	1.33E-17	-6.44	1.47E+01	9.48E+01
ENSMUSG00000025525	Apool	7.76E-19	1.34E-17	2.14	1.89E+02	8.81E+01
ENSMUSG00000030530	Furin	8.13E-19	1.40E-17	2.18	2.77E+03	1.27E+03
ENSMUSG00000049939	Lrrc4	8.69E-19	1.49E-17	29.01	2.71E+01	9.33E-01
ENSMUSG00000031242	2610002M06Rik	8.72E-19	1.50E-17	2.00	1.44E+02	7.17E+01
ENSMUSG00000032640	Chsy1	8.95E-19	1.53E-17	-2.65	4.10E+01	1.09E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000076441	Ass1	1.02E-18	1.75E-17	4.33	2.24E+02	5.17E+01
ENSMUSG00000021360	Gcnt2	1.04E-18	1.78E-17	3.30	1.14E+02	3.46E+01
ENSMUSG00000057367	Birc2	1.20E-18	2.04E-17	2.23	2.48E+02	1.11E+02
ENSMUSG00000000811	Txnrd3	1.30E-18	2.20E-17	-2.59	3.64E+01	9.45E+01
ENSMUSG00000028944	Prkag2	1.31E-18	2.22E-17	-4.22	4.74E+01	2.00E+02
ENSMUSG00000032750	Gab3	1.45E-18	2.46E-17	-3.65	5.39E+01	1.97E+02
ENSMUSG00000044700	Tmem201	1.57E-18	2.66E-17	-3.59	8.88E+00	3.19E+01
ENSMUSG00000061731	Ext1	1.59E-18	2.69E-17	2.56	4.39E+02	1.72E+02
ENSMUSG00000031458	Coprs	1.61E-18	2.72E-17	-2.05	1.74E+02	3.56E+02
ENSMUSG00000007987	Ift22	2.09E-18	3.53E-17	2.01	2.45E+02	1.22E+02
ENSMUSG00000079470	Utp14b	2.10E-18	3.53E-17	-3.48	2.37E+01	8.24E+01
ENSMUSG00000026648	Dclre1c	2.15E-18	3.61E-17	2.52	1.36E+02	5.41E+01
ENSMUSG00000068129	Cst7	2.21E-18	3.72E-17	5.34	2.44E+02	4.58E+01
ENSMUSG00000041707	Tmem273	2.30E-18	3.85E-17	-2.15	1.53E+02	3.27E+02
ENSMUSG00000008200	Fnbp4	2.60E-18	4.34E-17	2.57	6.70E+02	2.60E+02
ENSMUSG00000055296	Tmem245	2.68E-18	4.48E-17	-2.36	7.92E+01	1.87E+02
ENSMUSG00000037348	Paqr7	2.75E-18	4.60E-17	-2.48	1.84E+02	4.55E+02
ENSMUSG00000024335	Brd2	2.89E-18	4.82E-17	2.28	5.51E+03	2.42E+03
ENSMUSG00000052681	Rap1b	3.03E-18	5.04E-17	2.12	6.50E+03	3.06E+03
ENSMUSG00000061232	H2-K1	3.12E-18	5.19E-17	2.33	9.01E+03	3.87E+03
ENSMUSG00000034110	Kctd7	3.20E-18	5.31E-17	-3.18	1.09E+01	3.47E+01
ENSMUSG00000022641	Bbx	3.30E-18	5.48E-17	2.17	1.88E+03	8.67E+02
ENSMUSG00000055401	Fbxo6	3.54E-18	5.86E-17	2.06	4.73E+02	2.29E+02
ENSMUSG00000032855	Pkd1	3.76E-18	6.22E-17	-2.50	9.87E+01	2.47E+02
ENSMUSG00000024451	Arap3	3.97E-18	6.56E-17	-2.80	4.03E+01	1.13E+02

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ENSMUSG00000052631	Sh2d6	4.26E-18	7.03E-17	8.68	1.99E+01	2.29E+00
ENSMUSG00000030156	Cd69	4.37E-18	7.20E-17	41.29	3.78E+03	9.15E+01
ENSMUSG00000061536	Sec22c	4.37E-18	7.20E-17	-2.51	3.56E+01	8.96E+01
ENSMUSG00000040329	Il7	4.50E-18	7.40E-17	6.56	1.78E+01	2.71E+00
ENSMUSG00000026068	Il18rap	4.91E-18	8.07E-17	7.69	8.00E+01	1.04E+01
ENSMUSG00000040229	Gpr34	5.29E-18	8.67E-17	-3.95	1.67E+01	6.60E+01
ENSMUSG00000116927	Gm30881	5.48E-18	8.97E-17	6.21	2.04E+01	3.29E+00
ENSMUSG00000074211	Sdhaf1	5.75E-18	9.40E-17	-2.60	3.41E+01	8.85E+01
ENSMUSG00000001741	Il16	6.51E-18	1.06E-16	-3.55	2.53E+01	8.98E+01
ENSMUSG00000048897	Zfp710	6.56E-18	1.07E-16	2.05	5.06E+02	2.47E+02
ENSMUSG00000029204	Rhoh	6.60E-18	1.08E-16	5.18	2.71E+02	5.24E+01
ENSMUSG00000004814	Ccl24	6.77E-18	1.10E-16	10.32	2.30E+01	2.23E+00
ENSMUSG00000023088	Abcc1	7.17E-18	1.17E-16	-2.39	1.88E+02	4.50E+02
ENSMUSG00000066152	Slc31a2	7.23E-18	1.18E-16	2.90	1.14E+03	3.91E+02
ENSMUSG00000032175	Tyk2	7.45E-18	1.21E-16	3.25	9.49E+02	2.92E+02
ENSMUSG00000033282	Rpgrip1l	8.03E-18	1.30E-16	2.90	7.41E+01	2.55E+01
ENSMUSG00000050370	Ch25h	8.08E-18	1.31E-16	32.65	7.76E+01	2.38E+00
ENSMUSG00000031617	Tmem184c	8.92E-18	1.45E-16	-2.25	1.20E+02	2.71E+02
ENSMUSG00000002257	Def6	9.67E-18	1.56E-16	-2.22	1.04E+02	2.32E+02
ENSMUSG00000028773	Fabp3	1.02E-17	1.65E-16	5.37	6.88E+02	1.28E+02
ENSMUSG00000037461	Ints7	1.10E-17	1.77E-16	-2.19	9.27E+01	2.03E+02
ENSMUSG00000020091	Eif4ebp2	1.13E-17	1.82E-16	-2.47	1.85E+02	4.57E+02
ENSMUSG00000027827	Kcnab1	1.33E-17	2.13E-16	10.30	2.22E+01	2.16E+00
ENSMUSG00000024242	Map4k3	1.49E-17	2.38E-16	2.63	5.31E+02	2.02E+02
ENSMUSG00000111133	Gm5831	1.53E-17	2.44E-16	26.87	1.11E+01	4.15E-01

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ENSMUSG00000031826	Usp10	1.62E-17	2.58E-16	-3.42	2.65E+01	9.06E+01
ENSMUSG00000023903	Mmp25	1.67E-17	2.66E-16	27.27	4.51E+01	1.65E+00
ENSMUSG00000085741	5430405H02Rik	1.95E-17	3.09E-16	3.24	7.27E+01	2.24E+01
ENSMUSG00000035354	Uvrag	2.09E-17	3.31E-16	2.17	6.55E+02	3.01E+02
ENSMUSG00000028367	Txn1	2.24E-17	3.54E-16	2.06	6.71E+03	3.26E+03
ENSMUSG00000039842	Mcph1	2.26E-17	3.57E-16	-2.65	3.39E+01	8.97E+01
ENSMUSG00000034156	Tspoap1	2.29E-17	3.62E-16	4.09	1.51E+02	3.69E+01
ENSMUSG00000020057	Dram1	2.36E-17	3.73E-16	3.87	3.63E+02	9.37E+01
ENSMUSG00000015176	Nolc1	2.51E-17	3.96E-16	-2.89	1.10E+02	3.17E+02
ENSMUSG00000079197	Psme2	2.67E-17	4.21E-16	3.90	1.44E+02	3.68E+01
ENSMUSG00000031904	Slc7a6	2.68E-17	4.23E-16	-2.68	1.96E+01	5.26E+01
ENSMUSG00000042595	Fam199x	2.75E-17	4.33E-16	-2.17	5.30E+01	1.15E+02
ENSMUSG00000090110	Cmc4	2.78E-17	4.36E-16	2.27	1.09E+02	4.82E+01
ENSMUSG00000095609	Gm21188	2.79E-17	4.38E-16	4.64	4.35E+01	9.39E+00
ENSMUSG00000040570	Rundc3b	2.82E-17	4.43E-16	3.70	4.69E+01	1.27E+01
ENSMUSG00000042632	Pla2g6	2.99E-17	4.68E-16	-2.81	1.65E+01	4.63E+01
ENSMUSG00000030560	Ctsc	3.00E-17	4.70E-16	3.88	3.32E+03	8.55E+02
ENSMUSG00000022364	Tbc1d31	3.83E-17	5.96E-16	-3.20	1.74E+01	5.55E+01
ENSMUSG00000024660	Incenp	4.83E-17	7.48E-16	-2.07	2.99E+02	6.19E+02
ENSMUSG00000070883	Ccdc173	5.05E-17	7.80E-16	5.01	1.24E+02	2.47E+01
ENSMUSG00000040428	Plekha4	5.12E-17	7.91E-16	7.01	3.03E+01	4.32E+00
ENSMUSG00000116946	Gm41442	5.23E-17	8.06E-16	8.16	2.52E+01	3.09E+00
ENSMUSG00000106847	Peg13	5.54E-17	8.54E-16	-3.11	2.01E+01	6.25E+01
ENSMUSG00000043140	Tmem186	6.53E-17	1.00E-15	-3.33	1.16E+01	3.88E+01
ENSMUSG00000026694	Eef1aknmt	6.67E-17	1.02E-15	-4.51	1.48E+01	6.68E+01

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ENSMUSG00000018821	Avpi1	7.14E-17	1.09E-15	-2.50	3.10E+01	7.75E+01
ENSMUSG00000022744	Cldnd1	7.43E-17	1.14E-15	2.49	5.23E+02	2.10E+02
ENSMUSG00000032802	Srxn1	7.72E-17	1.18E-15	-2.49	9.32E+02	2.32E+03
ENSMUSG00000041057	Wdr43	7.85E-17	1.20E-15	2.17	1.25E+03	5.77E+02
ENSMUSG00000022856	Tmem41a	8.09E-17	1.23E-15	-2.65	2.52E+01	6.67E+01
ENSMUSG00000106990	Gm42547	8.44E-17	1.28E-15	6.87	1.50E+02	2.18E+01
ENSMUSG00000030269	Mtmr14	8.60E-17	1.31E-15	2.78	1.29E+03	4.65E+02
ENSMUSG00000079427	Mthfsl	9.40E-17	1.43E-15	2.19	3.13E+02	1.43E+02
ENSMUSG00000057335	Cep170	1.04E-16	1.57E-15	2.22	3.03E+02	1.37E+02
ENSMUSG00000034926	Dhcr24	1.05E-16	1.59E-15	-2.54	1.06E+02	2.68E+02
ENSMUSG00000021583	Erap1	1.10E-16	1.67E-15	2.19	3.73E+02	1.71E+02
ENSMUSG00000022822	Abcc5	1.19E-16	1.80E-15	2.52	6.49E+02	2.58E+02
ENSMUSG00000058392	Rrp1b	1.22E-16	1.84E-15	-3.43	3.92E+01	1.35E+02
ENSMUSG00000002602	Axl	1.23E-16	1.86E-15	3.94	1.32E+03	3.36E+02
ENSMUSG00000063694	Cycs	1.27E-16	1.91E-15	2.98	2.62E+02	8.82E+01
ENSMUSG00000016181	Utp25	1.30E-16	1.96E-15	-2.93	2.99E+01	8.78E+01
ENSMUSG00000024539	Ptpn2	1.31E-16	1.96E-15	2.16	3.09E+02	1.43E+02
ENSMUSG00000032766	Gng11	1.35E-16	2.03E-15	2.30	2.51E+02	1.09E+02
ENSMUSG00000021286	Zfyve21	1.39E-16	2.08E-15	-2.76	2.42E+01	6.67E+01
ENSMUSG00000034522	Zfp395	1.40E-16	2.09E-15	-5.34	7.82E+00	4.17E+01
ENSMUSG00000021474	Sfxn1	1.41E-16	2.12E-15	-2.27	3.14E+02	7.13E+02
ENSMUSG00000024974	Smc3	1.54E-16	2.31E-15	-2.16	2.76E+02	5.97E+02
ENSMUSG00000027068	Dhrs9	1.56E-16	2.33E-15	2.85	5.94E+02	2.09E+02
ENSMUSG00000100975	Gm28875	1.60E-16	2.38E-15	-2.16	9.78E+01	2.12E+02
ENSMUSG00000024754	Cemip2	1.68E-16	2.49E-15	3.64	7.45E+02	2.05E+02

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ENSMUSG00000036275	9530068E07Rik	1.79E-16	2.64E-15	2.24	1.26E+03	5.63E+02
ENSMUSG00000030201	Lrp6	1.92E-16	2.84E-15	-2.26	1.29E+02	2.90E+02
ENSMUSG00000034617	Mtrr	1.95E-16	2.88E-15	-2.81	1.76E+01	4.93E+01
ENSMUSG00000023953	Polh	2.04E-16	3.00E-15	-2.36	3.13E+01	7.41E+01
ENSMUSG00000112843	Gm46224	2.31E-16	3.41E-15	2.20	1.02E+02	4.62E+01
ENSMUSG00000022070	Bora	2.37E-16	3.48E-15	-4.78	7.46E+00	3.57E+01
ENSMUSG00000020910	Adprm	2.38E-16	3.49E-15	2.34	1.18E+02	5.04E+01
ENSMUSG00000024697	Gna14	2.68E-16	3.93E-15	33.91	1.10E+01	3.24E-01
ENSMUSG00000038658	Ric1	2.69E-16	3.94E-15	2.21	3.52E+02	1.60E+02
ENSMUSG00000045763	Basp1	2.78E-16	4.06E-15	2.55	1.73E+04	6.80E+03
ENSMUSG00000039682	Lap3	3.02E-16	4.41E-15	2.55	3.82E+02	1.50E+02
ENSMUSG00000021262	Evl	3.05E-16	4.44E-15	3.05	1.01E+03	3.33E+02
ENSMUSG00000045934	Mtmr11	3.35E-16	4.87E-15	3.41	6.49E+01	1.90E+01
ENSMUSG00000031337	Mtm1	3.42E-16	4.97E-15	2.00	1.82E+02	9.08E+01
ENSMUSG00000053801	Grwd1	3.49E-16	5.06E-15	-3.91	2.32E+01	9.06E+01
ENSMUSG00000039089	L3mbtl3	3.66E-16	5.31E-15	2.24	1.94E+02	8.63E+01
ENSMUSG00000097526	nan	3.80E-16	5.50E-15	5.88	1.94E+01	3.30E+00
ENSMUSG00000029186	Pi4k2b	3.91E-16	5.64E-15	2.02	1.80E+02	8.88E+01
ENSMUSG00000054976	Nyap2	4.04E-16	5.83E-15	7.39	3.88E+01	5.25E+00
ENSMUSG00000032375	Aph1b	4.12E-16	5.94E-15	-2.18	6.01E+01	1.31E+02
ENSMUSG00000039841	Zfp800	4.90E-16	7.03E-15	3.87	1.60E+03	4.15E+02
ENSMUSG00000032712	Resf1	5.10E-16	7.31E-15	2.78	3.48E+03	1.25E+03
ENSMUSG00000031785	Adgrg1	5.16E-16	7.39E-15	-3.56	1.53E+01	5.42E+01
ENSMUSG00000049090	Zadh2	6.00E-16	8.58E-15	-2.08	7.72E+01	1.61E+02
ENSMUSG00000026580	Selp	6.30E-16	8.97E-15	22.98	1.33E+01	5.78E-01

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ENSMUSG00000005362	Crbn	6.36E-16	9.06E-15	2.27	2.35E+02	1.03E+02
ENSMUSG00000043939	A530064D06Rik	6.70E-16	9.52E-15	5.32	1.38E+02	2.59E+01
ENSMUSG00000046169	Adamts6	6.81E-16	9.66E-15	6.86	2.59E+01	3.78E+00
ENSMUSG00000116961	Gm49662	6.87E-16	9.74E-15	29.54	1.23E+01	4.17E-01
ENSMUSG00000025036	Sfxn2	7.33E-16	1.04E-14	2.29	1.45E+02	6.34E+01
ENSMUSG00000001948	Spa17	7.40E-16	1.05E-14	2.00	9.20E+01	4.60E+01
ENSMUSG00000047153	Khnyn	7.95E-16	1.12E-14	2.19	1.33E+02	6.09E+01
ENSMUSG00000037318	Traf3ip3	7.97E-16	1.12E-14	-2.67	2.83E+01	7.56E+01
ENSMUSG00000038023	Atp6v0a2	8.17E-16	1.15E-14	2.13	4.22E+02	1.98E+02
ENSMUSG00000020156	Pwwp3a	8.31E-16	1.17E-14	-2.14	5.53E+01	1.18E+02
ENSMUSG00000086389	Gm15998	8.41E-16	1.18E-14	56.57	8.65E+00	1.53E-01
ENSMUSG00000020611	Gna13	8.71E-16	1.22E-14	2.15	5.42E+03	2.53E+03
ENSMUSG00000090812	Samd15	9.29E-16	1.30E-14	3.98	2.35E+01	5.89E+00
ENSMUSG00000025995	Wdr75	1.02E-15	1.42E-14	-3.03	3.80E+01	1.15E+02
ENSMUSG00000051339	2900026A02Rik	1.04E-15	1.45E-14	-2.67	3.53E+01	9.40E+01
ENSMUSG00000022020	Naa16	1.11E-15	1.55E-14	-2.02	6.83E+01	1.38E+02
ENSMUSG00000079491	H2-T10	1.13E-15	1.57E-14	4.56	2.59E+01	5.68E+00
ENSMUSG00000021079	Timm9	1.23E-15	1.71E-14	-2.53	4.25E+01	1.07E+02
ENSMUSG00000116564	Riok2	1.29E-15	1.79E-14	-2.36	4.00E+01	9.45E+01
ENSMUSG00000038188	Scarf1	1.31E-15	1.82E-14	3.35	1.16E+02	3.46E+01
ENSMUSG00000079144	A130010J15Rik	1.35E-15	1.87E-14	-4.07	8.57E+00	3.49E+01
ENSMUSG00000027253	Lrp4	1.45E-15	2.02E-14	3.55	4.41E+01	1.24E+01
ENSMUSG00000021880	Rnase6	1.60E-15	2.21E-14	3.75	1.11E+02	2.95E+01
ENSMUSG00000057914	Cacnb2	1.63E-15	2.26E-14	12.75	1.27E+01	9.94E-01
ENSMUSG00000041025	Iffo2	1.64E-15	2.26E-14	2.09	1.45E+02	6.95E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000050212	Eva1b	1.96E-15	2.71E-14	2.73	2.81E+02	1.03E+02
ENSMUSG00000020115	Tbk1	2.00E-15	2.75E-14	2.05	6.15E+02	3.00E+02
ENSMUSG00000026864	Hspa5	2.17E-15	2.98E-14	2.02	1.38E+04	6.81E+03
ENSMUSG00000042225	Ammecr1	2.37E-15	3.25E-14	2.05	3.19E+02	1.55E+02
ENSMUSG00000033706	Smyd5	2.45E-15	3.36E-14	-3.17	1.75E+01	5.54E+01
ENSMUSG00000057497	Fam136a	2.54E-15	3.46E-14	-2.21	2.92E+01	6.46E+01
ENSMUSG00000004100	Ppan	2.58E-15	3.52E-14	-3.90	1.26E+01	4.90E+01
ENSMUSG00000010663	Fads1	2.69E-15	3.67E-14	-2.03	1.97E+02	4.00E+02
ENSMUSG00000060261	Gtf2i	3.00E-15	4.08E-14	-2.23	1.44E+02	3.21E+02
ENSMUSG00000026021	Sumo1	3.18E-15	4.31E-14	2.03	2.52E+02	1.24E+02
ENSMUSG00000032119	Hinfp	3.21E-15	4.35E-14	2.56	1.37E+02	5.37E+01
ENSMUSG00000050628	Ubald2	3.46E-15	4.69E-14	2.01	2.84E+02	1.41E+02
ENSMUSG00000036099	Vezt	3.51E-15	4.75E-14	2.07	1.82E+02	8.80E+01
ENSMUSG00000053799	Exoc6	3.65E-15	4.93E-14	2.17	1.25E+02	5.74E+01
ENSMUSG00000026313	Hdac4	4.09E-15	5.52E-14	-2.01	9.49E+01	1.91E+02
ENSMUSG00000034297	Med13	4.30E-15	5.80E-14	2.17	9.11E+02	4.20E+02
ENSMUSG00000027663	Zmat3	4.79E-15	6.44E-14	-2.05	2.30E+02	4.72E+02
ENSMUSG00000026377	Nifk	4.79E-15	6.44E-14	-2.30	1.59E+02	3.67E+02
ENSMUSG00000021772	Nkiras1	4.92E-15	6.62E-14	2.45	7.57E+01	3.10E+01
ENSMUSG00000036693	Nop14	5.12E-15	6.88E-14	-2.12	1.58E+02	3.35E+02
ENSMUSG00000061186	Sfmbt2	5.23E-15	7.01E-14	3.85	3.17E+01	8.23E+00
ENSMUSG00000059970	Hspa2	5.25E-15	7.03E-14	2.57	8.70E+01	3.38E+01
ENSMUSG00000021569	Trip13	5.69E-15	7.62E-14	-2.38	3.28E+01	7.83E+01
ENSMUSG00000000776	Polr3d	5.81E-15	7.78E-14	-2.17	8.54E+01	1.85E+02
ENSMUSG00000032301	Psma4	5.85E-15	7.81E-14	2.13	1.44E+03	6.74E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000079523	Tmsb10	6.00E-15	8.01E-14	2.43	4.72E+02	1.94E+02
ENSMUSG00000043872	Zmym1	6.22E-15	8.29E-14	-3.02	1.92E+01	5.79E+01
ENSMUSG00000052384	Nrros	6.36E-15	8.47E-14	2.12	3.76E+03	1.77E+03
ENSMUSG00000006517	Mvd	6.42E-15	8.53E-14	-2.72	1.22E+02	3.31E+02
ENSMUSG00000020573	Pik3cg	6.42E-15	8.53E-14	-3.25	5.67E+01	1.84E+02
ENSMUSG00000020781	Tsen54	6.59E-15	8.74E-14	-2.74	1.48E+01	4.06E+01
ENSMUSG00000022962	Gart	7.29E-15	9.66E-14	-2.16	1.69E+02	3.64E+02
ENSMUSG00000061436	Hipk2	7.31E-15	9.68E-14	2.03	5.34E+02	2.63E+02
ENSMUSG00000057054	Inca1	8.09E-15	1.07E-13	5.15	3.16E+01	6.14E+00
ENSMUSG00000025997	Ikzf2	8.12E-15	1.07E-13	4.07	1.23E+02	3.02E+01
ENSMUSG00000042842	Serpinb6b	8.55E-15	1.13E-13	4.44	8.70E+02	1.96E+02
ENSMUSG00000029676	Pot1a	8.67E-15	1.14E-13	-2.25	2.26E+01	5.10E+01
ENSMUSG00000033671	Cep350	8.80E-15	1.16E-13	2.07	6.36E+02	3.08E+02
ENSMUSG00000044018	Mrpl50	9.04E-15	1.19E-13	-2.24	5.17E+01	1.16E+02
ENSMUSG00000020647	Ncoa1	9.39E-15	1.24E-13	2.84	5.43E+02	1.91E+02
ENSMUSG00000038126	Mphosph9	9.63E-15	1.27E-13	-3.59	8.71E+00	3.13E+01
ENSMUSG00000044447	Dock5	9.80E-15	1.29E-13	-2.80	3.58E+01	1.00E+02
ENSMUSG00000046688	Tifa	9.91E-15	1.30E-13	2.43	1.04E+03	4.26E+02
ENSMUSG00000060950	Trmt61a	1.16E-14	1.51E-13	-3.16	1.71E+01	5.42E+01
ENSMUSG00000021423	Ly86	1.19E-14	1.55E-13	5.27	1.35E+02	2.56E+01
ENSMUSG00000024142	Mlst8	1.25E-14	1.63E-13	-2.25	4.07E+01	9.15E+01
ENSMUSG00000027030	Stk39	1.39E-14	1.80E-13	4.37	3.36E+01	7.68E+00
ENSMUSG00000028863	Meaf6	1.46E-14	1.89E-13	-2.10	5.26E+01	1.11E+02
ENSMUSG00000044948	Cfap43	1.58E-14	2.04E-13	3.18	1.54E+02	4.83E+01
ENSMUSG00000022938	Fam3b	1.69E-14	2.18E-13	22.00	1.49E+01	6.79E-01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000090101	Snhg9	1.70E-14	2.19E-13	-2.08	1.41E+02	2.94E+02
ENSMUSG00000032834	Pwp2	1.78E-14	2.29E-13	-2.45	2.80E+01	6.88E+01
ENSMUSG00000035279	Ssc5d	1.87E-14	2.40E-13	5.50	2.78E+01	5.06E+00
ENSMUSG00000030088	Aldh1l1	1.93E-14	2.47E-13	2.66	8.74E+01	3.29E+01
ENSMUSG00000020393	Kremen1	2.00E-14	2.55E-13	2.00	1.65E+02	8.26E+01
ENSMUSG00000018537	Pcgf2	2.03E-14	2.59E-13	-2.21	2.61E+01	5.76E+01
ENSMUSG00000028683	Eif2b3	2.15E-14	2.75E-13	-2.68	2.22E+01	5.94E+01
ENSMUSG00000057469	E2f6	2.24E-14	2.85E-13	-2.84	3.20E+01	9.10E+01
ENSMUSG00000052085	Dock8	2.32E-14	2.95E-13	2.43	7.28E+02	2.99E+02
ENSMUSG00000027387	Zc3h8	2.36E-14	3.00E-13	-4.81	5.07E+00	2.44E+01
ENSMUSG00000031668	Eif2ak3	2.36E-14	3.00E-13	-2.54	3.61E+01	9.16E+01
ENSMUSG00000030094	Xpc	2.42E-14	3.07E-13	-2.53	4.89E+01	1.24E+02
ENSMUSG00000020802	Ube2o	2.72E-14	3.44E-13	-2.20	3.39E+01	7.47E+01
ENSMUSG00000038332	Sesn1	2.79E-14	3.53E-13	-5.69	7.95E+01	4.52E+02
ENSMUSG00000009621	Vav2	3.08E-14	3.89E-13	-2.29	5.65E+01	1.29E+02
ENSMUSG00000045287	Rtn4rl1	3.18E-14	4.01E-13	-4.50	8.45E+00	3.80E+01
ENSMUSG00000041037	Irgq	3.21E-14	4.04E-13	-2.26	9.05E+01	2.05E+02
ENSMUSG00000025010	Ccnj	3.22E-14	4.06E-13	5.13	2.92E+01	5.69E+00
ENSMUSG00000058624	Gda	3.29E-14	4.14E-13	2.47	4.78E+02	1.94E+02
ENSMUSG00000109715	Gm45606	3.35E-14	4.21E-13	-3.16	9.41E+00	2.98E+01
ENSMUSG00000032841	Prr5l	3.41E-14	4.28E-13	3.39	7.48E+02	2.21E+02
ENSMUSG00000027469	Tpx2	3.43E-14	4.30E-13	2.47	9.41E+02	3.82E+02
ENSMUSG00000030872	Gga2	3.50E-14	4.38E-13	-2.12	2.09E+02	4.43E+02
ENSMUSG00000086527	Gm15856	3.79E-14	4.72E-13	18.80	1.58E+01	8.41E-01
ENSMUSG00000038506	Dcun1d2	3.82E-14	4.75E-13	-2.05	2.85E+01	5.85E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000039813	Tbc1d2	4.53E-14	5.60E-13	-2.47	5.37E+01	1.33E+02
ENSMUSG00000021952	Xpo4	4.62E-14	5.71E-13	-2.00	4.87E+01	9.75E+01
ENSMUSG00000051498	Tlr6	5.00E-14	6.16E-13	2.37	1.76E+02	7.41E+01
ENSMUSG00000048170	Mcmbp	5.36E-14	6.59E-13	2.09	6.45E+02	3.09E+02
ENSMUSG00000015846	Rxra	5.59E-14	6.87E-13	-2.57	9.90E+01	2.54E+02
ENSMUSG00000027333	Smox	5.68E-14	6.97E-13	2.60	3.82E+02	1.47E+02
ENSMUSG00000061313	Ddhd2	5.69E-14	6.98E-13	-2.01	1.22E+02	2.45E+02
ENSMUSG00000021929	Kpna3	5.76E-14	7.06E-13	2.91	2.03E+03	6.99E+02
ENSMUSG00000111857	1190001M18Rik	6.15E-14	7.53E-13	6.26	2.16E+01	3.46E+00
ENSMUSG00000002728	Naa20	6.50E-14	7.94E-13	2.15	2.39E+02	1.11E+02
ENSMUSG00000058355	Abce1	6.68E-14	8.15E-13	-2.09	1.06E+02	2.22E+02
ENSMUSG00000036810	Cnep1r1	7.66E-14	9.34E-13	2.07	3.51E+02	1.69E+02
ENSMUSG00000028159	Dapp1	7.70E-14	9.38E-13	2.03	2.05E+02	1.01E+02
ENSMUSG00000093726	Gm20667	7.81E-14	9.50E-13	-9.47	1.49E+00	1.41E+01
ENSMUSG00000045045	Lrfn4	8.17E-14	9.92E-13	-4.64	4.50E+00	2.09E+01
ENSMUSG00000027018	Hat1	8.52E-14	1.03E-12	2.78	5.91E+02	2.13E+02
ENSMUSG00000030729	Pgm2l1	8.56E-14	1.04E-12	-2.06	1.65E+02	3.41E+02
ENSMUSG00000037151	Lrrc20	8.94E-14	1.08E-12	-2.63	4.41E+01	1.16E+02
ENSMUSG00000078956	Gm14221	9.00E-14	1.09E-12	-3.11	1.48E+01	4.61E+01
ENSMUSG00000026192	Atic	9.04E-14	1.09E-12	-2.03	1.51E+02	3.07E+02
ENSMUSG00000043257	Pigv	9.72E-14	1.17E-12	2.21	9.53E+01	4.30E+01
ENSMUSG00000031896	Ctrl	9.99E-14	1.20E-12	12.14	1.20E+01	9.86E-01
ENSMUSG00000090231	Cfb	1.05E-13	1.27E-12	66.71	1.16E+01	1.73E-01
ENSMUSG00000036912	Piwil4	1.06E-13	1.28E-12	11.85	1.46E+01	1.23E+00
ENSMUSG00000029174	Tbc1d1	1.14E-13	1.37E-12	2.04	4.51E+02	2.21E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000010554	Mettl16	1.17E-13	1.40E-12	-2.03	9.76E+01	1.98E+02
ENSMUSG00000041220	Elovl6	1.24E-13	1.48E-12	-4.27	1.24E+01	5.29E+01
ENSMUSG00000033576	Apol6	1.28E-13	1.54E-12	28.33	9.18E+00	3.24E-01
ENSMUSG00000072620	Slfn2	1.31E-13	1.56E-12	3.92	1.14E+04	2.92E+03
ENSMUSG00000054580	Pla2r1	1.32E-13	1.58E-12	4.69	2.42E+01	5.16E+00
ENSMUSG00000024691	Fam111a	1.33E-13	1.59E-12	2.22	2.55E+03	1.15E+03
ENSMUSG00000053957	Gm12474	1.35E-13	1.61E-12	8.10	1.05E+01	1.30E+00
ENSMUSG00000028028	Alpk1	1.48E-13	1.76E-12	2.49	9.18E+01	3.68E+01
ENSMUSG00000020706	Ftsj3	1.56E-13	1.85E-12	-2.01	2.00E+02	4.03E+02
ENSMUSG00000036995	Asap3	1.68E-13	2.00E-12	11.83	2.14E+01	1.81E+00
ENSMUSG00000090319	Gm4462	1.73E-13	2.05E-12	30.34	6.75E+00	2.23E-01
ENSMUSG00000042606	Hirip3	1.87E-13	2.21E-12	-3.64	2.35E+01	8.58E+01
ENSMUSG00000045411	2410002F23Rik	1.91E-13	2.26E-12	-2.97	1.51E+01	4.49E+01
ENSMUSG00000025869	Nop16	1.93E-13	2.28E-12	-2.96	5.68E+01	1.68E+02
ENSMUSG00000025203	Scd2	2.15E-13	2.53E-12	-3.80	4.37E+01	1.66E+02
ENSMUSG00000090176	Cd200r2	2.21E-13	2.60E-12	12.46	2.14E+01	1.72E+00
ENSMUSG00000033166	Dis3	2.37E-13	2.78E-12	-2.23	5.40E+01	1.21E+02
ENSMUSG00000020826	Nos2	2.37E-13	2.78E-12	63.07	7.60E+01	1.21E+00
ENSMUSG00000071713	Csf2rb	2.42E-13	2.84E-12	2.16	4.45E+03	2.07E+03
ENSMUSG00000000682	Cd52	2.43E-13	2.84E-12	2.10	5.11E+03	2.44E+03
ENSMUSG00000021514	Zfp369	2.51E-13	2.93E-12	-2.31	3.54E+01	8.16E+01
ENSMUSG00000029992	Gfpt1	2.64E-13	3.07E-12	2.21	7.50E+02	3.40E+02
ENSMUSG00000055493	Epm2a	2.97E-13	3.45E-12	-4.45	6.50E+00	2.89E+01
ENSMUSG00000090523	Gypc	3.00E-13	3.48E-12	2.44	7.48E+01	3.06E+01
ENSMUSG00000009905	Kdsr	3.21E-13	3.72E-12	-2.35	8.12E+01	1.91E+02

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ENSMUSG00000014773	Dll1	3.26E-13	3.78E-12	39.53	8.80E+00	2.23E-01
ENSMUSG00000005374	Tbl2	3.28E-13	3.80E-12	-3.04	1.90E+01	5.78E+01
ENSMUSG00000031304	Il2rg	3.33E-13	3.86E-12	2.60	1.73E+03	6.67E+02
ENSMUSG00000019979	Apaf1	3.33E-13	3.86E-12	2.27	3.31E+02	1.46E+02
ENSMUSG00000022747	St3gal6	3.37E-13	3.90E-12	3.99	2.61E+01	6.53E+00
ENSMUSG00000064340	mt-Tl1	3.39E-13	3.92E-12	3.09	1.97E+02	6.38E+01
ENSMUSG00000022793	B4galt4	3.52E-13	4.07E-12	2.40	7.65E+01	3.19E+01
ENSMUSG00000090881	Phf11	3.56E-13	4.11E-12	32.88	5.03E+00	1.53E-01
ENSMUSG00000063179	Pstk	3.70E-13	4.27E-12	-3.03	1.34E+01	4.06E+01
ENSMUSG00000070348	Ccnd1	3.71E-13	4.27E-12	3.69	1.37E+04	3.73E+03
ENSMUSG00000027322	Siglec1	3.83E-13	4.40E-12	3.10	6.72E+01	2.17E+01
ENSMUSG00000023940	Sgo1	3.96E-13	4.54E-12	-3.32	2.32E+01	7.70E+01
ENSMUSG00000024170	Telo2	3.98E-13	4.56E-12	-2.26	2.17E+01	4.90E+01
ENSMUSG00000112892	Gm8613	4.02E-13	4.61E-12	45.77	7.00E+00	1.53E-01
ENSMUSG00000029521	Chek2	4.06E-13	4.65E-12	-2.98	5.96E+01	1.78E+02
ENSMUSG00000035064	Eef2k	4.15E-13	4.74E-12	-4.23	2.74E+01	1.16E+02
ENSMUSG00000039934	Gsap	4.15E-13	4.74E-12	2.58	1.77E+02	6.87E+01
ENSMUSG00000068735	Trp53i11	4.20E-13	4.79E-12	16.16	2.01E+01	1.24E+00
ENSMUSG00000035547	Capn5	4.23E-13	4.82E-12	2.67	2.69E+02	1.01E+02
ENSMUSG00000028948	Nol9	4.23E-13	4.82E-12	-2.02	4.53E+01	9.14E+01
ENSMUSG00000021418	Rpp40	4.38E-13	4.99E-12	-4.04	8.11E+00	3.28E+01
ENSMUSG00000022052	Ppp2r2a	4.50E-13	5.11E-12	2.08	1.98E+03	9.53E+02
ENSMUSG00000007570	Fance	4.50E-13	5.11E-12	-2.29	4.99E+01	1.14E+02
ENSMUSG00000029033	Acap3	4.58E-13	5.20E-12	-2.13	4.11E+01	8.73E+01
ENSMUSG00000107761	2010008C14Rik	4.66E-13	5.29E-12	-3.99	1.30E+01	5.17E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000014164	Klhl3	4.81E-13	5.45E-12	-10.86	1.58E+00	1.71E+01
ENSMUSG00000058290	Espl1	4.88E-13	5.52E-12	-2.97	1.79E+01	5.31E+01
ENSMUSG00000033705	Stard9	4.89E-13	5.53E-12	-2.56	6.79E+01	1.74E+02
ENSMUSG00000028859	Csf3r	5.31E-13	6.00E-12	2.67	1.55E+02	5.82E+01
ENSMUSG00000040018	Cox15	5.56E-13	6.28E-12	2.26	2.80E+02	1.24E+02
ENSMUSG00000002017	Fam98a	5.57E-13	6.28E-12	-2.38	1.57E+01	3.73E+01
ENSMUSG00000021918	Nek4	6.43E-13	7.23E-12	-2.10	3.27E+01	6.86E+01
ENSMUSG00000037344	Slc12a9	7.10E-13	7.97E-12	2.06	3.55E+02	1.72E+02
ENSMUSG00000004266	Ptpn6	7.24E-13	8.12E-12	2.41	2.17E+03	9.01E+02
ENSMUSG00000016559	H3f3b	7.65E-13	8.56E-12	2.66	8.54E+03	3.21E+03
ENSMUSG00000039633	Lonrf1	8.07E-13	9.03E-12	-2.89	4.22E+01	1.22E+02
ENSMUSG00000035125	Gcfc2	8.39E-13	9.37E-12	-2.04	3.18E+01	6.50E+01
ENSMUSG00000031788	Kifc3	8.66E-13	9.64E-12	-2.25	5.01E+01	1.13E+02
ENSMUSG00000002997	Prkar2b	8.91E-13	9.91E-12	-2.54	1.31E+02	3.34E+02
ENSMUSG00000038335	Tsr1	9.30E-13	1.03E-11	-2.91	3.90E+01	1.13E+02
ENSMUSG00000078185	Chml	9.81E-13	1.09E-11	-2.45	1.68E+01	4.13E+01
ENSMUSG00000021451	Sema4d	1.03E-12	1.14E-11	2.59	2.23E+03	8.62E+02
ENSMUSG00000022504	Ciita	1.08E-12	1.19E-11	4.10	7.64E+01	1.86E+01
ENSMUSG00000025058	Tasl	1.11E-12	1.22E-11	3.48	3.33E+02	9.57E+01
ENSMUSG00000025195	Dnmbp	1.11E-12	1.22E-11	-3.02	1.94E+01	5.85E+01
ENSMUSG00000052566	Hook2	1.19E-12	1.30E-11	2.25	1.32E+02	5.85E+01
ENSMUSG00000070354	Evi2	1.20E-12	1.31E-11	2.12	5.76E+02	2.72E+02
ENSMUSG00000022554	Hgh1	1.22E-12	1.34E-11	-2.73	9.02E+00	2.47E+01
ENSMUSG00000051098	Mblac2	1.23E-12	1.35E-11	-2.69	2.31E+01	6.21E+01
ENSMUSG00000059325	Hopx	1.33E-12	1.46E-11	3.42	2.48E+01	7.25E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000017561	Crlf3	1.35E-12	1.47E-11	2.05	5.48E+02	2.68E+02
ENSMUSG00000084846	A730011C13Rik	1.39E-12	1.52E-11	7.85	1.22E+01	1.55E+00
ENSMUSG00000102243	Gm37718	1.39E-12	1.52E-11	3.98	4.22E+01	1.06E+01
ENSMUSG00000046591	Ticrr	1.39E-12	1.52E-11	-4.07	6.32E+00	2.57E+01
ENSMUSG00000064338	mt-Tv	1.40E-12	1.53E-11	3.05	3.41E+02	1.12E+02
ENSMUSG00000023905	Tnfrsf12a	1.45E-12	1.57E-11	2.44	1.90E+02	7.81E+01
ENSMUSG00000036353	P2ry12	1.45E-12	1.58E-11	3.35	3.20E+01	9.54E+00
ENSMUSG00000031292	Cdkl5	1.49E-12	1.62E-11	5.42	1.89E+01	3.49E+00
ENSMUSG00000033102	Cdc14b	1.63E-12	1.77E-11	-2.08	4.32E+01	8.96E+01
ENSMUSG00000020255	D10Wsu102e	1.66E-12	1.80E-11	-2.02	1.31E+02	2.66E+02
ENSMUSG00000032066	Bco2	1.71E-12	1.86E-11	5.57	2.49E+01	4.47E+00
ENSMUSG00000002814	Top3a	1.74E-12	1.88E-11	2.24	8.36E+01	3.74E+01
ENSMUSG00000036777	Anln	1.84E-12	1.99E-11	-3.47	2.29E+01	7.95E+01
ENSMUSG00000019823	Mical1	1.89E-12	2.03E-11	-2.17	1.42E+02	3.09E+02
ENSMUSG00000040613	Apobec1	1.91E-12	2.06E-11	2.11	3.19E+03	1.51E+03
ENSMUSG00000026626	Ppp2r5a	1.95E-12	2.10E-11	2.09	8.79E+02	4.21E+02
ENSMUSG00000027405	Nop56	2.12E-12	2.28E-11	-2.60	2.92E+01	7.61E+01
ENSMUSG00000047767	Atg16l2	2.19E-12	2.35E-11	-2.52	4.25E+01	1.07E+02
ENSMUSG00000039116	Adgrg6	2.23E-12	2.38E-11	2.41	9.33E+01	3.88E+01
ENSMUSG00000029814	Igf2bp3	2.45E-12	2.62E-11	2.29	2.38E+02	1.04E+02
ENSMUSG00000028410	Dnaja1	2.47E-12	2.63E-11	2.20	4.59E+02	2.09E+02
ENSMUSG00000092627	D130058E05Rik	2.65E-12	2.82E-11	-5.51	4.53E+00	2.50E+01
ENSMUSG00000014778	Fhod1	2.67E-12	2.84E-11	-2.27	8.52E+01	1.94E+02
ENSMUSG00000047632	Fgfbp3	2.74E-12	2.91E-11	3.27	5.86E+01	1.79E+01
ENSMUSG00000046908	Ltb4r1	2.80E-12	2.97E-11	4.75	2.22E+01	4.68E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000020328	Nudcd2	2.80E-12	2.97E-11	-2.03	1.90E+02	3.87E+02
ENSMUSG00000049130	C5ar1	2.80E-12	2.97E-11	-2.14	6.52E+02	1.40E+03
ENSMUSG00000033319	Fem1c	2.84E-12	3.01E-11	2.26	6.79E+02	3.00E+02
ENSMUSG00000031971	Ccsap	2.88E-12	3.05E-11	-4.62	1.43E+01	6.58E+01
ENSMUSG00000024151	Msh2	2.93E-12	3.10E-11	-3.03	5.46E+01	1.65E+02
ENSMUSG00000039989	Cbx4	2.94E-12	3.10E-11	2.21	2.80E+02	1.27E+02
ENSMUSG00000061607	Mdc1	2.96E-12	3.13E-11	-2.13	6.53E+01	1.39E+02
ENSMUSG00000099843	Gm7160	3.00E-12	3.17E-11	4.47	2.81E+01	6.27E+00
ENSMUSG00000025050	Pcgf6	3.07E-12	3.24E-11	-4.00	8.92E+00	3.56E+01
ENSMUSG00000018143	Mafk	3.12E-12	3.29E-11	2.94	7.55E+02	2.57E+02
ENSMUSG00000038594	Cep85l	3.35E-12	3.52E-11	2.74	7.43E+01	2.71E+01
ENSMUSG00000061979	Rcc1l	3.47E-12	3.65E-11	-2.35	2.91E+01	6.84E+01
ENSMUSG00000047881	Rell1	3.73E-12	3.90E-11	2.04	1.96E+03	9.62E+02
ENSMUSG00000032184	Lysmd2	3.78E-12	3.96E-11	2.86	2.40E+01	8.38E+00
ENSMUSG00000022034	Esco2	3.78E-12	3.96E-11	-4.59	8.75E+00	4.01E+01
ENSMUSG00000028633	Ctps	3.97E-12	4.15E-11	-3.37	1.28E+01	4.32E+01
ENSMUSG00000096954	nan	3.99E-12	4.16E-11	3.98	1.82E+02	4.59E+01
ENSMUSG00000034413	Neurl1b	4.00E-12	4.18E-11	-3.00	5.55E+01	1.66E+02
ENSMUSG00000020329	Polrmt	4.04E-12	4.22E-11	-2.46	2.29E+01	5.62E+01
ENSMUSG00000039697	Ncoa7	4.36E-12	4.54E-11	2.51	9.06E+02	3.61E+02
ENSMUSG00000024812	Tjp2	4.44E-12	4.63E-11	-2.28	1.27E+02	2.90E+02
ENSMUSG00000009575	Cbx5	4.62E-12	4.81E-11	-2.23	2.44E+02	5.43E+02
ENSMUSG00000002803	Btbd6	4.83E-12	5.02E-11	-2.45	1.46E+01	3.56E+01
ENSMUSG00000031652	N4bp1	4.84E-12	5.03E-11	2.82	1.08E+03	3.84E+02
ENSMUSG00000044469	Tnfaip8l1	4.88E-12	5.06E-11	-2.82	8.97E+00	2.53E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000114784	Gm47754	5.18E-12	5.36E-11	3.82	1.51E+01	3.94E+00
ENSMUSG00000097111	Peak1os	5.45E-12	5.64E-11	15.58	1.46E+01	9.39E-01
ENSMUSG00000025921	Rdh10	5.54E-12	5.73E-11	-2.55	2.44E+01	6.22E+01
ENSMUSG00000022476	Polr3h	5.69E-12	5.87E-11	-2.09	3.87E+01	8.07E+01
ENSMUSG00000097769	nan	5.81E-12	6.00E-11	-2.30	1.69E+01	3.87E+01
ENSMUSG00000051065	Mb21d2	5.84E-12	6.02E-11	3.63	2.04E+01	5.63E+00
ENSMUSG00000032526	Ss18l2	5.91E-12	6.09E-11	-2.07	5.44E+01	1.13E+02
ENSMUSG00000028010	Gar1	6.30E-12	6.48E-11	-2.58	6.48E+01	1.67E+02
ENSMUSG00000020075	Ddx21	6.37E-12	6.54E-11	-2.05	5.35E+02	1.10E+03
ENSMUSG00000031596	Slc7a2	6.89E-12	7.06E-11	5.72	2.48E+02	4.34E+01
ENSMUSG00000097145	9230114K14Rik	7.20E-12	7.37E-11	-3.02	1.36E+01	4.09E+01
ENSMUSG00000026566	Mpzl1	7.29E-12	7.46E-11	-2.40	2.97E+01	7.12E+01
ENSMUSG00000018428	Akap1	7.47E-12	7.63E-11	-2.76	1.73E+01	4.77E+01
ENSMUSG00000034265	Zdhhc14	7.48E-12	7.64E-11	-2.67	9.05E+01	2.42E+02
ENSMUSG00000029591	Ung	7.67E-12	7.83E-11	-4.55	1.51E+01	6.87E+01
ENSMUSG00000049932	H2ax	7.79E-12	7.95E-11	-3.15	7.79E+01	2.46E+02
ENSMUSG00000022508	Bcl6	8.07E-12	8.22E-11	2.71	8.56E+02	3.16E+02
ENSMUSG00000082229	Nap1l2	8.48E-12	8.62E-11	6.46	1.64E+01	2.53E+00
ENSMUSG00000042489	Clspn	8.79E-12	8.93E-11	-3.70	5.24E+01	1.94E+02
ENSMUSG00000107355	AI839979	9.43E-12	9.57E-11	-2.31	2.70E+01	6.25E+01
ENSMUSG00000027395	Polr1b	9.74E-12	9.87E-11	-4.39	4.66E+00	2.05E+01
ENSMUSG00000009566	Fpgs	9.92E-12	1.01E-10	-2.98	1.18E+01	3.52E+01
ENSMUSG00000022351	Sqle	9.94E-12	1.01E-10	-2.05	2.89E+02	5.94E+02
ENSMUSG00000040177	2310057M21Rik	1.04E-11	1.05E-10	-2.01	3.06E+01	6.16E+01
ENSMUSG00000022360	Atad2	1.09E-11	1.10E-10	-2.30	1.42E+02	3.27E+02

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ENSMUSG00000031657	Heatr3	1.11E-11	1.12E-10	-2.17	3.25E+01	7.06E+01
ENSMUSG00000026700	Tnfsf4	1.12E-11	1.13E-10	10.53	6.53E+01	6.21E+00
ENSMUSG00000022240	Ctnnd2	1.12E-11	1.13E-10	5.43	7.83E+01	1.44E+01
ENSMUSG00000041147	Brca2	1.14E-11	1.15E-10	-3.91	1.16E+01	4.51E+01
ENSMUSG00000062031	Pgghg	1.15E-11	1.15E-10	2.36	5.49E+01	2.32E+01
ENSMUSG00000073700	Klhl21	1.15E-11	1.16E-10	-3.22	8.39E+01	2.70E+02
ENSMUSG00000028613	Lrp8	1.17E-11	1.18E-10	-2.66	4.87E+01	1.30E+02
ENSMUSG00000030271	Ogg1	1.21E-11	1.22E-10	-2.25	1.90E+01	4.29E+01
ENSMUSG00000022548	Apod	1.23E-11	1.23E-10	13.28	9.62E+00	7.24E-01
ENSMUSG00000047649	Cd3eap	1.25E-11	1.25E-10	-2.06	8.90E+01	1.84E+02
ENSMUSG00000019863	Qrsl1	1.25E-11	1.25E-10	-2.16	3.11E+01	6.71E+01
ENSMUSG00000038205	Prkab2	1.39E-11	1.39E-10	-2.13	3.51E+01	7.49E+01
ENSMUSG00000021322	Aoah	1.39E-11	1.39E-10	2.30	3.61E+02	1.57E+02
ENSMUSG00000019987	Arg1	1.41E-11	1.40E-10	19.91	1.04E+01	5.22E-01
ENSMUSG00000078700	D030028A08Rik	1.59E-11	1.59E-10	-4.71	3.35E+00	1.58E+01
ENSMUSG00000098098	Bvht	1.60E-11	1.59E-10	-2.16	1.87E+01	4.04E+01
ENSMUSG00000061143	Maml3	1.66E-11	1.66E-10	-3.40	1.22E+01	4.16E+01
ENSMUSG00000030761	Myo7a	1.68E-11	1.67E-10	-2.11	4.58E+01	9.66E+01
ENSMUSG00000104388	Gm37033	1.70E-11	1.69E-10	2.51	1.13E+02	4.52E+01
ENSMUSG00000040675	Mthfd1l	1.72E-11	1.71E-10	-2.31	4.70E+01	1.09E+02
ENSMUSG00000055322	Tns1	1.75E-11	1.74E-10	-2.58	1.86E+02	4.79E+02
ENSMUSG00000042389	Tsen2	1.75E-11	1.74E-10	-3.33	1.04E+01	3.48E+01
ENSMUSG00000037275	Gemin5	1.76E-11	1.74E-10	-2.19	2.99E+01	6.54E+01
ENSMUSG00000033526	Ppip5k1	1.77E-11	1.76E-10	-2.08	4.12E+01	8.58E+01
ENSMUSG00000005718	Tfap4	1.88E-11	1.86E-10	-7.50	4.71E+00	3.53E+01

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ENSMUSG00000032513	Gorasp1	1.92E-11	1.90E-10	-2.54	2.12E+01	5.39E+01
ENSMUSG00000064366	mt-Tl2	2.08E-11	2.05E-10	2.89	1.26E+02	4.36E+01
ENSMUSG00000015944	Castor2	2.11E-11	2.08E-10	-2.20	9.71E+01	2.13E+02
ENSMUSG00000039763	Dnajc28	2.17E-11	2.14E-10	-4.36	7.10E+00	3.10E+01
ENSMUSG00000071632	2510002D24Rik	2.21E-11	2.17E-10	-2.33	3.20E+01	7.45E+01
ENSMUSG00000059851	Kmt5c	2.23E-11	2.19E-10	-2.24	4.55E+01	1.02E+02
ENSMUSG00000055110	A630012P03Rik	2.31E-11	2.27E-10	49.98	7.65E+00	1.53E-01
ENSMUSG00000072844	G530011O06Rik	2.32E-11	2.27E-10	20.86	9.64E+01	4.62E+00
ENSMUSG00000006362	Cbfa2t3	2.41E-11	2.35E-10	-3.20	3.96E+01	1.27E+02
ENSMUSG00000035842	Ddx11	2.52E-11	2.45E-10	-3.48	8.21E+00	2.86E+01
ENSMUSG00000045875	Adra1a	2.57E-11	2.50E-10	2.12	1.55E+02	7.31E+01
ENSMUSG00000027009	Itga4	2.64E-11	2.57E-10	2.30	1.64E+03	7.14E+02
ENSMUSG00000029817	Tra2a	2.65E-11	2.58E-10	2.00	1.40E+03	6.97E+02
ENSMUSG00000026473	Glul	2.74E-11	2.66E-10	-2.59	3.61E+02	9.33E+02
ENSMUSG00000005225	Plekha8	2.79E-11	2.71E-10	-2.02	3.09E+01	6.25E+01
ENSMUSG00000023805	Synj2	2.83E-11	2.75E-10	-2.04	3.90E+01	7.96E+01
ENSMUSG00000032411	Tfdp2	2.88E-11	2.78E-10	-2.26	5.66E+01	1.28E+02
ENSMUSG00000025086	Trub1	2.94E-11	2.84E-10	-3.57	1.17E+01	4.19E+01
ENSMUSG00000016498	Pdcd1lg2	3.20E-11	3.08E-10	15.89	9.23E+00	5.80E-01
ENSMUSG00000039911	Spsb1	3.48E-11	3.34E-10	2.67	2.16E+02	8.10E+01
ENSMUSG00000050751	Pgbd5	3.49E-11	3.35E-10	-14.58	9.29E-01	1.35E+01
ENSMUSG00000027115	Kif18a	3.55E-11	3.40E-10	-4.19	6.49E+00	2.72E+01
ENSMUSG00000112067	Gm48015	3.73E-11	3.57E-10	6.36	1.64E+01	2.57E+00
ENSMUSG00000053411	Cbx7	3.74E-11	3.58E-10	-3.98	7.03E+00	2.80E+01
ENSMUSG00000026655	Fam107b	3.83E-11	3.66E-10	-2.16	4.62E+01	9.96E+01

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ENSMUSG00000024786	Majin	3.88E-11	3.70E-10	24.54	4.25E+00	1.73E-01
ENSMUSG00000017715	Pgs1	3.92E-11	3.73E-10	2.18	4.59E+02	2.11E+02
ENSMUSG00000106959	Gm42548	4.04E-11	3.84E-10	4.82	2.01E+01	4.17E+00
ENSMUSG00000014846	Tppp3	4.12E-11	3.91E-10	4.99	5.10E+01	1.02E+01
ENSMUSG00000034858	Fam214a	4.14E-11	3.92E-10	-2.89	2.92E+01	8.43E+01
ENSMUSG00000031728	Zfp821	4.24E-11	4.02E-10	2.40	1.42E+02	5.93E+01
ENSMUSG00000031196	F8	4.51E-11	4.26E-10	6.81	2.67E+01	3.92E+00
ENSMUSG00000025591	Tma16	4.55E-11	4.30E-10	2.58	4.91E+02	1.90E+02
ENSMUSG00000021226	Acot2	4.98E-11	4.69E-10	-2.22	1.06E+02	2.35E+02
ENSMUSG00000026833	Olfm1	5.35E-11	5.03E-10	2.26	1.41E+02	6.25E+01
ENSMUSG00000028931	Kcnab2	5.76E-11	5.39E-10	-2.07	3.28E+02	6.79E+02
ENSMUSG00000107320	Gm42549	5.78E-11	5.41E-10	4.38	4.55E+01	1.04E+01
ENSMUSG00000019773	Fbxo5	5.96E-11	5.57E-10	-3.39	2.46E+01	8.34E+01
ENSMUSG00000020332	Meikin	6.18E-11	5.77E-10	35.72	5.46E+00	1.53E-01
ENSMUSG00000003848	Nob1	6.32E-11	5.89E-10	-2.59	2.22E+01	5.75E+01
ENSMUSG00000031506	Ptpn7	6.33E-11	5.90E-10	-2.26	1.32E+02	2.98E+02
ENSMUSG00000097000	Gm17435	6.63E-11	6.17E-10	6.23	1.61E+01	2.58E+00
ENSMUSG00000046679	C87436	6.65E-11	6.18E-10	-2.00	2.49E+01	4.98E+01
ENSMUSG00000033356	Pus7l	6.71E-11	6.23E-10	-2.88	7.04E+00	2.03E+01
ENSMUSG00000043252	Tmem64	6.84E-11	6.35E-10	-2.20	2.98E+01	6.56E+01
ENSMUSG00000015340	Cybb	6.88E-11	6.38E-10	2.37	1.57E+04	6.61E+03
ENSMUSG00000007827	Ankrd26	6.91E-11	6.41E-10	-2.27	2.98E+01	6.76E+01
ENSMUSG00000029863	Casp2	7.14E-11	6.60E-10	2.21	2.61E+02	1.18E+02
ENSMUSG00000028793	Rnf19b	7.40E-11	6.83E-10	3.37	3.98E+03	1.18E+03
ENSMUSG00000020262	Adarb1	7.63E-11	7.04E-10	-10.06	1.12E+00	1.12E+01

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ENSMUSG00000046994	Mars2	7.65E-11	7.05E-10	-3.23	7.58E+00	2.45E+01
ENSMUSG00000039270	Megf9	7.82E-11	7.21E-10	-3.39	2.10E+01	7.12E+01
ENSMUSG00000038046	Mrm3	7.97E-11	7.33E-10	-3.89	5.14E+00	2.00E+01
ENSMUSG00000022126	Acod1	8.57E-11	7.87E-10	15.31	1.01E+04	6.57E+02
ENSMUSG00000056529	Ptafr	8.87E-11	8.12E-10	2.56	3.00E+03	1.17E+03
ENSMUSG00000066735	Vkorc1l1	8.87E-11	8.12E-10	-2.20	2.35E+01	5.17E+01
ENSMUSG00000024891	Slc29a2	8.92E-11	8.16E-10	-4.01	3.16E+00	1.27E+01
ENSMUSG00000047496	Rnf152	8.98E-11	8.21E-10	20.77	7.62E+00	3.67E-01
ENSMUSG00000115855	Gm34643	9.03E-11	8.24E-10	4.69	1.99E+01	4.25E+00
ENSMUSG00000041774	Ydjc	9.14E-11	8.34E-10	-2.52	2.99E+01	7.54E+01
ENSMUSG00000026131	Dst	9.20E-11	8.38E-10	2.36	3.35E+02	1.42E+02
ENSMUSG00000075703	Selenoi	9.89E-11	8.99E-10	-2.02	3.89E+01	7.87E+01
ENSMUSG00000091906	1700099I09Rik	1.01E-10	9.19E-10	3.89	1.72E+01	4.42E+00
ENSMUSG00000035594	Chrna5	1.02E-10	9.28E-10	42.47	9.45E+00	2.23E-01
ENSMUSG00000055884	Fancm	1.03E-10	9.32E-10	-2.69	1.67E+01	4.48E+01
ENSMUSG00000009654	Oit3	1.03E-10	9.37E-10	-2.33	3.46E+01	8.06E+01
ENSMUSG00000039356	Exosc2	1.06E-10	9.58E-10	-2.30	1.79E+01	4.13E+01
ENSMUSG00000018983	E2f2	1.06E-10	9.59E-10	-2.40	1.09E+02	2.61E+02
ENSMUSG00000039396	Neil3	1.07E-10	9.69E-10	-3.90	9.31E+00	3.63E+01
ENSMUSG00000053436	Mapk14	1.08E-10	9.71E-10	-2.02	1.74E+02	3.52E+02
ENSMUSG00000060510	Zfp266	1.12E-10	1.01E-09	-2.28	2.85E+01	6.49E+01
ENSMUSG00000006398	Cdc20	1.12E-10	1.01E-09	-3.80	4.62E+01	1.75E+02
ENSMUSG00000089715	Cbx6	1.17E-10	1.05E-09	-2.54	9.18E+01	2.33E+02
ENSMUSG00000024795	Kif20b	1.17E-10	1.05E-09	-2.75	7.77E+01	2.14E+02
ENSMUSG00000026435	Slc45a3	1.18E-10	1.06E-09	5.03	3.10E+01	6.17E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000073739	Gm16287	1.21E-10	1.09E-09	-2.44	1.67E+01	4.08E+01
ENSMUSG00000079442	St6galnac4	1.23E-10	1.10E-09	2.34	8.47E+02	3.62E+02
ENSMUSG00000041633	Kctd12b	1.29E-10	1.15E-09	-2.85	3.19E+01	9.08E+01
ENSMUSG00000092051	Gm17229	1.32E-10	1.19E-09	4.31	3.45E+01	8.01E+00
ENSMUSG00000032344	Cgas	1.39E-10	1.24E-09	2.62	5.23E+02	2.00E+02
ENSMUSG00000031480	Thsd1	1.45E-10	1.29E-09	-4.35	3.52E+00	1.53E+01
ENSMUSG00000048707	Tprn	1.51E-10	1.34E-09	-2.46	2.02E+01	4.96E+01
ENSMUSG00000039232	Stx11	1.62E-10	1.44E-09	3.62	5.81E+02	1.60E+02
ENSMUSG00000051790	Nlgn2	1.64E-10	1.46E-09	2.74	5.11E+01	1.86E+01
ENSMUSG00000105062	Gm43113	1.67E-10	1.48E-09	2.84	3.93E+01	1.38E+01
ENSMUSG00000034906	Ncaph	1.75E-10	1.55E-09	-2.66	3.15E+01	8.38E+01
ENSMUSG00000020899	Pfas	1.80E-10	1.59E-09	-2.60	3.49E+01	9.10E+01
ENSMUSG00000033257	Ttll4	1.83E-10	1.61E-09	-2.28	1.67E+01	3.80E+01
ENSMUSG00000037851	Iars	1.90E-10	1.67E-09	-2.02	1.35E+02	2.72E+02
ENSMUSG00000054051	Ercc6	1.95E-10	1.71E-09	-2.35	4.62E+01	1.09E+02
ENSMUSG00000052821	Cysltr1	1.97E-10	1.73E-09	2.62	1.47E+02	5.59E+01
ENSMUSG00000007050	Lsm2	1.98E-10	1.74E-09	-2.28	7.45E+01	1.70E+02
ENSMUSG00000026558	Uck2	2.00E-10	1.76E-09	-2.82	5.74E+01	1.62E+02
ENSMUSG00000027318	Adam33	2.01E-10	1.76E-09	4.65	4.62E+01	9.93E+00
ENSMUSG00000031833	Mast3	2.09E-10	1.83E-09	-2.04	6.46E+01	1.32E+02
ENSMUSG00000018548	Trim37	2.14E-10	1.87E-09	-2.43	7.74E+01	1.88E+02
ENSMUSG00000024164	C3	2.16E-10	1.89E-09	8.01	9.09E+02	1.13E+02
ENSMUSG00000042351	Grap2	2.19E-10	1.91E-09	3.57	3.53E+01	9.88E+00
ENSMUSG00000024397	Aif1	2.20E-10	1.92E-09	2.86	6.81E+02	2.38E+02
ENSMUSG00000042812	Foxf1	2.22E-10	1.94E-09	11.88	8.73E+00	7.35E-01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000051517	Arhgef39	2.33E-10	2.03E-09	-2.69	1.33E+01	3.59E+01
ENSMUSG00000064307	Lrrc51	2.37E-10	2.07E-09	2.51	4.45E+01	1.78E+01
ENSMUSG00000103123	Gm37390	2.47E-10	2.15E-09	2.83	2.83E+01	1.00E+01
ENSMUSG00000042647	Acad12	2.52E-10	2.19E-09	-2.17	2.50E+01	5.44E+01
ENSMUSG00000041992	Rapgef5	2.56E-10	2.22E-09	-2.58	1.10E+02	2.83E+02
ENSMUSG00000022325	Pop1	2.79E-10	2.41E-09	-2.06	3.77E+01	7.78E+01
ENSMUSG00000041515	Irf8	2.83E-10	2.44E-09	2.32	2.28E+03	9.81E+02
ENSMUSG00000055485	Soga1	2.84E-10	2.45E-09	-2.27	7.57E+01	1.72E+02
ENSMUSG00000023832	Acat2	2.86E-10	2.47E-09	-2.48	6.48E+01	1.60E+02
ENSMUSG00000021699	Pde4d	3.04E-10	2.62E-09	-3.13	9.57E+00	3.00E+01
ENSMUSG00000025255	Zfhx4	3.09E-10	2.66E-09	5.32	1.46E+01	2.74E+00
ENSMUSG00000021338	Carmil1	3.26E-10	2.80E-09	3.03	1.18E+02	3.89E+01
ENSMUSG00000079445	B3gnt7	3.42E-10	2.93E-09	-3.09	7.09E+00	2.19E+01
ENSMUSG00000040943	Tet2	3.49E-10	2.99E-09	2.28	3.98E+02	1.74E+02
ENSMUSG00000038379	Ttk	3.51E-10	3.00E-09	-2.59	3.20E+01	8.31E+01
ENSMUSG00000000318	Clec10a	3.72E-10	3.18E-09	2.38	1.33E+02	5.58E+01
ENSMUSG00000042590	Ipo11	3.81E-10	3.25E-09	-2.27	4.30E+01	9.74E+01
ENSMUSG00000073821	8030451A03Rik	3.87E-10	3.30E-09	14.22	7.33E+00	5.16E-01
ENSMUSG00000038736	Nudcd1	3.89E-10	3.32E-09	-2.03	2.51E+01	5.10E+01
ENSMUSG00000031609	Sap30	3.92E-10	3.34E-09	2.56	2.82E+02	1.10E+02
ENSMUSG00000039908	Slc26a11	3.96E-10	3.37E-09	-2.87	8.47E+01	2.43E+02
ENSMUSG00000042978	Sbk1	4.03E-10	3.43E-09	-4.15	4.82E+00	2.00E+01
ENSMUSG00000073643	Wdfy1	4.45E-10	3.77E-09	2.05	4.50E+02	2.19E+02
ENSMUSG00000107179	Gm43069	4.56E-10	3.86E-09	9.38	6.83E+00	7.28E-01
ENSMUSG00000039976	Tbc1d16	4.61E-10	3.90E-09	-4.10	8.37E+00	3.43E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000033955	Tnks1bp1	4.63E-10	3.92E-09	2.36	4.02E+01	1.70E+01
ENSMUSG00000060098	Prmt7	4.77E-10	4.03E-09	-2.53	3.26E+01	8.25E+01
ENSMUSG00000055639	Dach1	4.78E-10	4.03E-09	2.66	1.69E+02	6.36E+01
ENSMUSG00000000392	Fap	4.93E-10	4.15E-09	6.34	1.01E+01	1.60E+00
ENSMUSG00000020739	Nup85	4.96E-10	4.17E-09	-2.21	6.07E+01	1.34E+02
ENSMUSG00000028089	Chd1l	4.97E-10	4.18E-09	-2.13	2.71E+01	5.77E+01
ENSMUSG00000074874	Ctla2b	5.37E-10	4.51E-09	2.19	4.99E+01	2.28E+01
ENSMUSG00000037509	Arhgef4	5.49E-10	4.60E-09	-3.51	5.50E+00	1.93E+01
ENSMUSG00000025582	Nptx1	5.51E-10	4.61E-09	-3.18	8.21E+01	2.61E+02
ENSMUSG00000041429	Nthl1	5.59E-10	4.67E-09	-3.99	4.15E+00	1.66E+01
ENSMUSG00000047473	Zfp30	5.74E-10	4.79E-09	-3.35	6.78E+00	2.27E+01
ENSMUSG00000026020	Nop58	5.76E-10	4.80E-09	-2.87	1.72E+02	4.95E+02
ENSMUSG00000025026	Add3	5.92E-10	4.93E-09	-2.71	1.09E+02	2.96E+02
ENSMUSG00000026039	Sgo2a	6.06E-10	5.05E-09	-2.90	4.29E+01	1.24E+02
ENSMUSG00000042182	Bend6	6.33E-10	5.27E-09	2.06	2.30E+01	1.12E+01
ENSMUSG00000021902	Phf7	6.71E-10	5.59E-09	-2.07	1.72E+01	3.57E+01
ENSMUSG00000086782	E130102H24Rik	6.82E-10	5.67E-09	3.28	5.30E+01	1.62E+01
ENSMUSG00000036825	Ssx2ip	7.47E-10	6.19E-09	-2.03	2.35E+01	4.76E+01
ENSMUSG00000072494	Ppp1r3e	7.62E-10	6.31E-09	-2.10	1.20E+01	2.52E+01
ENSMUSG00000007379	Dennd2c	7.75E-10	6.40E-09	-4.38	2.96E+00	1.30E+01
ENSMUSG00000019841	Rev3l	8.53E-10	7.03E-09	-2.10	4.07E+01	8.54E+01
ENSMUSG00000020649	Rrm2	8.86E-10	7.28E-09	-3.09	6.58E+01	2.03E+02
ENSMUSG00000038543	BC028528	8.88E-10	7.29E-09	2.37	4.64E+02	1.96E+02
ENSMUSG00000091556	Gm14569	9.03E-10	7.40E-09	33.25	6.53E+00	1.96E-01
ENSMUSG00000063760	Rnf217	9.24E-10	7.57E-09	2.05	1.24E+02	6.09E+01

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ENSMUSG00000004996	Mri1	9.52E-10	7.80E-09	-2.44	1.66E+01	4.04E+01
ENSMUSG00000000561	Wdr77	9.59E-10	7.85E-09	-2.04	7.47E+01	1.52E+02
ENSMUSG00000116673	A630089N07Rik	9.62E-10	7.87E-09	-3.08	6.70E+00	2.06E+01
ENSMUSG00000030882	Dnhd1	9.63E-10	7.87E-09	4.22	9.91E+00	2.35E+00
ENSMUSG00000052609	Plekhg3	9.74E-10	7.95E-09	-2.81	5.60E+01	1.57E+02
ENSMUSG00000029536	Gatc	9.74E-10	7.95E-09	-2.02	6.03E+01	1.22E+02
ENSMUSG00000082088	Gm15753	1.03E-09	8.38E-09	13.41	7.69E+00	5.73E-01
ENSMUSG00000026955	Sapcd2	1.05E-09	8.51E-09	-9.74	1.12E+00	1.09E+01
ENSMUSG00000031595	Pdgfrl	1.09E-09	8.82E-09	8.96	6.50E+00	7.26E-01
ENSMUSG00000041406	BC055324	1.13E-09	9.13E-09	-3.17	1.38E+01	4.36E+01
ENSMUSG00000022389	Tef	1.17E-09	9.47E-09	-2.18	2.29E+02	4.99E+02
ENSMUSG00000021838	Samd4	1.19E-09	9.66E-09	-2.38	4.12E+01	9.82E+01
ENSMUSG00000036223	Ska1	1.21E-09	9.78E-09	-3.47	2.20E+01	7.63E+01
ENSMUSG00000029082	Bst1	1.22E-09	9.81E-09	2.21	9.69E+01	4.39E+01
ENSMUSG00000045005	Fzd5	1.22E-09	9.84E-09	2.30	9.59E+01	4.17E+01
ENSMUSG00000003382	Etv3	1.24E-09	9.97E-09	2.58	1.87E+03	7.25E+02
ENSMUSG00000041135	Ripk2	1.30E-09	1.05E-08	3.94	5.65E+02	1.43E+02
ENSMUSG00000028687	Mutyh	1.31E-09	1.05E-08	-3.80	5.49E+00	2.09E+01
ENSMUSG00000064372	mt-Tp	1.33E-09	1.07E-08	2.15	1.35E+02	6.30E+01
ENSMUSG00000045316	Fahd1	1.43E-09	1.15E-08	-2.85	7.83E+00	2.23E+01
ENSMUSG00000032397	Tipin	1.51E-09	1.21E-08	-2.19	6.54E+01	1.43E+02
ENSMUSG00000031644	Nek1	1.52E-09	1.22E-08	-2.37	4.06E+01	9.62E+01
ENSMUSG00000028982	Slc25a33	1.54E-09	1.24E-08	-2.84	2.14E+01	6.07E+01
ENSMUSG00000022099	Dmtn	1.55E-09	1.24E-08	8.87	2.68E+01	3.03E+00
ENSMUSG00000044098	Rsbn1	1.55E-09	1.25E-08	2.10	5.30E+02	2.53E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000027605	Acss2	1.58E-09	1.26E-08	2.87	3.47E+01	1.21E+01
ENSMUSG00000034731	Dgkh	1.59E-09	1.28E-08	2.03	3.76E+02	1.85E+02
ENSMUSG00000079109	Pms2	1.60E-09	1.28E-08	-2.36	1.41E+01	3.33E+01
ENSMUSG00000015222	Map2	1.63E-09	1.30E-08	20.77	3.22E+01	1.55E+00
ENSMUSG00000030008	Pradc1	1.64E-09	1.31E-08	-2.31	1.39E+01	3.21E+01
ENSMUSG00000028884	Rpa2	1.71E-09	1.36E-08	-2.30	2.30E+02	5.30E+02
ENSMUSG00000041945	Mfsd9	1.79E-09	1.43E-08	2.53	7.14E+01	2.82E+01
ENSMUSG00000026429	Ube2t	1.82E-09	1.45E-08	-3.92	7.16E+00	2.80E+01
ENSMUSG00000038668	Lpar1	1.83E-09	1.45E-08	5.96	1.10E+02	1.85E+01
ENSMUSG00000015316	Slamf1	1.86E-09	1.48E-08	16.36	8.58E+00	5.24E-01
ENSMUSG00000020077	Srgn	1.88E-09	1.49E-08	2.39	2.67E+03	1.12E+03
ENSMUSG00000082079	Dnmt3c	1.92E-09	1.52E-08	27.96	4.28E+00	1.53E-01
ENSMUSG00000035373	Ccl7	2.00E-09	1.58E-08	10.82	4.95E+03	4.58E+02
ENSMUSG00000066687	Zbtb16	2.03E-09	1.61E-08	-11.69	7.44E-01	8.69E+00
ENSMUSG00000038587	Akap12	2.06E-09	1.63E-08	2.03	4.18E+01	2.06E+01
ENSMUSG00000021965	Ska3	2.08E-09	1.64E-08	-3.25	7.62E+00	2.48E+01
ENSMUSG00000040624	Plekhg1	2.09E-09	1.65E-08	3.12	6.44E+01	2.06E+01
ENSMUSG00000020228	Helb	2.09E-09	1.65E-08	-2.13	5.39E+01	1.15E+02
ENSMUSG00000018796	Acsl1	2.13E-09	1.68E-08	2.97	1.23E+03	4.14E+02
ENSMUSG00000049086	Bmyc	2.18E-09	1.72E-08	-2.06	4.15E+01	8.56E+01
ENSMUSG00000064344	mt-Tm	2.25E-09	1.77E-08	2.23	1.06E+03	4.75E+02
ENSMUSG00000022607	Ptk2	2.28E-09	1.80E-08	2.15	9.28E+01	4.31E+01
ENSMUSG00000018995	Nars2	2.31E-09	1.82E-08	-3.28	6.57E+00	2.15E+01
ENSMUSG00000026605	Cenpf	2.41E-09	1.89E-08	-2.84	1.28E+02	3.63E+02
ENSMUSG00000054423	Cadps	2.44E-09	1.92E-08	4.47	3.25E+01	7.28E+00

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ENSMUSG00000054942	Miga1	2.45E-09	1.92E-08	-2.17	2.15E+01	4.67E+01
ENSMUSG00000057329	Bcl2	2.45E-09	1.92E-08	-2.37	4.76E+01	1.13E+02
ENSMUSG00000061273	Mmgt1	2.53E-09	1.98E-08	-2.14	9.10E+01	1.95E+02
ENSMUSG00000086763	Plxna4os1	2.53E-09	1.98E-08	2.42	1.11E+02	4.59E+01
ENSMUSG00000038173	Enpp6	2.67E-09	2.09E-08	5.79	7.19E+00	1.24E+00
ENSMUSG00000037972	Snn	2.73E-09	2.13E-08	2.68	1.08E+02	4.05E+01
ENSMUSG00000086291	Gm15513	2.82E-09	2.20E-08	-7.71	3.73E+00	2.87E+01
ENSMUSG00000031754	Nudt21	2.93E-09	2.27E-08	-2.37	1.67E+01	3.96E+01
ENSMUSG00000106157	4930555A03Rik	2.96E-09	2.30E-08	-3.76	3.52E+00	1.33E+01
ENSMUSG00000041268	Dmxl2	2.97E-09	2.30E-08	-2.53	9.58E+01	2.42E+02
ENSMUSG00000042608	Stk40	3.06E-09	2.37E-08	2.23	8.54E+02	3.83E+02
ENSMUSG00000029246	Ppat	3.19E-09	2.47E-08	-2.50	2.70E+01	6.77E+01
ENSMUSG00000074825	Itpripl1	3.21E-09	2.48E-08	-2.25	5.44E+01	1.23E+02
ENSMUSG00000034317	Trim59	3.31E-09	2.56E-08	-2.37	4.20E+01	9.95E+01
ENSMUSG00000052632	Asap2	3.62E-09	2.79E-08	-3.55	8.78E+00	3.11E+01
ENSMUSG00000051212	Gpr183	3.66E-09	2.82E-08	-2.30	3.44E+01	7.91E+01
ENSMUSG00000024791	Cdca5	3.73E-09	2.87E-08	-2.57	1.85E+01	4.75E+01
ENSMUSG00000036862	Dchs1	3.83E-09	2.94E-08	-5.74	1.49E+00	8.54E+00
ENSMUSG00000107225	Gm43637	3.84E-09	2.95E-08	4.41	2.00E+01	4.54E+00
ENSMUSG00000064280	Ccdc146	3.90E-09	2.99E-08	30.15	5.92E+00	1.96E-01
ENSMUSG00000054008	Ndst1	4.03E-09	3.09E-08	-2.04	1.36E+02	2.78E+02
ENSMUSG00000021930	Spryd7	4.06E-09	3.10E-08	2.50	1.19E+03	4.77E+02
ENSMUSG00000116995	Gm21926	4.20E-09	3.21E-08	-2.21	3.20E+01	7.07E+01
ENSMUSG00000047604	Frat2	4.45E-09	3.39E-08	-3.17	3.63E+01	1.15E+02
ENSMUSG00000023067	Cdkn1a	5.22E-09	3.96E-08	2.42	1.62E+04	6.68E+03

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000019996	Map7	5.22E-09	3.96E-08	2.46	5.40E+01	2.20E+01
ENSMUSG00000024975	Pdcd4	5.22E-09	3.96E-08	-2.81	6.56E+01	1.84E+02
ENSMUSG00000029047	Pex10	5.24E-09	3.97E-08	-2.43	9.71E+00	2.36E+01
ENSMUSG00000083822	Hmgb1-ps5	5.32E-09	4.03E-08	3.09	3.12E+01	1.01E+01
ENSMUSG00000092118	Fancf	5.32E-09	4.03E-08	-3.85	3.67E+00	1.41E+01
ENSMUSG00000060550	H2-Q7	5.48E-09	4.14E-08	6.93	1.74E+01	2.51E+00
ENSMUSG00000116033	Gm49442	5.49E-09	4.14E-08	20.32	3.52E+00	1.73E-01
ENSMUSG00000046295	Ankle1	5.53E-09	4.17E-08	-5.15	2.89E+00	1.49E+01
ENSMUSG00000027203	Dut	5.71E-09	4.30E-08	-2.41	8.78E+01	2.11E+02
ENSMUSG00000064289	Tank	5.75E-09	4.32E-08	2.63	9.11E+02	3.47E+02
ENSMUSG00000036172	Cd200r3	5.81E-09	4.37E-08	16.69	1.15E+01	6.88E-01
ENSMUSG00000086247	Gm15787	5.85E-09	4.39E-08	5.80	8.16E+00	1.41E+00
ENSMUSG00000021087	Rtn1	5.88E-09	4.41E-08	2.44	2.87E+01	1.18E+01
ENSMUSG00000062232	Rapgef2	5.89E-09	4.42E-08	2.70	2.01E+02	7.43E+01
ENSMUSG00000020806	Rhbdf2	6.27E-09	4.69E-08	2.34	4.90E+02	2.09E+02
ENSMUSG00000043323	Fbrsl1	6.28E-09	4.70E-08	2.09	2.22E+02	1.06E+02
ENSMUSG00000038644	Pold1	6.31E-09	4.72E-08	-2.91	3.80E+01	1.11E+02
ENSMUSG00000055782	Abcd2	6.38E-09	4.76E-08	-4.34	1.09E+01	4.73E+01
ENSMUSG00000037224	Zfyve28	6.55E-09	4.89E-08	-4.55	5.90E+00	2.69E+01
ENSMUSG00000021365	Nedd9	6.57E-09	4.90E-08	-2.27	4.13E+01	9.37E+01
ENSMUSG00000027315	Spint1	6.68E-09	4.98E-08	3.41	2.98E+01	8.73E+00
ENSMUSG00000072066	6720489N17Rik	6.96E-09	5.18E-08	-5.38	2.14E+00	1.15E+01
ENSMUSG00000034883	Lrr1	7.11E-09	5.28E-08	-3.98	4.80E+00	1.91E+01
ENSMUSG00000075585	6330403L08Rik	7.30E-09	5.42E-08	-2.71	1.82E+01	4.93E+01
ENSMUSG00000037235	Mxd4	7.40E-09	5.49E-08	-2.54	3.67E+02	9.33E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000023988	Bysl	7.48E-09	5.54E-08	-2.01	4.43E+01	8.90E+01
ENSMUSG00000028318	Polr1e	7.77E-09	5.75E-08	-3.30	6.78E+00	2.24E+01
ENSMUSG00000019518	Ap4m1	7.79E-09	5.77E-08	-2.01	3.28E+01	6.58E+01
ENSMUSG00000090958	Lrrc32	7.88E-09	5.83E-08	2.76	2.92E+01	1.06E+01
ENSMUSG00000057982	Zfp809	8.20E-09	6.05E-08	-2.04	3.32E+01	6.78E+01
ENSMUSG00000027086	Fastkd1	8.29E-09	6.12E-08	-2.00	1.97E+01	3.94E+01
ENSMUSG00000025804	Ccr1	8.35E-09	6.16E-08	3.72	5.39E+02	1.45E+02
ENSMUSG00000033857	Engase	8.43E-09	6.22E-08	-3.12	2.11E+01	6.59E+01
ENSMUSG00000013629	Cad	8.68E-09	6.39E-08	-2.16	3.48E+01	7.54E+01
ENSMUSG00000032392	Parp16	8.73E-09	6.42E-08	-3.72	3.93E+00	1.46E+01
ENSMUSG00000054822	1700041G16Rik	8.73E-09	6.42E-08	3.80	9.76E+00	2.57E+00
ENSMUSG00000079737	3110001I22Rik	8.76E-09	6.44E-08	2.97	1.04E+02	3.52E+01
ENSMUSG00000096960	A230028O05Rik	8.76E-09	6.44E-08	2.71	3.55E+01	1.31E+01
ENSMUSG00000000686	Abhd15	9.60E-09	7.02E-08	-3.08	8.23E+00	2.54E+01
ENSMUSG00000030871	Ears2	9.99E-09	7.29E-08	-2.36	1.02E+01	2.40E+01
ENSMUSG00000002289	Angptl4	1.11E-08	8.12E-08	-3.43	9.28E+00	3.18E+01
ENSMUSG00000027510	Rbm38	1.12E-08	8.13E-08	-2.06	2.31E+01	4.77E+01
ENSMUSG00000086213	A330040F15Rik	1.12E-08	8.14E-08	8.85	1.63E+01	1.84E+00
ENSMUSG00000026656	Fcgr2b	1.12E-08	8.14E-08	2.41	5.36E+02	2.22E+02
ENSMUSG00000055184	Fam72a	1.13E-08	8.18E-08	2.53	5.45E+01	2.15E+01
ENSMUSG00000073771	Btbd19	1.21E-08	8.75E-08	-2.47	1.44E+01	3.54E+01
ENSMUSG00000102964	9430034N14Rik	1.21E-08	8.79E-08	2.75	4.72E+01	1.71E+01
ENSMUSG00000041075	Fzd7	1.23E-08	8.91E-08	2.13	5.09E+02	2.40E+02
ENSMUSG00000041235	Chd7	1.24E-08	8.95E-08	2.09	7.58E+02	3.62E+02
ENSMUSG00000066755	Tnfsf18	1.41E-08	1.01E-07	20.89	6.76E+00	3.24E-01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000021366	Hivep1	1.43E-08	1.03E-07	2.42	2.46E+02	1.02E+02
ENSMUSG00000032251	Irak1bp1	1.43E-08	1.03E-07	-2.02	2.93E+01	5.91E+01
ENSMUSG00000108004	Gm44080	1.49E-08	1.07E-07	4.18	1.84E+01	4.41E+00
ENSMUSG00000020032	Nuak1	1.52E-08	1.09E-07	-3.04	3.76E+01	1.15E+02
ENSMUSG00000019813	Cep57l1	1.56E-08	1.12E-07	-2.22	1.49E+01	3.31E+01
ENSMUSG00000082419	Gm11425	1.59E-08	1.13E-07	2.57	1.95E+01	7.60E+00
ENSMUSG00000015880	Ncapg	1.63E-08	1.17E-07	-2.52	4.38E+01	1.10E+02
ENSMUSG00000039865	Slc44a3	1.64E-08	1.17E-07	16.39	3.65E+00	2.23E-01
ENSMUSG00000005370	Msh6	1.65E-08	1.18E-07	-2.20	7.86E+01	1.73E+02
ENSMUSG00000111535	Gm35154	1.66E-08	1.19E-07	4.91	1.60E+01	3.26E+00
ENSMUSG00000031871	Cdh5	1.69E-08	1.20E-07	7.73	6.80E+00	8.79E-01
ENSMUSG00000038217	Tlcd2	1.79E-08	1.27E-07	2.22	5.43E+01	2.45E+01
ENSMUSG00000030878	Cdr2	1.83E-08	1.30E-07	-2.34	1.19E+01	2.79E+01
ENSMUSG00000072618	Gm10384	1.84E-08	1.31E-07	-17.23	3.40E-01	5.86E+00
ENSMUSG00000111521	Gm48529	1.84E-08	1.31E-07	2.50	2.10E+01	8.40E+00
ENSMUSG00000042349	Ikbke	1.88E-08	1.33E-07	2.20	5.50E+02	2.50E+02
ENSMUSG00000038295	Atg9b	1.88E-08	1.34E-07	-4.08	3.67E+00	1.49E+01
ENSMUSG00000104867	Gm43728	1.89E-08	1.34E-07	3.31	2.04E+01	6.18E+00
ENSMUSG00000001228	Uhrf1	1.89E-08	1.34E-07	-3.12	4.15E+01	1.30E+02
ENSMUSG00000020227	Irak3	1.95E-08	1.38E-07	-2.23	4.81E+01	1.07E+02
ENSMUSG00000110141	Gm45684	2.01E-08	1.42E-07	10.94	5.76E+00	5.26E-01
ENSMUSG00000023473	Celsr3	2.02E-08	1.43E-07	-2.56	6.57E+00	1.69E+01
ENSMUSG00000038305	Spats2l	2.10E-08	1.48E-07	10.07	1.41E+01	1.40E+00
ENSMUSG00000019487	Trip10	2.16E-08	1.52E-07	2.30	2.13E+02	9.27E+01
ENSMUSG00000074063	Osgin1	2.20E-08	1.54E-07	-2.28	5.49E+01	1.25E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000044066	Cep68	2.21E-08	1.55E-07	-2.20	2.02E+01	4.45E+01
ENSMUSG00000054640	Slc8a1	2.27E-08	1.59E-07	2.87	2.28E+01	7.94E+00
ENSMUSG00000022180	Slc7a8	2.28E-08	1.60E-07	2.11	3.07E+03	1.46E+03
ENSMUSG00000056220	Pla2g4a	2.30E-08	1.61E-07	2.64	1.39E+02	5.24E+01
ENSMUSG00000019796	Lrp11	2.31E-08	1.61E-07	2.03	7.12E+01	3.51E+01
ENSMUSG00000030717	Nupr1	2.40E-08	1.68E-07	2.83	5.38E+02	1.90E+02
ENSMUSG00000040734	Ppp1r13l	2.65E-08	1.84E-07	-2.77	6.52E+00	1.81E+01
ENSMUSG00000117239	Gpr31c	2.68E-08	1.86E-07	3.87	3.48E+01	8.98E+00
ENSMUSG00000026360	Rgs2	2.68E-08	1.86E-07	2.31	1.39E+04	6.00E+03
ENSMUSG00000030725	Lipt2	2.70E-08	1.88E-07	-3.47	3.99E+00	1.38E+01
ENSMUSG00000039781	Cep131	2.76E-08	1.91E-07	-2.88	1.00E+01	2.88E+01
ENSMUSG00000022471	Xrcc6	2.82E-08	1.95E-07	-2.19	2.20E+01	4.80E+01
ENSMUSG00000036390	Gadd45a	2.91E-08	2.01E-07	-3.10	1.05E+02	3.26E+02
ENSMUSG00000040264	Gbp2b	2.99E-08	2.06E-07	23.45	3.59E+00	1.53E-01
ENSMUSG00000007682	Dio2	3.08E-08	2.12E-07	3.90	4.92E+02	1.26E+02
ENSMUSG00000106962	Gm43633	3.23E-08	2.22E-07	7.87	6.54E+00	8.31E-01
ENSMUSG00000043183	Simc1	3.28E-08	2.25E-07	-2.59	1.27E+01	3.28E+01
ENSMUSG00000072244	Trim6	3.31E-08	2.27E-07	4.80	1.74E+01	3.63E+00
ENSMUSG00000045751	Mms22l	3.32E-08	2.28E-07	-2.16	3.92E+01	8.46E+01
ENSMUSG00000039748	Exo1	3.33E-08	2.28E-07	-3.96	6.76E+00	2.67E+01
ENSMUSG00000109560	Gm8463	3.34E-08	2.29E-07	5.90	8.63E+00	1.46E+00
ENSMUSG00000001305	Rrp15	3.35E-08	2.29E-07	-2.43	3.82E+01	9.29E+01
ENSMUSG00000061414	Cracr2a	3.43E-08	2.34E-07	-2.39	1.84E+01	4.41E+01
ENSMUSG00000032089	Il10ra	3.45E-08	2.35E-07	2.22	7.38E+02	3.33E+02
ENSMUSG00000040152	Thbs1	3.49E-08	2.38E-07	2.24	9.84E+02	4.40E+02

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ENSMUSG00000073705	Cenps	3.53E-08	2.41E-07	-2.56	2.00E+01	5.11E+01
ENSMUSG00000025574	Tk1	3.55E-08	2.42E-07	-2.66	1.05E+02	2.80E+02
ENSMUSG00000096967	Gm26621	3.62E-08	2.46E-07	3.65	2.41E+01	6.60E+00
ENSMUSG00000108650	Gm44867	3.65E-08	2.48E-07	40.94	7.10E+00	1.73E-01
ENSMUSG00000027347	Rasgrp1	3.70E-08	2.51E-07	11.51	6.66E+00	5.79E-01
ENSMUSG00000104436	Gm37423	3.74E-08	2.54E-07	2.73	3.50E+01	1.28E+01
ENSMUSG00000037447	Arid5a	3.83E-08	2.60E-07	4.60	5.26E+02	1.14E+02
ENSMUSG00000052798	Nup107	3.91E-08	2.65E-07	-2.02	5.58E+01	1.13E+02
ENSMUSG00000037347	Chst7	3.92E-08	2.65E-07	2.48	7.57E+01	3.05E+01
ENSMUSG00000034898	Filip1	3.93E-08	2.65E-07	5.68	6.19E+00	1.09E+00
ENSMUSG00000052270	Fpr2	4.00E-08	2.70E-07	8.40	8.03E+01	9.56E+00
ENSMUSG00000021453	Gadd45g	4.09E-08	2.76E-07	7.21	6.45E+03	8.94E+02
ENSMUSG00000104088	Gm38275	4.12E-08	2.78E-07	4.62	6.71E+00	1.45E+00
ENSMUSG00000079014	Serpina3i	4.25E-08	2.86E-07	18.03	2.76E+00	1.53E-01
ENSMUSG00000034842	Art3	4.30E-08	2.89E-07	26.57	4.61E+00	1.73E-01
ENSMUSG00000021287	Xrcc3	4.32E-08	2.90E-07	-3.10	6.67E+00	2.07E+01
ENSMUSG00000028957	Per3	4.32E-08	2.90E-07	-2.82	1.06E+01	3.00E+01
ENSMUSG00000020185	E2f7	4.35E-08	2.92E-07	-3.19	1.43E+01	4.56E+01
ENSMUSG00000092349	Smim40	4.54E-08	3.04E-07	3.87	8.60E+00	2.22E+00
ENSMUSG00000051969	Tlr11	4.55E-08	3.04E-07	19.06	4.24E+00	2.23E-01
ENSMUSG00000072949	Acot1	4.59E-08	3.06E-07	-9.08	1.02E+00	9.29E+00
ENSMUSG00000043391	2510009E07Rik	4.66E-08	3.11E-07	-2.43	5.55E+01	1.35E+02
ENSMUSG00000018169	Mfng	4.76E-08	3.17E-07	-3.12	6.03E+00	1.88E+01
ENSMUSG00000070808	Bicra	4.94E-08	3.29E-07	2.03	5.64E+01	2.78E+01
ENSMUSG00000027259	Adal	5.02E-08	3.34E-07	-2.51	8.78E+00	2.21E+01

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ENSMUSG00000020453	Patz1	5.12E-08	3.40E-07	-2.09	1.60E+01	3.34E+01
ENSMUSG00000021720	Rnf180	5.37E-08	3.56E-07	-2.11	2.43E+01	5.13E+01
ENSMUSG00000027765	P2ry1	5.41E-08	3.58E-07	-3.27	1.18E+01	3.86E+01
ENSMUSG00000004356	Utp20	5.42E-08	3.59E-07	-2.38	4.87E+01	1.16E+02
ENSMUSG00000097855	A930007I19Rik	5.68E-08	3.75E-07	2.05	6.69E+01	3.27E+01
ENSMUSG00000108461	AV356131	5.98E-08	3.95E-07	-4.82	1.68E+00	8.09E+00
ENSMUSG00000085327	Gm16104	6.12E-08	4.03E-07	-3.30	4.80E+00	1.58E+01
ENSMUSG00000030929	Eri2	6.15E-08	4.05E-07	-2.08	2.16E+01	4.49E+01
ENSMUSG00000051586	Mical3	6.24E-08	4.10E-07	-2.21	1.56E+01	3.45E+01
ENSMUSG00000040034	Nup43	6.24E-08	4.10E-07	-2.80	9.41E+00	2.63E+01
ENSMUSG00000029516	Cit	6.29E-08	4.13E-07	-2.14	6.18E+01	1.32E+02
ENSMUSG00000107586	Gm44283	6.39E-08	4.19E-07	2.66	6.29E+01	2.37E+01
ENSMUSG00000023393	Slc17a9	6.71E-08	4.39E-07	-2.35	1.25E+01	2.94E+01
ENSMUSG00000103688	Gm6321	7.06E-08	4.60E-07	13.80	3.48E+00	2.52E-01
ENSMUSG00000027456	Sdcbp2	7.19E-08	4.68E-07	4.38	1.78E+01	4.05E+00
ENSMUSG00000020895	Tmem107	7.29E-08	4.75E-07	-2.14	1.45E+01	3.12E+01
ENSMUSG00000036459	Wtip	7.30E-08	4.75E-07	-2.27	2.31E+01	5.24E+01
ENSMUSG00000074217	Misp3	7.81E-08	5.07E-07	-2.48	2.03E+01	5.05E+01
ENSMUSG00000097039	Pvt1	7.86E-08	5.10E-07	-2.30	1.62E+01	3.73E+01
ENSMUSG00000072640	Lyrm9	7.97E-08	5.16E-07	-2.42	2.11E+01	5.10E+01
ENSMUSG00000030498	Gas2	8.16E-08	5.28E-07	-2.59	6.55E+00	1.70E+01
ENSMUSG00000022718	Dgcr8	8.22E-08	5.32E-07	-2.22	4.54E+01	1.01E+02
ENSMUSG00000114761	Gm47242	8.58E-08	5.53E-07	78.35	1.20E+01	1.53E-01
ENSMUSG00000027961	Lrrc39	9.18E-08	5.91E-07	-2.46	1.45E+01	3.55E+01
ENSMUSG00000093765	Gm20658	9.37E-08	6.02E-07	-3.73	3.85E+00	1.43E+01

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ENSMUSG00000053226	Dand5	9.44E-08	6.06E-07	-2.70	5.29E+00	1.43E+01
ENSMUSG00000044345	Marveld1	9.48E-08	6.09E-07	-2.19	2.96E+01	6.47E+01
ENSMUSG00000078861	Zfp931	9.61E-08	6.16E-07	-2.55	7.25E+00	1.85E+01
ENSMUSG00000024301	Kifc5b	9.61E-08	6.16E-07	-3.47	4.06E+00	1.41E+01
ENSMUSG00000059461	Gm7331	9.62E-08	6.16E-07	4.58	1.19E+01	2.61E+00
ENSMUSG00000027654	Fam83d	9.67E-08	6.19E-07	-3.98	7.50E+00	2.99E+01
ENSMUSG00000042099	Kank3	1.01E-07	6.44E-07	-2.07	2.49E+01	5.16E+01
ENSMUSG00000021958	Pinx1	1.01E-07	6.45E-07	-2.09	7.83E+01	1.64E+02
ENSMUSG00000097705	Gm26740	1.05E-07	6.70E-07	-3.03	1.48E+01	4.47E+01
ENSMUSG00000027317	Ppp1r14d	1.07E-07	6.82E-07	18.81	3.26E+00	1.73E-01
ENSMUSG00000041911	Dlx1	1.12E-07	7.11E-07	16.95	6.22E+00	3.67E-01
ENSMUSG00000049526	Tmem202	1.15E-07	7.29E-07	2.08	5.27E+01	2.54E+01
ENSMUSG00000020589	Cyria	1.17E-07	7.40E-07	2.45	4.73E+02	1.93E+02
ENSMUSG00000020300	Cpeb4	1.18E-07	7.46E-07	2.37	2.33E+03	9.86E+02
ENSMUSG00000041859	Mcm3	1.19E-07	7.56E-07	-2.36	3.18E+02	7.51E+02
ENSMUSG00000032666	1700025G04Rik	1.19E-07	7.56E-07	-2.01	7.45E+01	1.50E+02
ENSMUSG00000008734	Gprc5b	1.27E-07	8.06E-07	2.34	1.97E+02	8.42E+01
ENSMUSG00000039994	Timeless	1.31E-07	8.27E-07	3.07	2.87E+02	9.36E+01
ENSMUSG00000031756	Cenpn	1.32E-07	8.36E-07	-2.24	2.24E+01	5.00E+01
ENSMUSG00000025870	Arl10	1.35E-07	8.52E-07	-2.05	1.54E+01	3.15E+01
ENSMUSG00000010048	Ifrd2	1.35E-07	8.52E-07	-3.10	4.85E+00	1.51E+01
ENSMUSG00000074505	Fat3	1.37E-07	8.61E-07	-2.31	3.79E+01	8.76E+01
ENSMUSG00000041396	Mettl18	1.43E-07	8.98E-07	-3.37	4.95E+00	1.67E+01
ENSMUSG00000035024	Ncapd3	1.51E-07	9.49E-07	-2.01	5.65E+01	1.13E+02
ENSMUSG00000027496	Aurka	1.55E-07	9.67E-07	-2.18	5.88E+01	1.28E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000031327	Chic1	1.56E-07	9.73E-07	10.62	4.94E+00	4.65E-01
ENSMUSG00000030207	Fam234b	1.58E-07	9.91E-07	-2.76	1.08E+01	2.99E+01
ENSMUSG00000046442	Ppm1e	1.62E-07	1.01E-06	5.46	2.41E+01	4.41E+00
ENSMUSG00000031004	Mki67	1.64E-07	1.02E-06	-2.57	1.38E+02	3.54E+02
ENSMUSG00000086513	Gvin-ps1	1.65E-07	1.03E-06	8.73	4.98E+00	5.71E-01
ENSMUSG00000030737	Slco2b1	1.68E-07	1.04E-06	-3.56	4.56E+00	1.62E+01
ENSMUSG00000085184	4933439K11Rik	1.84E-07	1.14E-06	3.13	9.66E+00	3.09E+00
ENSMUSG00000032527	Pccb	1.94E-07	1.20E-06	-2.25	1.40E+02	3.16E+02
ENSMUSG00000106472	Gm43111	2.02E-07	1.25E-06	2.19	7.36E+01	3.36E+01
ENSMUSG00000026274	Pask	2.03E-07	1.25E-06	-4.32	3.43E+00	1.48E+01
ENSMUSG00000020681	Ace	2.08E-07	1.28E-06	14.20	4.06E+00	2.86E-01
ENSMUSG00000020773	Trim47	2.13E-07	1.31E-06	-2.08	1.32E+02	2.74E+02
ENSMUSG00000105936	Gm43544	2.30E-07	1.41E-06	3.30	2.68E+01	8.13E+00
ENSMUSG00000041642	Kif21b	2.32E-07	1.42E-06	-2.26	7.09E+01	1.60E+02
ENSMUSG00000042190	Cmklr1	2.36E-07	1.44E-06	2.44	3.74E+01	1.53E+01
ENSMUSG00000021565	Slc6a19	2.40E-07	1.46E-06	4.68	1.14E+01	2.43E+00
ENSMUSG00000020808	Pimreg	2.44E-07	1.49E-06	-3.05	2.81E+01	8.57E+01
ENSMUSG00000025491	Ifitm1	2.50E-07	1.52E-06	2.99	4.56E+01	1.53E+01
ENSMUSG00000037907	Ankrd13b	2.52E-07	1.53E-06	-2.31	3.71E+01	8.58E+01
ENSMUSG00000028044	Cks1b	2.53E-07	1.54E-06	-2.01	1.32E+02	2.65E+02
ENSMUSG00000048058	Ldlrad3	2.56E-07	1.56E-06	-2.72	2.11E+01	5.74E+01
ENSMUSG00000035121	Neil2	2.60E-07	1.58E-06	-2.89	5.41E+00	1.57E+01
ENSMUSG00000020974	Pole2	2.64E-07	1.60E-06	-3.73	7.03E+00	2.63E+01
ENSMUSG00000021575	Ahrr	2.65E-07	1.60E-06	2.17	5.46E+01	2.51E+01
ENSMUSG00000055172	C1ra	2.67E-07	1.61E-06	3.35	1.52E+01	4.54E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000040321	Zfp770	2.70E-07	1.63E-06	-2.01	1.83E+01	3.69E+01
ENSMUSG00000024235	Map3k8	2.72E-07	1.64E-06	2.38	2.35E+02	9.91E+01
ENSMUSG00000039131	Gipc2	2.81E-07	1.70E-06	-3.99	2.30E+00	9.20E+00
ENSMUSG00000065080	Gm26497	2.83E-07	1.70E-06	3.30	4.07E+01	1.23E+01
ENSMUSG00000027358	Bmp2	2.84E-07	1.71E-06	4.03	8.10E+01	2.01E+01
ENSMUSG00000038323	1700066M21Rik	2.85E-07	1.72E-06	-2.06	1.50E+01	3.08E+01
ENSMUSG00000087361	0610043K17Rik	2.87E-07	1.73E-06	22.60	3.92E+00	1.73E-01
ENSMUSG00000114835	Gm48194	2.88E-07	1.73E-06	3.51	1.23E+01	3.51E+00
ENSMUSG00000107041	Gm42735	2.90E-07	1.74E-06	3.41	2.08E+01	6.09E+00
ENSMUSG00000002343	Armc6	3.24E-07	1.94E-06	-2.42	9.91E+00	2.40E+01
ENSMUSG00000089643	Gm16301	3.26E-07	1.95E-06	20.56	3.15E+00	1.53E-01
ENSMUSG00000024524	Gnal	3.32E-07	1.98E-06	3.27	2.18E+01	6.67E+00
ENSMUSG00000059277	R74862	3.39E-07	2.02E-06	-3.68	3.07E+00	1.13E+01
ENSMUSG00000020648	Dus4l	3.40E-07	2.03E-06	-3.41	3.95E+00	1.35E+01
ENSMUSG00000032782	Cntrob	3.48E-07	2.07E-06	-3.18	4.84E+00	1.54E+01
ENSMUSG00000018899	Irf1	3.69E-07	2.19E-06	4.20	1.08E+04	2.57E+03
ENSMUSG00000087593	Gm16174	3.73E-07	2.21E-06	2.85	1.75E+01	6.14E+00
ENSMUSG00000030283	St8sia1	3.75E-07	2.22E-06	12.51	4.59E+00	3.67E-01
ENSMUSG00000000562	Adora3	3.75E-07	2.22E-06	6.56	1.62E+01	2.47E+00
ENSMUSG00000015342	Xk	3.85E-07	2.28E-06	-3.32	3.39E+00	1.13E+01
ENSMUSG00000105950	Gm43679	4.09E-07	2.41E-06	3.82	8.63E+00	2.26E+00
ENSMUSG00000048142	Nat8l	4.10E-07	2.42E-06	-3.58	1.26E+01	4.53E+01
ENSMUSG00000037243	Zfp692	4.19E-07	2.47E-06	-2.24	1.63E+01	3.65E+01
ENSMUSG00000012443	Kif11	4.30E-07	2.53E-06	-2.16	4.82E+01	1.04E+02
ENSMUSG00000002076	Hsf2bp	4.36E-07	2.56E-06	4.47	1.20E+01	2.69E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000110185	Igip	4.43E-07	2.60E-06	-2.15	1.53E+01	3.28E+01
ENSMUSG00000025766	D3Ertd751e	4.66E-07	2.73E-06	-2.11	2.28E+01	4.80E+01
ENSMUSG00000071723	Gspt2	4.72E-07	2.76E-06	-2.13	1.66E+01	3.53E+01
ENSMUSG00000005470	Asf1b	4.94E-07	2.88E-06	-2.03	1.10E+02	2.24E+02
ENSMUSG00000022033	Pbk	5.02E-07	2.92E-06	-2.57	2.84E+01	7.30E+01
ENSMUSG00000022372	Sla	5.07E-07	2.95E-06	-2.64	6.69E+01	1.76E+02
ENSMUSG00000102882	Gm2065	5.11E-07	2.97E-06	27.02	5.31E+00	1.96E-01
ENSMUSG00000115142	Gm33251	5.12E-07	2.98E-06	2.62	1.74E+01	6.66E+00
ENSMUSG00000050410	Tcf19	5.14E-07	2.98E-06	-2.54	3.27E+01	8.29E+01
ENSMUSG00000030091	Nup210	5.18E-07	3.00E-06	-3.04	7.18E+00	2.18E+01
ENSMUSG00000004187	Kifc2	5.26E-07	3.05E-06	-3.26	2.97E+00	9.68E+00
ENSMUSG00000038235	F11r	5.45E-07	3.15E-06	2.16	1.09E+02	5.06E+01
ENSMUSG00000103291	Gm38235	5.46E-07	3.15E-06	4.16	1.12E+01	2.69E+00
ENSMUSG00000024013	Fgd2	5.66E-07	3.26E-06	2.06	2.87E+02	1.39E+02
ENSMUSG00000064105	Cnnm2	5.72E-07	3.29E-06	-2.03	2.93E+01	5.95E+01
ENSMUSG00000022887	Masp1	5.74E-07	3.30E-06	3.23	1.38E+01	4.27E+00
ENSMUSG00000048078	Tenm4	5.89E-07	3.38E-06	5.54	1.01E+01	1.82E+00
ENSMUSG00000042155	Klhl23	5.92E-07	3.40E-06	-5.10	3.13E+00	1.60E+01
ENSMUSG00000021591	Glrx	5.96E-07	3.42E-06	2.04	1.14E+03	5.57E+02
ENSMUSG00000022802	Lmln	5.98E-07	3.43E-06	-2.52	8.47E+00	2.14E+01
ENSMUSG00000035385	Ccl2	6.13E-07	3.51E-06	5.82	7.49E+03	1.29E+03
ENSMUSG00000022419	Deptor	6.16E-07	3.52E-06	-2.96	7.99E+01	2.37E+02
ENSMUSG00000101609	Kcnq1ot1	6.29E-07	3.59E-06	-2.11	1.54E+02	3.25E+02
ENSMUSG00000034773	Hrob	6.30E-07	3.59E-06	-2.57	1.62E+01	4.18E+01
ENSMUSG00000097115	1810019N24Rik	6.54E-07	3.72E-06	4.25	7.91E+00	1.86E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000050022	Amz1	6.76E-07	3.85E-06	-2.01	1.43E+02	2.87E+02
ENSMUSG00000027811	4930579G24Rik	6.93E-07	3.94E-06	-3.36	4.91E+00	1.65E+01
ENSMUSG00000026017	Carf	6.97E-07	3.95E-06	-2.50	1.20E+01	3.01E+01
ENSMUSG00000029730	Mcm7	7.00E-07	3.97E-06	-2.44	2.89E+02	7.06E+02
ENSMUSG00000059323	Tonsl	7.06E-07	4.00E-06	-2.98	1.64E+01	4.89E+01
ENSMUSG00000063550	Nup98	7.12E-07	4.03E-06	2.24	1.61E+02	7.17E+01
ENSMUSG00000027171	Prrg4	7.18E-07	4.06E-06	3.25	2.28E+01	7.01E+00
ENSMUSG00000023224	Serping1	7.38E-07	4.17E-06	2.82	1.52E+01	5.37E+00
ENSMUSG00000112226	Gm48786	7.48E-07	4.22E-06	3.44	1.20E+01	3.48E+00
ENSMUSG00000025577	Cbx2	7.53E-07	4.25E-06	-3.35	6.82E+00	2.29E+01
ENSMUSG00000031548	Sfrp1	7.55E-07	4.26E-06	9.21	6.35E+00	6.89E-01
ENSMUSG00000053541	Gvin-ps6	7.58E-07	4.27E-06	14.26	2.47E+00	1.73E-01
ENSMUSG00000047747	Rnf150	7.82E-07	4.40E-06	-2.74	1.50E+02	4.11E+02
ENSMUSG00000050592	Fam78a	7.82E-07	4.40E-06	-3.94	6.31E+00	2.48E+01
ENSMUSG00000049580	Tsku	7.86E-07	4.42E-06	-2.56	6.54E+00	1.68E+01
ENSMUSG00000022179	4931414P19Rik	7.94E-07	4.46E-06	2.06	3.15E+01	1.53E+01
ENSMUSG00000014786	Slc9a5	7.98E-07	4.48E-06	-2.53	7.59E+00	1.92E+01
ENSMUSG00000046567	4930430F08Rik	8.26E-07	4.62E-06	-2.07	2.09E+01	4.32E+01
ENSMUSG00000042498	Radx	8.33E-07	4.66E-06	-4.99	1.73E+00	8.66E+00
ENSMUSG00000046456	Tmem150b	8.43E-07	4.71E-06	-5.89	1.48E+00	8.71E+00
ENSMUSG00000027699	Ect2	8.54E-07	4.77E-06	-2.05	2.95E+01	6.05E+01
ENSMUSG00000050947	Amigo1	8.56E-07	4.78E-06	-3.05	4.66E+00	1.42E+01
ENSMUSG00000002055	Spag5	8.64E-07	4.82E-06	-2.46	4.16E+01	1.02E+02
ENSMUSG00000027324	Rpusd2	8.73E-07	4.87E-06	-3.53	2.50E+00	8.81E+00
ENSMUSG00000101389	Ms4a4a	8.89E-07	4.95E-06	4.73	1.07E+01	2.26E+00

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ENSMUSG00000054434	Tmem120b	9.06E-07	5.04E-06	-2.12	2.37E+01	5.02E+01
ENSMUSG00000002699	Lcp2	9.24E-07	5.13E-06	2.25	9.07E+02	4.04E+02
ENSMUSG00000086290	Snhg12	9.28E-07	5.15E-06	-2.07	3.01E+01	6.24E+01
ENSMUSG00000033450	Tagap	9.39E-07	5.21E-06	4.09	1.90E+02	4.64E+01
ENSMUSG00000023066	Rttn	9.80E-07	5.42E-06	-2.60	1.21E+01	3.13E+01
ENSMUSG00000039713	Plekhg5	9.96E-07	5.50E-06	-2.05	1.58E+01	3.24E+01
ENSMUSG00000072919	Noxred1	1.01E-06	5.58E-06	3.75	1.82E+01	4.87E+00
ENSMUSG00000098318	Lockd	1.04E-06	5.74E-06	-2.47	2.82E+01	6.96E+01
ENSMUSG00000097994	Gm26982	1.04E-06	5.75E-06	-2.05	1.93E+01	3.97E+01
ENSMUSG00000014030	Pax5	1.06E-06	5.81E-06	22.47	3.44E+00	1.53E-01
ENSMUSG00000038068	Rnf144b	1.07E-06	5.88E-06	2.51	2.26E+02	9.00E+01
ENSMUSG00000044716	Dok7	1.08E-06	5.94E-06	4.02	1.39E+01	3.46E+00
ENSMUSG00000054675	Tmem119	1.10E-06	6.06E-06	-3.19	5.00E+00	1.59E+01
ENSMUSG00000020263	Appl2	1.13E-06	6.20E-06	-2.15	1.14E+02	2.45E+02
ENSMUSG00000015217	Hmgb3	1.14E-06	6.23E-06	-2.49	1.87E+01	4.65E+01
ENSMUSG00000033508	Asprv1	1.14E-06	6.23E-06	15.83	5.13E+00	3.24E-01
ENSMUSG00000055210	Foxd2	1.17E-06	6.39E-06	-3.17	4.44E+00	1.41E+01
ENSMUSG00000113328	Gm47260	1.17E-06	6.40E-06	2.28	4.50E+01	1.98E+01
ENSMUSG00000051413	Plagl2	1.20E-06	6.54E-06	2.17	5.08E+02	2.34E+02
ENSMUSG00000025934	Gsta3	1.20E-06	6.54E-06	-2.08	2.18E+01	4.54E+01
ENSMUSG00000027488	Snta1	1.22E-06	6.64E-06	-2.06	3.79E+01	7.80E+01
ENSMUSG00000105008	Gm43652	1.22E-06	6.64E-06	2.87	2.07E+01	7.20E+00
ENSMUSG00000040084	Bub1b	1.29E-06	6.98E-06	-2.33	2.61E+01	6.08E+01
ENSMUSG00000040557	Mettl27	1.36E-06	7.32E-06	-2.42	5.24E+01	1.27E+02
ENSMUSG00000028690	Mmachc	1.38E-06	7.45E-06	-2.01	1.60E+01	3.20E+01

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ENSMUSG00000038860	Garnl3	1.41E-06	7.58E-06	2.35	1.96E+01	8.36E+00
ENSMUSG00000074738	Fndc10	1.42E-06	7.63E-06	-3.06	5.76E+00	1.76E+01
ENSMUSG00000001518	Itfg2	1.44E-06	7.74E-06	-2.10	1.20E+01	2.53E+01
ENSMUSG00000047669	Msl3l2	1.44E-06	7.75E-06	2.50	3.83E+01	1.53E+01
ENSMUSG00000032860	P2ry2	1.48E-06	7.93E-06	-2.67	5.48E+01	1.46E+02
ENSMUSG00000028630	Dyrk2	1.48E-06	7.93E-06	2.22	1.29E+03	5.80E+02
ENSMUSG00000073242	Dnmt3aos	1.48E-06	7.94E-06	2.58	1.11E+02	4.31E+01
ENSMUSG00000029490	Mfsd7a	1.56E-06	8.34E-06	2.86	8.62E+01	3.02E+01
ENSMUSG00000025586	Cpeb1	1.58E-06	8.43E-06	-2.31	1.07E+02	2.47E+02
ENSMUSG00000041498	Kif14	1.61E-06	8.58E-06	-2.78	2.40E+01	6.66E+01
ENSMUSG00000027832	Ptx3	1.61E-06	8.60E-06	3.55	1.50E+01	4.21E+00
ENSMUSG00000035900	Gramd4	1.62E-06	8.62E-06	-2.90	6.16E+00	1.79E+01
ENSMUSG00000029312	Klhl8	1.63E-06	8.69E-06	-2.30	7.93E+00	1.82E+01
ENSMUSG00000024118	Tedc2	1.64E-06	8.74E-06	-2.32	9.44E+00	2.19E+01
ENSMUSG00000092368	A930015D03Rik	1.64E-06	8.75E-06	2.49	1.35E+01	5.43E+00
ENSMUSG00000004500	Zfp324	1.66E-06	8.86E-06	2.57	3.98E+01	1.55E+01
ENSMUSG00000074934	Grem1	1.74E-06	9.24E-06	2.34	9.22E+01	3.94E+01
ENSMUSG00000039910	Cited2	1.75E-06	9.31E-06	3.70	3.58E+03	9.67E+02
ENSMUSG00000018845	Unc45b	1.82E-06	9.65E-06	18.42	3.19E+00	1.73E-01
ENSMUSG00000024730	Ms4a8a	1.83E-06	9.69E-06	16.54	3.25E+00	1.96E-01
ENSMUSG00000001630	Stk38l	1.85E-06	9.80E-06	2.24	1.14E+02	5.08E+01
ENSMUSG00000075054	Yae1d1	1.86E-06	9.83E-06	-2.38	9.57E+00	2.28E+01
ENSMUSG00000036898	Zfp157	1.86E-06	9.84E-06	-2.65	1.19E+01	3.15E+01
ENSMUSG00000049285	Mblac1	1.88E-06	9.91E-06	-2.94	7.73E+00	2.27E+01
ENSMUSG00000033762	Recql4	1.89E-06	1.00E-05	-3.69	2.23E+00	8.24E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000021367	Edn1	1.93E-06	1.02E-05	13.60	1.94E+02	1.43E+01
ENSMUSG00000044827	Tlr1	1.94E-06	1.02E-05	2.59	1.61E+02	6.23E+01
ENSMUSG00000033985	Tesk2	2.02E-06	1.06E-05	-2.75	5.93E+00	1.63E+01
ENSMUSG00000039958	Etfbkmt	2.03E-06	1.07E-05	-3.28	4.56E+00	1.49E+01
ENSMUSG00000079049	Serpinb1c	2.09E-06	1.10E-05	2.97	6.86E+01	2.31E+01
ENSMUSG00000025408	Ddit3	2.12E-06	1.11E-05	2.79	2.11E+03	7.57E+02
ENSMUSG00000114536	Gm48837	2.13E-06	1.12E-05	4.17	9.41E+00	2.26E+00
ENSMUSG00000027242	Wdr76	2.25E-06	1.18E-05	-2.54	3.57E+01	9.08E+01
ENSMUSG00000066800	Rnasel	2.28E-06	1.19E-05	2.18	7.89E+02	3.62E+02
ENSMUSG00000026950	Neb	2.29E-06	1.20E-05	13.85	4.49E+00	3.24E-01
ENSMUSG00000070997	1700055D18Rik	2.32E-06	1.21E-05	3.42	1.21E+01	3.52E+00
ENSMUSG00000045282	Tmem86b	2.34E-06	1.22E-05	2.18	1.92E+01	8.81E+00
ENSMUSG00000099757	BE692007	2.38E-06	1.24E-05	6.88	6.72E+00	9.77E-01
ENSMUSG00000099974	Bcl2a1d	2.39E-06	1.25E-05	7.59	1.52E+01	2.00E+00
ENSMUSG00000037649	H2-DMa	2.40E-06	1.25E-05	2.08	4.26E+02	2.05E+02
ENSMUSG00000112093	Gm47941	2.51E-06	1.31E-05	9.94	2.51E+00	2.52E-01
ENSMUSG00000103772	Gm36933	2.53E-06	1.31E-05	2.96	1.15E+01	3.89E+00
ENSMUSG00000066647	Gm5113	2.57E-06	1.33E-05	-3.14	3.51E+00	1.10E+01
ENSMUSG00000018925	Heatr9	2.58E-06	1.34E-05	16.10	3.16E+00	1.96E-01
ENSMUSG00000040350	Trim7	2.72E-06	1.41E-05	-3.01	5.16E+00	1.55E+01
ENSMUSG00000038252	Ncapd2	2.73E-06	1.41E-05	-2.22	2.02E+02	4.49E+02
ENSMUSG00000071324	Armc2	2.78E-06	1.44E-05	-2.30	1.43E+01	3.28E+01
ENSMUSG00000100954	Gm10138	2.81E-06	1.45E-05	-2.22	1.02E+01	2.27E+01
ENSMUSG00000056394	Lig1	2.87E-06	1.48E-05	-2.03	7.99E+02	1.62E+03
ENSMUSG00000034800	Zfp661	2.87E-06	1.48E-05	-2.97	3.78E+00	1.12E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000046080	Clec9a	2.96E-06	1.52E-05	13.13	1.27E+01	9.64E-01
ENSMUSG00000025912	Mybl1	2.97E-06	1.53E-05	-2.52	1.04E+01	2.62E+01
ENSMUSG00000027715	Ccna2	3.00E-06	1.54E-05	-2.33	9.80E+01	2.29E+02
ENSMUSG00000073627	C130036L24Rik	3.00E-06	1.54E-05	-2.62	4.25E+00	1.11E+01
ENSMUSG00000022583	Ly6f	3.02E-06	1.55E-05	13.13	2.28E+00	1.73E-01
ENSMUSG00000099470	Gm29340	3.03E-06	1.55E-05	3.19	2.08E+01	6.51E+00
ENSMUSG00000027570	Col9a3	3.05E-06	1.56E-05	8.77	6.33E+00	7.21E-01
ENSMUSG00000106209	Gm42918	3.08E-06	1.58E-05	3.45	9.07E+00	2.63E+00
ENSMUSG00000059772	Slx1b	3.14E-06	1.61E-05	-2.03	2.11E+01	4.27E+01
ENSMUSG00000042215	Bag2	3.26E-06	1.66E-05	-2.75	5.90E+00	1.62E+01
ENSMUSG00000028696	Ipp	3.29E-06	1.68E-05	-2.65	5.13E+00	1.36E+01
ENSMUSG00000039431	Mtmr7	3.34E-06	1.70E-05	4.08	1.51E+01	3.70E+00
ENSMUSG00000026641	Usf1	3.38E-06	1.72E-05	2.23	3.20E+01	1.43E+01
ENSMUSG00000033952	Aspm	3.40E-06	1.73E-05	-3.18	5.43E+01	1.72E+02
ENSMUSG00000036964	Trim17	3.42E-06	1.74E-05	10.19	5.31E+00	5.22E-01
ENSMUSG00000113017	Gm46401	3.44E-06	1.75E-05	7.21	9.42E+00	1.31E+00
ENSMUSG00000036882	Arhgap33	3.47E-06	1.76E-05	-4.67	1.67E+00	7.82E+00
ENSMUSG00000040978	Gm11992	3.48E-06	1.77E-05	6.13	6.36E+00	1.04E+00
ENSMUSG00000038351	Sgsm2	3.50E-06	1.78E-05	-2.32	1.51E+01	3.51E+01
ENSMUSG00000030313	Dennd5b	3.56E-06	1.80E-05	-2.29	1.16E+01	2.65E+01
ENSMUSG00000042641	Rgsl1	3.60E-06	1.82E-05	2.47	1.59E+01	6.46E+00
ENSMUSG00000108291	Gm44292	3.65E-06	1.85E-05	3.84	3.20E+02	8.32E+01
ENSMUSG00000017861	Mybl2	3.87E-06	1.95E-05	-3.83	4.76E+00	1.82E+01
ENSMUSG00000028718	Stil	3.97E-06	2.00E-05	-2.26	2.68E+01	6.06E+01
ENSMUSG00000029189	Sel1l3	4.07E-06	2.05E-05	-2.56	1.16E+01	2.97E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000031442	Mcf2l	4.16E-06	2.10E-05	2.51	1.46E+01	5.80E+00
ENSMUSG00000026077	Npas2	4.20E-06	2.11E-05	-2.77	5.51E+00	1.52E+01
ENSMUSG00000044702	Palb2	4.21E-06	2.12E-05	-3.10	6.59E+00	2.04E+01
ENSMUSG00000026134	Prim2	4.30E-06	2.16E-05	-2.02	3.89E+01	7.87E+01
ENSMUSG00000078521	Aunip	4.31E-06	2.16E-05	-2.53	1.70E+01	4.30E+01
ENSMUSG00000027379	Bub1	4.32E-06	2.17E-05	-2.24	3.66E+01	8.19E+01
ENSMUSG00000025950	Idh1	4.36E-06	2.19E-05	-2.01	5.50E+02	1.10E+03
ENSMUSG00000026622	Nek2	4.51E-06	2.25E-05	-2.46	1.88E+01	4.62E+01
ENSMUSG00000020692	Nle1	4.53E-06	2.27E-05	-2.26	1.33E+01	3.00E+01
ENSMUSG00000025395	Prim1	4.62E-06	2.31E-05	-2.10	3.67E+01	7.70E+01
ENSMUSG00000022881	Rfc4	4.62E-06	2.31E-05	-2.16	2.21E+01	4.77E+01
ENSMUSG00000051378	Kif18b	4.64E-06	2.32E-05	-2.66	8.05E+00	2.14E+01
ENSMUSG00000097734	nan	4.85E-06	2.42E-05	-2.92	3.23E+00	9.44E+00
ENSMUSG00000037640	Zfp60	4.86E-06	2.42E-05	-2.15	1.01E+01	2.18E+01
ENSMUSG00000028680	Plk3	4.86E-06	2.42E-05	-2.74	1.76E+01	4.83E+01
ENSMUSG00000102776	Gm38162	4.89E-06	2.43E-05	4.36	1.14E+01	2.62E+00
ENSMUSG00000102749	Gm37598	4.92E-06	2.45E-05	3.02	2.71E+01	8.98E+00
ENSMUSG00000051235	Gen1	4.94E-06	2.45E-05	-2.10	2.64E+01	5.54E+01
ENSMUSG00000026096	Osgepl1	5.11E-06	2.53E-05	-2.62	8.50E+00	2.23E+01
ENSMUSG00000035186	Ubd	5.21E-06	2.58E-05	11.57	2.27E+00	1.96E-01
ENSMUSG00000104272	Gm38297	5.27E-06	2.61E-05	6.79	7.98E+00	1.18E+00
ENSMUSG00000037846	Rtkn2	5.27E-06	2.61E-05	-10.89	3.40E-01	3.70E+00
ENSMUSG00000085135	Lrrc55os	5.38E-06	2.66E-05	25.99	3.98E+00	1.53E-01
ENSMUSG00000057541	Pus7	5.39E-06	2.66E-05	-2.28	2.37E+01	5.42E+01
ENSMUSG00000024617	Camk2a	5.39E-06	2.66E-05	-2.37	8.42E+00	2.00E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000049823	Zbtb12	5.45E-06	2.69E-05	-2.18	1.12E+01	2.44E+01
ENSMUSG00000020381	Mrnip	5.60E-06	2.76E-05	-2.63	1.00E+01	2.64E+01
ENSMUSG00000050174	Nudt6	5.72E-06	2.81E-05	-2.16	1.43E+01	3.08E+01
ENSMUSG00000029385	Ccng2	5.84E-06	2.87E-05	2.28	4.83E+02	2.12E+02
ENSMUSG00000028933	Xrcc2	5.88E-06	2.89E-05	-3.05	5.50E+00	1.67E+01
ENSMUSG00000003779	Kif20a	5.96E-06	2.92E-05	-2.67	4.24E+01	1.13E+02
ENSMUSG00000085355	3010003L21Rik	5.99E-06	2.94E-05	-2.28	6.43E+00	1.47E+01
ENSMUSG00000085295	4930430E12Rik	6.10E-06	2.99E-05	2.67	1.41E+02	5.29E+01
ENSMUSG00000060301	2610008E11Rik	6.29E-06	3.07E-05	-2.11	1.27E+01	2.69E+01
ENSMUSG00000087660	B230398E01Rik	6.35E-06	3.10E-05	2.18	1.98E+01	9.06E+00
ENSMUSG00000084964	Gm15503	6.35E-06	3.10E-05	-2.86	8.01E+00	2.29E+01
ENSMUSG00000032561	Acpp	6.44E-06	3.14E-05	-5.05	1.49E+00	7.52E+00
ENSMUSG00000109679	Gm45342	6.44E-06	3.14E-05	2.58	2.16E+01	8.40E+00
ENSMUSG00000032489	Kif9	6.50E-06	3.17E-05	2.80	3.55E+01	1.27E+01
ENSMUSG00000010751	Tnfrsf22	6.54E-06	3.19E-05	-2.10	1.09E+01	2.30E+01
ENSMUSG00000073236	2500004C02Rik	6.84E-06	3.33E-05	-2.29	8.17E+00	1.87E+01
ENSMUSG00000031555	Adam9	6.88E-06	3.34E-05	2.09	4.75E+02	2.28E+02
ENSMUSG00000001053	N4bp3	7.26E-06	3.51E-05	-2.16	8.59E+00	1.86E+01
ENSMUSG00000072082	Ccnf	7.36E-06	3.55E-05	-2.03	3.55E+01	7.20E+01
ENSMUSG00000040829	Zmynd15	7.42E-06	3.58E-05	2.26	3.45E+01	1.52E+01
ENSMUSG00000106054	Gm43623	7.43E-06	3.59E-05	3.99	1.18E+01	2.96E+00
ENSMUSG00000038807	Rap1gap2	7.44E-06	3.59E-05	2.63	1.24E+01	4.70E+00
ENSMUSG00000005686	Ampd3	7.61E-06	3.66E-05	-2.72	4.91E+01	1.34E+02
ENSMUSG00000035378	Shq1	7.71E-06	3.71E-05	-2.19	9.44E+00	2.07E+01
ENSMUSG00000041552	Ptchd1	7.72E-06	3.72E-05	2.68	8.56E+01	3.19E+01

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ENSMUSG00000027353	Mcm8	7.73E-06	3.72E-05	-2.58	1.02E+01	2.63E+01
ENSMUSG00000079020	Slc45a4	7.78E-06	3.74E-05	-2.35	1.95E+01	4.58E+01
ENSMUSG00000064336	mt-Tf	7.85E-06	3.77E-05	3.88	1.38E+01	3.55E+00
ENSMUSG00000108207	1810059H22Rik	7.98E-06	3.83E-05	7.28	4.13E+00	5.68E-01
ENSMUSG00000048924	Ccdc125	8.06E-06	3.86E-05	-3.56	6.28E+00	2.24E+01
ENSMUSG00000062519	Zfp398	8.23E-06	3.94E-05	-2.39	1.50E+01	3.60E+01
ENSMUSG00000022114	Spry2	8.37E-06	4.01E-05	3.46	5.48E+02	1.58E+02
ENSMUSG00000000884	Gnb1l	8.48E-06	4.06E-05	-2.55	7.13E+00	1.82E+01
ENSMUSG00000073018	Gm1070	8.63E-06	4.12E-05	4.74	5.16E+00	1.09E+00
ENSMUSG00000032221	Mns1	8.63E-06	4.12E-05	-2.49	1.50E+01	3.74E+01
ENSMUSG00000057897	Camk2b	8.64E-06	4.12E-05	2.44	2.54E+01	1.04E+01
ENSMUSG00000070942	Il1rl2	8.65E-06	4.13E-05	-2.61	4.37E+00	1.14E+01
ENSMUSG00000005986	Ankrd13d	8.65E-06	4.13E-05	-2.20	1.29E+01	2.83E+01
ENSMUSG00000024575	Pde6a	8.76E-06	4.17E-05	8.60	4.09E+00	4.76E-01
ENSMUSG00000053749	Gm9920	8.76E-06	4.17E-05	-3.53	3.05E+00	1.07E+01
ENSMUSG00000097295	Hmgb1-ps8	8.82E-06	4.20E-05	-2.65	9.91E+00	2.63E+01
ENSMUSG00000055994	Nod2	8.92E-06	4.24E-05	3.86	1.62E+02	4.19E+01
ENSMUSG00000085385	Snhg17	9.11E-06	4.33E-05	-2.34	1.04E+01	2.45E+01
ENSMUSG00000029414	Kntc1	9.27E-06	4.40E-05	-2.36	1.72E+01	4.05E+01
ENSMUSG00000110344	Gm45716	9.29E-06	4.41E-05	-2.40	8.18E+00	1.96E+01
ENSMUSG00000024989	Cep55	9.41E-06	4.45E-05	-2.06	3.56E+01	7.33E+01
ENSMUSG00000033847	Pla2g4c	9.43E-06	4.46E-05	6.56	8.53E+00	1.30E+00
ENSMUSG00000038732	Mboat1	1.02E-05	4.79E-05	-2.42	2.03E+01	4.90E+01
ENSMUSG00000107017	Gm43196	1.02E-05	4.80E-05	4.26	7.19E+00	1.69E+00
ENSMUSG00000105541	Gm43136	1.03E-05	4.83E-05	4.38	4.75E+00	1.08E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000007080	Pole	1.03E-05	4.84E-05	-2.11	2.88E+01	6.07E+01
ENSMUSG00000036067	Slc2a6	1.03E-05	4.85E-05	3.18	6.60E+02	2.08E+02
ENSMUSG00000030748	Il4ra	1.05E-05	4.93E-05	2.19	1.66E+03	7.57E+02
ENSMUSG00000033316	Galnt9	1.07E-05	5.00E-05	-4.33	2.89E+00	1.25E+01
ENSMUSG00000022177	Haus4	1.08E-05	5.04E-05	-2.01	4.59E+01	9.20E+01
ENSMUSG00000020988	L2hgdh	1.09E-05	5.08E-05	-3.63	1.96E+00	7.13E+00
ENSMUSG00000019214	Chtf18	1.09E-05	5.12E-05	-2.41	1.11E+01	2.68E+01
ENSMUSG00000034640	Tiparp	1.11E-05	5.17E-05	2.25	1.31E+03	5.83E+02
ENSMUSG00000026031	Cflar	1.12E-05	5.23E-05	3.21	3.45E+03	1.07E+03
ENSMUSG00000114736	Gm47336	1.13E-05	5.25E-05	37.76	5.78E+00	1.53E-01
ENSMUSG00000020657	Dnajc27	1.17E-05	5.46E-05	-2.05	1.06E+01	2.17E+01
ENSMUSG00000002847	Pla1a	1.22E-05	5.69E-05	2.72	1.34E+01	4.90E+00
ENSMUSG00000036875	Dna2	1.22E-05	5.69E-05	-2.12	2.29E+01	4.84E+01
ENSMUSG00000040860	Crocc	1.25E-05	5.80E-05	-2.83	6.96E+00	1.97E+01
ENSMUSG00000047003	Zfp41	1.27E-05	5.88E-05	-2.22	1.14E+01	2.53E+01
ENSMUSG00000020105	Lrig3	1.28E-05	5.93E-05	-2.12	9.49E+00	2.01E+01
ENSMUSG00000100018	Gm7776	1.32E-05	6.12E-05	3.09	8.18E+00	2.64E+00
ENSMUSG00000072572	Slc39a2	1.36E-05	6.29E-05	3.89	6.40E+00	1.65E+00
ENSMUSG00000113918	Gm6566	1.37E-05	6.32E-05	3.27	7.03E+00	2.15E+00
ENSMUSG00000018334	Ksr1	1.37E-05	6.33E-05	-2.66	6.80E+00	1.81E+01
ENSMUSG00000066975	Cryba4	1.41E-05	6.51E-05	2.08	2.09E+01	1.00E+01
ENSMUSG00000036053	Fmnl2	1.44E-05	6.61E-05	2.70	2.79E+02	1.03E+02
ENSMUSG00000010342	Tex14	1.47E-05	6.73E-05	9.83	4.59E+00	4.67E-01
ENSMUSG00000043833	2900005J15Rik	1.47E-05	6.75E-05	-4.34	2.21E+00	9.58E+00
ENSMUSG00000108046	Gm43924	1.47E-05	6.76E-05	2.04	2.47E+01	1.21E+01

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ENSMUSG00000087452	Gm11998	1.49E-05	6.82E-05	9.67	3.13E+00	3.24E-01
ENSMUSG00000023826	Prkn	1.56E-05	7.13E-05	2.11	1.31E+01	6.22E+00
ENSMUSG00000028862	Map3k6	1.60E-05	7.32E-05	-2.01	1.25E+01	2.52E+01
ENSMUSG00000037216	Lipt1	1.63E-05	7.41E-05	-2.45	5.52E+00	1.35E+01
ENSMUSG00000018920	Cxcl16	1.64E-05	7.46E-05	2.14	2.37E+03	1.11E+03
ENSMUSG00000097166	9330179D12Rik	1.64E-05	7.48E-05	4.59	5.94E+00	1.29E+00
ENSMUSG00000090290	Tarbp1	1.67E-05	7.59E-05	-4.55	1.21E+00	5.52E+00
ENSMUSG00000046865	Fbl	1.68E-05	7.65E-05	-2.35	8.25E+00	1.94E+01
ENSMUSG00000049709	Nlrp10	1.70E-05	7.72E-05	2.56	3.89E+01	1.52E+01
ENSMUSG00000093277	Gm26236	1.70E-05	7.73E-05	4.34	9.53E+00	2.19E+00
ENSMUSG00000029587	Zfp12	1.76E-05	7.99E-05	-2.04	2.20E+01	4.48E+01
ENSMUSG00000037636	Slc25a43	1.80E-05	8.13E-05	2.20	3.53E+01	1.61E+01
ENSMUSG00000026942	Traf2	1.82E-05	8.23E-05	2.09	1.33E+02	6.38E+01
ENSMUSG00000060470	Adgrg3	1.83E-05	8.27E-05	-2.38	3.04E+01	7.23E+01
ENSMUSG00000027326	Knl1	1.83E-05	8.28E-05	-2.01	4.11E+01	8.27E+01
ENSMUSG00000054115	Skp2	1.85E-05	8.36E-05	-2.32	2.09E+01	4.84E+01
ENSMUSG00000030671	Pde3b	1.87E-05	8.46E-05	-2.07	6.52E+01	1.35E+02
ENSMUSG00000020042	Btbd11	1.89E-05	8.50E-05	-3.63	1.77E+00	6.44E+00
ENSMUSG00000027692	Tnik	1.95E-05	8.76E-05	3.28	2.52E+01	7.68E+00
ENSMUSG00000056476	Med12l	1.96E-05	8.80E-05	2.55	1.40E+01	5.47E+00
ENSMUSG00000108238	Gm43984	1.96E-05	8.80E-05	2.88	1.17E+01	4.07E+00
ENSMUSG00000033904	Ccp110	1.97E-05	8.84E-05	-2.34	6.08E+00	1.42E+01
ENSMUSG00000071724	Smpd5	1.97E-05	8.86E-05	-3.29	2.60E+00	8.53E+00
ENSMUSG00000051323	Pcdh19	1.97E-05	8.86E-05	2.27	2.82E+01	1.24E+01
ENSMUSG00000036949	Slc39a12	1.98E-05	8.89E-05	2.79	2.21E+01	7.94E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000002870	Mcm2	2.02E-05	9.04E-05	-2.21	1.36E+02	3.02E+02
ENSMUSG00000022686	B3gnt5	2.06E-05	9.24E-05	2.66	3.09E+01	1.16E+01
ENSMUSG00000039242	B3galnt2	2.11E-05	9.45E-05	-2.21	8.28E+00	1.83E+01
ENSMUSG00000021364	Elovl2	2.14E-05	9.53E-05	10.12	3.28E+00	3.24E-01
ENSMUSG00000021411	Pxdc1	2.14E-05	9.56E-05	-3.91	2.91E+00	1.14E+01
ENSMUSG00000073557	Ppp1r12b	2.18E-05	9.70E-05	-2.63	2.03E+01	5.34E+01
ENSMUSG00000093622	Gm20703	2.22E-05	9.87E-05	-2.10	1.07E+01	2.26E+01
ENSMUSG00000037759	Ptger2	2.22E-05	9.88E-05	-2.52	1.04E+01	2.62E+01
ENSMUSG00000055546	Timd4	2.26E-05	1.00E-04	9.00	4.17E+00	4.63E-01
ENSMUSG00000043415	Otud1	2.28E-05	1.01E-04	4.08	7.61E+02	1.87E+02
ENSMUSG00000027254	Map1a	2.29E-05	1.01E-04	-2.14	7.01E+00	1.50E+01
ENSMUSG00000087203	Gm13986	2.29E-05	1.02E-04	7.26	4.52E+00	6.23E-01
ENSMUSG00000000325	nan	2.30E-05	1.02E-04	-2.81	4.27E+00	1.20E+01
ENSMUSG00000097287	D130017N08Rik	2.32E-05	1.03E-04	-2.68	3.52E+00	9.43E+00
ENSMUSG00000020309	Chac2	2.33E-05	1.03E-04	2.14	1.80E+01	8.41E+00
ENSMUSG00000078954	Arhgap8	2.35E-05	1.04E-04	7.96	3.31E+00	4.16E-01
ENSMUSG00000044149	Nkrf	2.36E-05	1.04E-04	-2.27	7.38E+00	1.67E+01
ENSMUSG00000022146	Osmr	2.36E-05	1.04E-04	3.16	8.92E+00	2.82E+00
ENSMUSG00000014543	Klra17	2.39E-05	1.05E-04	3.99	7.85E+00	1.97E+00
ENSMUSG00000005947	Itgae	2.41E-05	1.06E-04	7.08	3.65E+00	5.15E-01
ENSMUSG00000002835	Chaf1a	2.42E-05	1.07E-04	-2.19	7.55E+01	1.65E+02
ENSMUSG00000044231	Nhlrc1	2.43E-05	1.07E-04	-3.53	5.40E+00	1.91E+01
ENSMUSG00000030134	Rasgef1a	2.45E-05	1.08E-04	-2.16	2.77E+01	5.98E+01
ENSMUSG00000097558	Gm26902	2.50E-05	1.10E-04	7.60	4.36E+00	5.74E-01
ENSMUSG00000032113	Chek1	2.57E-05	1.13E-04	-2.82	1.40E+01	3.95E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000026866	Kynu	2.58E-05	1.13E-04	5.27	1.74E+01	3.30E+00
ENSMUSG00000061603	Akap6	2.68E-05	1.17E-04	2.66	2.35E+01	8.83E+00
ENSMUSG00000097412	1810014B01Rik	2.75E-05	1.20E-04	-2.09	1.15E+01	2.40E+01
ENSMUSG00000021846	Peli2	2.83E-05	1.23E-04	-2.20	4.68E+01	1.03E+02
ENSMUSG00000022900	Ildr1	2.88E-05	1.25E-04	12.02	2.36E+00	1.96E-01
ENSMUSG00000049608	Gpr55	2.90E-05	1.26E-04	8.77	4.58E+00	5.22E-01
ENSMUSG00000051444	Bbs12	2.91E-05	1.27E-04	-6.45	9.15E-01	5.90E+00
ENSMUSG00000105161	Gm42595	2.92E-05	1.27E-04	-2.10	8.10E+00	1.70E+01
ENSMUSG00000087259	2610035D17Rik	3.00E-05	1.30E-04	-3.76	3.18E+00	1.20E+01
ENSMUSG00000017639	Rab11fip4	3.01E-05	1.31E-04	-4.17	1.21E+00	5.03E+00
ENSMUSG00000091549	Gm6548	3.03E-05	1.32E-04	2.18	1.92E+01	8.80E+00
ENSMUSG00000052125	F730043M19Rik	3.05E-05	1.32E-04	2.24	1.60E+01	7.14E+00
ENSMUSG00000006641	Slc5a6	3.06E-05	1.33E-04	-2.52	8.35E+00	2.10E+01
ENSMUSG00000109244	Gm44751	3.07E-05	1.33E-04	2.95	1.17E+01	3.99E+00
ENSMUSG00000024462	Gabbr1	3.08E-05	1.33E-04	2.72	1.10E+01	4.06E+00
ENSMUSG00000056071	S100a9	3.13E-05	1.35E-04	2.23	1.07E+02	4.80E+01
ENSMUSG00000005410	Mcm5	3.17E-05	1.37E-04	-2.11	1.73E+02	3.65E+02
ENSMUSG00000104018	4833412K13Rik	3.25E-05	1.40E-04	-3.42	4.96E+00	1.70E+01
ENSMUSG00000028841	Cnksr1	3.28E-05	1.41E-04	12.11	3.46E+00	2.86E-01
ENSMUSG00000106202	Gm43727	3.29E-05	1.42E-04	2.65	8.21E+00	3.11E+00
ENSMUSG00000062661	Ncs1	3.38E-05	1.45E-04	-2.15	8.40E+00	1.81E+01
ENSMUSG00000110360	Gm45380	3.54E-05	1.52E-04	-2.33	4.54E+00	1.06E+01
ENSMUSG00000000861	Bcl11a	3.54E-05	1.52E-04	-2.90	5.25E+00	1.52E+01
ENSMUSG00000013089	Etv5	3.55E-05	1.52E-04	-2.27	5.33E+01	1.21E+02
ENSMUSG00000040204	Pclaf	3.56E-05	1.53E-04	-2.08	1.91E+02	3.96E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000021579	Lrrc14b	3.57E-05	1.53E-04	2.53	3.41E+01	1.35E+01
ENSMUSG00000092626	9130230N09Rik	3.59E-05	1.54E-04	2.35	1.31E+01	5.57E+00
ENSMUSG00000028078	Dclk2	3.61E-05	1.54E-04	-3.33	2.32E+00	7.75E+00
ENSMUSG00000040270	Bach2	3.62E-05	1.55E-04	-3.81	5.34E+00	2.03E+01
ENSMUSG00000060568	Fam78b	3.65E-05	1.56E-04	-2.65	4.60E+00	1.22E+01
ENSMUSG00000025436	Atp23	3.76E-05	1.60E-04	-2.25	1.87E+01	4.20E+01
ENSMUSG00000042066	Tmcc2	3.78E-05	1.61E-04	-2.26	1.09E+01	2.46E+01
ENSMUSG00000003282	Plag1	3.94E-05	1.68E-04	3.22	1.23E+01	3.82E+00
ENSMUSG00000037568	Vash2	3.99E-05	1.70E-04	-2.51	6.89E+00	1.73E+01
ENSMUSG00000106951	5930430L01Rik	3.99E-05	1.70E-04	-4.26	1.57E+00	6.71E+00
ENSMUSG00000046272	Olfr1444	4.01E-05	1.70E-04	6.97	3.97E+00	5.70E-01
ENSMUSG00000038456	Dennd2a	4.02E-05	1.71E-04	2.26	3.54E+01	1.56E+01
ENSMUSG00000110647	Gm17745	4.02E-05	1.71E-04	-2.41	5.73E+00	1.38E+01
ENSMUSG00000065610	Mir29a	4.04E-05	1.72E-04	2.86	1.67E+01	5.83E+00
ENSMUSG00000066191	Anks6	4.09E-05	1.73E-04	-2.04	8.48E+00	1.73E+01
ENSMUSG00000024678	Ms4a4d	4.16E-05	1.76E-04	8.74	3.21E+00	3.67E-01
ENSMUSG00000036206	Sh3bp4	4.17E-05	1.77E-04	2.08	4.98E+01	2.40E+01
ENSMUSG00000055240	Zfp101	4.23E-05	1.79E-04	-2.40	9.73E+00	2.33E+01
ENSMUSG00000025429	Pstpip2	4.26E-05	1.80E-04	3.77	7.56E+00	2.00E+00
ENSMUSG00000028678	Kif2c	4.29E-05	1.81E-04	-2.53	2.08E+01	5.26E+01
ENSMUSG00000045381	Olfr433	4.31E-05	1.82E-04	5.70	6.14E+00	1.08E+00
ENSMUSG00000086564	Cd101	4.35E-05	1.84E-04	-2.50	5.13E+00	1.28E+01
ENSMUSG00000042213	Zfand4	4.37E-05	1.84E-04	-2.45	5.87E+00	1.44E+01
ENSMUSG00000055809	Dnaaf3	4.48E-05	1.88E-04	2.13	2.49E+01	1.17E+01
ENSMUSG00000111938	2900045O20Rik	4.52E-05	1.90E-04	4.08	7.06E+00	1.73E+00

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ENSMUSG00000067889	Sptbn2	4.63E-05	1.95E-04	12.38	4.01E+00	3.24E-01
ENSMUSG00000053263	Gm12592	4.65E-05	1.96E-04	18.44	2.82E+00	1.53E-01
ENSMUSG00000100235	Gm28557	4.66E-05	1.96E-04	-3.84	1.58E+00	6.08E+00
ENSMUSG00000097832	Gm26912	4.69E-05	1.97E-04	-3.91	2.47E+00	9.67E+00
ENSMUSG00000030046	Bmp10	4.73E-05	1.98E-04	14.44	2.84E+00	1.96E-01
ENSMUSG00000036412	Arsi	4.74E-05	1.99E-04	17.78	3.96E+00	2.23E-01
ENSMUSG00000107429	Gm44206	4.81E-05	2.02E-04	-3.89	1.94E+00	7.55E+00
ENSMUSG00000043336	Filip1l	4.83E-05	2.02E-04	2.16	5.00E+02	2.32E+02
ENSMUSG00000063889	Crem	4.87E-05	2.04E-04	2.19	3.93E+02	1.79E+02
ENSMUSG00000031200	Mtcp1	4.93E-05	2.06E-04	2.42	1.29E+01	5.32E+00
ENSMUSG00000035735	Dagla	4.94E-05	2.07E-04	-2.18	1.63E+01	3.56E+01
ENSMUSG00000039384	Dusp10	4.96E-05	2.07E-04	3.03	5.19E+01	1.71E+01
ENSMUSG00000084806	Gm15232	5.06E-05	2.11E-04	-2.71	3.16E+00	8.58E+00
ENSMUSG00000061878	Sphk1	5.13E-05	2.14E-04	3.08	2.74E+01	8.89E+00
ENSMUSG00000108359	C430039J01Rik	5.22E-05	2.18E-04	-2.22	6.38E+00	1.42E+01
ENSMUSG00000026930	Gpsm1	5.26E-05	2.19E-04	-2.10	6.75E+00	1.42E+01
ENSMUSG00000034872	Gipc3	5.31E-05	2.21E-04	7.57	2.45E+00	3.24E-01
ENSMUSG00000032940	Rbm11	5.32E-05	2.21E-04	3.69	6.13E+00	1.66E+00
ENSMUSG00000032035	Ets1	5.54E-05	2.30E-04	-2.31	8.45E+00	1.95E+01
ENSMUSG00000047583	Tyw3	5.76E-05	2.38E-04	-2.13	7.37E+00	1.57E+01
ENSMUSG00000020086	Macroh2a2	5.86E-05	2.42E-04	2.47	1.43E+01	5.81E+00
ENSMUSG00000004791	Pgf	5.87E-05	2.42E-04	4.51	1.67E+01	3.69E+00
ENSMUSG00000032783	Troap	5.89E-05	2.43E-04	-2.38	2.03E+01	4.84E+01
ENSMUSG00000113789	Gm47322	5.92E-05	2.44E-04	-8.31	4.01E-01	3.34E+00
ENSMUSG00000029158	Yipf7	6.02E-05	2.48E-04	3.13	1.12E+01	3.59E+00

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ENSMUSG00000045868	Gvin1	6.06E-05	2.49E-04	18.24	2.79E+00	1.53E-01
ENSMUSG00000028943	Espn	6.14E-05	2.52E-04	2.96	8.04E+00	2.71E+00
ENSMUSG00000104654	Gm43814	6.25E-05	2.57E-04	5.36	2.19E+02	4.08E+01
ENSMUSG00000022661	Cd200	6.28E-05	2.58E-04	3.31	1.06E+02	3.21E+01
ENSMUSG00000030677	Kif22	6.29E-05	2.58E-04	-2.20	4.12E+01	9.06E+01
ENSMUSG00000106212	Gm43112	6.41E-05	2.62E-04	3.01	1.81E+01	6.02E+00
ENSMUSG00000107946	Gm44066	6.47E-05	2.65E-04	9.73	2.78E+00	2.86E-01
ENSMUSG00000037375	Hhat	6.52E-05	2.67E-04	2.35	1.33E+01	5.65E+00
ENSMUSG00000025938	Slco5a1	6.58E-05	2.69E-04	-3.19	2.05E+00	6.53E+00
ENSMUSG00000099773	Hmgb1-rs16	6.62E-05	2.70E-04	2.45	1.45E+01	5.90E+00
ENSMUSG00000003992	Ssbp2	6.66E-05	2.72E-04	2.10	1.47E+01	7.02E+00
ENSMUSG00000048232	Fbxo10	6.80E-05	2.77E-04	-2.27	8.51E+00	1.93E+01
ENSMUSG00000116632	Magef1	6.81E-05	2.78E-04	-2.37	6.91E+00	1.64E+01
ENSMUSG00000098055	Gm26947	6.92E-05	2.82E-04	-2.43	5.18E+00	1.26E+01
ENSMUSG00000060923	Acyp2	6.98E-05	2.84E-04	3.47	7.39E+00	2.13E+00
ENSMUSG00000085882	2610507I01Rik	7.08E-05	2.88E-04	-2.77	3.68E+00	1.02E+01
ENSMUSG00000002100	Mybpc3	7.09E-05	2.88E-04	2.27	3.17E+01	1.39E+01
ENSMUSG00000108030	9530062K07Rik	7.09E-05	2.88E-04	-3.61	1.40E+00	5.06E+00
ENSMUSG00000020897	Aurkb	7.14E-05	2.90E-04	-2.05	2.47E+01	5.08E+01
ENSMUSG00000045322	Tlr9	7.19E-05	2.92E-04	8.30	3.45E+00	4.15E-01
ENSMUSG00000076431	Sox4	7.20E-05	2.92E-04	-2.15	1.94E+02	4.16E+02
ENSMUSG00000078762	Haus5	7.25E-05	2.94E-04	-2.25	4.43E+00	9.98E+00
ENSMUSG00000074863	Platr25	7.27E-05	2.94E-04	-2.20	1.12E+01	2.46E+01
ENSMUSG00000034023	Fancd2	7.28E-05	2.95E-04	-2.12	1.72E+01	3.63E+01
ENSMUSG00000021572	Cep72	7.29E-05	2.95E-04	-2.24	6.82E+00	1.52E+01

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ENSMUSG00000000028	Cdc45	7.33E-05	2.96E-04	-2.10	2.93E+01	6.17E+01
ENSMUSG00000074892	B3galt5	7.33E-05	2.97E-04	-4.16	3.42E+00	1.42E+01
ENSMUSG00000033083	Tbc1d4	7.38E-05	2.99E-04	-2.06	6.63E+01	1.37E+02
ENSMUSG00000087252	Gm14379	7.43E-05	3.00E-04	2.84	8.07E+00	2.84E+00
ENSMUSG00000085175	Gm11423	7.49E-05	3.03E-04	-2.18	7.26E+00	1.58E+01
ENSMUSG00000086184	Gm12764	7.52E-05	3.04E-04	16.28	2.49E+00	1.53E-01
ENSMUSG00000104524	Gm37333	7.53E-05	3.04E-04	-2.18	1.05E+01	2.29E+01
ENSMUSG00000102157	Gm37470	7.55E-05	3.05E-04	2.77	1.00E+01	3.62E+00
ENSMUSG00000050395	Tnfsf15	7.72E-05	3.11E-04	5.99	6.62E+01	1.10E+01
ENSMUSG00000045502	Hcar2	7.83E-05	3.15E-04	5.57	1.92E+02	3.44E+01
ENSMUSG00000062510	Nsl1	7.94E-05	3.20E-04	-2.10	1.24E+01	2.61E+01
ENSMUSG00000026778	Prkcq	8.12E-05	3.26E-04	9.08	2.29E+00	2.52E-01
ENSMUSG00000039410	Prdm16	8.17E-05	3.28E-04	-2.41	8.90E+00	2.14E+01
ENSMUSG00000025746	Il6	8.26E-05	3.31E-04	13.82	5.38E+01	3.89E+00
ENSMUSG00000046101	Mcmdc2	8.31E-05	3.33E-04	4.47	4.64E+00	1.04E+00
ENSMUSG00000104891	2510017J16Rik	8.35E-05	3.34E-04	2.25	2.13E+01	9.44E+00
ENSMUSG00000041491	Cep78	8.50E-05	3.40E-04	-2.23	1.01E+01	2.24E+01
ENSMUSG00000114980	4933432I03Rik	8.51E-05	3.40E-04	3.19	6.97E+00	2.18E+00
ENSMUSG00000027962	Vcam1	9.04E-05	3.61E-04	2.26	2.00E+02	8.87E+01
ENSMUSG00000045382	Cxcr4	9.04E-05	3.61E-04	-2.35	4.76E+02	1.12E+03
ENSMUSG00000024402	Lta	9.16E-05	3.65E-04	6.89	6.83E+00	9.90E-01
ENSMUSG00000074006	Omp	9.23E-05	3.68E-04	3.93	8.69E+00	2.21E+00
ENSMUSG00000051037	Zfp455	9.26E-05	3.69E-04	2.02	2.20E+01	1.09E+01
ENSMUSG00000044026	Slc35g1	9.31E-05	3.70E-04	-2.65	5.00E+00	1.32E+01
ENSMUSG00000073234	Gm8773	9.51E-05	3.78E-04	8.43	2.41E+00	2.86E-01

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ENSMUSG00000090556	Olfr753-ps1	9.57E-05	3.80E-04	10.35	1.79E+00	1.73E-01
ENSMUSG00000039648	Kyat1	9.67E-05	3.84E-04	-2.30	6.90E+00	1.59E+01
ENSMUSG00000048905	Bnip5	9.71E-05	3.85E-04	3.69	6.82E+00	1.85E+00
ENSMUSG00000087256	Gm15990	9.80E-05	3.88E-04	16.13	3.17E+00	1.96E-01
ENSMUSG00000105851	9130604C24Rik	9.83E-05	3.89E-04	-3.93	1.36E+00	5.36E+00
ENSMUSG00000112767	Gm47532	9.98E-05	3.95E-04	16.08	2.46E+00	1.53E-01
ENSMUSG00000099481	Xndc1	9.99E-05	3.95E-04	-2.12	1.28E+01	2.72E+01
ENSMUSG00000103284	3110080O07Rik	1.00E-04	3.97E-04	-6.32	6.53E-01	4.13E+00
ENSMUSG00000097023	Mir9-3hg	1.02E-04	4.04E-04	12.68	2.82E+00	2.23E-01
ENSMUSG00000014599	Csf1	1.02E-04	4.05E-04	2.28	1.29E+03	5.67E+02
ENSMUSG00000101462	Gm3052	1.04E-04	4.10E-04	-3.23	2.08E+00	6.73E+00
ENSMUSG00000026646	Suv39h2	1.05E-04	4.13E-04	-2.16	9.31E+00	2.01E+01
ENSMUSG00000035239	Neu3	1.06E-04	4.16E-04	2.28	1.05E+01	4.61E+00
ENSMUSG00000026532	Spta1	1.06E-04	4.18E-04	6.43	4.66E+00	7.25E-01
ENSMUSG00000112095	A130077B15Rik	1.08E-04	4.25E-04	-4.10	2.70E+00	1.11E+01
ENSMUSG00000075225	Ccdc162	1.11E-04	4.37E-04	10.33	2.30E+00	2.23E-01
ENSMUSG00000101903	Gm29291	1.11E-04	4.38E-04	-12.56	2.06E-01	2.59E+00
ENSMUSG00000064284	Cdpf1	1.13E-04	4.43E-04	-2.01	1.01E+01	2.02E+01
ENSMUSG00000109685	Gvin-ps1	1.13E-04	4.44E-04	8.43	2.41E+00	2.86E-01
ENSMUSG00000114409	Gm9042	1.17E-04	4.59E-04	3.96	6.51E+00	1.64E+00
ENSMUSG00000050350	Gpr18	1.19E-04	4.64E-04	2.92	1.45E+01	4.94E+00
ENSMUSG00000104339	C130089K02Rik	1.19E-04	4.65E-04	-3.14	2.74E+00	8.58E+00
ENSMUSG00000112571	Gm48207	1.19E-04	4.65E-04	7.42	2.72E+00	3.67E-01
ENSMUSG00000030532	Hddc3	1.19E-04	4.65E-04	-2.04	1.24E+01	2.52E+01
ENSMUSG00000045326	Fndc7	1.19E-04	4.67E-04	4.81	6.19E+00	1.29E+00

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ENSMUSG00000109428	Gm45698	1.20E-04	4.71E-04	4.40	9.21E+00	2.09E+00
ENSMUSG00000105889	Gm42776	1.22E-04	4.77E-04	13.13	4.25E+00	3.24E-01
ENSMUSG00000062345	Serpinb2	1.23E-04	4.82E-04	2.24	4.73E+01	2.11E+01
ENSMUSG00000066000	Zfp979	1.25E-04	4.86E-04	-2.67	3.54E+00	9.47E+00
ENSMUSG00000108059	Gm44369	1.25E-04	4.88E-04	4.90	6.56E+00	1.34E+00
ENSMUSG00000043953	Ccrl2	1.28E-04	4.98E-04	4.15	4.93E+03	1.19E+03
ENSMUSG00000115124	Gm49201	1.29E-04	5.01E-04	-7.70	4.01E-01	3.09E+00
ENSMUSG00000015812	Gnrh1	1.34E-04	5.18E-04	-2.55	3.53E+00	9.02E+00
ENSMUSG00000022704	Qtrt2	1.38E-04	5.34E-04	-2.12	7.09E+00	1.50E+01
ENSMUSG00000051682	Treml4	1.38E-04	5.35E-04	-2.79	4.46E+00	1.24E+01
ENSMUSG00000091764	Zfp964	1.39E-04	5.40E-04	-8.66	2.88E-01	2.49E+00
ENSMUSG00000029406	Pitpnm2	1.40E-04	5.42E-04	-2.31	5.89E+00	1.36E+01
ENSMUSG00000035458	Tnni3	1.41E-04	5.44E-04	2.45	1.06E+01	4.32E+00
ENSMUSG00000026463	Atp2b4	1.42E-04	5.49E-04	-2.31	3.28E+01	7.57E+01
ENSMUSG00000054589	Gm9949	1.45E-04	5.58E-04	-3.14	2.13E+00	6.70E+00
ENSMUSG00000043487	Acot6	1.47E-04	5.68E-04	-2.72	4.19E+00	1.14E+01
ENSMUSG00000037725	Ckap2	1.50E-04	5.76E-04	-2.45	2.05E+01	5.04E+01
ENSMUSG00000098176	Ccdc166	1.51E-04	5.80E-04	-2.55	4.75E+00	1.21E+01
ENSMUSG00000090329	Gm17160	1.51E-04	5.81E-04	2.99	9.31E+00	3.11E+00
ENSMUSG00000086150	Bach2os	1.52E-04	5.85E-04	-5.89	9.36E-01	5.51E+00
ENSMUSG00000026492	Tfb2m	1.53E-04	5.88E-04	-2.05	8.68E+00	1.78E+01
ENSMUSG00000102133	Gm37106	1.56E-04	5.99E-04	3.16	6.72E+00	2.12E+00
ENSMUSG00000045231	BC106179	1.56E-04	6.01E-04	-7.60	4.01E-01	3.05E+00
ENSMUSG00000020330	Hmmr	1.58E-04	6.07E-04	-2.15	1.11E+02	2.39E+02
ENSMUSG00000022584	Ly6c2	1.62E-04	6.22E-04	2.91	1.12E+01	3.86E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000109675	Nxpe1-ps	1.64E-04	6.28E-04	2.73	1.12E+01	4.11E+00
ENSMUSG00000032815	Fanca	1.65E-04	6.31E-04	2.04	4.80E+01	2.36E+01
ENSMUSG00000052934	Fbxo31	1.66E-04	6.34E-04	-2.17	5.83E+01	1.27E+02
ENSMUSG00000053062	Jam2	1.66E-04	6.34E-04	4.06	8.02E+00	1.98E+00
ENSMUSG00000042784	Muc1	1.68E-04	6.40E-04	7.66	3.19E+00	4.16E-01
ENSMUSG00000079808	ENSMUSG00000079808	1.68E-04	6.40E-04	11.70	1.79E+00	1.53E-01
ENSMUSG00000028794	A3galt2	1.70E-04	6.46E-04	8.34	4.82E+00	5.79E-01
ENSMUSG00000110388	Gm30329	1.70E-04	6.47E-04	-2.32	1.25E+01	2.91E+01
ENSMUSG00000110088	Gm45343	1.73E-04	6.58E-04	2.12	2.68E+01	1.27E+01
ENSMUSG00000082319	Actr3-ps	1.78E-04	6.76E-04	2.70	6.35E+00	2.35E+00
ENSMUSG00000034336	Ina	1.78E-04	6.76E-04	-3.17	2.24E+00	7.10E+00
ENSMUSG00000103507	Gm38375	1.80E-04	6.83E-04	3.97	5.10E+00	1.28E+00
ENSMUSG00000048445	Ccdc57	1.81E-04	6.85E-04	-2.53	4.62E+00	1.17E+01
ENSMUSG00000057402	Cldn34b2	1.82E-04	6.88E-04	7.78	4.77E+00	6.13E-01
ENSMUSG00000114094	Gm48375	1.84E-04	6.94E-04	2.10	1.42E+01	6.75E+00
ENSMUSG00000024421	Lama3	1.84E-04	6.94E-04	-2.86	4.55E+00	1.30E+01
ENSMUSG00000025001	Hells	1.88E-04	7.10E-04	-2.27	7.86E+01	1.78E+02
ENSMUSG00000067199	Frat1	1.92E-04	7.22E-04	-2.99	1.12E+01	3.36E+01
ENSMUSG00000063851	Rnf183	1.92E-04	7.23E-04	-6.95	4.74E-01	3.30E+00
ENSMUSG00000102059	Gm20257	1.98E-04	7.45E-04	2.40	1.31E+01	5.48E+00
ENSMUSG00000109481	Gm45130	1.98E-04	7.45E-04	2.32	8.36E+00	3.61E+00
ENSMUSG00000035299	Mid1	2.01E-04	7.55E-04	8.08	3.37E+00	4.17E-01
ENSMUSG00000087385	Frg2f1	2.06E-04	7.70E-04	-2.08	5.13E+00	1.07E+01
ENSMUSG00000032417	Rwdd2a	2.10E-04	7.83E-04	-2.32	9.45E+00	2.20E+01
ENSMUSG00000030145	Zfp248	2.16E-04	8.07E-04	-4.05	1.20E+00	4.85E+00

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ENSMUSG00000096959	4930509G22Rik	2.19E-04	8.18E-04	9.42	3.46E+00	3.67E-01
ENSMUSG00000032641	Gpr19	2.22E-04	8.29E-04	-2.08	6.21E+00	1.29E+01
ENSMUSG00000087231	E230016M11Rik	2.23E-04	8.30E-04	-2.41	3.31E+00	7.98E+00
ENSMUSG00000003309	Ap1m2	2.24E-04	8.33E-04	16.38	2.84E+00	1.73E-01
ENSMUSG00000109864	Eid3	2.25E-04	8.39E-04	-2.31	1.49E+01	3.44E+01
ENSMUSG00000051219	nan	2.33E-04	8.67E-04	10.50	3.40E+00	3.24E-01
ENSMUSG00000086287	Gm15972	2.37E-04	8.80E-04	-3.10	2.58E+00	8.00E+00
ENSMUSG00000035435	Abca17	2.40E-04	8.91E-04	10.03	2.53E+00	2.52E-01
ENSMUSG00000038930	Rccd1	2.50E-04	9.25E-04	-2.87	2.34E+00	6.74E+00
ENSMUSG00000073434	Wdr90	2.54E-04	9.38E-04	-2.62	3.79E+00	9.92E+00
ENSMUSG00000026821	Ralgds	2.58E-04	9.52E-04	2.02	1.52E+03	7.55E+02
ENSMUSG00000005824	Tnfsf14	2.60E-04	9.59E-04	2.23	5.11E+01	2.29E+01
ENSMUSG00000054931	Zkscan4	2.64E-04	9.72E-04	-8.20	4.74E-01	3.89E+00
ENSMUSG00000044339	Alkbh2	2.65E-04	9.77E-04	-2.03	7.33E+00	1.49E+01
ENSMUSG00000038777	Sema6c	2.66E-04	9.78E-04	-6.72	4.01E-01	2.70E+00
ENSMUSG00000097636	Mirt1	2.73E-04	1.00E-03	-2.98	3.94E+00	1.17E+01
ENSMUSG00000022586	Ly6i	2.74E-04	1.01E-03	7.64	3.19E+00	4.17E-01
ENSMUSG00000044033	Ccdc141	2.75E-04	1.01E-03	4.03	4.58E+00	1.14E+00
ENSMUSG00000024121	Atp6v0c	2.79E-04	1.02E-03	2.12	1.11E+01	5.22E+00
ENSMUSG00000075511	1700001L05Rik	2.84E-04	1.04E-03	-3.29	2.05E+00	6.73E+00
ENSMUSG00000097128	nan	2.89E-04	1.06E-03	5.57	2.60E+00	4.67E-01
ENSMUSG00000020838	Slc6a4	2.93E-04	1.07E-03	10.50	5.39E+00	5.14E-01
ENSMUSG00000029283	Cdc7	2.97E-04	1.08E-03	-2.15	1.16E+01	2.50E+01
ENSMUSG00000000730	Dnmt3l	2.99E-04	1.09E-03	-2.94	2.57E+00	7.57E+00
ENSMUSG00000031382	Asb11	2.99E-04	1.09E-03	13.12	2.27E+00	1.73E-01

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ENSMUSG00000056749	Nfil3	3.05E-04	1.11E-03	2.46	1.84E+02	7.48E+01
ENSMUSG00000107278	Gm42600	3.06E-04	1.11E-03	-6.24	4.74E-01	2.96E+00
ENSMUSG00000025959	Klf7	3.11E-04	1.13E-03	-2.45	1.92E+02	4.70E+02
ENSMUSG00000109408	A930037H05Rik	3.11E-04	1.13E-03	-6.87	4.74E-01	3.25E+00
ENSMUSG00000110928	Gm48114	3.13E-04	1.14E-03	-4.74	9.47E-01	4.48E+00
ENSMUSG00000042745	Id1	3.14E-04	1.14E-03	2.05	2.80E+02	1.37E+02
ENSMUSG00000027983	Cyp2u1	3.18E-04	1.15E-03	-3.03	2.23E+00	6.78E+00
ENSMUSG00000051716	Apon	3.20E-04	1.16E-03	5.92	4.07E+00	6.88E-01
ENSMUSG00000103400	Gm15853	3.22E-04	1.17E-03	-2.35	6.43E+00	1.51E+01
ENSMUSG00000034614	Pik3ip1	3.31E-04	1.20E-03	2.03	9.44E+01	4.64E+01
ENSMUSG00000104164	Gm38248	3.32E-04	1.20E-03	-2.12	7.15E+00	1.52E+01
ENSMUSG00000092277	Gm19684	3.40E-04	1.23E-03	4.09	4.27E+00	1.04E+00
ENSMUSG00000050605	Zfp61	3.48E-04	1.25E-03	-2.47	7.60E+00	1.88E+01
ENSMUSG00000022197	Pdzd2	3.49E-04	1.26E-03	8.98	2.26E+00	2.52E-01
ENSMUSG00000043419	Rnf227	3.50E-04	1.26E-03	-3.08	3.63E+00	1.12E+01
ENSMUSG00000032281	Acsbg1	3.50E-04	1.26E-03	-4.03	1.69E+00	6.82E+00
ENSMUSG00000055632	Hmcn2	3.53E-04	1.27E-03	2.53	1.01E+01	3.97E+00
ENSMUSG00000090230	Gm16315	3.56E-04	1.28E-03	3.26	6.93E+00	2.13E+00
ENSMUSG00000080797	Gm15760	3.56E-04	1.28E-03	-6.42	4.01E-01	2.58E+00
ENSMUSG00000115764	Gm18811	3.66E-04	1.31E-03	2.84	1.06E+01	3.74E+00
ENSMUSG00000028031	Dkk2	3.76E-04	1.35E-03	-5.33	7.41E-01	3.95E+00
ENSMUSG00000103382	Gm37755	3.79E-04	1.36E-03	7.35	2.70E+00	3.67E-01
ENSMUSG00000086728	Man2c1os	3.80E-04	1.36E-03	-2.50	3.05E+00	7.62E+00
ENSMUSG00000046605	B3gntl1	3.82E-04	1.37E-03	-2.04	9.25E+00	1.89E+01
ENSMUSG00000020546	Stxbp4	3.86E-04	1.38E-03	-2.07	8.65E+00	1.79E+01

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ENSMUSG00000102423	Gm37465	3.89E-04	1.39E-03	-7.64	2.88E-01	2.20E+00
ENSMUSG00000021097	Clmn	4.00E-04	1.43E-03	-6.10	2.88E-01	1.76E+00
ENSMUSG00000049555	Tmie	4.01E-04	1.43E-03	2.70	9.99E+00	3.70E+00
ENSMUSG00000087263	Gm15726	4.05E-04	1.44E-03	12.60	2.80E+00	2.23E-01
ENSMUSG00000091014	Gm5244	4.09E-04	1.45E-03	2.65	1.28E+01	4.82E+00
ENSMUSG00000044628	Rnf208	4.09E-04	1.45E-03	-7.61	2.43E-01	1.85E+00
ENSMUSG00000046159	Chrm3	4.15E-04	1.47E-03	7.03	6.30E+00	8.97E-01
ENSMUSG00000043671	Dpy19l3	4.17E-04	1.48E-03	2.19	1.13E+01	5.19E+00
ENSMUSG00000018417	Myo1b	4.21E-04	1.49E-03	-2.02	2.03E+01	4.10E+01
ENSMUSG00000020834	Dhrs13	4.24E-04	1.50E-03	-2.05	8.55E+00	1.75E+01
ENSMUSG00000028555	Ttc39a	4.25E-04	1.50E-03	-2.06	9.82E+00	2.02E+01
ENSMUSG00000031549	Ido2	4.44E-04	1.57E-03	8.17	1.60E+00	1.96E-01
ENSMUSG00000024810	Il33	4.49E-04	1.58E-03	10.12	1.75E+00	1.73E-01
ENSMUSG00000025422	Agap2	4.50E-04	1.59E-03	-2.89	2.50E+00	7.22E+00
ENSMUSG00000086075	Gm15728	4.55E-04	1.60E-03	2.38	8.05E+00	3.38E+00
ENSMUSG00000063810	Alms1	4.58E-04	1.61E-03	-2.22	6.10E+00	1.35E+01
ENSMUSG00000025578	Cbx8	4.57E-04	1.61E-03	-2.51	9.57E+00	2.40E+01
ENSMUSG00000092090	Gm3294	4.61E-04	1.62E-03	10.44	1.81E+00	1.73E-01
ENSMUSG00000097804	Gm16685	4.66E-04	1.64E-03	4.35	7.07E+00	1.62E+00
ENSMUSG00000032595	Cdhr4	4.68E-04	1.64E-03	2.51	9.35E+00	3.73E+00
ENSMUSG00000074282	Zfp94	4.68E-04	1.64E-03	-2.58	3.73E+00	9.61E+00
ENSMUSG00000088689	Scarna17	4.68E-04	1.64E-03	2.49	1.45E+01	5.80E+00
ENSMUSG00000049811	Fam161a	4.73E-04	1.66E-03	-2.52	5.29E+00	1.33E+01
ENSMUSG00000051169	Rpusd3	4.77E-04	1.68E-03	-2.53	3.91E+00	9.91E+00
ENSMUSG00000039960	Rhou	4.79E-04	1.68E-03	2.16	3.53E+01	1.64E+01

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ENSMUSG00000085054	Gm15834	4.91E-04	1.72E-03	-2.65	5.87E+00	1.56E+01
ENSMUSG00000034173	Zbed5	4.96E-04	1.73E-03	-4.31	1.11E+00	4.78E+00
ENSMUSG00000001036	Epn2	5.12E-04	1.79E-03	-2.11	5.76E+00	1.22E+01
ENSMUSG00000097566	nan	5.12E-04	1.79E-03	10.15	2.26E+00	2.23E-01
ENSMUSG00000114608	Gm36161	5.12E-04	1.79E-03	3.46	7.35E+00	2.12E+00
ENSMUSG00000110920	Gm48858	5.26E-04	1.83E-03	3.14	6.30E+00	2.01E+00
ENSMUSG00000104324	Gm37320	5.39E-04	1.87E-03	3.88	6.36E+00	1.64E+00
ENSMUSG00000009248	Ascl2	5.43E-04	1.88E-03	-5.87	6.45E-01	3.78E+00
ENSMUSG00000022519	Srl	5.43E-04	1.88E-03	-2.96	2.79E+00	8.27E+00
ENSMUSG00000031949	Adat1	5.47E-04	1.90E-03	-2.71	2.13E+00	5.78E+00
ENSMUSG00000103822	6030460B20Rik	5.47E-04	1.90E-03	-4.63	1.09E+00	5.05E+00
ENSMUSG00000102672	Gm37105	5.47E-04	1.90E-03	-2.23	4.34E+00	9.66E+00
ENSMUSG00000059897	Zfp930	5.55E-04	1.92E-03	-2.08	7.72E+00	1.61E+01
ENSMUSG00000027173	Depdc7	5.57E-04	1.93E-03	-2.09	2.91E+01	6.10E+01
ENSMUSG00000027579	Srms	5.66E-04	1.96E-03	12.36	1.89E+00	1.53E-01
ENSMUSG00000116639	Gm49730	5.87E-04	2.02E-03	12.82	2.22E+00	1.73E-01
ENSMUSG00000031714	Gab1	5.90E-04	2.03E-03	-2.15	3.36E+01	7.24E+01
ENSMUSG00000030747	Dgat2	6.06E-04	2.08E-03	2.60	1.42E+01	5.46E+00
ENSMUSG00000058046	4933430I17Rik	6.09E-04	2.09E-03	2.79	1.35E+01	4.84E+00
ENSMUSG00000097885	5031434O11Rik	6.17E-04	2.11E-03	-2.34	4.23E+00	9.91E+00
ENSMUSG00000051920	Rspo2	6.20E-04	2.12E-03	2.28	1.38E+01	6.05E+00
ENSMUSG00000049134	Nrap	6.22E-04	2.13E-03	2.49	9.61E+00	3.86E+00
ENSMUSG00000105843	Gm19439	6.33E-04	2.16E-03	2.11	1.63E+01	7.72E+00
ENSMUSG00000052565	H1f3	6.34E-04	2.17E-03	-2.62	7.40E+00	1.94E+01
ENSMUSG00000063556	Gm10132	6.38E-04	2.18E-03	6.70	2.46E+00	3.67E-01

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ENSMUSG00000109051	Gm44913	6.42E-04	2.19E-03	-2.26	5.16E+00	1.17E+01
ENSMUSG00000059395	Nkapl	6.50E-04	2.22E-03	-7.14	4.01E-01	2.87E+00
ENSMUSG00000117182	Gm18068	6.61E-04	2.25E-03	3.57	1.09E+01	3.05E+00
ENSMUSG00000048911	Rnf24	6.68E-04	2.27E-03	2.04	3.94E+01	1.93E+01
ENSMUSG00000036526	Card11	6.71E-04	2.28E-03	2.92	8.13E+01	2.78E+01
ENSMUSG00000107529	Gm44291	6.90E-04	2.34E-03	2.02	5.08E+01	2.51E+01
ENSMUSG00000101452	Gm28530	7.07E-04	2.40E-03	-2.47	4.08E+00	1.01E+01
ENSMUSG00000109861	4930458B22Rik	7.21E-04	2.44E-03	10.62	1.62E+00	1.53E-01
ENSMUSG00000034171	Faah	7.30E-04	2.46E-03	10.73	3.47E+00	3.24E-01
ENSMUSG00000053128	Rnf26	7.34E-04	2.48E-03	-2.01	7.44E+00	1.50E+01
ENSMUSG00000022468	Endou	7.35E-04	2.48E-03	4.51	5.39E+00	1.20E+00
ENSMUSG00000051650	B3gnt2	7.46E-04	2.51E-03	5.10	3.78E+00	7.40E-01
ENSMUSG00000113587	Gm36287	7.48E-04	2.52E-03	4.36	4.53E+00	1.04E+00
ENSMUSG00000100121	1700025N23Rik	7.54E-04	2.54E-03	11.38	1.97E+00	1.73E-01
ENSMUSG00000041907	Gpr45	7.56E-04	2.54E-03	2.82	4.84E+00	1.72E+00
ENSMUSG00000093314	Mir5136	7.70E-04	2.59E-03	-2.46	4.99E+00	1.23E+01
ENSMUSG00000044854	1700056E22Rik	7.71E-04	2.59E-03	2.40	5.98E+00	2.49E+00
ENSMUSG00000051427	Ccdc157	7.73E-04	2.60E-03	-2.26	4.19E+00	9.45E+00
ENSMUSG00000110079	Gm45292	7.81E-04	2.62E-03	-2.65	3.04E+00	8.06E+00
ENSMUSG00000110030	Gm45546	7.91E-04	2.65E-03	-2.91	2.22E+00	6.44E+00
ENSMUSG00000047363	Cstad	7.99E-04	2.67E-03	-2.97	2.04E+00	6.06E+00
ENSMUSG00000112280	A830082N09Rik	8.02E-04	2.68E-03	-4.04	1.11E+00	4.50E+00
ENSMUSG00000106943	Dancr	8.06E-04	2.69E-03	-2.23	3.84E+00	8.57E+00
ENSMUSG00000107531	E330037G11Rik	8.06E-04	2.69E-03	-2.30	6.29E+00	1.44E+01
ENSMUSG00000032372	Plscr2	8.20E-04	2.73E-03	2.78	7.06E+00	2.54E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000066175	2510046G10Rik	8.25E-04	2.75E-03	-2.57	3.40E+00	8.73E+00
ENSMUSG00000024530	Prelid3a	8.25E-04	2.75E-03	-2.24	5.52E+00	1.24E+01
ENSMUSG00000028532	Cachd1	8.36E-04	2.78E-03	3.10	3.53E+00	1.14E+00
ENSMUSG00000059921	Unc5c	8.38E-04	2.79E-03	3.42	4.39E+00	1.28E+00
ENSMUSG00000107932	Gm44432	8.47E-04	2.82E-03	-3.47	1.80E+00	6.23E+00
ENSMUSG00000086370	Ftx	8.54E-04	2.84E-03	-2.83	1.77E+00	5.00E+00
ENSMUSG00000026303	Mlph	8.54E-04	2.84E-03	-7.44	4.01E-01	2.99E+00
ENSMUSG00000068631	Gm7676	8.62E-04	2.86E-03	6.16	3.18E+00	5.17E-01
ENSMUSG00000097061	9330151L19Rik	8.67E-04	2.88E-03	-2.46	6.09E+00	1.50E+01
ENSMUSG00000108695	Siglecl1	8.90E-04	2.95E-03	4.72	3.20E+00	6.79E-01
ENSMUSG00000019845	Tube1	8.99E-04	2.98E-03	-2.16	8.20E+00	1.77E+01
ENSMUSG00000082361	Btc	9.05E-04	3.00E-03	6.43	3.32E+00	5.17E-01
ENSMUSG00000107792	Gm43914	9.12E-04	3.02E-03	11.84	1.81E+00	1.53E-01
ENSMUSG00000078656	Vps25	9.13E-04	3.02E-03	2.04	1.13E+01	5.53E+00
ENSMUSG00000067869	Tcea1-ps1	9.34E-04	3.08E-03	2.70	6.04E+00	2.24E+00
ENSMUSG00000000303	Cdh1	9.40E-04	3.10E-03	3.87	8.13E+00	2.10E+00
ENSMUSG00000025738	Fbxl16	9.67E-04	3.18E-03	-2.60	2.52E+00	6.55E+00
ENSMUSG00000027246	Ell3	9.70E-04	3.19E-03	4.07	3.66E+00	8.98E-01
ENSMUSG00000026650	Meig1	9.79E-04	3.22E-03	2.06	7.26E+00	3.52E+00
ENSMUSG00000107759	Gm44258	9.81E-04	3.22E-03	3.09	4.93E+00	1.59E+00
ENSMUSG00000097325	Gm16897	1.00E-03	3.30E-03	6.02	2.48E+00	4.12E-01
ENSMUSG00000070691	Runx3	1.01E-03	3.31E-03	2.19	3.41E+02	1.56E+02
ENSMUSG00000030137	Tuba8	1.01E-03	3.32E-03	5.99	3.47E+00	5.79E-01
ENSMUSG00000042010	Acacb	1.01E-03	3.33E-03	3.02	4.43E+00	1.47E+00
ENSMUSG00000030159	Clec1b	1.02E-03	3.34E-03	2.03	7.19E+00	3.55E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000114828	AI463229	1.03E-03	3.37E-03	3.83	4.91E+00	1.28E+00
ENSMUSG00000105534	Gm42435	1.04E-03	3.39E-03	9.58	2.42E+00	2.52E-01
ENSMUSG00000106032	Gm42463	1.04E-03	3.42E-03	-6.39	4.74E-01	3.03E+00
ENSMUSG00000094619	Trav14d-3-dv8	1.07E-03	3.51E-03	3.50	4.55E+00	1.30E+00
ENSMUSG00000114768	Gm48857	1.13E-03	3.69E-03	17.96	2.75E+00	1.53E-01
ENSMUSG00000034538	Zfp418	1.15E-03	3.74E-03	-3.17	1.40E+00	4.43E+00
ENSMUSG00000022885	St6gal1	1.15E-03	3.74E-03	-2.22	1.28E+02	2.83E+02
ENSMUSG00000066894	Vsig10	1.16E-03	3.75E-03	-2.49	3.66E+00	9.11E+00
ENSMUSG00000074607	Tox2	1.17E-03	3.79E-03	-2.35	9.34E+01	2.20E+02
ENSMUSG00000040102	Klhl42	1.17E-03	3.80E-03	-2.11	9.38E+00	1.98E+01
ENSMUSG00000110945	Gm9856	1.18E-03	3.82E-03	-2.37	2.95E+00	6.99E+00
ENSMUSG00000048478	Spata33	1.19E-03	3.84E-03	-3.12	1.41E+00	4.38E+00
ENSMUSG00000035067	Xkr6	1.19E-03	3.86E-03	-6.50	3.40E-01	2.21E+00
ENSMUSG00000038508	Gdf15	1.20E-03	3.89E-03	-2.60	4.04E+03	1.05E+04
ENSMUSG00000098183	Gm27010	1.21E-03	3.91E-03	2.02	1.44E+01	7.13E+00
ENSMUSG00000034957	Cebpa	1.23E-03	3.95E-03	-2.03	8.62E+02	1.75E+03
ENSMUSG00000027931	Npr1	1.23E-03	3.96E-03	3.12	5.67E+00	1.82E+00
ENSMUSG00000032484	Ngp	1.25E-03	4.01E-03	2.18	3.26E+01	1.49E+01
ENSMUSG00000024228	Nudt12	1.25E-03	4.03E-03	-2.40	3.41E+00	8.19E+00
ENSMUSG00000058773	H1f5	1.29E-03	4.12E-03	-2.99	3.24E+00	9.69E+00
ENSMUSG00000085316	D330050G23Rik	1.29E-03	4.13E-03	2.36	8.78E+00	3.72E+00
ENSMUSG00000110378	Gm45242	1.29E-03	4.14E-03	3.11	4.48E+00	1.44E+00
ENSMUSG00000087249	Gm16062	1.29E-03	4.15E-03	-3.15	2.50E+00	7.85E+00
ENSMUSG00000017607	Tns4	1.29E-03	4.15E-03	-2.53	2.86E+00	7.25E+00
ENSMUSG00000079018	Ly6c1	1.30E-03	4.16E-03	3.97	2.47E+00	6.20E-01

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ENSMUSG00000026494	Kif26b	1.31E-03	4.18E-03	-2.72	2.31E+00	6.28E+00
ENSMUSG00000054939	Zfp174	1.32E-03	4.23E-03	-3.04	1.94E+00	5.91E+00
ENSMUSG00000084910	C630043F03Rik	1.35E-03	4.30E-03	-8.73	2.06E-01	1.80E+00
ENSMUSG00000045838	Ccdc9b	1.35E-03	4.31E-03	-5.64	4.74E-01	2.68E+00
ENSMUSG00000112294	Gm4129	1.37E-03	4.37E-03	2.81	8.28E+00	2.95E+00
ENSMUSG00000044551	9930012K11Rik	1.39E-03	4.44E-03	-2.35	3.89E+00	9.15E+00
ENSMUSG00000104060	Gm37954	1.40E-03	4.44E-03	2.39	1.11E+01	4.62E+00
ENSMUSG00000018930	Ccl4	1.41E-03	4.50E-03	4.02	9.78E+03	2.43E+03
ENSMUSG00000086015	4833417C18Rik	1.41E-03	4.50E-03	-3.09	1.67E+00	5.17E+00
ENSMUSG00000087187	Gm13431	1.42E-03	4.52E-03	-2.32	3.46E+00	8.02E+00
ENSMUSG00000048261	Gm4879	1.49E-03	4.72E-03	-2.63	2.03E+00	5.33E+00
ENSMUSG00000114169	Gm47075	1.49E-03	4.73E-03	8.50	1.67E+00	1.96E-01
ENSMUSG00000102970	Gm37349	1.50E-03	4.75E-03	-2.42	5.95E+00	1.44E+01
ENSMUSG00000036863	Syde2	1.50E-03	4.75E-03	-4.91	4.74E-01	2.33E+00
ENSMUSG00000026620	Mark1	1.51E-03	4.77E-03	2.46	5.09E+00	2.07E+00
ENSMUSG00000066829	Zfp810	1.52E-03	4.81E-03	-2.01	1.11E+01	2.23E+01
ENSMUSG00000018427	Ypel2	1.54E-03	4.85E-03	-2.03	4.33E+01	8.79E+01
ENSMUSG00000085129	5031425F14Rik	1.58E-03	4.97E-03	-3.31	1.22E+00	4.03E+00
ENSMUSG00000105031	Gm3511	1.58E-03	4.97E-03	2.05	7.12E+00	3.47E+00
ENSMUSG00000045259	Klhdc9	1.60E-03	5.03E-03	5.39	2.52E+00	4.68E-01
ENSMUSG00000020656	Grhl1	1.60E-03	5.05E-03	2.16	1.18E+01	5.49E+00
ENSMUSG00000112955	Gm48889	1.61E-03	5.05E-03	-5.31	4.01E-01	2.13E+00
ENSMUSG00000044860	Gm1123	1.63E-03	5.11E-03	5.58	2.33E+00	4.17E-01
ENSMUSG00000064984	Snord73a	1.64E-03	5.14E-03	-8.64	2.43E-01	2.10E+00
ENSMUSG00000073409	H2-Q6	1.64E-03	5.14E-03	4.52	3.51E+00	7.78E-01

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ENSMUSG00000068957	4930589L23Rik	1.69E-03	5.29E-03	3.30	4.48E+00	1.36E+00
ENSMUSG00000086851	A430108G06Rik	1.71E-03	5.35E-03	-4.06	1.02E+00	4.14E+00
ENSMUSG00000084024	Gm15937	1.74E-03	5.44E-03	-2.44	4.07E+00	9.93E+00
ENSMUSG00000116796	Gm49784	1.78E-03	5.55E-03	2.29	1.06E+01	4.61E+00
ENSMUSG00000032607	Amt	1.80E-03	5.60E-03	-6.08	4.74E-01	2.88E+00
ENSMUSG00000114070	Gm47727	1.80E-03	5.62E-03	2.70	1.45E+01	5.36E+00
ENSMUSG00000003585	Sec14l2	1.82E-03	5.67E-03	-6.24	4.01E-01	2.50E+00
ENSMUSG00000115116	Gm46496	1.83E-03	5.68E-03	4.46	2.32E+00	5.22E-01
ENSMUSG00000089774	Slc5a3	1.86E-03	5.75E-03	-2.11	1.22E+01	2.57E+01
ENSMUSG00000109876	Gm45449	1.86E-03	5.78E-03	-5.74	4.01E-01	2.30E+00
ENSMUSG00000031434	Morc4	1.87E-03	5.79E-03	-2.04	5.99E+00	1.22E+01
ENSMUSG00000037474	Dtl	1.89E-03	5.84E-03	-2.03	4.81E+01	9.78E+01
ENSMUSG00000105270	Gm42863	1.91E-03	5.90E-03	4.18	2.40E+00	5.74E-01
ENSMUSG00000114055	Gm32089	1.91E-03	5.91E-03	3.07	6.36E+00	2.07E+00
ENSMUSG00000065100	Gm26132	1.91E-03	5.91E-03	-5.23	4.74E-01	2.48E+00
ENSMUSG00000101662	Gm28499	1.94E-03	5.98E-03	-5.36	4.01E-01	2.15E+00
ENSMUSG00000020812	Snhg16	1.98E-03	6.11E-03	-2.41	4.21E+00	1.02E+01
ENSMUSG00000101024	Gm5692	2.02E-03	6.23E-03	5.80	2.67E+00	4.61E-01
ENSMUSG00000030393	Zik1	2.04E-03	6.28E-03	-3.51	1.47E+00	5.16E+00
ENSMUSG00000073590	3222401L13Rik	2.04E-03	6.28E-03	-2.66	3.09E+00	8.23E+00
ENSMUSG00000098024	Gm27003	2.05E-03	6.29E-03	-2.04	3.54E+00	7.23E+00
ENSMUSG00000029861	Fam131b	2.05E-03	6.30E-03	6.88	1.35E+00	1.96E-01
ENSMUSG00000032826	Ank2	2.07E-03	6.34E-03	2.25	1.49E+01	6.63E+00
ENSMUSG00000104693	Gm42941	2.08E-03	6.37E-03	-4.25	6.52E-01	2.77E+00
ENSMUSG00000099375	Gm28187	2.09E-03	6.40E-03	-3.26	1.04E+00	3.39E+00

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ENSMUSG00000047115	Fam221a	2.10E-03	6.43E-03	-2.50	2.45E+00	6.10E+00
ENSMUSG00000031465	Angpt2	2.13E-03	6.51E-03	2.27	1.64E+01	7.23E+00
ENSMUSG00000006435	Neurl1a	2.14E-03	6.53E-03	-3.96	9.17E-01	3.63E+00
ENSMUSG00000055567	Unc80	2.14E-03	6.55E-03	9.06	2.28E+00	2.52E-01
ENSMUSG00000097165	nan	2.15E-03	6.57E-03	-3.28	1.77E+00	5.82E+00
ENSMUSG00000024014	Pim1	2.16E-03	6.60E-03	2.07	4.18E+03	2.02E+03
ENSMUSG00000047143	Dmrta2	2.20E-03	6.70E-03	-2.57	2.13E+00	5.47E+00
ENSMUSG00000035105	Egln3	2.24E-03	6.81E-03	-2.13	4.18E+00	8.91E+00
ENSMUSG00000032648	Pygm	2.26E-03	6.87E-03	2.09	1.14E+01	5.49E+00
ENSMUSG00000048806	Ifnb1	2.26E-03	6.87E-03	11.55	6.22E+00	5.39E-01
ENSMUSG00000106115	Gm43420	2.26E-03	6.88E-03	2.19	9.54E+00	4.35E+00
ENSMUSG00000033669	Zfp7	2.26E-03	6.88E-03	-2.59	2.33E+00	6.02E+00
ENSMUSG00000014791	Elmo3	2.27E-03	6.91E-03	-5.96	2.88E-01	1.71E+00
ENSMUSG00000062040	Zfp27	2.32E-03	7.05E-03	-2.03	4.89E+00	9.94E+00
ENSMUSG00000063522	Ly6m	2.36E-03	7.15E-03	6.68	2.45E+00	3.67E-01
ENSMUSG00000106590	Gm42879	2.39E-03	7.24E-03	-3.76	1.33E+00	4.98E+00
ENSMUSG00000060512	0610040J01Rik	2.43E-03	7.34E-03	-4.74	7.52E-01	3.57E+00
ENSMUSG00000083678	Gm12989	2.45E-03	7.41E-03	3.22	3.34E+00	1.04E+00
ENSMUSG00000047842	Diras2	2.46E-03	7.43E-03	3.33	3.46E+00	1.04E+00
ENSMUSG00000058979	Hdhd5	2.48E-03	7.48E-03	-2.26	2.70E+00	6.08E+00
ENSMUSG00000069920	B3gnt9	2.49E-03	7.52E-03	-2.59	2.38E+00	6.17E+00
ENSMUSG00000000078	Klf6	2.50E-03	7.52E-03	2.29	1.70E+04	7.43E+03
ENSMUSG00000024784	Gpha2	2.53E-03	7.62E-03	10.78	1.87E+00	1.73E-01
ENSMUSG00000107216	2210412B16Rik	2.55E-03	7.66E-03	8.45	1.46E+00	1.73E-01
ENSMUSG00000019437	Tlcd1	2.60E-03	7.82E-03	-2.36	4.49E+00	1.06E+01

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ENSMUSG00000024186	Rgs11	2.61E-03	7.83E-03	-2.22	3.79E+00	8.40E+00
ENSMUSG00000105607	Gm43513	2.65E-03	7.94E-03	-6.58	4.01E-01	2.64E+00
ENSMUSG00000041444	Arhgap32	2.67E-03	7.98E-03	-2.23	6.60E+00	1.47E+01
ENSMUSG00000097149	G630030J09Rik	2.68E-03	8.01E-03	-5.20	4.01E-01	2.09E+00
ENSMUSG00000103006	4933417C20Rik	2.74E-03	8.18E-03	4.43	2.99E+00	6.74E-01
ENSMUSG00000098789	Jmjd7	2.75E-03	8.23E-03	-2.23	3.81E+00	8.50E+00
ENSMUSG00000052435	Cebpe	2.76E-03	8.23E-03	3.49	4.16E+00	1.19E+00
ENSMUSG00000113757	Gm47507	2.77E-03	8.26E-03	3.09	8.35E+00	2.70E+00
ENSMUSG00000112927	Gm48332	2.79E-03	8.32E-03	8.33	2.38E+00	2.86E-01
ENSMUSG00000104554	Gm4610	2.79E-03	8.32E-03	3.05	4.41E+00	1.44E+00
ENSMUSG00000020623	Map2k6	2.84E-03	8.45E-03	-2.28	4.85E+00	1.10E+01
ENSMUSG00000089687	Rab42	2.87E-03	8.53E-03	-2.17	3.16E+00	6.84E+00
ENSMUSG00000035769	Xylb	2.87E-03	8.54E-03	-2.02	6.80E+00	1.38E+01
ENSMUSG00000008845	Cd163	2.89E-03	8.58E-03	-2.66	2.64E+00	7.03E+00
ENSMUSG00000049353	Rd3	2.91E-03	8.65E-03	2.01	1.03E+01	5.16E+00
ENSMUSG00000030032	Wdr54	2.94E-03	8.72E-03	-2.14	4.84E+00	1.04E+01
ENSMUSG00000028128	F3	2.94E-03	8.74E-03	5.66	1.04E+01	1.83E+00
ENSMUSG00000022218	Tgm1	2.97E-03	8.81E-03	6.05	1.53E+00	2.52E-01
ENSMUSG00000020682	Mmp28	3.00E-03	8.90E-03	4.50	3.25E+00	7.22E-01
ENSMUSG00000017499	Cdc6	3.04E-03	8.99E-03	-2.14	2.19E+01	4.67E+01
ENSMUSG00000053964	Lgals4	3.06E-03	9.05E-03	-2.47	2.05E+00	5.05E+00
ENSMUSG00000055866	Per2	3.06E-03	9.06E-03	-2.34	7.03E+00	1.64E+01
ENSMUSG00000030600	Lrfn1	3.08E-03	9.10E-03	-2.34	2.53E+00	5.92E+00
ENSMUSG00000096140	Ankrd66	3.12E-03	9.22E-03	4.32	3.95E+00	9.15E-01
ENSMUSG00000087141	Plcxd2	3.14E-03	9.26E-03	2.29	9.26E+01	4.04E+01

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ENSMUSG00000035165	Kcne3	3.16E-03	9.31E-03	-3.23	1.65E+00	5.34E+00
ENSMUSG00000021090	Lrrc9	3.21E-03	9.45E-03	8.05	2.61E+00	3.24E-01
ENSMUSG00000039328	Rnf122	3.23E-03	9.51E-03	-2.09	2.87E+00	6.00E+00
ENSMUSG00000103646	Gm37706	3.26E-03	9.59E-03	2.57	6.26E+00	2.43E+00
ENSMUSG00000051074	4930579K19Rik	3.33E-03	9.76E-03	-2.24	2.51E+00	5.61E+00
ENSMUSG00000033900	Map9	3.34E-03	9.80E-03	-2.40	3.51E+00	8.42E+00
ENSMUSG00000094334	Fabp5l2	3.37E-03	9.88E-03	2.39	6.04E+00	2.53E+00
ENSMUSG00000078773	Rad54b	3.38E-03	9.89E-03	-2.05	1.16E+01	2.37E+01
ENSMUSG00000099098	1110035H17Rik	3.48E-03	1.02E-02	-2.36	2.73E+00	6.44E+00
ENSMUSG00000009628	Tex15	3.48E-03	1.02E-02	-2.95	1.40E+00	4.12E+00
ENSMUSG00000051727	Kctd14	3.52E-03	1.03E-02	3.98	3.08E+00	7.75E-01
ENSMUSG00000028133	Rwdd3	3.53E-03	1.03E-02	-2.10	3.55E+00	7.47E+00
ENSMUSG00000097842	9330104G04Rik	3.60E-03	1.05E-02	-2.29	4.13E+00	9.43E+00
ENSMUSG00000031298	Adgrg2	3.64E-03	1.06E-02	3.73	3.49E+00	9.37E-01
ENSMUSG00000067878	Map7d3	3.65E-03	1.06E-02	-3.71	8.30E-01	3.08E+00
ENSMUSG00000097773	Gm10614	3.65E-03	1.06E-02	-6.36	4.01E-01	2.55E+00
ENSMUSG00000108122	Gm44116	3.66E-03	1.06E-02	-2.36	2.68E+00	6.32E+00
ENSMUSG00000034382	AI661453	3.67E-03	1.06E-02	-2.37	2.22E+00	5.28E+00
ENSMUSG00000002799	Jag2	3.72E-03	1.08E-02	-2.51	2.22E+00	5.59E+00
ENSMUSG00000068855	H2ac20	3.77E-03	1.09E-02	-3.24	1.29E+00	4.19E+00
ENSMUSG00000065647	Gm25896	3.86E-03	1.11E-02	-3.23	1.23E+00	3.97E+00
ENSMUSG00000097632	nan	3.88E-03	1.12E-02	3.18	4.69E+00	1.48E+00
ENSMUSG00000056832	Ttc26	3.90E-03	1.12E-02	2.17	9.35E+00	4.31E+00
ENSMUSG00000085929	Gm13421	3.91E-03	1.13E-02	-4.80	4.74E-01	2.28E+00
ENSMUSG00000045968	Teddm2	3.94E-03	1.13E-02	-3.41	1.02E+00	3.47E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000053004	Hrh1	3.96E-03	1.14E-02	-3.14	1.41E+00	4.41E+00
ENSMUSG00000049109	Themis	3.96E-03	1.14E-02	7.48	1.47E+00	1.96E-01
ENSMUSG00000041064	Pif1	3.98E-03	1.14E-02	-2.33	9.48E+00	2.21E+01
ENSMUSG00000038214	Bend3	3.98E-03	1.14E-02	-2.07	4.79E+00	9.93E+00
ENSMUSG00000098702	1500015A07Rik	4.09E-03	1.17E-02	-2.08	5.17E+00	1.08E+01
ENSMUSG00000045659	Plekha7	4.20E-03	1.20E-02	3.42	3.85E+00	1.13E+00
ENSMUSG00000102863	Gm37639	4.24E-03	1.21E-02	2.20	7.44E+00	3.38E+00
ENSMUSG00000047878	A4galt	4.24E-03	1.22E-02	3.46	3.40E+00	9.85E-01
ENSMUSG00000023947	Nfkbie	4.25E-03	1.22E-02	2.60	4.84E+02	1.86E+02
ENSMUSG00000016756	Cmah	4.32E-03	1.24E-02	-2.23	9.67E+00	2.16E+01
ENSMUSG00000109708	Gm45809	4.33E-03	1.24E-02	-5.93	2.88E-01	1.71E+00
ENSMUSG00000086401	Gm15559	4.36E-03	1.24E-02	3.82	2.53E+00	6.62E-01
ENSMUSG00000084883	Ccdc85c	4.38E-03	1.25E-02	-4.06	6.60E-01	2.68E+00
ENSMUSG00000021636	Marveld2	4.39E-03	1.25E-02	5.84	3.35E+00	5.73E-01
ENSMUSG00000036186	Dipk1b	4.40E-03	1.25E-02	-2.32	2.58E+00	5.99E+00
ENSMUSG00000035266	Helq	4.43E-03	1.26E-02	-2.08	4.47E+00	9.31E+00
ENSMUSG00000101823	Gm29438	4.44E-03	1.27E-02	2.07	8.33E+00	4.03E+00
ENSMUSG00000026343	Gpr39	4.48E-03	1.28E-02	3.31	3.76E+00	1.14E+00
ENSMUSG00000102929	Gm37154	4.52E-03	1.29E-02	-3.45	1.02E+00	3.53E+00
ENSMUSG00000078768	Zfp566	4.53E-03	1.29E-02	-2.83	1.60E+00	4.52E+00
ENSMUSG00000097904	nan	4.56E-03	1.30E-02	11.80	2.32E+00	1.96E-01
ENSMUSG00000103914	Gm38073	4.57E-03	1.30E-02	10.32	1.79E+00	1.73E-01
ENSMUSG00000067928	Zfp760	4.62E-03	1.31E-02	-2.05	3.91E+00	8.02E+00
ENSMUSG00000110393	Gm36445	4.66E-03	1.32E-02	-2.68	1.95E+00	5.23E+00
ENSMUSG00000065808	nan	4.69E-03	1.33E-02	4.66	4.20E+00	9.02E-01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000042097	Zfp239	4.71E-03	1.34E-02	-5.62	3.40E-01	1.91E+00
ENSMUSG00000102840	Gm38037	4.72E-03	1.34E-02	-2.99	1.93E+00	5.77E+00
ENSMUSG00000026736	4930426L09Rik	4.75E-03	1.35E-02	3.21	4.38E+00	1.36E+00
ENSMUSG00000024486	Hbegf	4.86E-03	1.37E-02	2.82	2.12E+02	7.51E+01
ENSMUSG00000111151	Gm5120	4.91E-03	1.39E-02	2.47	5.15E+00	2.08E+00
ENSMUSG00000040464	Gtpbp10	4.93E-03	1.39E-02	-2.29	3.52E+00	8.05E+00
ENSMUSG00000054178	nan	4.93E-03	1.39E-02	-2.16	3.15E+00	6.80E+00
ENSMUSG00000032528	Vipr1	4.93E-03	1.39E-02	-4.58	5.57E-01	2.55E+00
ENSMUSG00000087351	Gm11464	4.94E-03	1.40E-02	3.45	3.34E+00	9.68E-01
ENSMUSG00000007207	Stx1a	4.98E-03	1.40E-02	-2.46	2.96E+00	7.26E+00
ENSMUSG00000031444	F10	5.02E-03	1.42E-02	2.18	7.67E+01	3.52E+01
ENSMUSG00000097944	A130014A01Rik	5.05E-03	1.42E-02	-2.49	4.47E+00	1.11E+01
ENSMUSG00000079053	Gm14010	5.08E-03	1.43E-02	13.98	2.14E+00	1.53E-01
ENSMUSG00000102207	Gm10344	5.09E-03	1.43E-02	7.87	2.25E+00	2.86E-01
ENSMUSG00000099746	Ppnr	5.09E-03	1.43E-02	2.41	4.03E+00	1.67E+00
ENSMUSG00000049791	Fzd4	5.16E-03	1.45E-02	-2.42	2.11E+00	5.11E+00
ENSMUSG00000097303	3110083C13Rik	5.16E-03	1.45E-02	-3.67	1.04E+00	3.80E+00
ENSMUSG00000041658	Rragb	5.19E-03	1.46E-02	-4.12	7.41E-01	3.05E+00
ENSMUSG00000063488	Zkscan7	5.21E-03	1.46E-02	-2.10	2.99E+00	6.28E+00
ENSMUSG00000032352	Lrrc1	5.29E-03	1.48E-02	-2.06	2.98E+00	6.12E+00
ENSMUSG00000082536	Gm13456	5.34E-03	1.49E-02	5.19	1.48E+00	2.86E-01
ENSMUSG00000055560	Zfp459	5.42E-03	1.51E-02	3.32	2.26E+00	6.79E-01
ENSMUSG00000002346	Slc25a42	5.43E-03	1.52E-02	-2.46	2.55E+00	6.28E+00
ENSMUSG00000114670	Gm18072	5.44E-03	1.52E-02	5.89	1.68E+00	2.86E-01
ENSMUSG00000112301	Gm10752	5.47E-03	1.53E-02	2.81	3.38E+00	1.21E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000010021	Kif19a	5.48E-03	1.53E-02	3.18	4.57E+00	1.44E+00
ENSMUSG00000110424	1700012D14Rik	5.51E-03	1.54E-02	-3.30	1.04E+00	3.44E+00
ENSMUSG00000019935	Slc17a8	5.52E-03	1.54E-02	2.19	6.07E+00	2.77E+00
ENSMUSG00000031562	Dctd	5.53E-03	1.54E-02	-2.09	5.12E+00	1.07E+01
ENSMUSG00000045007	Tubg2	5.55E-03	1.54E-02	-5.60	2.43E-01	1.36E+00
ENSMUSG00000065750	Gm23346	5.55E-03	1.54E-02	-2.35	1.96E+00	4.59E+00
ENSMUSG00000029848	Stra8	5.56E-03	1.55E-02	8.34	1.64E+00	1.96E-01
ENSMUSG00000108214	Gm43982	5.56E-03	1.55E-02	2.50	7.39E+00	2.95E+00
ENSMUSG00000043993	2900052L18Rik	5.56E-03	1.55E-02	-2.48	2.94E+00	7.31E+00
ENSMUSG00000104897	Gm43203	5.59E-03	1.55E-02	3.33	2.95E+00	8.85E-01
ENSMUSG00000114453	Gm17805	5.60E-03	1.56E-02	-3.41	8.27E-01	2.82E+00
ENSMUSG00000040093	Bmf	5.69E-03	1.58E-02	-2.63	3.69E+00	9.68E+00
ENSMUSG00000072573	Gm10369	5.70E-03	1.58E-02	-3.66	7.40E-01	2.71E+00
ENSMUSG00000085105	Gm12758	5.70E-03	1.58E-02	-3.82	6.50E-01	2.48E+00
ENSMUSG00000107604	Gm44041	5.75E-03	1.59E-02	-5.81	4.01E-01	2.33E+00
ENSMUSG00000086600	C030005K06Rik	5.82E-03	1.61E-02	-5.22	3.40E-01	1.77E+00
ENSMUSG00000024871	Doc2g	5.83E-03	1.62E-02	-2.78	1.39E+00	3.86E+00
ENSMUSG00000086108	Gm5602	5.88E-03	1.63E-02	-3.76	8.07E-01	3.04E+00
ENSMUSG00000035000	Dpp4	5.89E-03	1.63E-02	4.63	1.70E+00	3.67E-01
ENSMUSG00000036111	Lmo1	5.89E-03	1.63E-02	3.31	3.46E+00	1.04E+00
ENSMUSG00000011267	Zfp296	5.91E-03	1.63E-02	2.08	6.95E+00	3.35E+00
ENSMUSG00000097383	1500026H17Rik	6.10E-03	1.68E-02	2.13	7.06E+00	3.31E+00
ENSMUSG00000031906	Smpd3	6.17E-03	1.70E-02	-2.93	2.24E+00	6.56E+00
ENSMUSG00000021697	Depdc1b	6.22E-03	1.71E-02	-3.38	9.20E-01	3.11E+00
ENSMUSG00000097357	Gm16793	6.30E-03	1.73E-02	-4.36	5.51E-01	2.40E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000048012	Zfp473	6.36E-03	1.75E-02	-2.30	2.31E+00	5.30E+00
ENSMUSG00000071633	Gm4952	6.41E-03	1.76E-02	7.51	1.48E+00	1.96E-01
ENSMUSG00000050921	P2ry10	6.41E-03	1.76E-02	4.17	5.04E+00	1.21E+00
ENSMUSG00000087138	Gm15545	6.41E-03	1.76E-02	-2.84	1.79E+00	5.07E+00
ENSMUSG00000022790	Igsf11	6.45E-03	1.77E-02	2.29	6.41E+00	2.80E+00
ENSMUSG00000083649	Rasl2-9	6.46E-03	1.77E-02	-4.85	2.43E-01	1.18E+00
ENSMUSG00000075576	Gm12359	6.50E-03	1.78E-02	-4.77	3.40E-01	1.62E+00
ENSMUSG00000028602	Tnfrsf8	6.53E-03	1.79E-02	2.31	1.61E+01	6.98E+00
ENSMUSG00000073415	Gm10501	6.57E-03	1.80E-02	-2.50	1.59E+00	3.98E+00
ENSMUSG00000073437	D330041H03Rik	6.65E-03	1.82E-02	-2.95	1.31E+00	3.87E+00
ENSMUSG00000103715	4933431K14Rik	6.68E-03	1.82E-02	-3.16	1.12E+00	3.52E+00
ENSMUSG00000042826	Fgf11	6.68E-03	1.82E-02	-2.06	4.10E+00	8.45E+00
ENSMUSG00000048655	Ccdc169	6.68E-03	1.82E-02	-4.72	4.01E-01	1.89E+00
ENSMUSG00000017300	Tnnc2	6.70E-03	1.83E-02	6.07	1.53E+00	2.52E-01
ENSMUSG00000112944	Gm48885	6.71E-03	1.83E-02	-5.92	2.43E-01	1.44E+00
ENSMUSG00000032515	Csrnp1	6.71E-03	1.83E-02	3.22	1.22E+03	3.80E+02
ENSMUSG00000021779	Thrb	6.71E-03	1.83E-02	2.08	9.24E+00	4.43E+00
ENSMUSG00000052572	Dlg2	6.75E-03	1.84E-02	-3.59	7.51E-01	2.70E+00
ENSMUSG00000045319	Proser2	6.82E-03	1.86E-02	-2.86	1.40E+00	4.00E+00
ENSMUSG00000097762	4732463B04Rik	6.87E-03	1.87E-02	2.55	6.81E+00	2.68E+00
ENSMUSG00000090963	Gm17655	6.90E-03	1.88E-02	2.12	6.06E+00	2.85E+00
ENSMUSG00000085663	Gm15718	6.92E-03	1.88E-02	-2.68	1.68E+00	4.52E+00
ENSMUSG00000115743	Gm7004	6.99E-03	1.90E-02	-4.11	4.74E-01	1.95E+00
ENSMUSG00000038180	Spag4	7.20E-03	1.95E-02	-2.74	1.52E+00	4.17E+00
ENSMUSG00000035211	Xrra1	7.20E-03	1.95E-02	-3.52	1.02E+00	3.59E+00

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ENSMUSG00000116898	Gm49785	7.26E-03	1.97E-02	-3.44	9.27E-01	3.19E+00
ENSMUSG00000098609	Anxa11os	7.29E-03	1.97E-02	9.22	1.60E+00	1.73E-01
ENSMUSG00000104069	Gm37198	7.35E-03	1.99E-02	-2.05	5.69E+00	1.16E+01
ENSMUSG00000036136	Fam110c	7.35E-03	1.99E-02	2.25	1.60E+01	7.09E+00
ENSMUSG00000030446	Zfp273	7.36E-03	1.99E-02	-3.31	1.30E+00	4.31E+00
ENSMUSG00000046323	Dppa3	7.40E-03	2.00E-02	2.05	5.83E+00	2.84E+00
ENSMUSG00000015665	Awat1	7.43E-03	2.00E-02	2.06	4.98E+00	2.42E+00
ENSMUSG00000098434	2010110E17Rik	7.47E-03	2.02E-02	7.51	3.63E+00	4.83E-01
ENSMUSG00000021485	Mxd3	7.49E-03	2.02E-02	-2.32	2.88E+00	6.68E+00
ENSMUSG00000094595	Fsbp	7.60E-03	2.05E-02	-2.37	3.35E+00	7.94E+00
ENSMUSG00000087163	Gm16230	7.69E-03	2.07E-02	4.02	3.28E+00	8.17E-01
ENSMUSG00000114456	H2bc9	7.70E-03	2.07E-02	-4.80	6.44E-01	3.09E+00
ENSMUSG00000112744	Gm48880	7.77E-03	2.09E-02	-5.14	4.74E-01	2.44E+00
ENSMUSG00000017446	C1qtnf1	7.78E-03	2.09E-02	7.89	1.99E+00	2.52E-01
ENSMUSG00000015709	Arnt2	7.80E-03	2.09E-02	2.67	6.56E+00	2.46E+00
ENSMUSG00000116789	Gm49579	7.82E-03	2.10E-02	5.80	1.66E+00	2.86E-01
ENSMUSG00000115164	Gm30159	7.83E-03	2.10E-02	3.43	4.01E+00	1.17E+00
ENSMUSG00000112009	Gm48591	7.93E-03	2.13E-02	-4.72	3.40E-01	1.60E+00
ENSMUSG00000055413	H2-Q5	7.96E-03	2.13E-02	3.11	4.12E+00	1.32E+00
ENSMUSG00000085705	Gm16046	8.02E-03	2.15E-02	-2.06	4.76E+00	9.78E+00
ENSMUSG00000092241	Gm20522	8.06E-03	2.16E-02	-2.42	2.37E+00	5.73E+00
ENSMUSG00000100599	1700120C14Rik	8.08E-03	2.16E-02	-2.24	2.66E+00	5.95E+00
ENSMUSG00000040841	Six5	8.11E-03	2.17E-02	-2.51	3.03E+00	7.61E+00
ENSMUSG00000052392	Acot4	8.23E-03	2.20E-02	-5.36	2.88E-01	1.54E+00
ENSMUSG00000054598	9130230L23Rik	8.26E-03	2.20E-02	2.48	7.29E+00	2.94E+00

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ENSMUSG00000048621	Gm6377	8.33E-03	2.22E-02	2.45	3.54E+02	1.44E+02
ENSMUSG00000115543	B230362B09Rik	8.38E-03	2.23E-02	-2.02	4.42E+00	8.94E+00
ENSMUSG00000040247	Tbc1d10c	8.40E-03	2.24E-02	-4.16	6.38E-01	2.65E+00
ENSMUSG00000045662	Henmt1	8.61E-03	2.29E-02	4.90	1.59E+00	3.24E-01
ENSMUSG00000086700	Gm15747	8.72E-03	2.31E-02	2.57	3.66E+00	1.42E+00
ENSMUSG00000110156	Gm42067	8.72E-03	2.31E-02	-3.46	9.44E-01	3.27E+00
ENSMUSG00000078154	Gm12184	8.74E-03	2.32E-02	-3.42	9.16E-01	3.13E+00
ENSMUSG00000045730	Adrb2	8.84E-03	2.34E-02	-2.17	7.06E+00	1.53E+01
ENSMUSG00000099377	Gm6159	8.90E-03	2.36E-02	-4.39	3.40E-01	1.49E+00
ENSMUSG00000059058	Tma7-ps	8.92E-03	2.36E-02	2.94	2.45E+00	8.32E-01
ENSMUSG00000108625	Gm44711	8.95E-03	2.37E-02	6.27	1.23E+00	1.96E-01
ENSMUSG00000110773	Gm39326	8.96E-03	2.37E-02	2.37	6.36E+00	2.68E+00
ENSMUSG00000023045	Soat2	8.99E-03	2.38E-02	2.28	6.05E+00	2.66E+00
ENSMUSG00000104467	Gm37660	9.05E-03	2.39E-02	-2.01	5.29E+00	1.06E+01
ENSMUSG00000032487	Ptgs2	9.07E-03	2.40E-02	3.85	1.73E+03	4.48E+02
ENSMUSG00000103808	Gm37060	9.12E-03	2.41E-02	-2.74	1.59E+00	4.36E+00
ENSMUSG00000105382	Gm43339	9.14E-03	2.41E-02	-4.63	2.88E-01	1.33E+00
ENSMUSG00000115497	Gm49207	9.19E-03	2.43E-02	2.63	4.41E+00	1.67E+00
ENSMUSG00000077457	Snord65	9.20E-03	2.43E-02	-3.02	1.01E+00	3.06E+00
ENSMUSG00000045349	Sh2d5	9.28E-03	2.45E-02	3.06	8.50E+00	2.77E+00
ENSMUSG00000041377	Ninj2	9.30E-03	2.45E-02	4.71	1.96E+00	4.16E-01
ENSMUSG00000024987	Cyp26a1	9.39E-03	2.47E-02	8.07	1.40E+00	1.73E-01
ENSMUSG00000065494	Mir28a	9.54E-03	2.51E-02	4.11	2.97E+00	7.22E-01
ENSMUSG00000102919	Gm37726	9.56E-03	2.51E-02	2.31	8.99E+00	3.89E+00
ENSMUSG00000027858	Tspan2	9.60E-03	2.52E-02	-2.35	2.23E+00	5.22E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000105565	Gm43566	9.61E-03	2.52E-02	-2.29	2.13E+00	4.88E+00
ENSMUSG00000015134	Aldh1a3	9.61E-03	2.52E-02	-3.58	8.48E-01	3.03E+00
ENSMUSG00000097047	1110020A21Rik	9.68E-03	2.54E-02	-2.36	1.97E+00	4.65E+00
ENSMUSG00000049804	Armcx4	9.73E-03	2.55E-02	-3.73	5.59E-01	2.08E+00
ENSMUSG00000035298	Klhl35	9.74E-03	2.55E-02	-2.30	2.86E+00	6.59E+00
ENSMUSG00000109434	Gm44937	9.74E-03	2.55E-02	6.45	1.27E+00	1.96E-01
ENSMUSG00000051243	Islr2	9.89E-03	2.59E-02	6.07	1.53E+00	2.52E-01
ENSMUSG00000021265	Slc25a29	9.90E-03	2.59E-02	-2.77	1.82E+00	5.05E+00
ENSMUSG00000115355	4930445E18Rik	9.93E-03	2.60E-02	4.88	1.23E+00	2.52E-01
ENSMUSG00000026875	Traf1	9.93E-03	2.60E-02	2.94	3.71E+02	1.26E+02
ENSMUSG00000093862	Gm5117	1.00E-02	2.61E-02	3.09	3.39E+00	1.10E+00
ENSMUSG00000028978	Nos3	1.00E-02	2.62E-02	-3.25	8.31E-01	2.70E+00
ENSMUSG00000007655	Cav1	1.01E-02	2.62E-02	-2.15	1.82E+01	3.91E+01
ENSMUSG00000032420	Nt5e	1.01E-02	2.63E-02	-3.97	5.59E-01	2.22E+00
ENSMUSG00000100747	1700084E18Rik	1.01E-02	2.63E-02	-2.20	2.05E+00	4.51E+00
ENSMUSG00000108048	Gm43990	1.01E-02	2.64E-02	2.21	1.14E+01	5.16E+00
ENSMUSG00000097583	6430590A07Rik	1.02E-02	2.65E-02	-2.22	3.33E+00	7.40E+00
ENSMUSG00000097754	Ptgs2os2	1.02E-02	2.67E-02	2.50	3.41E+01	1.36E+01
ENSMUSG00000074824	Rslcan18	1.03E-02	2.68E-02	-3.52	6.43E-01	2.26E+00
ENSMUSG00000075270	Pde11a	1.04E-02	2.70E-02	6.81	1.95E+00	2.86E-01
ENSMUSG00000073600	Prob1	1.04E-02	2.70E-02	-3.37	7.45E-01	2.51E+00
ENSMUSG00000021719	Rgs7bp	1.05E-02	2.73E-02	-2.52	3.35E+00	8.44E+00
ENSMUSG00000039577	Nphp4	1.05E-02	2.74E-02	-3.28	1.02E+00	3.34E+00
ENSMUSG00000097060	Gm26759	1.06E-02	2.75E-02	2.67	3.46E+00	1.30E+00
ENSMUSG00000089671	Gm16537	1.07E-02	2.76E-02	-2.54	1.97E+00	5.01E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000001095	Slc13a2	1.07E-02	2.77E-02	-2.37	2.17E+00	5.14E+00
ENSMUSG00000040717	Il17rd	1.08E-02	2.78E-02	3.76	2.74E+00	7.30E-01
ENSMUSG00000038781	Stap2	1.09E-02	2.81E-02	-4.10	4.74E-01	1.94E+00
ENSMUSG00000031257	Nox1	1.09E-02	2.82E-02	3.16	3.58E+00	1.13E+00
ENSMUSG00000047238	Mageh1	1.11E-02	2.87E-02	-2.08	2.79E+00	5.80E+00
ENSMUSG00000005089	Slc1a2	1.12E-02	2.89E-02	2.74	3.99E+00	1.46E+00
ENSMUSG00000030401	Rtn2	1.13E-02	2.91E-02	2.62	7.51E+00	2.87E+00
ENSMUSG00000097635	Gm26826	1.13E-02	2.91E-02	3.16	2.99E+00	9.47E-01
ENSMUSG00000030516	Tjp1	1.13E-02	2.92E-02	2.64	5.00E+00	1.89E+00
ENSMUSG00000047911	Npm2	1.14E-02	2.93E-02	-3.22	9.18E-01	2.95E+00
ENSMUSG00000092300	Cdk3	1.15E-02	2.95E-02	2.09	6.02E+00	2.87E+00
ENSMUSG00000031613	Hpgd	1.15E-02	2.96E-02	-2.10	6.17E+00	1.30E+01
ENSMUSG00000044937	Ttc41	1.15E-02	2.96E-02	-4.49	4.74E-01	2.13E+00
ENSMUSG00000091955	Gm9844	1.15E-02	2.96E-02	3.21	2.16E+00	6.72E-01
ENSMUSG00000096351	Samd11	1.15E-02	2.97E-02	2.99	7.25E+00	2.42E+00
ENSMUSG00000028456	Unc13b	1.16E-02	2.98E-02	-2.75	1.63E+00	4.49E+00
ENSMUSG00000062704	9430002A10Rik	1.17E-02	2.99E-02	-2.70	1.72E+00	4.64E+00
ENSMUSG00000110218	Tincr	1.17E-02	3.00E-02	2.32	7.81E+00	3.37E+00
ENSMUSG00000027200	Sema6d	1.19E-02	3.04E-02	-3.05	1.58E+00	4.82E+00
ENSMUSG00000018849	Wwc1	1.19E-02	3.05E-02	2.00	1.99E+01	9.92E+00
ENSMUSG00000063060	Sox7	1.20E-02	3.08E-02	-6.22	2.43E-01	1.52E+00
ENSMUSG00000024770	Lipn	1.20E-02	3.08E-02	2.62	4.22E+00	1.61E+00
ENSMUSG00000049536	Tceal1	1.20E-02	3.08E-02	-2.02	3.20E+00	6.46E+00
ENSMUSG00000114547	Gm3226	1.20E-02	3.08E-02	-2.69	1.30E+00	3.50E+00
ENSMUSG00000054206	Gzmm	1.20E-02	3.08E-02	-3.74	7.60E-01	2.84E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000106840	Gm42790	1.22E-02	3.13E-02	6.34	1.60E+00	2.52E-01
ENSMUSG00000109297	Gm31522	1.23E-02	3.13E-02	4.81	3.26E+00	6.78E-01
ENSMUSG00000034930	Rtkn	1.24E-02	3.16E-02	-2.18	2.47E+00	5.38E+00
ENSMUSG00000007033	Hspa1l	1.24E-02	3.18E-02	2.24	9.60E+00	4.29E+00
ENSMUSG00000115656	4930556J02Rik	1.25E-02	3.20E-02	15.26	2.33E+00	1.53E-01
ENSMUSG00000023912	Slc25a27	1.26E-02	3.21E-02	-3.66	6.33E-01	2.32E+00
ENSMUSG00000032578	Cish	1.27E-02	3.23E-02	2.57	1.14E+02	4.43E+01
ENSMUSG00000069763	Tmem100	1.27E-02	3.23E-02	3.90	2.04E+00	5.22E-01
ENSMUSG00000019817	Plagl1	1.27E-02	3.24E-02	2.25	1.55E+01	6.89E+00
ENSMUSG00000003452	Bicd1	1.28E-02	3.25E-02	-2.05	3.93E+00	8.05E+00
ENSMUSG00000057766	Ankrd29	1.29E-02	3.28E-02	-2.21	1.75E+00	3.87E+00
ENSMUSG00000101191	Gm28809	1.29E-02	3.28E-02	2.45	3.77E+00	1.54E+00
ENSMUSG00000009614	Sardh	1.30E-02	3.31E-02	-2.07	3.83E+00	7.92E+00
ENSMUSG00000097892	Gm26801	1.30E-02	3.31E-02	2.45	6.01E+00	2.46E+00
ENSMUSG00000038210	Hoxa11	1.31E-02	3.31E-02	-3.69	6.49E-01	2.40E+00
ENSMUSG00000070643	Sox13	1.31E-02	3.32E-02	-3.40	7.53E-01	2.56E+00
ENSMUSG00000113601	Gm48735	1.31E-02	3.33E-02	-3.89	7.42E-01	2.88E+00
ENSMUSG00000087610	Gm16253	1.31E-02	3.33E-02	2.66	4.14E+00	1.56E+00
ENSMUSG00000035148	Gpr33	1.32E-02	3.34E-02	14.36	2.20E+00	1.53E-01
ENSMUSG00000092181	Gm20432	1.33E-02	3.37E-02	3.91	1.62E+00	4.14E-01
ENSMUSG00000088595	nan	1.34E-02	3.38E-02	4.73	1.53E+00	3.24E-01
ENSMUSG00000049532	Sall2	1.35E-02	3.40E-02	-3.13	7.47E-01	2.34E+00
ENSMUSG00000071041	Impdh2-ps	1.36E-02	3.43E-02	-2.62	1.49E+00	3.90E+00
ENSMUSG00000101875	Gm6028	1.39E-02	3.49E-02	2.77	2.97E+00	1.07E+00
ENSMUSG00000086495	Gm13778	1.39E-02	3.49E-02	-4.54	4.74E-01	2.15E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000115405	Gm41307	1.41E-02	3.55E-02	-5.35	2.43E-01	1.30E+00
ENSMUSG00000000320	Alox12	1.41E-02	3.55E-02	5.56	9.63E-01	1.73E-01
ENSMUSG00000086644	Gm13470	1.42E-02	3.56E-02	3.19	2.95E+00	9.27E-01
ENSMUSG00000043421	Hilpda	1.42E-02	3.56E-02	2.12	3.82E+03	1.81E+03
ENSMUSG00000112198	Gm4065	1.43E-02	3.58E-02	3.54	3.13E+00	8.85E-01
ENSMUSG00000082895	Rpsa-ps9	1.43E-02	3.59E-02	-4.15	2.88E-01	1.19E+00
ENSMUSG00000079457	Gm7609	1.44E-02	3.61E-02	10.46	1.60E+00	1.53E-01
ENSMUSG00000067149	Jchain	1.44E-02	3.61E-02	8.27	1.84E+00	2.23E-01
ENSMUSG00000031478	Nek3	1.44E-02	3.62E-02	-2.66	1.96E+00	5.20E+00
ENSMUSG00000113076	Gm47088	1.45E-02	3.64E-02	2.73	5.59E+00	2.04E+00
ENSMUSG00000087222	E030042O20Rik	1.46E-02	3.65E-02	-4.87	2.43E-01	1.19E+00
ENSMUSG00000098122	Gm27039	1.48E-02	3.69E-02	-3.97	3.40E-01	1.35E+00
ENSMUSG00000115480	Gm49249	1.48E-02	3.71E-02	-2.26	2.22E+00	5.02E+00
ENSMUSG00000085030	2810455O05Rik	1.50E-02	3.74E-02	-2.05	4.02E+00	8.23E+00
ENSMUSG00000095202	Gm6100	1.50E-02	3.74E-02	2.29	2.96E+00	1.29E+00
ENSMUSG00000110500	Gm32568	1.50E-02	3.75E-02	5.18	8.98E-01	1.73E-01
ENSMUSG00000070822	Zscan18	1.51E-02	3.76E-02	-2.78	1.21E+00	3.35E+00
ENSMUSG00000001420	Tmem79	1.52E-02	3.79E-02	-4.10	2.88E-01	1.18E+00
ENSMUSG00000106025	Gm42940	1.53E-02	3.81E-02	-2.61	1.37E+00	3.57E+00
ENSMUSG00000111078	Gm35028	1.53E-02	3.81E-02	10.57	1.62E+00	1.53E-01
ENSMUSG00000110575	6330537M06Rik	1.54E-02	3.83E-02	-4.50	2.88E-01	1.29E+00
ENSMUSG00000092354	Gm20548	1.54E-02	3.83E-02	5.21	1.49E+00	2.86E-01
ENSMUSG00000006586	Runx1t1	1.54E-02	3.84E-02	2.11	4.51E+00	2.14E+00
ENSMUSG00000049872	Calhm5	1.55E-02	3.86E-02	2.15	4.09E+00	1.90E+00
ENSMUSG00000073802	Cdkn2b	1.56E-02	3.87E-02	-2.15	2.05E+00	4.39E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000047369	Dnah14	1.56E-02	3.87E-02	5.77	1.13E+00	1.96E-01
ENSMUSG00000064246	Chil1	1.56E-02	3.87E-02	4.97	2.28E+00	4.58E-01
ENSMUSG00000106617	Gm36266	1.57E-02	3.90E-02	-2.08	5.06E+00	1.06E+01
ENSMUSG00000037279	Ovol2	1.59E-02	3.93E-02	8.32	1.27E+00	1.53E-01
ENSMUSG00000030606	Hapln3	1.59E-02	3.93E-02	-4.20	5.65E-01	2.37E+00
ENSMUSG00000110845	Gm47481	1.59E-02	3.93E-02	2.66	2.61E+00	9.81E-01
ENSMUSG00000103703	Gm42568	1.59E-02	3.93E-02	-4.42	2.88E-01	1.27E+00
ENSMUSG00000029343	Crybb1	1.59E-02	3.93E-02	4.12	1.71E+00	4.15E-01
ENSMUSG00000086196	Gm13571	1.59E-02	3.94E-02	4.81	4.16E+00	8.64E-01
ENSMUSG00000109154	Gm44822	1.60E-02	3.96E-02	-4.40	2.43E-01	1.07E+00
ENSMUSG00000098056	Gm8100	1.60E-02	3.96E-02	-4.24	2.88E-01	1.22E+00
ENSMUSG00000096948	Gm4221	1.61E-02	3.97E-02	-6.69	2.06E-01	1.38E+00
ENSMUSG00000115384	Gm49205	1.61E-02	3.98E-02	5.15	1.47E+00	2.86E-01
ENSMUSG00000048029	Eno4	1.62E-02	4.00E-02	3.27	2.69E+00	8.22E-01
ENSMUSG00000047945	Marcksl1	1.63E-02	4.03E-02	2.31	1.09E+03	4.73E+02
ENSMUSG00000111425	Gm47324	1.65E-02	4.08E-02	-3.01	1.06E+00	3.18E+00
ENSMUSG00000042333	Tnfrsf14	1.67E-02	4.10E-02	3.00	2.93E+00	9.79E-01
ENSMUSG00000081650	Gm16181	1.67E-02	4.12E-02	3.21	3.24E+00	1.01E+00
ENSMUSG00000105864	Gm10484	1.68E-02	4.14E-02	3.07	2.22E+00	7.23E-01
ENSMUSG00000022178	Ajuba	1.71E-02	4.19E-02	-2.09	3.58E+00	7.47E+00
ENSMUSG00000112883	Gm48023	1.71E-02	4.20E-02	4.29	1.23E+00	2.86E-01
ENSMUSG00000015314	Slamf6	1.72E-02	4.21E-02	2.80	3.22E+00	1.15E+00
ENSMUSG00000082560	Gm15157	1.73E-02	4.25E-02	2.08	9.80E+00	4.70E+00
ENSMUSG00000102662	Gm38377	1.74E-02	4.26E-02	2.05	1.77E+01	8.63E+00
ENSMUSG00000098292	Gm27194	1.74E-02	4.26E-02	4.16	1.53E+00	3.67E-01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000086391	1700042O10Rik	1.76E-02	4.30E-02	5.96	1.33E+00	2.23E-01
ENSMUSG00000027977	Ndst3	1.76E-02	4.31E-02	5.91	1.16E+00	1.96E-01
ENSMUSG00000070732	Rbm44	1.77E-02	4.32E-02	-4.32	5.54E-01	2.39E+00
ENSMUSG00000021638	Ocln	1.77E-02	4.32E-02	8.80	1.35E+00	1.53E-01
ENSMUSG00000104900	4930596I21Rik	1.78E-02	4.34E-02	3.40	2.88E+00	8.49E-01
ENSMUSG00000055494	Gm14168	1.78E-02	4.35E-02	-3.62	4.01E-01	1.45E+00
ENSMUSG00000090293	Gm17034	1.78E-02	4.35E-02	6.33	1.10E+00	1.73E-01
ENSMUSG00000108049	Gm44168	1.79E-02	4.37E-02	-4.31	3.40E-01	1.47E+00
ENSMUSG00000064653	Gm26129	1.80E-02	4.39E-02	2.15	7.93E+00	3.68E+00
ENSMUSG00000042564	Fam227a	1.81E-02	4.42E-02	-2.24	4.61E+00	1.03E+01
ENSMUSG00000024901	Peli3	1.82E-02	4.42E-02	-2.72	1.81E+00	4.92E+00
ENSMUSG00000035283	Adrb1	1.82E-02	4.43E-02	-2.37	1.77E+00	4.19E+00
ENSMUSG00000055235	Wdr86	1.83E-02	4.45E-02	9.02	1.38E+00	1.53E-01
ENSMUSG00000039814	Xkr5	1.83E-02	4.46E-02	-2.03	9.29E+00	1.89E+01
ENSMUSG00000028919	Arhgef19	1.84E-02	4.46E-02	-3.78	6.50E-01	2.46E+00
ENSMUSG00000032373	Car12	1.85E-02	4.49E-02	3.23	2.37E+00	7.33E-01
ENSMUSG00000031099	Smarca1	1.86E-02	4.50E-02	-4.40	2.88E-01	1.26E+00
ENSMUSG00000104116	Gm37296	1.86E-02	4.51E-02	3.29	2.91E+00	8.83E-01
ENSMUSG00000053574	4930563E22Rik	1.90E-02	4.60E-02	-3.90	5.49E-01	2.14E+00
ENSMUSG00000089679	Gm16299	1.92E-02	4.64E-02	-4.81	2.88E-01	1.38E+00
ENSMUSG00000031297	Slc7a3	1.96E-02	4.73E-02	2.42	5.18E+00	2.14E+00
ENSMUSG00000025141	Myadml2	1.98E-02	4.79E-02	-3.76	5.46E-01	2.05E+00
ENSMUSG00000083462	Gm12501	2.00E-02	4.82E-02	-4.36	3.40E-01	1.48E+00
ENSMUSG00000048481	Mypop	2.01E-02	4.83E-02	-2.02	2.13E+00	4.32E+00
ENSMUSG00000115793	Gm48961	2.01E-02	4.85E-02	3.27	2.70E+00	8.26E-01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-α+β)	LSMean (unstimulated)
ENSMUSG00000105512	Gm43714	2.02E-02	4.85E-02	3.72	2.72E+00	7.30E-01
ENSMUSG00000075571	Defb30	2.02E-02	4.86E-02	2.42	4.01E+00	1.65E+00
ENSMUSG00000100625	1700016G22Rik	2.02E-02	4.86E-02	7.16	1.41E+00	1.96E-01
ENSMUSG00000083902	Tent2-ps1	2.03E-02	4.88E-02	4.73	1.53E+00	3.24E-01
ENSMUSG00000083829	Gm2199	2.04E-02	4.89E-02	2.31	3.35E+00	1.45E+00
ENSMUSG00000062248	Cks2	2.06E-02	4.94E-02	-4.59	4.01E-01	1.84E+00
ENSMUSG00000040605	Bace2	2.07E-02	4.96E-02	3.00	3.80E+00	1.26E+00
ENSMUSG00000025777	Gdap1	2.07E-02	4.97E-02	2.00	4.66E+00	2.32E+00
ENSMUSG00000021221	Dpf3	2.08E-02	4.99E-02	-5.13	2.43E-01	1.25E+00

Appendix 3 Complete list of differentially expressed genes upon IFN-γ stimulation

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000078853	Igtp	0.00E+00	0.00E+00	93.70	4.84E+03	5.17E+01
ENSMUSG00000046879	Irgm1	0.00E+00	0.00E+00	51.60	2.96E+03	5.73E+01
ENSMUSG00000074151	Nlrc5	1.92E-274	1.04E-270	18.32	8.14E+02	4.44E+01
ENSMUSG00000078920	Ifi47	3.22E-266	1.31E-262	105.15	7.75E+03	7.37E+01
ENSMUSG00000069874	Irgm2	6.07E-257	1.97E-253	44.04	1.16E+03	2.64E+01
ENSMUSG00000040253	Gbp7	5.23E-250	1.42E-246	72.61	6.61E+03	9.10E+01
ENSMUSG00000045932	Ifit2	1.63E-207	3.78E-204	121.61	2.49E+03	2.05E+01
ENSMUSG00000028894	Inpp5b	6.17E-203	1.25E-199	7.12	1.05E+03	1.48E+02
ENSMUSG00000027639	Samhd1	3.65E-202	6.59E-199	14.89	1.35E+04	9.04E+02
ENSMUSG00000082292	Gm12250	6.00E-200	9.75E-197	181.45	9.02E+02	4.97E+00
ENSMUSG00000054072	Iigp1	1.62E-199	2.39E-196	3,055.28	1.83E+04	6.00E+00
ENSMUSG00000029298	Gbp9	5.54E-194	7.49E-191	40.34	5.52E+02	1.37E+01
ENSMUSG00000073555	Gm4951	8.71E-189	1.09E-185	899.42	1.46E+03	1.62E+00
ENSMUSG00000039699	Batf2	7.61E-184	8.83E-181	196.91	1.49E+03	7.57E+00
ENSMUSG00000028270	Gbp2	1.58E-183	1.71E-180	321.71	2.79E+04	8.67E+01
ENSMUSG00000090272	Mndal	8.29E-177	8.41E-174	12.71	9.04E+03	7.11E+02
ENSMUSG00000033355	Rtp4	2.67E-157	2.55E-154	15.62	1.98E+03	1.27E+02
ENSMUSG00000037321	Tap1	1.56E-156	1.41E-153	18.92	7.52E+03	3.98E+02
ENSMUSG00000028268	Gbp3	5.70E-153	4.87E-150	97.52	3.78E+03	3.87E+01
ENSMUSG00000030921	Trim30a	7.27E-153	5.91E-150	8.38	3.91E+03	4.67E+02
ENSMUSG00000020572	Nampt	1.67E-152	1.29E-149	14.23	1.09E+04	7.65E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000059089	Fcgr4	6.49E-152	4.79E-149	13.90	2.48E+03	1.78E+02
ENSMUSG00000063268	Parp10	2.33E-149	1.64E-146	6.68	4.66E+02	6.97E+01
ENSMUSG00000049502	Dtx3l	1.95E-144	1.32E-141	12.03	2.45E+03	2.04E+02
ENSMUSG00000041481	Serpina3g	1.56E-138	1.01E-135	351.06	9.41E+02	2.68E+00
ENSMUSG00000027514	Zbp1	6.21E-132	3.88E-129	71.77	1.46E+03	2.03E+01
ENSMUSG00000024349	Sting1	6.08E-131	3.66E-128	8.01	1.55E+03	1.94E+02
ENSMUSG00000029561	Oasl2	3.88E-123	2.25E-120	23.57	1.27E+03	5.38E+01
ENSMUSG00000054404	Slfn5	2.04E-118	1.14E-115	14.32	5.17E+03	3.61E+02
ENSMUSG00000070327	Rnf213	4.50E-116	2.43E-113	13.31	2.22E+03	1.67E+02
ENSMUSG00000004040	Stat3	1.22E-114	6.41E-112	4.41	4.46E+03	1.01E+03
ENSMUSG00000042726	Trafd1	4.58E-114	2.32E-111	6.74	2.59E+03	3.85E+02
ENSMUSG00000070730	Rmdn3	3.70E-113	1.82E-110	5.56	1.39E+03	2.50E+02
ENSMUSG00000058163	Gm5431	5.31E-111	2.54E-108	15.96	1.67E+02	1.05E+01
ENSMUSG00000029417	Cxcl9	1.05E-110	4.89E-108	3,479.08	1.07E+04	3.07E+00
ENSMUSG00000053318	Slamf8	1.22E-109	5.49E-107	126.12	3.44E+03	2.73E+01
ENSMUSG00000079363	Gbp4	3.17E-109	1.39E-106	2,190.82	1.48E+03	6.76E-01
ENSMUSG00000040328	Olfr56	8.68E-102	3.71E-99	145.05	1.80E+02	1.24E+00
ENSMUSG00000073489	Ifi204	5.85E-100	2.43E-97	7.85	3.78E+03	4.82E+02
ENSMUSG00000074896	Ifit3	1.87E-99	7.58E-97	31.27	1.06E+03	3.38E+01
ENSMUSG00000039899	Fgl2	7.75E-97	3.00E-94	81.47	5.18E+03	6.35E+01
ENSMUSG00000034422	Parp14	7.75E-97	3.00E-94	17.54	7.68E+03	4.37E+02
ENSMUSG00000021266	Wars	1.27E-96	4.80E-94	10.04	1.86E+03	1.85E+02
ENSMUSG00000022906	Parp9	1.78E-96	6.57E-94	10.22	2.16E+03	2.11E+02
ENSMUSG00000009585	Apobec3	1.43E-95	5.16E-93	6.73	1.16E+03	1.73E+02
ENSMUSG00000066363	Serpina3f	2.02E-94	7.14E-92	3,194.99	9.13E+02	2.86E-01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000024581	Napg	2.25E-94	7.78E-92	2.20	8.64E+02	3.92E+02
ENSMUSG00000017830	Dhx58	2.36E-93	7.98E-91	6.99	3.31E+02	4.73E+01
ENSMUSG00000090222	Ifi203-ps	9.25E-93	3.06E-90	15.65	1.69E+02	1.08E+01
ENSMUSG00000033213	AA467197	2.23E-92	7.24E-90	75.88	2.02E+03	2.66E+01
ENSMUSG00000046031	Calhm6	4.82E-91	1.53E-88	152.40	3.87E+03	2.54E+01
ENSMUSG00000034438	Gbp8	1.35E-90	4.22E-88	85.16	3.30E+02	3.88E+00
ENSMUSG00000027669	Gnb4	3.93E-89	1.20E-86	9.69	7.06E+02	7.28E+01
ENSMUSG00000029798	Herc6	9.89E-88	2.97E-85	12.60	9.13E+02	7.24E+01
ENSMUSG00000024079	Eif2ak2	2.64E-86	7.78E-84	5.32	6.74E+02	1.27E+02
ENSMUSG00000020638	Cmpk2	1.07E-84	3.11E-82	41.04	1.24E+03	3.03E+01
ENSMUSG00000043263	Ifi209	1.30E-84	3.70E-82	33.41	6.41E+02	1.92E+01
ENSMUSG00000009185	Ccl8	1.13E-81	3.16E-79	220.89	2.40E+02	1.09E+00
ENSMUSG00000063286	Gvin-ps7	7.86E-81	2.16E-78	19.49	5.40E+03	2.77E+02
ENSMUSG00000034459	Ifit1	3.26E-79	8.82E-77	55.26	2.09E+03	3.79E+01
ENSMUSG00000027951	Adar	8.55E-79	2.28E-76	4.01	5.23E+02	1.30E+02
ENSMUSG00000069892	9930111J21Rik2	2.27E-78	5.94E-76	6.38	3.06E+02	4.80E+01
ENSMUSG00000035692	Isg15	6.26E-78	1.61E-75	43.76	2.35E+03	5.37E+01
ENSMUSG00000036986	Pml	8.72E-78	2.21E-75	5.83	8.56E+02	1.47E+02
ENSMUSG00000050029	Rap2c	3.00E-77	7.49E-75	3.53	1.86E+03	5.25E+02
ENSMUSG00000078616	Trim30c	4.91E-77	1.21E-74	46.66	2.68E+02	5.73E+00
ENSMUSG00000059498	Fcgr3	8.90E-77	2.16E-74	3.14	1.11E+04	3.53E+03
ENSMUSG00000031712	Il15	9.29E-77	2.22E-74	8.36	6.83E+02	8.17E+01
ENSMUSG00000030275	Etnk1	1.32E-76	3.12E-74	2.98	6.53E+02	2.19E+02
ENSMUSG00000090942	F830016B08Rik	1.92E-75	4.45E-73	1,260.43	1.93E+02	1.53E-01
ENSMUSG00000036381	P2ry14	7.16E-75	1.64E-72	7.02	5.76E+02	8.20E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000025498	Irf7	3.16E-74	7.13E-72	19.64	1.11E+03	5.63E+01
ENSMUSG00000040033	Stat2	1.23E-73	2.74E-71	9.80	1.04E+03	1.06E+02
ENSMUSG00000035208	Slfn8	1.10E-72	2.42E-70	12.67	1.09E+03	8.61E+01
ENSMUSG00000002307	Daxx	7.50E-72	1.62E-69	6.72	1.69E+03	2.51E+02
ENSMUSG00000030341	Tnfrsf1a	4.61E-71	9.85E-69	3.96	2.11E+03	5.32E+02
ENSMUSG00000038507	Parp12	9.76E-71	2.06E-68	6.20	7.12E+02	1.15E+02
ENSMUSG00000068606	Gm4841	1.23E-69	2.56E-67	1,242.46	1.90E+02	1.53E-01
ENSMUSG00000053931	Cnn3	1.76E-69	3.62E-67	20.19	8.64E+02	4.28E+01
ENSMUSG00000063236	1110038F14Rik	2.26E-69	4.59E-67	4.58	7.35E+02	1.61E+02
ENSMUSG00000078921	Tgtp2	1.73E-68	3.47E-66	780.50	2.53E+02	3.24E-01
ENSMUSG00000016496	Cd274	3.55E-68	7.04E-66	29.48	9.61E+03	3.26E+02
ENSMUSG00000026104	Stat1	4.95E-68	9.69E-66	14.58	4.35E+03	2.99E+02
ENSMUSG00000022504	Ciita	7.30E-67	1.41E-64	44.63	8.32E+02	1.86E+01
ENSMUSG00000031792	Usb1	6.46E-66	1.23E-63	3.00	7.47E+02	2.49E+02
ENSMUSG00000030966	Trim21	1.62E-65	3.06E-63	6.59	2.43E+02	3.69E+01
ENSMUSG00000017057	Il13ra1	2.14E-65	3.99E-63	7.22	2.35E+02	3.25E+01
ENSMUSG00000037816	Fbxw17	4.01E-65	7.40E-63	4.28	4.34E+02	1.02E+02
ENSMUSG00000057596	Trim30d	1.02E-64	1.86E-62	9.74	8.87E+02	9.11E+01
ENSMUSG00000060519	Tor3a	2.34E-64	4.22E-62	6.40	2.34E+03	3.65E+02
ENSMUSG00000020407	Upp1	2.68E-63	4.78E-61	265.89	8.37E+02	3.15E+00
ENSMUSG00000038058	Nod1	4.73E-63	8.34E-61	15.08	7.35E+02	4.88E+01
ENSMUSG00000070034	Sp110	5.57E-63	9.72E-61	7.42	5.04E+02	6.80E+01
ENSMUSG00000029860	Zyx	9.01E-63	1.56E-60	11.27	4.31E+03	3.82E+02
ENSMUSG00000026088	Mitd1	4.39E-62	7.50E-60	3.44	3.63E+02	1.06E+02
ENSMUSG00000070031	Sp140	5.06E-62	8.56E-60	6.85	3.36E+02	4.91E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000023307	Marchf5	5.37E-62	8.99E-60	3.74	1.30E+03	3.47E+02
ENSMUSG00000040483	Xaf1	5.90E-62	9.78E-60	10.96	1.49E+02	1.36E+01
ENSMUSG00000026222	Sp100	1.33E-61	2.18E-59	4.71	1.42E+03	3.01E+02
ENSMUSG00000090125	Pou3f1	1.73E-60	2.82E-58	26.70	2.78E+02	1.04E+01
ENSMUSG00000034118	Tpst1	4.65E-60	7.47E-58	5.74	2.05E+02	3.57E+01
ENSMUSG00000073902	Gvin3	5.22E-60	8.30E-58	38.13	2.33E+02	6.11E+00
ENSMUSG00000066150	Slc31a1	3.11E-56	4.91E-54	2.81	1.72E+03	6.12E+02
ENSMUSG00000034320	Slc26a2	3.08E-55	4.81E-53	3.20	8.58E+02	2.68E+02
ENSMUSG00000040296	Ddx58	3.49E-55	5.39E-53	5.68	6.29E+02	1.11E+02
ENSMUSG00000092021	Gbp11	4.50E-55	6.90E-53	694.04	1.06E+02	1.53E-01
ENSMUSG00000029780	Nt5c3	4.55E-55	6.90E-53	5.60	1.41E+03	2.51E+02
ENSMUSG00000030107	Usp18	4.83E-55	7.27E-53	21.06	4.51E+02	2.14E+01
ENSMUSG00000035352	Ccl12	1.40E-54	2.09E-52	69.33	9.04E+02	1.30E+01
ENSMUSG00000029502	Golga3	2.68E-53	3.96E-51	3.29	4.80E+02	1.46E+02
ENSMUSG00000037849	Ifi206	5.65E-53	8.27E-51	96.05	2.06E+02	2.14E+00
ENSMUSG00000000386	Mx1	1.82E-52	2.64E-50	77.70	6.06E+02	7.80E+00
ENSMUSG00000041515	Irf8	2.01E-52	2.88E-50	10.02	9.83E+03	9.81E+02
ENSMUSG00000037685	Atp8a1	2.68E-52	3.82E-50	2.90	7.87E+02	2.72E+02
ENSMUSG00000029771	Irf5	4.43E-52	6.26E-50	3.32	2.94E+03	8.87E+02
ENSMUSG00000039157	Fam102a	2.10E-51	2.94E-49	3.60	8.27E+02	2.30E+02
ENSMUSG00000057137	Tmem140	4.38E-51	6.07E-49	4.33	3.01E+03	6.94E+02
ENSMUSG00000039982	Dtx4	4.65E-51	6.40E-49	-4.48	1.52E+02	6.82E+02
ENSMUSG00000059436	Max	5.02E-51	6.85E-49	2.90	1.99E+03	6.85E+02
ENSMUSG00000037731	Themis2	5.82E-51	7.88E-49	10.27	1.73E+03	1.68E+02
ENSMUSG00000032690	Oas2	1.09E-50	1.46E-48	5.90	3.23E+02	5.47E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000039997	Ifi203	1.54E-50	2.05E-48	14.29	6.83E+03	4.78E+02
ENSMUSG00000061981	Flot2	1.62E-50	2.14E-48	2.00	9.03E+02	4.50E+02
ENSMUSG00000035725	Prkx	3.63E-50	4.75E-48	3.18	1.63E+03	5.13E+02
ENSMUSG00000025165	Sectm1a	3.85E-50	5.00E-48	496.04	1.10E+02	2.23E-01
ENSMUSG00000026946	Nmi	1.20E-49	1.54E-47	4.60	4.95E+02	1.07E+02
ENSMUSG00000007036	Abhd16a	1.27E-49	1.62E-47	4.06	1.35E+03	3.32E+02
ENSMUSG00000091649	Phf11b	2.09E-49	2.65E-47	19.56	1.19E+03	6.10E+01
ENSMUSG00000015947	Fcgr1	2.12E-49	2.66E-47	8.75	2.04E+03	2.33E+02
ENSMUSG00000022765	Snap29	4.09E-49	5.11E-47	2.76	6.08E+02	2.21E+02
ENSMUSG00000028657	Ppt1	1.05E-48	1.30E-46	2.15	1.64E+03	7.61E+02
ENSMUSG00000097194	9330175E14Rik	1.18E-48	1.45E-46	12.62	1.26E+02	9.98E+00
ENSMUSG00000022035	Ccdc25	5.69E-48	6.94E-46	4.53	2.10E+03	4.63E+02
ENSMUSG00000056692	Ilrun	5.83E-48	7.07E-46	2.29	2.50E+03	1.09E+03
ENSMUSG00000047735	Samd9l	1.37E-47	1.65E-45	5.18	9.10E+02	1.76E+02
ENSMUSG00000074342	I830077J02Rik	2.02E-47	2.41E-45	6.87	1.97E+02	2.87E+01
ENSMUSG00000002797	Ggct	4.52E-47	5.36E-45	9.36	3.70E+02	3.95E+01
ENSMUSG00000025888	Casp1	5.84E-47	6.87E-45	3.51	2.09E+03	5.95E+02
ENSMUSG00000027952	Pmvk	1.02E-46	1.19E-44	5.22	6.40E+02	1.22E+02
ENSMUSG00000023206	Il15ra	1.38E-46	1.60E-44	22.99	2.33E+02	1.01E+01
ENSMUSG00000037400	Atp11b	1.49E-46	1.72E-44	3.07	9.08E+02	2.96E+02
ENSMUSG00000022186	Oxct1	6.58E-46	7.53E-44	2.25	5.56E+03	2.47E+03
ENSMUSG00000026896	Ifih1	1.12E-45	1.27E-43	7.59	7.20E+02	9.49E+01
ENSMUSG00000037921	Ddx60	1.70E-45	1.92E-43	6.39	2.88E+02	4.50E+01
ENSMUSG00000029279	Brdt	3.67E-45	4.10E-43	5.59	9.63E+01	1.72E+01
ENSMUSG00000062380	Tubb3	6.18E-45	6.87E-43	12.22	1.38E+02	1.13E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000060183	Cxcl11	1.95E-44	2.15E-42	1,783.34	6.54E+02	3.67E-01
ENSMUSG00000010358	Ifi35	2.89E-44	3.17E-42	5.37	4.69E+02	8.73E+01
ENSMUSG00000034855	Cxcl10	5.15E-44	5.62E-42	180.62	2.27E+04	1.26E+02
ENSMUSG00000041827	Oasl1	1.14E-43	1.23E-41	94.96	5.27E+02	5.55E+00
ENSMUSG00000020641	Rsad2	1.40E-43	1.50E-41	39.88	1.35E+04	3.39E+02
ENSMUSG00000026536	Ifi211	2.50E-43	2.67E-41	14.49	1.17E+03	8.05E+01
ENSMUSG00000049401	Ogfr	3.22E-43	3.42E-41	3.33	8.33E+02	2.50E+02
ENSMUSG00000038213	Tapbpl	3.78E-43	3.99E-41	8.84	8.75E+02	9.90E+01
ENSMUSG00000023961	Enpp4	3.45E-42	3.61E-40	12.30	7.97E+01	6.48E+00
ENSMUSG00000039753	Fbxl5	3.70E-42	3.85E-40	3.43	3.99E+02	1.16E+02
ENSMUSG00000029474	Rnf34	4.36E-42	4.51E-40	3.49	4.68E+02	1.34E+02
ENSMUSG00000029082	Bst1	4.67E-42	4.80E-40	7.06	3.10E+02	4.39E+01
ENSMUSG00000104713	Gbp6	6.15E-42	6.29E-40	420.81	6.44E+01	1.53E-01
ENSMUSG00000032661	Oas3	9.83E-42	9.98E-40	7.34	3.11E+02	4.24E+01
ENSMUSG00000019806	Aig1	2.11E-41	2.13E-39	4.37	3.68E+02	8.41E+01
ENSMUSG00000048852	Gm12185	2.28E-41	2.29E-39	234.00	9.72E+01	4.15E-01
ENSMUSG00000022901	Cd86	2.57E-41	2.56E-39	9.54	8.93E+02	9.36E+01
ENSMUSG00000068245	Phf11d	4.80E-41	4.75E-39	21.13	2.71E+02	1.28E+01
ENSMUSG00000012519	Mlkl	7.78E-41	7.61E-39	5.30	3.06E+02	5.76E+01
ENSMUSG00000078922	Tgtp1	1.30E-40	1.27E-38	436.54	6.68E+01	1.53E-01
ENSMUSG00000115338	Pnp	5.45E-40	5.27E-38	6.61	1.20E+03	1.82E+02
ENSMUSG00000039304	Tnfsf10	8.67E-40	8.33E-38	102.29	1.62E+02	1.58E+00
ENSMUSG00000053007	Creb5	1.06E-39	1.01E-37	4.11	2.09E+03	5.07E+02
ENSMUSG00000045092	S1pr1	1.24E-39	1.18E-37	-7.65	5.30E+01	4.05E+02
ENSMUSG00000066677	Ifi208	1.61E-39	1.52E-37	215.45	7.91E+01	3.67E-01

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ENSMUSG00000049488	Tmem67	1.94E-39	1.82E-37	6.06	1.52E+02	2.51E+01
ENSMUSG00000026767	Mindy3	2.59E-39	2.42E-37	2.06	4.31E+02	2.09E+02
ENSMUSG00000006418	Rnf114	4.37E-39	4.05E-37	2.85	7.60E+02	2.66E+02
ENSMUSG00000096727	Psmb9	6.17E-39	5.69E-37	8.10	2.45E+03	3.03E+02
ENSMUSG00000051065	Mb21d2	1.13E-38	1.04E-36	12.87	7.24E+01	5.63E+00
ENSMUSG00000054203	Ifi205	1.50E-38	1.37E-36	68.87	6.84E+02	9.93E+00
ENSMUSG00000046908	Ltb4r1	6.15E-38	5.58E-36	21.56	1.01E+02	4.68E+00
ENSMUSG00000019794	Katna1	8.89E-38	8.02E-36	3.56	8.61E+02	2.42E+02
ENSMUSG00000112627	4933412E12Rik	9.00E-38	8.07E-36	9.87	8.39E+01	8.49E+00
ENSMUSG00000054720	Lrrc8c	2.39E-37	2.13E-35	3.70	5.75E+02	1.56E+02
ENSMUSG00000021880	Rnase6	2.46E-37	2.18E-35	10.65	3.14E+02	2.95E+01
ENSMUSG00000025790	Slco3a1	4.17E-37	3.68E-35	22.17	1.15E+03	5.17E+01
ENSMUSG00000020089	Ppa1	4.30E-37	3.77E-35	3.83	4.39E+02	1.15E+02
ENSMUSG00000023959	Clic5	4.45E-37	3.89E-35	96.54	1.68E+02	1.74E+00
ENSMUSG00000028619	Tceanc2	4.65E-37	4.04E-35	2.09	3.83E+02	1.84E+02
ENSMUSG00000075010	AW112010	5.10E-37	4.39E-35	50.43	2.05E+03	4.06E+01
ENSMUSG00000050565	Tor1aip2	5.11E-37	4.39E-35	2.86	1.42E+03	4.96E+02
ENSMUSG00000028037	Ifi44	9.65E-37	8.20E-35	93.81	5.23E+02	5.57E+00
ENSMUSG00000031897	Psmb10	4.19E-36	3.54E-34	6.41	2.39E+03	3.74E+02
ENSMUSG00000052336	Cx3cr1	1.15E-35	9.71E-34	-12.58	3.24E+01	4.07E+02
ENSMUSG00000024308	Tapbp	1.43E-35	1.20E-33	3.73	1.11E+04	2.98E+03
ENSMUSG00000028019	Pdgfc	1.52E-35	1.26E-33	4.28	1.74E+02	4.08E+01
ENSMUSG00000038301	Snx10	1.68E-35	1.39E-33	3.60	1.91E+03	5.30E+02
ENSMUSG00000021196	Pfkp	3.27E-35	2.70E-33	3.44	1.88E+03	5.48E+02
ENSMUSG00000004952	Rasa4	4.60E-35	3.77E-33	2.66	1.14E+03	4.27E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000066258	Trim12a	5.47E-35	4.46E-33	4.04	2.16E+02	5.33E+01
ENSMUSG00000045210	Vcpip1	5.67E-35	4.60E-33	2.35	7.40E+02	3.15E+02
ENSMUSG00000021725	Parp8	1.48E-34	1.19E-32	5.30	2.26E+02	4.26E+01
ENSMUSG00000037997	Parp11	1.55E-34	1.24E-32	5.83	4.45E+02	7.63E+01
ENSMUSG00000025887	Casp12	4.87E-34	3.87E-32	13.99	5.36E+01	3.83E+00
ENSMUSG00000029104	Htt	6.30E-34	4.99E-32	2.25	3.61E+02	1.60E+02
ENSMUSG00000035392	Dennd1a	8.35E-34	6.55E-32	2.63	6.76E+02	2.57E+02
ENSMUSG00000037649	H2-DMa	1.00E-33	7.83E-32	8.35	1.71E+03	2.05E+02
ENSMUSG00000038037	Socs1	1.57E-33	1.22E-31	60.84	8.71E+02	1.43E+01
ENSMUSG00000039531	Zup1	2.59E-33	2.00E-31	4.68	4.18E+02	8.93E+01
ENSMUSG00000035186	Ubd	3.22E-33	2.47E-31	602.97	1.18E+02	1.96E-01
ENSMUSG00000023106	Denr	1.04E-32	7.96E-31	4.07	2.87E+03	7.03E+02
ENSMUSG00000028796	Phc2	1.17E-32	8.92E-31	2.48	7.21E+02	2.91E+02
ENSMUSG00000026110	Mgat4a	4.42E-32	3.35E-30	2.69	3.79E+02	1.41E+02
ENSMUSG00000050549	Fam241a	4.51E-32	3.40E-30	4.13	6.41E+02	1.55E+02
ENSMUSG00000052749	Trim30b	7.03E-32	5.29E-30	22.20	4.50E+01	2.03E+00
ENSMUSG00000000247	Lhx2	1.21E-31	9.06E-30	19.64	1.02E+02	5.17E+00
ENSMUSG00000025492	Ifitm3	1.71E-31	1.27E-29	3.73	6.05E+03	1.62E+03
ENSMUSG00000024338	Psmb8	2.43E-31	1.79E-29	4.62	3.81E+03	8.25E+02
ENSMUSG00000042228	Lyn	3.43E-31	2.52E-29	2.39	3.51E+03	1.46E+03
ENSMUSG00000047798	Cd300lf	4.24E-31	3.10E-29	3.44	3.45E+03	1.00E+03
ENSMUSG00000073491	Ifi213	5.10E-31	3.71E-29	136.87	1.30E+02	9.48E-01
ENSMUSG00000078153	Psme2b	5.64E-31	4.07E-29	6.92	3.95E+01	5.70E+00
ENSMUSG00000026580	Selp	5.96E-31	4.28E-29	103.85	6.00E+01	5.78E-01
ENSMUSG00000027035	Cers6	6.21E-31	4.44E-29	5.63	1.47E+03	2.62E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000019866	Crybg1	7.95E-31	5.66E-29	3.18	7.06E+02	2.22E+02
ENSMUSG00000002325	Irf9	1.60E-30	1.13E-28	2.30	6.69E+02	2.91E+02
ENSMUSG00000033581	Igf2bp2	2.48E-30	1.75E-28	4.45	1.12E+03	2.51E+02
ENSMUSG00000085977	Gm5970	2.61E-30	1.83E-28	162.20	2.81E+01	1.73E-01
ENSMUSG00000027835	Pdcd10	4.86E-30	3.40E-28	2.09	4.30E+02	2.06E+02
ENSMUSG00000105504	Gbp5	5.52E-30	3.85E-28	103.35	2.00E+04	1.94E+02
ENSMUSG00000022257	Laptm4b	6.14E-30	4.26E-28	2.78	1.84E+02	6.62E+01
ENSMUSG00000026395	Ptprc	1.63E-29	1.11E-27	2.13	4.78E+03	2.24E+03
ENSMUSG00000029413	Naaa	3.09E-29	2.10E-27	4.14	2.16E+02	5.21E+01
ENSMUSG00000056144	Trim34a	4.14E-29	2.80E-27	3.62	1.95E+02	5.38E+01
ENSMUSG00000062488	Ifit3b	5.67E-29	3.82E-27	14.21	8.46E+01	5.95E+00
ENSMUSG00000104955	1700016F12Rik	6.09E-29	4.09E-27	226.41	3.46E+01	1.53E-01
ENSMUSG00000079442	St6galnac4	6.30E-29	4.21E-27	5.28	1.91E+03	3.62E+02
ENSMUSG00000058624	Gda	7.91E-29	5.26E-27	4.47	8.66E+02	1.94E+02
ENSMUSG00000044734	Serpinb1a	1.54E-28	1.02E-26	5.51	4.61E+02	8.37E+01
ENSMUSG00000039501	Znfx1	1.54E-28	1.02E-26	4.12	1.83E+03	4.45E+02
ENSMUSG00000000628	Hk2	1.66E-28	1.09E-26	3.40	1.77E+03	5.19E+02
ENSMUSG00000041238	Rbbp8	1.78E-28	1.17E-26	3.17	7.57E+02	2.39E+02
ENSMUSG00000027466	Rbck1	2.15E-28	1.40E-26	2.01	6.39E+02	3.18E+02
ENSMUSG00000106734	Gm20559	3.30E-28	2.14E-26	3.52	1.99E+02	5.64E+01
ENSMUSG00000052512	Nav2	3.45E-28	2.23E-26	-3.69	1.41E+02	5.20E+02
ENSMUSG00000027475	Kif3b	5.02E-28	3.23E-26	2.02	1.72E+03	8.54E+02
ENSMUSG00000053338	Tarm1	8.40E-28	5.39E-26	10.27	1.16E+02	1.13E+01
ENSMUSG00000030199	Etv6	9.79E-28	6.26E-26	2.88	1.13E+03	3.94E+02
ENSMUSG00000060675	Plaat3	1.11E-27	7.10E-26	11.08	1.43E+03	1.29E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000028233	Tgs1	1.20E-27	7.62E-26	2.60	7.31E+02	2.81E+02
ENSMUSG00000051185	Fam174a	1.75E-27	1.11E-25	2.09	8.22E+02	3.94E+02
ENSMUSG00000031627	Irf2	1.85E-27	1.16E-25	2.32	1.26E+03	5.44E+02
ENSMUSG00000032508	Myd88	2.19E-27	1.37E-25	3.47	1.84E+03	5.29E+02
ENSMUSG00000036362	P2ry13	3.44E-27	2.15E-25	4.98	1.54E+02	3.09E+01
ENSMUSG00000031903	Pla2g15	5.30E-27	3.30E-25	2.11	1.84E+03	8.74E+02
ENSMUSG00000019966	Kitl	7.62E-27	4.72E-25	4.13	3.13E+02	7.57E+01
ENSMUSG00000020225	Tmbim4	8.63E-27	5.33E-25	2.10	1.62E+03	7.69E+02
ENSMUSG00000029428	Stx2	8.77E-27	5.40E-25	3.72	9.67E+02	2.60E+02
ENSMUSG00000071068	Treml2	1.25E-26	7.67E-25	4.72	1.22E+02	2.59E+01
ENSMUSG00000057143	Trim12c	1.33E-26	8.09E-25	3.45	5.97E+02	1.73E+02
ENSMUSG00000093507	Gm20627	1.44E-26	8.73E-25	22.76	2.12E+01	9.31E-01
ENSMUSG00000096954	nan	1.50E-26	9.08E-25	10.91	5.00E+02	4.59E+01
ENSMUSG00000048120	Entpd1	2.18E-26	1.31E-24	2.43	1.30E+03	5.33E+02
ENSMUSG00000024942	Capn1	4.26E-26	2.56E-24	2.13	8.59E+02	4.03E+02
ENSMUSG00000024805	Pcgf5	4.29E-26	2.57E-24	3.51	3.03E+02	8.63E+01
ENSMUSG00000060802	B2m	4.61E-26	2.75E-24	2.52	9.54E+04	3.79E+04
ENSMUSG00000018341	Il12rb2	5.11E-26	3.04E-24	3.40	3.54E+02	1.04E+02
ENSMUSG00000030560	Ctsc	5.97E-26	3.54E-24	6.81	5.82E+03	8.55E+02
ENSMUSG00000037752	Xkr8	9.87E-26	5.81E-24	5.33	1.62E+02	3.04E+01
ENSMUSG00000020057	Dram1	1.33E-25	7.79E-24	6.60	6.19E+02	9.37E+01
ENSMUSG00000087477	Gm13822	1.56E-25	9.04E-24	36.98	2.69E+01	7.28E-01
ENSMUSG00000046157	Tmem229b	1.65E-25	9.51E-24	2.91	4.39E+02	1.51E+02
ENSMUSG00000029605	Oas1b	2.34E-25	1.35E-23	5.74	4.65E+01	8.10E+00
ENSMUSG00000050350	Gpr18	2.37E-25	1.36E-23	22.62	1.12E+02	4.94E+00

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ENSMUSG00000042182	Bend6	2.41E-25	1.38E-23	3.51	3.94E+01	1.12E+01
ENSMUSG00000030149	Klrk1	2.45E-25	1.40E-23	133.32	6.18E+01	4.63E-01
ENSMUSG00000027009	Itga4	2.60E-25	1.48E-23	4.34	3.10E+03	7.14E+02
ENSMUSG00000029265	Dr1	2.76E-25	1.56E-23	2.85	6.36E+02	2.23E+02
ENSMUSG00000091144	Phf11c	3.14E-25	1.77E-23	5.80	6.50E+01	1.12E+01
ENSMUSG00000039936	Pik3cd	4.63E-25	2.60E-23	2.97	9.24E+02	3.11E+02
ENSMUSG00000053101	Gpr141	4.85E-25	2.72E-23	3.98	5.13E+02	1.29E+02
ENSMUSG00000038517	Tbkbp1	4.98E-25	2.78E-23	2.51	4.32E+02	1.72E+02
ENSMUSG00000023341	Mx2	5.73E-25	3.18E-23	33.51	2.46E+02	7.35E+00
ENSMUSG00000027078	Ube2l6	6.07E-25	3.36E-23	4.93	9.48E+01	1.92E+01
ENSMUSG00000049130	C5ar1	6.87E-25	3.79E-23	-3.61	3.87E+02	1.40E+03
ENSMUSG00000022378	Cyrib	7.12E-25	3.92E-23	2.19	3.03E+03	1.38E+03
ENSMUSG00000037242	Clic4	8.58E-25	4.70E-23	3.30	7.00E+03	2.12E+03
ENSMUSG00000017715	Pgs1	1.20E-24	6.56E-23	3.90	8.24E+02	2.11E+02
ENSMUSG00000033088	Triobp	1.26E-24	6.89E-23	2.19	4.46E+02	2.04E+02
ENSMUSG00000027219	Slc28a2	1.54E-24	8.35E-23	6.18	2.35E+02	3.79E+01
ENSMUSG00000027199	Gatm	1.94E-24	1.05E-22	2.25	3.59E+02	1.59E+02
ENSMUSG00000044468	Tent5c	1.97E-24	1.06E-22	2.75	1.77E+03	6.46E+02
ENSMUSG00000024777	Ppp2r5b	2.52E-24	1.35E-22	2.32	3.25E+02	1.40E+02
ENSMUSG00000036636	Clcn7	2.81E-24	1.50E-22	3.29	2.43E+03	7.38E+02
ENSMUSG00000075602	Ly6a	4.65E-24	2.48E-22	27.16	2.56E+03	9.44E+01
ENSMUSG00000005583	Mef2c	4.78E-24	2.54E-22	-2.33	6.68E+02	1.56E+03
ENSMUSG00000079659	Tmem243	6.04E-24	3.20E-22	3.29	2.86E+02	8.67E+01
ENSMUSG00000025877	Hk3	7.66E-24	4.01E-22	3.62	3.91E+03	1.08E+03
ENSMUSG00000093661	Eif4e3	8.79E-24	4.58E-22	2.08	5.76E+02	2.78E+02

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ENSMUSG00000002227	Mov10	1.21E-23	6.26E-22	4.28	2.57E+02	6.02E+01
ENSMUSG00000024098	Twsg1	1.22E-23	6.31E-22	2.44	3.63E+02	1.49E+02
ENSMUSG00000000791	Il12rb1	1.52E-23	7.82E-22	53.20	1.25E+02	2.36E+00
ENSMUSG00000032232	Cgnl1	1.62E-23	8.30E-22	-4.86	2.69E+01	1.31E+02
ENSMUSG00000020134	Peli1	2.02E-23	1.03E-21	4.01	1.86E+03	4.65E+02
ENSMUSG00000032265	Tent5a	2.28E-23	1.16E-21	2.95	9.29E+02	3.15E+02
ENSMUSG00000011148	Adssl1	2.47E-23	1.25E-21	-2.37	1.79E+02	4.23E+02
ENSMUSG00000017652	Cd40	2.72E-23	1.37E-21	46.41	3.91E+03	8.42E+01
ENSMUSG00000038179	Slamf7	3.11E-23	1.56E-21	6.08	5.98E+03	9.84E+02
ENSMUSG00000019768	Esr1	3.43E-23	1.71E-21	4.96	6.44E+01	1.30E+01
ENSMUSG00000051285	Pcmtd1	3.42E-23	1.71E-21	2.16	1.00E+03	4.63E+02
ENSMUSG00000021583	Erap1	3.45E-23	1.72E-21	2.87	4.91E+02	1.71E+02
ENSMUSG00000028466	Creb3	3.75E-23	1.86E-21	2.55	9.35E+02	3.66E+02
ENSMUSG00000078606	Gvin2	4.77E-23	2.35E-21	69.02	1.74E+01	2.52E-01
ENSMUSG00000037820	Tgm2	4.93E-23	2.42E-21	2.77	6.75E+03	2.43E+03
ENSMUSG00000050075	Gpr171	6.13E-23	3.00E-21	12.03	1.16E+02	9.67E+00
ENSMUSG00000027340	Slc23a2	8.28E-23	4.04E-21	2.60	7.80E+02	3.00E+02
ENSMUSG00000081769	Gm12216	9.32E-23	4.53E-21	7.95	4.32E+01	5.44E+00
ENSMUSG00000044703	Phf11a	1.28E-22	6.21E-21	48.78	7.10E+01	1.46E+00
ENSMUSG00000078763	Slfn1	1.58E-22	7.62E-21	98.15	1.93E+01	1.96E-01
ENSMUSG00000033487	Fndc3a	1.83E-22	8.83E-21	2.38	9.82E+02	4.14E+02
ENSMUSG00000071714	Csf2rb2	1.85E-22	8.90E-21	2.12	2.84E+03	1.34E+03
ENSMUSG00000009418	Nav1	2.39E-22	1.14E-20	-2.43	2.72E+02	6.61E+02
ENSMUSG00000048118	Arid4a	2.82E-22	1.35E-20	2.46	1.68E+03	6.84E+02
ENSMUSG00000015850	Adamtsl4	2.85E-22	1.36E-20	4.77	6.93E+01	1.45E+01

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ENSMUSG00000026068	Il18rap	3.43E-22	1.63E-20	12.88	1.34E+02	1.04E+01
ENSMUSG00000024789	Jak2	3.56E-22	1.69E-20	3.92	5.36E+02	1.37E+02
ENSMUSG00000025372	Baiap2	3.78E-22	1.78E-20	-2.57	1.77E+02	4.54E+02
ENSMUSG00000024539	Ptpn2	3.97E-22	1.87E-20	2.76	3.95E+02	1.43E+02
ENSMUSG00000032883	Acsl3	4.58E-22	2.15E-20	-3.25	8.67E+01	2.82E+02
ENSMUSG00000030102	Itpr1	4.68E-22	2.19E-20	5.29	1.86E+02	3.51E+01
ENSMUSG00000034297	Med13	5.37E-22	2.51E-20	2.93	1.23E+03	4.20E+02
ENSMUSG00000024472	Dcp2	5.71E-22	2.66E-20	2.20	2.83E+02	1.28E+02
ENSMUSG00000037926	Ssh2	5.85E-22	2.72E-20	-3.12	9.09E+01	2.83E+02
ENSMUSG00000039285	Azi2	5.99E-22	2.77E-20	2.23	3.34E+02	1.50E+02
ENSMUSG00000050957	Insl6	6.98E-22	3.22E-20	3.53	2.11E+02	5.97E+01
ENSMUSG00000040339	Fam102b	1.02E-21	4.71E-20	3.62	3.76E+03	1.04E+03
ENSMUSG00000022564	Grina	1.14E-21	5.25E-20	2.13	2.47E+03	1.16E+03
ENSMUSG00000017756	Slc12a7	1.37E-21	6.28E-20	2.39	3.10E+02	1.29E+02
ENSMUSG00000041075	Fzd7	1.96E-21	8.96E-20	4.15	9.95E+02	2.40E+02
ENSMUSG00000029534	St7	2.09E-21	9.50E-20	3.47	1.19E+02	3.42E+01
ENSMUSG00000026814	Eng	2.27E-21	1.03E-19	2.48	6.15E+02	2.48E+02
ENSMUSG00000071042	Rasgrp3	2.37E-21	1.07E-19	-4.62	3.02E+01	1.40E+02
ENSMUSG00000038910	Plcl2	2.45E-21	1.11E-19	2.72	7.39E+02	2.72E+02
ENSMUSG00000032596	Uba7	2.51E-21	1.13E-19	3.25	7.24E+02	2.23E+02
ENSMUSG00000052776	Oas1a	2.94E-21	1.32E-19	4.34	7.21E+01	1.66E+01
ENSMUSG00000032841	Prr5l	3.47E-21	1.55E-19	5.59	1.23E+03	2.21E+02
ENSMUSG00000063800	Prpf38a	3.56E-21	1.58E-19	2.64	2.92E+02	1.11E+02
ENSMUSG00000033306	Lpp	3.65E-21	1.62E-19	2.01	1.54E+03	7.66E+02
ENSMUSG00000020611	Gna13	4.17E-21	1.84E-19	2.76	6.97E+03	2.53E+03

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ENSMUSG00000053846	Lipg	4.47E-21	1.97E-19	104.18	5.33E+01	5.12E-01
ENSMUSG00000039682	Lap3	5.03E-21	2.21E-19	3.37	5.07E+02	1.50E+02
ENSMUSG00000024030	Abcg1	5.06E-21	2.22E-19	3.07	8.34E+02	2.72E+02
ENSMUSG00000050002	Idnk	5.46E-21	2.39E-19	2.64	2.56E+02	9.72E+01
ENSMUSG00000039934	Gsap	5.49E-21	2.40E-19	3.97	2.73E+02	6.87E+01
ENSMUSG00000054676	1600014C10Rik	6.66E-21	2.90E-19	4.60	5.37E+02	1.17E+02
ENSMUSG00000024074	Crim1	6.71E-21	2.91E-19	3.22	2.58E+02	8.01E+01
ENSMUSG00000004846	Plod3	6.81E-21	2.95E-19	2.09	9.31E+02	4.45E+02
ENSMUSG00000079339	Ifit1bl1	6.84E-21	2.96E-19	12.55	6.43E+01	5.12E+00
ENSMUSG00000020826	Nos2	7.11E-21	3.06E-19	369.43	4.45E+02	1.21E+00
ENSMUSG00000056220	Pla2g4a	9.87E-21	4.23E-19	6.21	3.25E+02	5.24E+01
ENSMUSG00000042901	Aida	1.04E-20	4.44E-19	2.62	4.08E+02	1.55E+02
ENSMUSG00000063193	Cd300lb	1.12E-20	4.76E-19	-4.52	2.34E+02	1.06E+03
ENSMUSG00000049657	Zbtb5	1.12E-20	4.76E-19	2.83	1.49E+02	5.25E+01
ENSMUSG00000061132	Blnk	1.14E-20	4.85E-19	-2.21	4.57E+02	1.01E+03
ENSMUSG00000025279	Dnase1l3	1.49E-20	6.32E-19	97.68	4.55E+01	4.65E-01
ENSMUSG00000037965	Zc3h7a	1.70E-20	7.17E-19	2.40	6.71E+02	2.79E+02
ENSMUSG00000022501	Prm1	1.78E-20	7.47E-19	79.75	1.22E+01	1.53E-01
ENSMUSG00000026544	Dusp23	1.85E-20	7.75E-19	2.08	3.84E+02	1.84E+02
ENSMUSG00000070427	Il18bp	2.12E-20	8.84E-19	8.33	4.04E+02	4.85E+01
ENSMUSG00000021895	Arhgef3	2.52E-20	1.05E-18	4.93	1.15E+03	2.34E+02
ENSMUSG00000029826	Zc3hav1	3.16E-20	1.31E-18	2.10	1.48E+03	7.07E+02
ENSMUSG00000063388	BC023105	3.82E-20	1.58E-18	58.64	8.97E+00	1.53E-01
ENSMUSG00000029156	Sgcb	3.96E-20	1.63E-18	2.62	3.53E+02	1.34E+02
ENSMUSG00000021483	Cdk20	4.22E-20	1.73E-18	-4.22	3.76E+01	1.59E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000036469	Marchf1	4.93E-20	2.02E-18	2.94	5.45E+02	1.85E+02
ENSMUSG00000055013	Agap1	5.47E-20	2.24E-18	-3.00	1.16E+02	3.49E+02
ENSMUSG00000030530	Furin	6.78E-20	2.76E-18	2.49	3.16E+03	1.27E+03
ENSMUSG00000020564	Atxn7l1	7.74E-20	3.15E-18	2.46	2.83E+02	1.15E+02
ENSMUSG00000023903	Mmp25	7.91E-20	3.21E-18	49.85	8.25E+01	1.65E+00
ENSMUSG00000034111	Tmed8	8.05E-20	3.26E-18	2.32	1.63E+02	7.03E+01
ENSMUSG00000029862	Clcn1	8.34E-20	3.37E-18	10.46	1.52E+01	1.46E+00
ENSMUSG00000023249	Parp3	8.39E-20	3.38E-18	4.35	6.21E+02	1.43E+02
ENSMUSG00000055172	C1ra	8.58E-20	3.45E-18	9.86	4.47E+01	4.54E+00
ENSMUSG00000028385	Snx30	1.04E-19	4.16E-18	-2.16	1.95E+02	4.20E+02
ENSMUSG00000022216	Psme1	1.20E-19	4.80E-18	2.94	3.28E+03	1.12E+03
ENSMUSG00000030852	Tacc2	1.23E-19	4.91E-18	-5.38	1.17E+01	6.30E+01
ENSMUSG00000094796	BC147527	1.38E-19	5.49E-18	44.04	8.65E+00	1.96E-01
ENSMUSG00000024778	Fas	1.40E-19	5.54E-18	4.85	3.14E+02	6.49E+01
ENSMUSG00000026482	Rgl1	1.48E-19	5.86E-18	4.44	7.34E+02	1.65E+02
ENSMUSG00000026764	Kif5c	1.58E-19	6.22E-18	3.83	7.35E+01	1.92E+01
ENSMUSG00000022814	Umps	1.91E-19	7.51E-18	-3.42	4.10E+01	1.40E+02
ENSMUSG00000028480	Glipr2	1.96E-19	7.68E-18	3.92	3.41E+02	8.69E+01
ENSMUSG00000028266	Lmo4	2.01E-19	7.87E-18	3.69	3.96E+03	1.07E+03
ENSMUSG00000079547	H2-DMb1	2.27E-19	8.86E-18	3.90	9.95E+02	2.55E+02
ENSMUSG00000033538	Casp4	2.72E-19	1.06E-17	4.79	1.58E+03	3.31E+02
ENSMUSG00000035954	Dock4	2.89E-19	1.12E-17	3.17	3.56E+02	1.13E+02
ENSMUSG00000026466	Tor1aip1	2.98E-19	1.15E-17	2.36	1.73E+03	7.31E+02
ENSMUSG00000054520	Sh3bp2	3.16E-19	1.22E-17	2.02	1.75E+03	8.65E+02
ENSMUSG00000032724	Abtb2	3.54E-19	1.36E-17	9.44	1.47E+02	1.55E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000020128	Vps54	3.54E-19	1.36E-17	2.22	2.70E+02	1.22E+02
ENSMUSG00000035439	Haus8	3.71E-19	1.42E-17	-2.15	2.09E+02	4.49E+02
ENSMUSG00000051212	Gpr183	6.19E-19	2.36E-17	-4.72	1.68E+01	7.91E+01
ENSMUSG00000027360	Hdc	6.52E-19	2.48E-17	22.20	2.07E+01	9.33E-01
ENSMUSG00000037434	Slc30a1	7.25E-19	2.74E-17	3.28	1.27E+03	3.86E+02
ENSMUSG00000001156	Mxd1	7.44E-19	2.80E-17	5.47	2.14E+03	3.91E+02
ENSMUSG00000031824	6430548M08Rik	1.17E-18	4.38E-17	-4.31	3.96E+01	1.71E+02
ENSMUSG00000027580	Helz2	1.18E-18	4.41E-17	9.97	1.26E+03	1.27E+02
ENSMUSG00000040430	Pitpnc1	1.48E-18	5.51E-17	-2.49	3.49E+02	8.68E+02
ENSMUSG00000034987	Hrh2	1.54E-18	5.69E-17	13.92	3.78E+01	2.72E+00
ENSMUSG00000070501	Ifi214	1.54E-18	5.70E-17	51.14	1.14E+01	2.23E-01
ENSMUSG00000026981	Il1rn	1.84E-18	6.80E-17	6.62	3.68E+03	5.57E+02
ENSMUSG00000026797	Stxbp1	2.35E-18	8.63E-17	2.95	3.66E+02	1.24E+02
ENSMUSG00000021892	Sh3bp5	2.59E-18	9.48E-17	-2.17	7.12E+02	1.54E+03
ENSMUSG00000022272	Myo10	2.67E-18	9.74E-17	2.97	1.02E+03	3.43E+02
ENSMUSG00000005580	Adcy9	3.23E-18	1.18E-16	-3.27	3.95E+01	1.29E+02
ENSMUSG00000031805	Jak3	3.27E-18	1.19E-16	2.22	9.46E+01	4.26E+01
ENSMUSG00000026786	Apbb1ip	3.92E-18	1.42E-16	-2.28	8.04E+02	1.83E+03
ENSMUSG00000046062	Ppp1r15b	3.98E-18	1.44E-16	2.08	8.75E+02	4.21E+02
ENSMUSG00000025969	Nrp2	6.82E-18	2.46E-16	2.23	6.41E+03	2.88E+03
ENSMUSG00000007617	Homer1	6.90E-18	2.48E-16	2.58	3.09E+02	1.20E+02
ENSMUSG00000085501	Gm11772	7.33E-18	2.63E-16	5.85	5.32E+01	9.09E+00
ENSMUSG00000068015	Lrch1	7.37E-18	2.64E-16	3.32	3.37E+02	1.02E+02
ENSMUSG00000026012	Cd28	8.42E-18	2.99E-16	-2.25	6.87E+02	1.55E+03
ENSMUSG00000051339	2900026A02Rik	8.47E-18	3.00E-16	-3.47	2.71E+01	9.40E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000042719	Naa25	8.60E-18	3.04E-16	2.54	5.37E+02	2.12E+02
ENSMUSG00000000318	Clec10a	8.79E-18	3.10E-16	3.81	2.13E+02	5.58E+01
ENSMUSG00000032333	Stoml1	1.24E-17	4.36E-16	2.35	1.84E+02	7.83E+01
ENSMUSG00000047534	Mis18bp1	1.24E-17	4.36E-16	-2.62	8.65E+01	2.27E+02
ENSMUSG00000054976	Nyap2	1.46E-17	5.11E-16	10.25	5.38E+01	5.25E+00
ENSMUSG00000097457	nan	1.51E-17	5.26E-16	26.32	1.89E+01	7.18E-01
ENSMUSG00000028064	Sema4a	1.79E-17	6.21E-16	4.91	2.40E+02	4.88E+01
ENSMUSG00000021109	Hif1a	2.01E-17	6.94E-16	2.81	1.20E+03	4.28E+02
ENSMUSG00000085184	4933439K11Rik	2.16E-17	7.42E-16	6.80	2.10E+01	3.09E+00
ENSMUSG00000020868	Xylt2	2.28E-17	7.80E-16	-2.82	1.50E+02	4.21E+02
ENSMUSG00000025582	Nptx1	2.53E-17	8.63E-16	-6.24	4.19E+01	2.61E+02
ENSMUSG00000027882	Stxbp3	2.94E-17	1.00E-15	2.68	6.45E+02	2.41E+02
ENSMUSG00000016087	Fli1	2.95E-17	1.00E-15	-2.41	2.97E+02	7.14E+02
ENSMUSG00000041649	Klf8	3.08E-17	1.04E-15	3.49	7.18E+01	2.06E+01
ENSMUSG00000022587	Ly6e	3.24E-17	1.10E-15	4.55	4.64E+03	1.02E+03
ENSMUSG00000073421	H2-Ab1	3.44E-17	1.16E-15	4.94	3.31E+03	6.70E+02
ENSMUSG00000079470	Utp14b	3.68E-17	1.24E-15	-4.09	2.01E+01	8.24E+01
ENSMUSG00000052423	B4galt3	3.71E-17	1.25E-15	3.74	2.54E+02	6.77E+01
ENSMUSG00000025591	Tma16	4.16E-17	1.39E-15	3.94	7.49E+02	1.90E+02
ENSMUSG00000032434	Cmtm6	4.41E-17	1.48E-15	2.27	6.42E+02	2.84E+02
ENSMUSG00000027366	Sppl2a	4.92E-17	1.64E-15	2.53	2.71E+03	1.07E+03
ENSMUSG00000112226	Gm48786	5.80E-17	1.93E-15	9.23	3.21E+01	3.48E+00
ENSMUSG00000036712	Cyld	6.00E-17	2.00E-15	2.00	5.38E+02	2.69E+02
ENSMUSG00000050953	Gja1	6.51E-17	2.16E-15	3.61	2.03E+02	5.62E+01
ENSMUSG00000041483	Zfp281	8.24E-17	2.72E-15	2.82	6.17E+02	2.19E+02

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ENSMUSG00000029313	Aff1	1.03E-16	3.37E-15	2.44	8.02E+02	3.29E+02
ENSMUSG00000024660	Incenp	1.07E-16	3.51E-15	-2.28	2.72E+02	6.19E+02
ENSMUSG00000029204	Rhoh	1.26E-16	4.11E-15	5.96	3.12E+02	5.24E+01
ENSMUSG00000018796	Acsl1	1.35E-16	4.42E-15	5.48	2.27E+03	4.14E+02
ENSMUSG00000025059	Gk	1.69E-16	5.51E-15	2.62	4.82E+02	1.84E+02
ENSMUSG00000021067	Sav1	1.69E-16	5.51E-15	2.14	3.51E+02	1.64E+02
ENSMUSG00000020707	Rnf135	1.76E-16	5.71E-15	2.13	2.46E+02	1.15E+02
ENSMUSG00000026112	Coa5	2.24E-16	7.23E-15	2.17	1.33E+03	6.11E+02
ENSMUSG00000049091	Sephs2	2.53E-16	8.14E-15	-2.66	1.76E+02	4.68E+02
ENSMUSG00000041707	Tmem273	2.92E-16	9.32E-15	-2.26	1.45E+02	3.27E+02
ENSMUSG00000106959	Gm42548	3.02E-16	9.63E-15	8.36	3.49E+01	4.17E+00
ENSMUSG00000068749	Psma5	3.07E-16	9.77E-15	2.24	4.99E+02	2.23E+02
ENSMUSG00000100975	Gm28875	3.13E-16	9.95E-15	-2.41	8.78E+01	2.12E+02
ENSMUSG00000041736	Tspo	3.29E-16	1.04E-14	2.51	1.98E+03	7.90E+02
ENSMUSG00000071350	Setdb2	3.36E-16	1.06E-14	4.43	7.06E+01	1.59E+01
ENSMUSG00000024052	Lpin2	3.77E-16	1.19E-14	2.08	1.32E+03	6.36E+02
ENSMUSG00000064181	Rab3ip	3.84E-16	1.21E-14	2.69	6.24E+01	2.32E+01
ENSMUSG00000060012	Kif13b	4.02E-16	1.26E-14	-2.45	1.44E+02	3.52E+02
ENSMUSG00000037533	Rapgef6	4.48E-16	1.40E-14	2.74	6.14E+02	2.24E+02
ENSMUSG00000022575	Gsdmd	4.70E-16	1.47E-14	2.97	4.53E+02	1.52E+02
ENSMUSG00000032479	Map4	4.72E-16	1.47E-14	2.02	8.23E+02	4.08E+02
ENSMUSG00000034731	Dgkh	5.94E-16	1.84E-14	2.92	5.40E+02	1.85E+02
ENSMUSG00000057561	Eif1a	6.20E-16	1.91E-14	2.30	1.25E+03	5.42E+02
ENSMUSG00000026821	Ralgds	6.38E-16	1.96E-14	5.82	4.39E+03	7.55E+02
ENSMUSG00000038527	C1rl	8.44E-16	2.58E-14	3.86	5.06E+01	1.31E+01

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ENSMUSG00000040774	Cept1	8.62E-16	2.63E-14	2.70	1.32E+03	4.91E+02
ENSMUSG00000026389	Steap3	9.41E-16	2.87E-14	-2.43	1.71E+02	4.15E+02
ENSMUSG00000039116	Adgrg6	1.32E-15	3.99E-14	3.07	1.19E+02	3.88E+01
ENSMUSG00000025997	Ikzf2	1.35E-15	4.07E-14	5.09	1.54E+02	3.02E+01
ENSMUSG00000021175	Cdca7l	1.35E-15	4.07E-14	-3.93	6.22E+01	2.45E+02
ENSMUSG00000009772	Nuak2	1.37E-15	4.13E-14	2.26	6.06E+02	2.68E+02
ENSMUSG00000059142	Zfp945	1.39E-15	4.18E-14	2.91	1.32E+02	4.55E+01
ENSMUSG00000053835	H2-T24	1.41E-15	4.23E-14	8.19	3.90E+01	4.77E+00
ENSMUSG00000033576	Apol6	1.42E-15	4.26E-14	43.55	1.41E+01	3.24E-01
ENSMUSG00000057191	AB124611	1.46E-15	4.37E-14	2.14	7.74E+02	3.62E+02
ENSMUSG00000106990	Gm42547	1.55E-15	4.63E-14	8.03	1.75E+02	2.18E+01
ENSMUSG00000044340	Phlpp1	1.79E-15	5.32E-14	3.96	2.37E+02	6.00E+01
ENSMUSG00000021384	Susd3	1.85E-15	5.50E-14	-3.58	9.49E+01	3.40E+02
ENSMUSG00000026131	Dst	1.95E-15	5.78E-14	3.29	4.66E+02	1.42E+02
ENSMUSG00000033792	Atp7a	2.07E-15	6.15E-14	2.17	7.94E+02	3.66E+02
ENSMUSG00000005370	Msh6	2.22E-15	6.57E-14	-3.63	4.76E+01	1.73E+02
ENSMUSG00000068129	Cst7	2.63E-15	7.75E-14	5.54	2.54E+02	4.58E+01
ENSMUSG00000079197	Psme2	2.94E-15	8.62E-14	4.19	1.54E+02	3.68E+01
ENSMUSG00000112843	Gm46224	3.02E-15	8.82E-14	2.35	1.08E+02	4.62E+01
ENSMUSG00000025429	Pstpip2	3.06E-15	8.93E-14	14.86	2.98E+01	2.00E+00
ENSMUSG00000044701	Il27	3.10E-15	9.01E-14	37.59	2.04E+02	5.42E+00
ENSMUSG00000116549	Gm49728	3.17E-15	9.21E-14	26.01	7.43E+00	2.86E-01
ENSMUSG00000002699	Lcp2	4.47E-15	1.29E-13	4.32	1.75E+03	4.04E+02
ENSMUSG00000029009	Mthfr	4.46E-15	1.29E-13	2.65	2.13E+02	8.04E+01
ENSMUSG00000038256	Bcl9	4.62E-15	1.33E-13	2.78	2.30E+02	8.27E+01

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ENSMUSG00000048534	Jaml	5.00E-15	1.44E-13	10.76	1.41E+01	1.31E+00
ENSMUSG00000087175	Gm15133	5.00E-15	1.44E-13	5.14	1.72E+01	3.36E+00
ENSMUSG00000001741	Il16	5.03E-15	1.44E-13	-3.78	2.37E+01	8.98E+01
ENSMUSG00000045795	Whamm	5.27E-15	1.51E-13	2.88	1.21E+02	4.21E+01
ENSMUSG00000109244	Gm44751	5.52E-15	1.58E-13	8.69	3.47E+01	3.99E+00
ENSMUSG00000030157	Clec2d	5.61E-15	1.60E-13	4.16	1.85E+02	4.45E+01
ENSMUSG00000045827	Serpinb9	5.63E-15	1.60E-13	5.89	3.63E+02	6.16E+01
ENSMUSG00000035042	Ccl5	6.40E-15	1.82E-13	41.75	2.94E+03	7.05E+01
ENSMUSG00000052125	F730043M19Rik	6.88E-15	1.95E-13	5.01	3.57E+01	7.14E+00
ENSMUSG00000063506	Arhgap22	7.44E-15	2.11E-13	-2.69	1.33E+02	3.58E+02
ENSMUSG00000043279	Trim56	8.15E-15	2.30E-13	2.25	6.40E+02	2.84E+02
ENSMUSG00000020272	Stk10	8.91E-15	2.50E-13	-2.53	6.96E+01	1.76E+02
ENSMUSG00000023224	Serping1	9.47E-15	2.65E-13	5.70	3.06E+01	5.37E+00
ENSMUSG00000031442	Mcf2l	1.01E-14	2.82E-13	5.21	3.02E+01	5.80E+00
ENSMUSG00000006134	Crkl	1.04E-14	2.90E-13	2.22	5.27E+02	2.37E+02
ENSMUSG00000021614	Vcan	1.06E-14	2.95E-13	4.71	1.28E+02	2.71E+01
ENSMUSG00000024222	Fkbp5	1.07E-14	2.96E-13	-2.55	4.52E+01	1.15E+02
ENSMUSG00000018899	Irf1	1.29E-14	3.59E-13	11.77	3.03E+04	2.57E+03
ENSMUSG00000004266	Ptpn6	1.33E-14	3.66E-13	2.91	2.63E+03	9.01E+02
ENSMUSG00000032359	Ctsh	1.37E-14	3.76E-13	2.21	3.23E+03	1.47E+03
ENSMUSG00000067212	H2-T23	1.44E-14	3.95E-13	8.67	6.49E+01	7.49E+00
ENSMUSG00000028212	Ccne2	1.54E-14	4.22E-13	-5.75	4.02E+01	2.31E+02
ENSMUSG00000026893	Gca	1.67E-14	4.55E-13	4.54	6.09E+01	1.34E+01
ENSMUSG00000025764	Jade1	1.74E-14	4.72E-13	-2.91	7.65E+01	2.22E+02
ENSMUSG00000031595	Pdgfrl	1.78E-14	4.81E-13	17.41	1.26E+01	7.26E-01

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ENSMUSG00000059970	Hspa2	1.87E-14	5.06E-13	2.83	9.57E+01	3.38E+01
ENSMUSG00000024953	Prdx5	2.21E-14	5.98E-13	2.92	4.62E+03	1.58E+03
ENSMUSG00000022014	Epsti1	2.31E-14	6.22E-13	2.69	6.83E+02	2.54E+02
ENSMUSG00000024245	Tmem178	2.74E-14	7.38E-13	9.36	8.45E+01	9.03E+00
ENSMUSG00000024675	Ms4a4c	2.85E-14	7.63E-13	14.65	1.00E+02	6.84E+00
ENSMUSG00000034265	Zdhhc14	2.93E-14	7.83E-13	-3.50	6.91E+01	2.42E+02
ENSMUSG00000024339	Tap2	3.09E-14	8.25E-13	7.10	4.16E+03	5.86E+02
ENSMUSG00000042167	Tent2	3.11E-14	8.28E-13	2.26	9.73E+01	4.30E+01
ENSMUSG00000004099	Dnmt1	3.42E-14	9.08E-13	-2.40	2.28E+02	5.48E+02
ENSMUSG00000029366	Dck	3.49E-14	9.23E-13	2.79	2.93E+02	1.05E+02
ENSMUSG00000060441	Trim5	3.54E-14	9.37E-13	2.54	1.01E+02	3.97E+01
ENSMUSG00000066152	Slc31a2	3.63E-14	9.59E-13	2.89	1.13E+03	3.91E+02
ENSMUSG00000025278	Flnb	3.77E-14	9.94E-13	2.73	4.13E+02	1.51E+02
ENSMUSG00000037826	Ppm1k	3.82E-14	1.00E-12	3.13	1.21E+02	3.86E+01
ENSMUSG00000006411	Nectin4	3.99E-14	1.05E-12	3.08	1.40E+02	4.55E+01
ENSMUSG00000019947	Arid5b	4.03E-14	1.06E-12	2.57	1.15E+03	4.46E+02
ENSMUSG00000042350	Arel1	4.60E-14	1.21E-12	2.30	4.45E+02	1.94E+02
ENSMUSG00000001123	Lgals9	5.77E-14	1.50E-12	2.33	2.73E+03	1.17E+03
ENSMUSG00000105283	Gm33370	5.83E-14	1.51E-12	3.93	4.04E+01	1.03E+01
ENSMUSG00000031669	Gins3	6.27E-14	1.62E-12	-3.29	1.74E+01	5.73E+01
ENSMUSG00000031639	Tlr3	7.48E-14	1.92E-12	2.94	1.33E+02	4.52E+01
ENSMUSG00000016206	H2-M3	7.85E-14	2.02E-12	2.76	2.19E+02	7.93E+01
ENSMUSG00000028793	Rnf19b	8.83E-14	2.26E-12	4.84	5.71E+03	1.18E+03
ENSMUSG00000035232	Pdk3	9.58E-14	2.45E-12	2.26	2.01E+02	8.90E+01
ENSMUSG00000003283	Hck	9.72E-14	2.49E-12	2.86	1.12E+03	3.92E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000020092	Pald1	9.99E-14	2.55E-12	-4.11	1.64E+01	6.74E+01
ENSMUSG00000087700	Gm15283	1.07E-13	2.72E-12	30.74	7.75E+00	2.52E-01
ENSMUSG00000024451	Arap3	1.08E-13	2.73E-12	-2.75	4.11E+01	1.13E+02
ENSMUSG00000030745	Il21r	1.10E-13	2.79E-12	2.34	9.00E+02	3.85E+02
ENSMUSG00000005973	Rcn1	1.11E-13	2.80E-12	2.38	1.27E+02	5.32E+01
ENSMUSG00000031497	Tnfsf13b	1.29E-13	3.27E-12	4.94	3.84E+01	7.78E+00
ENSMUSG00000039841	Zfp800	1.32E-13	3.32E-12	4.05	1.68E+03	4.15E+02
ENSMUSG00000035929	H2-Q4	1.37E-13	3.44E-12	6.38	6.13E+01	9.60E+00
ENSMUSG00000061232	H2-K1	1.62E-13	4.06E-12	2.25	8.72E+03	3.87E+03
ENSMUSG00000022867	Usp25	1.63E-13	4.07E-12	2.19	1.14E+03	5.22E+02
ENSMUSG00000024164	C3	1.66E-13	4.15E-12	15.47	1.75E+03	1.13E+02
ENSMUSG00000046159	Chrm3	2.04E-13	5.05E-12	81.34	7.29E+01	8.97E-01
ENSMUSG00000036594	H2-Aa	2.28E-13	5.64E-12	3.70	3.56E+03	9.63E+02
ENSMUSG00000054150	Syne3	2.49E-13	6.14E-12	-2.53	3.15E+01	7.96E+01
ENSMUSG00000035469	Rcbtb1	2.85E-13	7.01E-12	2.31	2.08E+02	9.00E+01
ENSMUSG00000020023	Tmcc3	2.91E-13	7.17E-12	2.99	5.76E+02	1.93E+02
ENSMUSG00000025612	Bach1	3.01E-13	7.40E-12	2.42	1.43E+03	5.91E+02
ENSMUSG00000021877	Arf4	3.02E-13	7.41E-12	2.19	1.75E+03	7.97E+02
ENSMUSG00000026866	Kynu	3.04E-13	7.45E-12	24.26	8.00E+01	3.30E+00
ENSMUSG00000050394	Armcx6	3.16E-13	7.71E-12	4.33	2.11E+01	4.89E+00
ENSMUSG00000053390	Zfp952	3.55E-13	8.63E-12	2.04	9.17E+01	4.50E+01
ENSMUSG00000031596	Slc7a2	3.59E-13	8.73E-12	8.09	3.51E+02	4.34E+01
ENSMUSG00000024610	Cd74	3.71E-13	8.99E-12	3.87	4.92E+03	1.27E+03
ENSMUSG00000031785	Adgrg1	4.40E-13	1.06E-11	-3.75	1.45E+01	5.42E+01
ENSMUSG00000005514	Por	4.51E-13	1.08E-11	-2.49	1.82E+03	4.53E+03

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000021624	Cd180	4.73E-13	1.13E-11	2.08	2.40E+03	1.15E+03
ENSMUSG00000049871	Nlrc3	4.81E-13	1.15E-11	-2.78	1.76E+01	4.89E+01
ENSMUSG00000005802	Slc30a4	4.83E-13	1.15E-11	3.67	2.75E+02	7.50E+01
ENSMUSG00000052477	C130026I21Rik	4.87E-13	1.16E-11	6.04	1.88E+01	3.12E+00
ENSMUSG00000064326	Siva1	4.95E-13	1.18E-11	-2.39	8.10E+01	1.93E+02
ENSMUSG00000025491	Ifitm1	5.04E-13	1.20E-11	5.53	8.44E+01	1.53E+01
ENSMUSG00000030748	Il4ra	5.09E-13	1.21E-11	4.30	3.26E+03	7.57E+02
ENSMUSG00000035441	Myo1d	5.32E-13	1.26E-11	3.13	8.06E+01	2.57E+01
ENSMUSG00000042489	Clspn	5.44E-13	1.29E-11	-4.90	3.96E+01	1.94E+02
ENSMUSG00000027822	Slc33a1	5.47E-13	1.29E-11	2.02	3.24E+02	1.60E+02
ENSMUSG00000038843	Gcnt1	5.52E-13	1.30E-11	-2.38	1.47E+02	3.51E+02
ENSMUSG00000023147	Get1	6.03E-13	1.42E-11	-2.57	4.77E+01	1.22E+02
ENSMUSG00000032750	Gab3	8.06E-13	1.89E-11	-3.31	5.94E+01	1.97E+02
ENSMUSG00000023953	Polh	8.60E-13	2.02E-11	-2.38	3.12E+01	7.41E+01
ENSMUSG00000026107	Nabp1	8.65E-13	2.03E-11	3.18	4.20E+02	1.32E+02
ENSMUSG00000017412	Cacnb4	8.74E-13	2.04E-11	6.18	1.66E+01	2.69E+00
ENSMUSG00000026827	Gpd2	9.96E-13	2.32E-11	3.02	1.25E+03	4.13E+02
ENSMUSG00000079293	Clec7a	1.07E-12	2.50E-11	2.79	3.24E+03	1.16E+03
ENSMUSG00000107320	Gm42549	1.11E-12	2.57E-11	6.03	6.25E+01	1.04E+01
ENSMUSG00000024601	Isoc1	1.12E-12	2.60E-11	2.09	2.84E+02	1.36E+02
ENSMUSG00000027347	Rasgrp1	1.14E-12	2.64E-11	27.82	1.61E+01	5.79E-01
ENSMUSG00000062373	Tmem65	1.18E-12	2.74E-11	-2.10	3.00E+02	6.28E+02
ENSMUSG00000047098	Rnf31	1.27E-12	2.93E-11	2.67	3.86E+01	1.45E+01
ENSMUSG00000038172	Ttc39b	1.31E-12	3.02E-11	2.53	2.25E+02	8.89E+01
ENSMUSG00000076431	Sox4	1.39E-12	3.20E-11	-4.76	8.73E+01	4.16E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000019487	Trip10	1.49E-12	3.41E-11	3.27	3.04E+02	9.27E+01
ENSMUSG00000034575	Tent4a	1.52E-12	3.49E-11	3.09	1.49E+02	4.83E+01
ENSMUSG00000090231	Cfb	1.53E-12	3.50E-11	76.12	1.32E+01	1.73E-01
ENSMUSG00000025089	Gfra1	1.57E-12	3.59E-11	6.78	1.02E+01	1.50E+00
ENSMUSG00000025076	Casp7	1.62E-12	3.69E-11	2.35	1.97E+02	8.36E+01
ENSMUSG00000020357	Flt4	1.63E-12	3.72E-11	17.53	1.55E+01	8.82E-01
ENSMUSG00000060586	H2-Eb1	1.73E-12	3.93E-11	3.77	1.86E+03	4.94E+02
ENSMUSG00000035455	Fignl1	1.75E-12	3.95E-11	-5.05	1.01E+01	5.12E+01
ENSMUSG00000079014	Serpina3i	1.94E-12	4.37E-11	46.96	7.18E+00	1.53E-01
ENSMUSG00000066026	Dhrs3	2.02E-12	4.54E-11	-2.64	9.03E+02	2.39E+03
ENSMUSG00000021838	Samd4	2.20E-12	4.95E-11	-3.23	3.04E+01	9.82E+01
ENSMUSG00000052760	A630001G21Rik	2.24E-12	5.03E-11	2.27	1.44E+02	6.35E+01
ENSMUSG00000032715	Trib3	2.58E-12	5.75E-11	2.42	3.80E+02	1.57E+02
ENSMUSG00000045216	Hs6st1	2.74E-12	6.08E-11	-2.37	1.46E+02	3.47E+02
ENSMUSG00000046718	Bst2	3.01E-12	6.63E-11	3.02	2.81E+03	9.32E+02
ENSMUSG00000044258	Ctla2a	3.04E-12	6.69E-11	-2.11	9.31E+01	1.96E+02
ENSMUSG00000041633	Kctd12b	3.23E-12	7.08E-11	-3.76	2.41E+01	9.08E+01
ENSMUSG00000035125	Gcfc2	3.25E-12	7.12E-11	-2.27	2.86E+01	6.50E+01
ENSMUSG00000029648	Flt1	3.26E-12	7.14E-11	6.25	1.38E+02	2.20E+01
ENSMUSG00000019699	Akt3	3.42E-12	7.46E-11	2.42	3.92E+02	1.62E+02
ENSMUSG00000038774	Ascc3	3.60E-12	7.82E-11	2.06	3.28E+02	1.60E+02
ENSMUSG00000033880	Lgals3bp	4.02E-12	8.70E-11	2.13	4.00E+03	1.88E+03
ENSMUSG00000032397	Tipin	4.40E-12	9.47E-11	-2.82	5.07E+01	1.43E+02
ENSMUSG00000031304	Il2rg	4.42E-12	9.52E-11	2.80	1.87E+03	6.67E+02
ENSMUSG00000057135	Scimp	4.46E-12	9.59E-11	6.34	2.27E+01	3.59E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000024732	Ccdc86	4.93E-12	1.05E-10	2.15	6.51E+02	3.02E+02
ENSMUSG00000022364	Tbc1d31	5.12E-12	1.09E-10	-2.98	1.86E+01	5.55E+01
ENSMUSG00000044350	Lacc1	5.35E-12	1.14E-10	2.72	8.57E+02	3.15E+02
ENSMUSG00000056394	Lig1	5.72E-12	1.21E-10	-3.26	4.97E+02	1.62E+03
ENSMUSG00000014846	Tppp3	5.79E-12	1.22E-10	6.56	6.70E+01	1.02E+01
ENSMUSG00000044700	Tmem201	5.88E-12	1.24E-10	-3.11	1.02E+01	3.19E+01
ENSMUSG00000037966	Ninj1	5.98E-12	1.26E-10	2.06	4.45E+03	2.16E+03
ENSMUSG00000037860	Aim2	6.12E-12	1.29E-10	2.09	4.92E+02	2.35E+02
ENSMUSG00000030269	Mtmr14	7.28E-12	1.53E-10	2.59	1.21E+03	4.65E+02
ENSMUSG00000024786	Majin	7.78E-12	1.62E-10	33.32	5.78E+00	1.73E-01
ENSMUSG00000021758	Ddx4	7.77E-12	1.62E-10	7.82	1.33E+01	1.70E+00
ENSMUSG00000035198	Tubg1	7.90E-12	1.64E-10	-2.06	9.92E+01	2.05E+02
ENSMUSG00000023952	Gtpbp2	8.05E-12	1.67E-10	2.13	6.78E+02	3.18E+02
ENSMUSG00000051786	Tubgcp6	9.00E-12	1.86E-10	-2.14	3.05E+01	6.51E+01
ENSMUSG00000054728	Phactr1	9.07E-12	1.87E-10	8.07	1.12E+01	1.39E+00
ENSMUSG00000018920	Cxcl16	9.10E-12	1.87E-10	3.91	4.34E+03	1.11E+03
ENSMUSG00000048756	Foxo3	9.29E-12	1.91E-10	-2.33	1.73E+02	4.03E+02
ENSMUSG00000018983	E2f2	9.41E-12	1.93E-10	-2.87	9.08E+01	2.61E+02
ENSMUSG00000063760	Rnf217	9.73E-12	1.99E-10	2.45	1.49E+02	6.09E+01
ENSMUSG00000027315	Spint1	1.00E-11	2.04E-10	4.95	4.32E+01	8.73E+00
ENSMUSG00000005413	Hmox1	1.07E-11	2.19E-10	-2.31	1.28E+03	2.96E+03
ENSMUSG00000022586	Ly6i	1.09E-11	2.21E-10	51.36	2.14E+01	4.17E-01
ENSMUSG00000073490	Ifi207	1.10E-11	2.24E-10	2.73	2.03E+03	7.45E+02
ENSMUSG00000057367	Birc2	1.12E-11	2.28E-10	2.02	2.24E+02	1.11E+02
ENSMUSG00000055884	Fancm	1.24E-11	2.51E-10	-3.47	1.29E+01	4.48E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000020476	Dbnl	1.28E-11	2.59E-10	2.22	1.24E+03	5.60E+02
ENSMUSG00000046688	Tifa	1.32E-11	2.67E-10	2.41	1.03E+03	4.26E+02
ENSMUSG00000024754	Cemip2	1.43E-11	2.88E-10	3.32	6.79E+02	2.05E+02
ENSMUSG00000026770	Il2ra	1.47E-11	2.95E-10	15.51	5.02E+00	3.24E-01
ENSMUSG00000024899	Papss2	1.47E-11	2.95E-10	2.30	1.04E+02	4.55E+01
ENSMUSG00000009575	Cbx5	1.56E-11	3.11E-10	-2.43	2.23E+02	5.43E+02
ENSMUSG00000047409	Ctdspl	1.60E-11	3.19E-10	-2.75	3.59E+01	9.86E+01
ENSMUSG00000050777	Tmem37	1.61E-11	3.22E-10	-3.45	8.99E+01	3.10E+02
ENSMUSG00000004446	Bid	1.73E-11	3.43E-10	2.08	7.15E+02	3.43E+02
ENSMUSG00000040276	Pacsin1	1.79E-11	3.55E-10	15.91	1.49E+01	9.39E-01
ENSMUSG00000000184	Ccnd2	1.88E-11	3.71E-10	3.05	2.40E+03	7.86E+02
ENSMUSG00000022790	Igsf11	2.03E-11	4.00E-10	8.45	2.36E+01	2.80E+00
ENSMUSG00000061607	Mdc1	2.15E-11	4.23E-10	-2.30	6.04E+01	1.39E+02
ENSMUSG00000071713	Csf2rb	2.33E-11	4.56E-10	2.21	4.57E+03	2.07E+03
ENSMUSG00000039217	Il18	2.39E-11	4.67E-10	2.32	2.40E+02	1.03E+02
ENSMUSG00000086742	Gm16201	2.53E-11	4.93E-10	-2.91	1.74E+01	5.06E+01
ENSMUSG00000018909	Arrb1	2.61E-11	5.07E-10	-2.29	2.06E+02	4.72E+02
ENSMUSG00000029722	Agfg2	2.70E-11	5.22E-10	-2.64	1.35E+02	3.56E+02
ENSMUSG00000029438	Bcl7a	2.83E-11	5.45E-10	-4.03	9.56E+00	3.86E+01
ENSMUSG00000037972	Snn	3.07E-11	5.87E-10	3.46	1.40E+02	4.05E+01
ENSMUSG00000022126	Acod1	3.13E-11	5.98E-10	23.70	1.56E+04	6.57E+02
ENSMUSG00000092564	BC051226	3.35E-11	6.39E-10	2.00	1.26E+02	6.28E+01
ENSMUSG00000020694	Tlk2	3.46E-11	6.59E-10	2.04	5.15E+02	2.52E+02
ENSMUSG00000026365	Cfh	3.52E-11	6.68E-10	2.44	1.47E+02	6.02E+01
ENSMUSG00000068417	Pnp2	3.58E-11	6.80E-10	6.15	1.14E+01	1.86E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000031647	Mfap3l	3.99E-11	7.57E-10	-2.54	2.45E+01	6.22E+01
ENSMUSG00000054871	Tmem158	4.15E-11	7.86E-10	-2.85	6.91E+01	1.97E+02
ENSMUSG00000110141	Gm45684	4.46E-11	8.43E-10	18.93	9.95E+00	5.26E-01
ENSMUSG00000045502	Hcar2	4.60E-11	8.67E-10	25.56	8.79E+02	3.44E+01
ENSMUSG00000026357	Rgs18	4.63E-11	8.72E-10	-2.28	1.01E+02	2.30E+02
ENSMUSG00000000409	Lck	4.99E-11	9.37E-10	4.89	9.68E+00	1.98E+00
ENSMUSG00000031403	Dkc1	5.33E-11	9.97E-10	-3.02	8.99E+01	2.71E+02
ENSMUSG00000038658	Ric1	5.37E-11	1.00E-09	2.05	3.28E+02	1.60E+02
ENSMUSG00000023067	Cdkn1a	6.04E-11	1.12E-09	3.08	2.06E+04	6.68E+03
ENSMUSG00000033450	Tagap	6.15E-11	1.14E-09	8.37	3.88E+02	4.64E+01
ENSMUSG00000028702	Rad54l	6.53E-11	1.21E-09	-2.87	4.73E+01	1.36E+02
ENSMUSG00000026974	Zmynd19	6.79E-11	1.25E-09	-2.29	3.48E+01	7.98E+01
ENSMUSG00000046096	Mosmo	6.81E-11	1.25E-09	2.07	1.40E+02	6.79E+01
ENSMUSG00000038332	Sesn1	6.87E-11	1.26E-09	-5.43	8.32E+01	4.52E+02
ENSMUSG00000037406	Htra4	7.42E-11	1.36E-09	6.37	3.99E+01	6.26E+00
ENSMUSG00000022684	Bfar	7.55E-11	1.38E-09	2.20	7.08E+02	3.22E+02
ENSMUSG00000031971	Ccsap	7.64E-11	1.39E-09	-5.22	1.26E+01	6.58E+01
ENSMUSG00000037697	Ddhd1	7.83E-11	1.42E-09	2.27	1.43E+02	6.31E+01
ENSMUSG00000039055	Eme1	8.84E-11	1.60E-09	-3.27	9.48E+00	3.10E+01
ENSMUSG00000026581	Sell	9.25E-11	1.66E-09	10.71	7.21E+00	6.73E-01
ENSMUSG00000007570	Fance	9.99E-11	1.79E-09	-2.33	4.88E+01	1.14E+02
ENSMUSG00000048922	Cdca2	1.01E-10	1.80E-09	-3.34	4.27E+01	1.42E+02
ENSMUSG00000045751	Mms22l	1.06E-10	1.90E-09	-2.87	2.95E+01	8.46E+01
ENSMUSG00000038866	Zcchc2	1.07E-10	1.91E-09	2.51	3.00E+02	1.20E+02
ENSMUSG00000033960	Jcad	1.08E-10	1.92E-09	2.67	8.60E+01	3.22E+01

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ENSMUSG00000020464	Pnpt1	1.08E-10	1.92E-09	2.47	1.16E+02	4.69E+01
ENSMUSG00000047446	Arl4a	1.08E-10	1.93E-09	2.22	2.05E+02	9.21E+01
ENSMUSG00000055782	Abcd2	1.09E-10	1.94E-09	-7.11	6.65E+00	4.73E+01
ENSMUSG00000042744	Hectd4	1.12E-10	1.98E-09	2.09	1.42E+02	6.82E+01
ENSMUSG00000020593	Lpin1	1.18E-10	2.09E-09	-2.91	7.89E+01	2.29E+02
ENSMUSG00000076441	Ass1	1.23E-10	2.18E-09	3.36	1.74E+02	5.17E+01
ENSMUSG00000055322	Tns1	1.27E-10	2.25E-09	-2.80	1.71E+02	4.79E+02
ENSMUSG00000101013	A630072M18Rik	1.30E-10	2.29E-09	2.71	2.51E+02	9.26E+01
ENSMUSG00000027490	E2f1	1.32E-10	2.33E-09	-2.20	1.31E+02	2.88E+02
ENSMUSG00000031788	Kifc3	1.38E-10	2.43E-09	-2.31	4.88E+01	1.13E+02
ENSMUSG00000056116	H2-T22	1.61E-10	2.82E-09	3.03	2.80E+02	9.26E+01
ENSMUSG00000032555	Topbp1	1.61E-10	2.82E-09	-2.33	8.83E+01	2.06E+02
ENSMUSG00000033470	Cysltr2	1.75E-10	3.06E-09	5.21	3.88E+01	7.45E+00
ENSMUSG00000107355	AI839979	1.76E-10	3.07E-09	-2.49	2.51E+01	6.25E+01
ENSMUSG00000049969	Plekhf2	2.28E-10	3.95E-09	2.07	4.79E+02	2.31E+02
ENSMUSG00000032184	Lysmd2	2.35E-10	4.04E-09	2.92	2.44E+01	8.38E+00
ENSMUSG00000047810	Ccdc88b	2.67E-10	4.59E-09	2.69	4.42E+02	1.64E+02
ENSMUSG00000032350	Gclc	2.81E-10	4.81E-09	-2.36	2.72E+02	6.43E+02
ENSMUSG00000086513	Gvin-ps1	2.84E-10	4.85E-09	15.26	8.71E+00	5.71E-01
ENSMUSG00000027296	Itpka	2.84E-10	4.86E-09	32.10	9.17E+00	2.86E-01
ENSMUSG00000006818	Sod2	2.98E-10	5.08E-09	3.71	4.71E+03	1.27E+03
ENSMUSG00000029640	Usp12	3.16E-10	5.37E-09	2.93	5.00E+01	1.71E+01
ENSMUSG00000048186	Bend7	3.31E-10	5.62E-09	6.50	1.25E+01	1.93E+00
ENSMUSG00000040987	Mill2	3.31E-10	5.62E-09	2.99	6.13E+01	2.05E+01
ENSMUSG00000046727	Cystm1	3.32E-10	5.63E-09	2.55	4.14E+01	1.63E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000035842	Ddx11	3.47E-10	5.86E-09	-4.09	6.99E+00	2.86E+01
ENSMUSG00000025153	Fasn	3.53E-10	5.96E-09	-2.25	1.10E+02	2.48E+02
ENSMUSG00000050234	Gja4	3.55E-10	5.99E-09	45.52	6.96E+00	1.53E-01
ENSMUSG00000035852	Misp	3.89E-10	6.54E-09	14.62	4.73E+00	3.24E-01
ENSMUSG00000041859	Mcm3	4.32E-10	7.22E-09	-3.16	2.37E+02	7.51E+02
ENSMUSG00000026630	Batf3	4.43E-10	7.40E-09	4.82	4.37E+01	9.06E+00
ENSMUSG00000019842	Traf3ip2	4.56E-10	7.60E-09	2.68	4.92E+01	1.84E+01
ENSMUSG00000026566	Mpzl1	4.60E-10	7.66E-09	-2.51	2.84E+01	7.12E+01
ENSMUSG00000039748	Exo1	4.67E-10	7.77E-09	-7.16	3.73E+00	2.67E+01
ENSMUSG00000089940	Gm4117	5.01E-10	8.33E-09	3.21	1.67E+01	5.19E+00
ENSMUSG00000004151	Etv1	5.33E-10	8.86E-09	-2.85	1.68E+01	4.77E+01
ENSMUSG00000031662	Snx20	5.45E-10	9.03E-09	2.18	1.02E+03	4.67E+02
ENSMUSG00000052446	Zfp961	5.60E-10	9.25E-09	3.30	4.94E+01	1.50E+01
ENSMUSG00000109715	Gm45606	5.83E-10	9.62E-09	-2.95	1.01E+01	2.98E+01
ENSMUSG00000111118	Gm6545	5.92E-10	9.76E-09	18.85	1.91E+01	1.01E+00
ENSMUSG00000018537	Pcgf2	6.06E-10	9.97E-09	-2.09	2.76E+01	5.76E+01
ENSMUSG00000021133	Susd6	6.07E-10	9.98E-09	2.26	9.75E+02	4.31E+02
ENSMUSG00000049744	Arhgap15	7.02E-10	1.15E-08	2.13	1.85E+02	8.66E+01
ENSMUSG00000032204	Aqp9	7.15E-10	1.17E-08	3.78	5.21E+01	1.38E+01
ENSMUSG00000097113	Gm19705	7.37E-10	1.20E-08	2.37	4.23E+01	1.79E+01
ENSMUSG00000067642	Adgrf3	7.84E-10	1.27E-08	56.38	8.63E+00	1.53E-01
ENSMUSG00000021575	Ahrr	7.92E-10	1.29E-08	2.82	7.09E+01	2.51E+01
ENSMUSG00000039713	Plekhg5	7.94E-10	1.29E-08	-3.07	1.05E+01	3.24E+01
ENSMUSG00000037474	Dtl	8.27E-10	1.34E-08	-5.20	1.88E+01	9.78E+01
ENSMUSG00000029730	Mcm7	8.31E-10	1.34E-08	-3.51	2.01E+02	7.06E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000059851	Kmt5c	8.69E-10	1.40E-08	-2.34	4.35E+01	1.02E+02
ENSMUSG00000041936	Agrn	9.26E-10	1.49E-08	2.02	9.33E+01	4.61E+01
ENSMUSG00000022833	Ccdc14	9.81E-10	1.57E-08	-3.48	6.65E+00	2.31E+01
ENSMUSG00000039908	Slc26a11	1.02E-09	1.64E-08	-3.24	7.51E+01	2.43E+02
ENSMUSG00000055435	Maf	1.06E-09	1.70E-08	-2.29	2.43E+03	5.57E+03
ENSMUSG00000005470	Asf1b	1.09E-09	1.74E-08	-2.67	8.38E+01	2.24E+02
ENSMUSG00000047649	Cd3eap	1.10E-09	1.75E-08	-2.10	8.72E+01	1.84E+02
ENSMUSG00000040229	Gpr34	1.11E-09	1.77E-08	-2.95	2.24E+01	6.60E+01
ENSMUSG00000030978	Rrm1	1.14E-09	1.81E-08	-2.35	2.14E+02	5.03E+02
ENSMUSG00000039497	Dse	1.26E-09	1.99E-08	2.33	8.51E+02	3.66E+02
ENSMUSG00000001995	Sipa1l2	1.33E-09	2.08E-08	-2.11	8.58E+01	1.81E+02
ENSMUSG00000000811	Txnrd3	1.44E-09	2.26E-08	-2.09	4.53E+01	9.45E+01
ENSMUSG00000026228	Htr2b	1.47E-09	2.29E-08	-2.55	5.56E+01	1.42E+02
ENSMUSG00000049939	Lrrc4	1.47E-09	2.29E-08	12.81	1.20E+01	9.33E-01
ENSMUSG00000003153	Slc2a3	1.49E-09	2.32E-08	-2.92	8.98E+00	2.63E+01
ENSMUSG00000041147	Brca2	1.50E-09	2.33E-08	-4.08	1.11E+01	4.51E+01
ENSMUSG00000021287	Xrcc3	1.64E-09	2.53E-08	-4.96	4.17E+00	2.07E+01
ENSMUSG00000039804	Ncoa5	1.76E-09	2.71E-08	2.26	3.85E+02	1.71E+02
ENSMUSG00000029322	Plac8	1.79E-09	2.76E-08	5.47	1.68E+01	3.08E+00
ENSMUSG00000035891	Cerk	1.82E-09	2.80E-08	-2.11	4.69E+02	9.90E+02
ENSMUSG00000097567	nan	1.88E-09	2.89E-08	2.85	1.85E+01	6.48E+00
ENSMUSG00000025911	Adhfe1	1.92E-09	2.93E-08	5.70	2.05E+01	3.60E+00
ENSMUSG00000023913	Pla2g7	2.12E-09	3.23E-08	2.60	1.53E+02	5.88E+01
ENSMUSG00000019823	Mical1	2.22E-09	3.36E-08	-2.11	1.46E+02	3.09E+02
ENSMUSG00000026596	Abl2	2.29E-09	3.47E-08	2.54	7.03E+02	2.77E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000021322	Aoah	2.31E-09	3.49E-08	2.30	3.62E+02	1.57E+02
ENSMUSG00000037151	Lrrc20	2.41E-09	3.63E-08	-2.41	4.80E+01	1.16E+02
ENSMUSG00000000686	Abhd15	2.51E-09	3.78E-08	-4.21	6.03E+00	2.54E+01
ENSMUSG00000053617	Sh3pxd2a	2.58E-09	3.87E-08	-2.36	4.71E+01	1.11E+02
ENSMUSG00000033294	Noc4l	2.58E-09	3.87E-08	3.14	2.22E+02	7.06E+01
ENSMUSG00000022788	Fgd4	2.61E-09	3.90E-08	-3.38	6.40E+01	2.16E+02
ENSMUSG00000032089	Il10ra	2.65E-09	3.96E-08	2.65	8.81E+02	3.33E+02
ENSMUSG00000048911	Rnf24	2.83E-09	4.22E-08	4.00	7.74E+01	1.93E+01
ENSMUSG00000021366	Hivep1	2.83E-09	4.22E-08	2.85	2.90E+02	1.02E+02
ENSMUSG00000093726	Gm20667	2.88E-09	4.29E-08	-6.69	2.11E+00	1.41E+01
ENSMUSG00000028527	Ak4	3.00E-09	4.45E-08	4.18	3.27E+01	7.83E+00
ENSMUSG00000040264	Gbp2b	3.24E-09	4.79E-08	37.14	5.68E+00	1.53E-01
ENSMUSG00000061878	Sphk1	3.29E-09	4.86E-08	6.26	5.56E+01	8.89E+00
ENSMUSG00000000751	Rpa1	3.36E-09	4.95E-08	-2.10	1.45E+02	3.03E+02
ENSMUSG00000037405	Icam1	3.44E-09	5.06E-08	5.91	8.64E+03	1.46E+03
ENSMUSG00000022360	Atad2	3.51E-09	5.17E-08	-2.28	1.43E+02	3.27E+02
ENSMUSG00000064090	Vrk2	3.52E-09	5.17E-08	2.57	4.66E+02	1.81E+02
ENSMUSG00000015846	Rxra	3.58E-09	5.26E-08	-2.32	1.10E+02	2.54E+02
ENSMUSG00000019082	Slc25a22	3.78E-09	5.53E-08	3.09	1.63E+02	5.26E+01
ENSMUSG00000038485	Socs7	3.78E-09	5.53E-08	2.19	5.22E+02	2.39E+02
ENSMUSG00000020077	Srgn	3.80E-09	5.55E-08	2.63	2.94E+03	1.12E+03
ENSMUSG00000021565	Slc6a19	3.87E-09	5.63E-08	6.86	1.66E+01	2.43E+00
ENSMUSG00000092627	D130058E05Rik	4.01E-09	5.81E-08	-5.27	4.74E+00	2.50E+01
ENSMUSG00000033781	Asb13	4.12E-09	5.96E-08	2.46	7.86E+01	3.19E+01
ENSMUSG00000005410	Mcm5	4.30E-09	6.19E-08	-3.33	1.09E+02	3.65E+02

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ENSMUSG00000039842	Mcph1	4.33E-09	6.22E-08	-2.13	4.20E+01	8.97E+01
ENSMUSG00000079505	Gm11131	4.39E-09	6.30E-08	5.51	9.79E+00	1.78E+00
ENSMUSG00000039232	Stx11	4.44E-09	6.36E-08	3.81	6.12E+02	1.60E+02
ENSMUSG00000041406	BC055324	4.48E-09	6.40E-08	-3.67	1.19E+01	4.36E+01
ENSMUSG00000027676	Ccdc39	4.76E-09	6.79E-08	5.26	9.50E+00	1.81E+00
ENSMUSG00000041836	Ptpre	5.26E-09	7.47E-08	-2.31	5.51E+02	1.28E+03
ENSMUSG00000022177	Haus4	5.40E-09	7.65E-08	-2.93	3.14E+01	9.20E+01
ENSMUSG00000097534	Gm16675	5.69E-09	8.05E-08	6.16	9.28E+00	1.51E+00
ENSMUSG00000036206	Sh3bp4	5.68E-09	8.05E-08	3.19	7.66E+01	2.40E+01
ENSMUSG00000046080	Clec9a	5.75E-09	8.12E-08	34.50	3.33E+01	9.64E-01
ENSMUSG00000002289	Angptl4	5.83E-09	8.23E-08	-4.50	7.07E+00	3.18E+01
ENSMUSG00000027242	Wdr76	5.85E-09	8.25E-08	-3.80	2.39E+01	9.08E+01
ENSMUSG00000041685	Fcho2	5.95E-09	8.38E-08	2.17	1.05E+03	4.82E+02
ENSMUSG00000039236	Isg20	6.41E-09	8.99E-08	5.36	4.73E+01	8.83E+00
ENSMUSG00000110235	Gm5086	6.56E-09	9.18E-08	-3.86	7.72E+00	2.98E+01
ENSMUSG00000032826	Ank2	6.64E-09	9.29E-08	5.31	3.52E+01	6.63E+00
ENSMUSG00000114980	4933432I03Rik	7.12E-09	9.92E-08	6.17	1.35E+01	2.18E+00
ENSMUSG00000027330	Cdc25b	7.31E-09	1.02E-07	-2.24	9.90E+01	2.22E+02
ENSMUSG00000078349	AW011738	7.32E-09	1.02E-07	5.86	7.59E+00	1.30E+00
ENSMUSG00000051341	Zfp52	7.35E-09	1.02E-07	-2.51	3.43E+01	8.63E+01
ENSMUSG00000067297	Ifit1bl2	7.39E-09	1.02E-07	10.55	4.38E+00	4.15E-01
ENSMUSG00000036067	Slc2a6	7.56E-09	1.05E-07	5.57	1.16E+03	2.08E+02
ENSMUSG00000027351	Spred1	7.77E-09	1.07E-07	2.75	1.53E+03	5.57E+02
ENSMUSG00000063889	Crem	7.98E-09	1.10E-07	3.53	6.34E+02	1.79E+02
ENSMUSG00000022070	Bora	8.23E-09	1.13E-07	-3.34	1.07E+01	3.57E+01

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ENSMUSG00000041199	Rpusd1	8.27E-09	1.14E-07	-2.12	2.81E+01	5.95E+01
ENSMUSG00000022673	Mcm4	8.31E-09	1.14E-07	-2.59	1.15E+02	2.97E+02
ENSMUSG00000071855	Ccdc112	8.59E-09	1.18E-07	-2.13	4.15E+01	8.84E+01
ENSMUSG00000055809	Dnaaf3	8.81E-09	1.20E-07	3.23	3.79E+01	1.17E+01
ENSMUSG00000041058	Wwp1	9.00E-09	1.23E-07	-2.10	5.56E+02	1.17E+03
ENSMUSG00000030830	Itgal	9.56E-09	1.30E-07	3.14	8.57E+02	2.73E+02
ENSMUSG00000089844	A530032D15Rik	9.75E-09	1.33E-07	13.10	4.81E+00	3.67E-01
ENSMUSG00000027171	Prrg4	9.92E-09	1.35E-07	4.55	3.19E+01	7.01E+00
ENSMUSG00000036599	Chst12	1.03E-08	1.40E-07	-2.00	7.42E+01	1.49E+02
ENSMUSG00000047712	Ust	1.07E-08	1.45E-07	2.77	8.55E+01	3.08E+01
ENSMUSG00000073705	Cenps	1.09E-08	1.47E-07	-3.13	1.63E+01	5.11E+01
ENSMUSG00000116961	Gm49662	1.10E-08	1.48E-07	13.49	5.62E+00	4.17E-01
ENSMUSG00000034522	Zfp395	1.10E-08	1.49E-07	-3.56	1.17E+01	4.17E+01
ENSMUSG00000115855	Gm34643	1.13E-08	1.52E-07	4.58	1.95E+01	4.25E+00
ENSMUSG00000027203	Dut	1.16E-08	1.55E-07	-2.67	7.92E+01	2.11E+02
ENSMUSG00000030156	Cd69	1.18E-08	1.58E-07	16.03	1.47E+03	9.15E+01
ENSMUSG00000053957	Gm12474	1.24E-08	1.66E-07	5.97	7.77E+00	1.30E+00
ENSMUSG00000029314	Gpat3	1.24E-08	1.66E-07	3.94	3.64E+01	9.24E+00
ENSMUSG00000058392	Rrp1b	1.26E-08	1.68E-07	-2.60	5.18E+01	1.35E+02
ENSMUSG00000027832	Ptx3	1.27E-08	1.70E-07	5.24	2.21E+01	4.21E+00
ENSMUSG00000090394	4930523C07Rik	1.35E-08	1.79E-07	2.30	7.19E+01	3.13E+01
ENSMUSG00000043872	Zmym1	1.36E-08	1.81E-07	-2.47	2.34E+01	5.79E+01
ENSMUSG00000029992	Gfpt1	1.40E-08	1.85E-07	2.01	6.82E+02	3.40E+02
ENSMUSG00000025025	Mxi1	1.42E-08	1.88E-07	-2.18	1.66E+02	3.63E+02
ENSMUSG00000112093	Gm47941	1.43E-08	1.89E-07	17.52	4.42E+00	2.52E-01

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ENSMUSG00000021338	Carmil1	1.46E-08	1.93E-07	3.10	1.21E+02	3.89E+01
ENSMUSG00000069844	Sco1	1.46E-08	1.93E-07	2.22	1.18E+02	5.31E+01
ENSMUSG00000033857	Engase	1.47E-08	1.94E-07	-3.66	1.80E+01	6.59E+01
ENSMUSG00000095609	Gm21188	1.50E-08	1.98E-07	3.22	3.03E+01	9.39E+00
ENSMUSG00000066861	Oas1g	1.63E-08	2.15E-07	4.15	1.43E+01	3.45E+00
ENSMUSG00000061603	Akap6	1.64E-08	2.15E-07	4.31	3.80E+01	8.83E+00
ENSMUSG00000057315	Arhgap24	1.69E-08	2.21E-07	-2.17	9.19E+01	1.99E+02
ENSMUSG00000021714	Cenpk	1.70E-08	2.22E-07	-2.68	2.81E+01	7.54E+01
ENSMUSG00000049409	Prokr1	1.84E-08	2.39E-07	-6.09	2.98E+00	1.81E+01
ENSMUSG00000038807	Rap1gap2	1.90E-08	2.47E-07	3.75	1.76E+01	4.70E+00
ENSMUSG00000073599	Ecscr	1.91E-08	2.49E-07	4.44	1.17E+01	2.64E+00
ENSMUSG00000020185	E2f7	1.92E-08	2.50E-07	-4.04	1.13E+01	4.56E+01
ENSMUSG00000097471	5830432E09Rik	2.03E-08	2.63E-07	-3.33	9.03E+00	3.01E+01
ENSMUSG00000042659	Arrdc4	2.05E-08	2.65E-07	2.44	2.05E+02	8.39E+01
ENSMUSG00000050370	Ch25h	2.07E-08	2.68E-07	12.91	3.07E+01	2.38E+00
ENSMUSG00000055200	Sertad3	2.10E-08	2.71E-07	2.32	4.58E+02	1.97E+02
ENSMUSG00000031758	Cdyl2	2.10E-08	2.71E-07	2.26	1.36E+02	6.01E+01
ENSMUSG00000028128	F3	2.17E-08	2.80E-07	37.48	6.88E+01	1.83E+00
ENSMUSG00000038608	Dock10	2.18E-08	2.81E-07	2.12	1.25E+03	5.91E+02
ENSMUSG00000030589	Rasgrp4	2.21E-08	2.84E-07	2.22	6.39E+01	2.88E+01
ENSMUSG00000062082	Cd200r4	2.24E-08	2.87E-07	2.00	8.67E+02	4.33E+02
ENSMUSG00000069793	Slfn9	2.25E-08	2.88E-07	2.65	1.47E+02	5.56E+01
ENSMUSG00000016528	Mapkapk2	2.32E-08	2.97E-07	2.27	3.07E+03	1.35E+03
ENSMUSG00000056124	B4galt6	2.34E-08	2.98E-07	-2.12	4.25E+02	9.01E+02
ENSMUSG00000034110	Kctd7	2.35E-08	2.99E-07	-2.22	1.56E+01	3.47E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000022583	Ly6f	2.43E-08	3.09E-07	25.30	4.39E+00	1.73E-01
ENSMUSG00000033610	Pank1	2.49E-08	3.16E-07	-2.95	3.13E+01	9.25E+01
ENSMUSG00000072109	A530040E14Rik	2.53E-08	3.21E-07	15.67	3.49E+00	2.23E-01
ENSMUSG00000028885	Smpdl3b	2.57E-08	3.24E-07	2.80	1.18E+02	4.22E+01
ENSMUSG00000022945	Chaf1b	2.58E-08	3.26E-07	-2.21	6.74E+01	1.49E+02
ENSMUSG00000066357	Wdr6	2.78E-08	3.50E-07	-2.30	4.54E+01	1.04E+02
ENSMUSG00000090812	Samd15	2.95E-08	3.71E-07	2.97	1.75E+01	5.89E+00
ENSMUSG00000042284	Itga1	2.97E-08	3.73E-07	3.87	3.50E+01	9.05E+00
ENSMUSG00000032402	Smad3	3.01E-08	3.79E-07	-2.26	4.94E+01	1.12E+02
ENSMUSG00000068264	Ap5s1	3.04E-08	3.81E-07	-2.32	7.57E+01	1.76E+02
ENSMUSG00000026773	Pfkfb3	3.18E-08	3.99E-07	2.39	4.15E+02	1.73E+02
ENSMUSG00000028093	Acp6	3.19E-08	4.01E-07	-2.04	3.29E+01	6.70E+01
ENSMUSG00000022184	Fbxo4	3.24E-08	4.06E-07	2.17	2.72E+02	1.25E+02
ENSMUSG00000101823	Gm29438	3.26E-08	4.07E-07	4.49	1.81E+01	4.03E+00
ENSMUSG00000025574	Tk1	3.29E-08	4.11E-07	-3.05	9.17E+01	2.80E+02
ENSMUSG00000040978	Gm11992	3.31E-08	4.13E-07	10.21	1.06E+01	1.04E+00
ENSMUSG00000079018	Ly6c1	3.42E-08	4.26E-07	10.78	6.69E+00	6.20E-01
ENSMUSG00000047067	Dusp28	3.51E-08	4.36E-07	2.22	8.60E+01	3.86E+01
ENSMUSG00000086109	Gm13391	3.65E-08	4.53E-07	-2.41	1.76E+01	4.24E+01
ENSMUSG00000026355	Mcm6	3.66E-08	4.54E-07	-2.41	3.12E+02	7.52E+02
ENSMUSG00000045980	Tmem104	3.70E-08	4.58E-07	-2.01	4.55E+02	9.16E+02
ENSMUSG00000054263	Lifr	3.79E-08	4.68E-07	2.36	4.09E+01	1.73E+01
ENSMUSG00000020649	Rrm2	3.92E-08	4.84E-07	-3.16	6.42E+01	2.03E+02
ENSMUSG00000059323	Tonsl	3.94E-08	4.86E-07	-4.13	1.18E+01	4.89E+01
ENSMUSG00000039031	Arhgap18	3.98E-08	4.91E-07	-2.36	4.11E+02	9.67E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000097128	nan	4.06E-08	4.99E-07	14.11	6.59E+00	4.67E-01
ENSMUSG00000034041	Lyl1	4.54E-08	5.58E-07	-2.41	1.38E+02	3.34E+02
ENSMUSG00000040329	Il7	4.64E-08	5.69E-07	3.90	1.06E+01	2.71E+00
ENSMUSG00000025577	Cbx2	4.64E-08	5.69E-07	-5.22	4.38E+00	2.29E+01
ENSMUSG00000038705	Gmeb2	4.95E-08	6.05E-07	2.03	2.11E+02	1.04E+02
ENSMUSG00000002602	Axl	5.06E-08	6.18E-07	2.78	9.35E+02	3.36E+02
ENSMUSG00000036768	Kif15	5.07E-08	6.19E-07	-2.06	7.16E+01	1.47E+02
ENSMUSG00000027323	Rad51	5.48E-08	6.64E-07	-2.87	3.52E+01	1.01E+02
ENSMUSG00000023940	Sgo1	5.49E-08	6.64E-07	-2.76	2.79E+01	7.70E+01
ENSMUSG00000030722	Nfatc2ip	5.66E-08	6.84E-07	-2.28	1.92E+01	4.38E+01
ENSMUSG00000018427	Ypel2	6.15E-08	7.40E-07	-4.10	2.14E+01	8.79E+01
ENSMUSG00000028381	Ugcg	6.20E-08	7.44E-07	2.29	2.86E+02	1.25E+02
ENSMUSG00000047473	Zfp30	6.33E-08	7.60E-07	-3.45	6.59E+00	2.27E+01
ENSMUSG00000050410	Tcf19	6.40E-08	7.67E-07	-3.19	2.60E+01	8.29E+01
ENSMUSG00000025195	Dnmbp	6.55E-08	7.83E-07	-2.59	2.26E+01	5.85E+01
ENSMUSG00000069893	9930111J21Rik1	6.65E-08	7.93E-07	6.39	6.29E+00	9.84E-01
ENSMUSG00000024151	Msh2	6.79E-08	8.09E-07	-2.64	6.26E+01	1.65E+02
ENSMUSG00000028633	Ctps	6.85E-08	8.14E-07	-2.92	1.48E+01	4.32E+01
ENSMUSG00000033364	Usp37	7.16E-08	8.50E-07	-2.14	2.58E+01	5.52E+01
ENSMUSG00000055612	Cdca7	7.52E-08	8.89E-07	-9.32	3.33E+00	3.10E+01
ENSMUSG00000028664	Ephb2	7.68E-08	9.06E-07	8.40	1.10E+01	1.31E+00
ENSMUSG00000027962	Vcam1	7.75E-08	9.14E-07	3.54	3.14E+02	8.87E+01
ENSMUSG00000001228	Uhrf1	7.89E-08	9.29E-07	-3.47	3.74E+01	1.30E+02
ENSMUSG00000037509	Arhgef4	7.93E-08	9.32E-07	-3.59	5.38E+00	1.93E+01
ENSMUSG00000045045	Lrfn4	8.49E-08	9.96E-07	-3.30	6.34E+00	2.09E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000097415	AU020206	8.69E-08	1.02E-06	2.36	9.51E+02	4.04E+02
ENSMUSG00000044066	Cep68	8.74E-08	1.02E-06	-2.42	1.84E+01	4.45E+01
ENSMUSG00000033985	Tesk2	8.82E-08	1.03E-06	-4.34	3.76E+00	1.63E+01
ENSMUSG00000053801	Grwd1	8.87E-08	1.04E-06	-2.71	3.34E+01	9.06E+01
ENSMUSG00000029923	Rab19	9.10E-08	1.06E-06	2.28	4.59E+01	2.01E+01
ENSMUSG00000022494	Shisa9	9.62E-08	1.12E-06	-3.17	8.89E+00	2.81E+01
ENSMUSG00000021929	Kpna3	9.76E-08	1.13E-06	2.36	1.65E+03	6.99E+02
ENSMUSG00000054008	Ndst1	9.96E-08	1.15E-06	-2.09	1.33E+02	2.78E+02
ENSMUSG00000038644	Pold1	1.01E-07	1.17E-06	-3.06	3.61E+01	1.11E+02
ENSMUSG00000025001	Hells	1.03E-07	1.19E-06	-3.82	4.67E+01	1.78E+02
ENSMUSG00000020739	Nup85	1.07E-07	1.24E-06	-2.16	6.19E+01	1.34E+02
ENSMUSG00000038379	Ttk	1.08E-07	1.24E-06	-2.51	3.31E+01	8.31E+01
ENSMUSG00000089715	Cbx6	1.13E-07	1.29E-06	-2.39	9.75E+01	2.33E+02
ENSMUSG00000009654	Oit3	1.16E-07	1.33E-06	-2.21	3.65E+01	8.06E+01
ENSMUSG00000006715	Gmnn	1.18E-07	1.35E-06	-2.48	6.48E+01	1.60E+02
ENSMUSG00000030346	Rad51ap1	1.18E-07	1.35E-06	-2.76	3.06E+01	8.44E+01
ENSMUSG00000032254	Kif23	1.26E-07	1.43E-06	-2.08	1.88E+02	3.91E+02
ENSMUSG00000002997	Prkar2b	1.29E-07	1.47E-06	-2.19	1.53E+02	3.34E+02
ENSMUSG00000024791	Cdca5	1.34E-07	1.52E-06	-2.65	1.79E+01	4.75E+01
ENSMUSG00000074217	Misp3	1.34E-07	1.52E-06	-2.82	1.79E+01	5.05E+01
ENSMUSG00000002870	Mcm2	1.35E-07	1.53E-06	-3.07	9.85E+01	3.02E+02
ENSMUSG00000034773	Hrob	1.40E-07	1.59E-06	-3.23	1.29E+01	4.18E+01
ENSMUSG00000025921	Rdh10	1.44E-07	1.63E-06	-2.25	2.76E+01	6.22E+01
ENSMUSG00000007827	Ankrd26	1.47E-07	1.67E-06	-2.12	3.18E+01	6.76E+01
ENSMUSG00000038668	Lpar1	1.49E-07	1.68E-06	5.83	1.08E+02	1.85E+01

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ENSMUSG00000028687	Mutyh	1.50E-07	1.69E-06	-3.87	5.40E+00	2.09E+01
ENSMUSG00000049872	Calhm5	1.54E-07	1.73E-06	5.50	1.04E+01	1.90E+00
ENSMUSG00000018986	Slfn3	1.56E-07	1.76E-06	3.36	2.21E+01	6.59E+00
ENSMUSG00000027454	Gins1	1.61E-07	1.81E-06	-2.93	2.09E+01	6.12E+01
ENSMUSG00000072082	Ccnf	1.74E-07	1.95E-06	-2.61	2.76E+01	7.20E+01
ENSMUSG00000040964	Arhgef10l	1.84E-07	2.05E-06	-2.95	4.02E+01	1.19E+02
ENSMUSG00000073144	4930599N23Rik	1.89E-07	2.11E-06	3.31	1.74E+01	5.26E+00
ENSMUSG00000097754	Ptgs2os2	1.90E-07	2.11E-06	8.07	1.10E+02	1.36E+01
ENSMUSG00000030737	Slco2b1	1.99E-07	2.21E-06	-4.80	3.39E+00	1.62E+01
ENSMUSG00000041774	Ydjc	2.23E-07	2.45E-06	-2.32	3.25E+01	7.54E+01
ENSMUSG00000048142	Nat8l	2.26E-07	2.48E-06	-4.58	9.88E+00	4.53E+01
ENSMUSG00000063160	Numbl	2.32E-07	2.55E-06	-2.14	2.45E+01	5.24E+01
ENSMUSG00000030657	Xylt1	2.34E-07	2.56E-06	-2.42	1.15E+02	2.79E+02
ENSMUSG00000061143	Maml3	2.37E-07	2.60E-06	-2.90	1.44E+01	4.16E+01
ENSMUSG00000032567	Aste1	2.46E-07	2.69E-06	2.47	7.58E+01	3.06E+01
ENSMUSG00000034906	Ncaph	2.46E-07	2.69E-06	-2.46	3.40E+01	8.38E+01
ENSMUSG00000025395	Prim1	2.60E-07	2.83E-06	-2.63	2.93E+01	7.70E+01
ENSMUSG00000034266	Batf	2.67E-07	2.90E-06	3.03	1.24E+02	4.10E+01
ENSMUSG00000002835	Chaf1a	2.69E-07	2.92E-06	-2.99	5.54E+01	1.65E+02
ENSMUSG00000027611	Procr	2.82E-07	3.05E-06	5.78	7.69E+02	1.33E+02
ENSMUSG00000046295	Ankle1	2.85E-07	3.08E-06	-5.62	2.65E+00	1.49E+01
ENSMUSG00000053541	Gvin-ps6	2.86E-07	3.08E-06	19.11	3.31E+00	1.73E-01
ENSMUSG00000037235	Mxd4	2.86E-07	3.08E-06	-2.56	3.65E+02	9.33E+02
ENSMUSG00000035024	Ncapd3	2.93E-07	3.16E-06	-2.18	5.20E+01	1.13E+02
ENSMUSG00000021298	Gpr132	2.95E-07	3.17E-06	4.98	4.86E+02	9.75E+01

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ENSMUSG00000040321	Zfp770	3.07E-07	3.29E-06	-2.27	1.63E+01	3.69E+01
ENSMUSG00000032411	Tfdp2	3.25E-07	3.47E-06	-2.04	6.28E+01	1.28E+02
ENSMUSG00000018654	Ikzf1	3.28E-07	3.50E-06	2.42	5.09E+02	2.10E+02
ENSMUSG00000019478	Rab4a	3.37E-07	3.59E-06	-2.24	2.97E+01	6.65E+01
ENSMUSG00000034601	2700049A03Rik	3.39E-07	3.61E-06	-2.22	1.70E+01	3.77E+01
ENSMUSG00000078122	F630028O10Rik	3.46E-07	3.68E-06	-4.46	1.15E+01	5.13E+01
ENSMUSG00000020806	Rhbdf2	3.49E-07	3.70E-06	2.33	4.88E+02	2.09E+02
ENSMUSG00000022957	Itsn1	3.49E-07	3.70E-06	-2.41	2.57E+02	6.19E+02
ENSMUSG00000027284	Cdan1	3.52E-07	3.74E-06	-2.27	1.98E+01	4.50E+01
ENSMUSG00000003992	Ssbp2	3.58E-07	3.79E-06	2.81	1.97E+01	7.02E+00
ENSMUSG00000017550	Atad5	3.66E-07	3.87E-06	-2.77	3.12E+01	8.67E+01
ENSMUSG00000052485	Tmem171	3.68E-07	3.89E-06	2.64	3.86E+02	1.46E+02
ENSMUSG00000041135	Ripk2	3.70E-07	3.90E-06	3.68	5.27E+02	1.43E+02
ENSMUSG00000022034	Esco2	3.72E-07	3.92E-06	-3.48	1.15E+01	4.01E+01
ENSMUSG00000023022	Lima1	3.77E-07	3.97E-06	-2.09	1.81E+02	3.78E+02
ENSMUSG00000025950	Idh1	3.84E-07	4.04E-06	-2.40	4.60E+02	1.10E+03
ENSMUSG00000039395	Mreg	3.86E-07	4.06E-06	14.30	1.08E+01	7.53E-01
ENSMUSG00000020427	Igfbp3	4.10E-07	4.29E-06	13.59	5.65E+00	4.16E-01
ENSMUSG00000107761	2010008C14Rik	4.28E-07	4.47E-06	-2.95	1.75E+01	5.17E+01
ENSMUSG00000019773	Fbxo5	4.30E-07	4.49E-06	-2.91	2.86E+01	8.34E+01
ENSMUSG00000029189	Sel1l3	4.34E-07	4.54E-06	-3.42	8.69E+00	2.97E+01
ENSMUSG00000051278	Zgrf1	4.43E-07	4.62E-06	-2.95	1.33E+01	3.91E+01
ENSMUSG00000024397	Aif1	4.80E-07	4.98E-06	2.57	6.12E+02	2.38E+02
ENSMUSG00000019813	Cep57l1	4.88E-07	5.05E-06	-2.28	1.45E+01	3.31E+01
ENSMUSG00000004113	Cacna1b	4.97E-07	5.13E-06	3.07	7.37E+01	2.40E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000074578	Zfas1	4.97E-07	5.13E-06	2.03	5.53E+02	2.72E+02
ENSMUSG00000020781	Tsen54	5.04E-07	5.20E-06	-2.04	1.99E+01	4.06E+01
ENSMUSG00000004100	Ppan	5.07E-07	5.22E-06	-2.59	1.89E+01	4.90E+01
ENSMUSG00000035834	Polr3g	5.15E-07	5.30E-06	-3.19	2.98E+01	9.48E+01
ENSMUSG00000045273	Cenph	5.19E-07	5.33E-06	-2.22	5.68E+01	1.26E+02
ENSMUSG00000079109	Pms2	5.47E-07	5.59E-06	-2.27	1.47E+01	3.33E+01
ENSMUSG00000022686	B3gnt5	5.59E-07	5.71E-06	3.63	4.21E+01	1.16E+01
ENSMUSG00000048376	F2r	5.92E-07	6.03E-06	4.15	1.36E+01	3.28E+00
ENSMUSG00000061186	Sfmbt2	6.24E-07	6.34E-06	2.68	2.21E+01	8.23E+00
ENSMUSG00000025203	Scd2	6.33E-07	6.41E-06	-2.78	5.98E+01	1.66E+02
ENSMUSG00000042606	Hirip3	6.40E-07	6.48E-06	-2.67	3.21E+01	8.58E+01
ENSMUSG00000030671	Pde3b	6.58E-07	6.65E-06	-2.64	5.12E+01	1.35E+02
ENSMUSG00000023050	Map3k12	7.11E-07	7.16E-06	-2.56	1.29E+01	3.30E+01
ENSMUSG00000062960	Kdr	7.36E-07	7.40E-06	2.91	1.41E+02	4.82E+01
ENSMUSG00000039396	Neil3	7.66E-07	7.68E-06	-3.25	1.12E+01	3.63E+01
ENSMUSG00000028362	Tnfsf8	8.23E-07	8.23E-06	3.10	4.55E+01	1.47E+01
ENSMUSG00000087598	Zfp111	8.45E-07	8.45E-06	-2.21	1.54E+01	3.41E+01
ENSMUSG00000031629	Cenpu	8.50E-07	8.48E-06	-2.37	1.99E+01	4.72E+01
ENSMUSG00000030365	Clec2i	8.53E-07	8.51E-06	-2.53	8.96E+00	2.27E+01
ENSMUSG00000038679	Trps1	8.97E-07	8.92E-06	2.12	8.93E+02	4.21E+02
ENSMUSG00000026779	Mastl	9.07E-07	9.00E-06	-2.15	2.37E+01	5.08E+01
ENSMUSG00000027641	Rbl1	9.43E-07	9.33E-06	2.06	1.86E+02	9.05E+01
ENSMUSG00000023032	Slc4a8	9.51E-07	9.39E-06	10.65	1.17E+01	1.09E+00
ENSMUSG00000021062	Rab15	9.89E-07	9.76E-06	3.19	5.34E+01	1.68E+01
ENSMUSG00000067591	Klra3	9.90E-07	9.77E-06	2.99	1.22E+01	4.08E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000116380	Gm39556	1.00E-06	9.87E-06	5.42	6.75E+00	1.25E+00
ENSMUSG00000000028	Cdc45	1.01E-06	9.91E-06	-2.91	2.12E+01	6.17E+01
ENSMUSG00000073739	Gm16287	1.06E-06	1.04E-05	-2.16	1.89E+01	4.08E+01
ENSMUSG00000029516	Cit	1.06E-06	1.04E-05	-2.19	6.04E+01	1.32E+02
ENSMUSG00000107041	Gm42735	1.09E-06	1.06E-05	3.69	2.25E+01	6.09E+00
ENSMUSG00000037224	Zfyve28	1.09E-06	1.06E-05	-4.31	6.23E+00	2.69E+01
ENSMUSG00000104969	Gm43445	1.09E-06	1.06E-05	2.94	4.99E+01	1.70E+01
ENSMUSG00000030505	Prmt3	1.09E-06	1.06E-05	-2.16	7.08E+01	1.53E+02
ENSMUSG00000022471	Xrcc6	1.09E-06	1.07E-05	-2.21	2.18E+01	4.80E+01
ENSMUSG00000037946	Fgd3	1.13E-06	1.10E-05	-2.26	1.50E+02	3.39E+02
ENSMUSG00000032666	1700025G04Rik	1.14E-06	1.11E-05	-2.08	7.20E+01	1.50E+02
ENSMUSG00000015340	Cybb	1.14E-06	1.11E-05	2.08	1.37E+04	6.61E+03
ENSMUSG00000026023	Cdk15	1.15E-06	1.12E-05	-2.79	1.56E+01	4.37E+01
ENSMUSG00000093677	Gm20712	1.15E-06	1.12E-05	-2.38	1.82E+01	4.32E+01
ENSMUSG00000068246	Apol9b	1.16E-06	1.13E-05	16.48	3.24E+00	1.96E-01
ENSMUSG00000020228	Helb	1.19E-06	1.15E-05	-2.01	5.71E+01	1.15E+02
ENSMUSG00000024534	Sncaip	1.19E-06	1.16E-05	-3.33	6.91E+00	2.30E+01
ENSMUSG00000047747	Rnf150	1.20E-06	1.17E-05	-3.09	1.33E+02	4.11E+02
ENSMUSG00000050947	Amigo1	1.21E-06	1.17E-05	-3.90	3.65E+00	1.42E+01
ENSMUSG00000034959	Rubcnl	1.24E-06	1.20E-05	3.33	2.94E+01	8.81E+00
ENSMUSG00000041180	Hectd2	1.26E-06	1.22E-05	4.80	1.06E+01	2.21E+00
ENSMUSG00000062510	Nsl1	1.26E-06	1.22E-05	-3.01	8.67E+00	2.61E+01
ENSMUSG00000034023	Fancd2	1.29E-06	1.24E-05	-2.96	1.23E+01	3.63E+01
ENSMUSG00000086291	Gm15513	1.30E-06	1.25E-05	-6.61	4.35E+00	2.87E+01
ENSMUSG00000031549	Ido2	1.31E-06	1.26E-05	20.17	3.96E+00	1.96E-01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000021403	Serpinb9b	1.31E-06	1.26E-05	3.50	7.61E+01	2.17E+01
ENSMUSG00000021965	Ska3	1.32E-06	1.27E-05	-2.97	8.34E+00	2.48E+01
ENSMUSG00000032586	Traip	1.33E-06	1.27E-05	-2.35	1.93E+01	4.54E+01
ENSMUSG00000024795	Kif20b	1.34E-06	1.28E-05	-2.36	9.04E+01	2.14E+02
ENSMUSG00000028312	Smc2	1.36E-06	1.30E-05	-2.00	3.58E+02	7.17E+02
ENSMUSG00000112571	Gm48207	1.36E-06	1.30E-05	13.92	5.11E+00	3.67E-01
ENSMUSG00000046591	Ticrr	1.40E-06	1.33E-05	-2.84	9.06E+00	2.57E+01
ENSMUSG00000026196	Bard1	1.45E-06	1.37E-05	-2.69	1.65E+01	4.45E+01
ENSMUSG00000028944	Prkag2	1.47E-06	1.39E-05	-2.41	8.29E+01	2.00E+02
ENSMUSG00000004996	Mri1	1.47E-06	1.39E-05	-2.23	1.81E+01	4.04E+01
ENSMUSG00000018143	Mafk	1.47E-06	1.39E-05	2.33	5.98E+02	2.57E+02
ENSMUSG00000039270	Megf9	1.48E-06	1.40E-05	-2.78	2.56E+01	7.12E+01
ENSMUSG00000037447	Arid5a	1.50E-06	1.41E-05	4.54	5.20E+02	1.14E+02
ENSMUSG00000050931	Sgms2	1.50E-06	1.42E-05	-2.01	2.56E+01	5.14E+01
ENSMUSG00000042265	Trem1	1.50E-06	1.42E-05	-4.44	8.62E+00	3.82E+01
ENSMUSG00000108004	Gm44080	1.62E-06	1.52E-05	3.90	1.72E+01	4.41E+00
ENSMUSG00000040204	Pclaf	1.63E-06	1.53E-05	-2.62	1.51E+02	3.96E+02
ENSMUSG00000032000	Birc3	1.64E-06	1.54E-05	2.76	6.40E+02	2.32E+02
ENSMUSG00000097804	Gm16685	1.68E-06	1.58E-05	9.01	1.46E+01	1.62E+00
ENSMUSG00000027646	Src	1.73E-06	1.61E-05	3.45	1.41E+02	4.08E+01
ENSMUSG00000104524	Gm37333	1.79E-06	1.66E-05	-3.15	7.28E+00	2.29E+01
ENSMUSG00000043140	Tmem186	1.85E-06	1.72E-05	-2.08	1.86E+01	3.88E+01
ENSMUSG00000031840	Rab3a	1.86E-06	1.73E-05	-2.94	7.35E+00	2.16E+01
ENSMUSG00000071862	Lrrtm2	1.87E-06	1.74E-05	27.22	4.72E+00	1.73E-01
ENSMUSG00000030930	Chst15	1.90E-06	1.75E-05	2.55	1.40E+01	5.50E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000013089	Etv5	1.90E-06	1.75E-05	-2.96	4.09E+01	1.21E+02
ENSMUSG00000020573	Pik3cg	1.95E-06	1.80E-05	-2.25	8.19E+01	1.84E+02
ENSMUSG00000097166	9330179D12Rik	1.96E-06	1.81E-05	6.20	8.02E+00	1.29E+00
ENSMUSG00000072620	Slfn2	2.02E-06	1.86E-05	2.70	7.89E+03	2.92E+03
ENSMUSG00000053749	Gm9920	2.18E-06	1.99E-05	-5.94	1.81E+00	1.07E+01
ENSMUSG00000062232	Rapgef2	2.21E-06	2.02E-05	2.50	1.86E+02	7.43E+01
ENSMUSG00000037847	Nmrk1	2.29E-06	2.09E-05	-2.04	2.25E+01	4.60E+01
ENSMUSG00000035561	Aldh1b1	2.35E-06	2.14E-05	2.17	1.91E+02	8.82E+01
ENSMUSG00000030929	Eri2	2.48E-06	2.25E-05	-2.09	2.15E+01	4.49E+01
ENSMUSG00000108371	Gm38832	2.52E-06	2.28E-05	-2.43	1.14E+01	2.76E+01
ENSMUSG00000027115	Kif18a	2.52E-06	2.28E-05	-3.09	8.79E+00	2.72E+01
ENSMUSG00000029084	Cd38	2.56E-06	2.31E-05	7.64	1.03E+01	1.35E+00
ENSMUSG00000031480	Thsd1	2.62E-06	2.36E-05	-3.25	4.71E+00	1.53E+01
ENSMUSG00000086782	E130102H24Rik	2.66E-06	2.39E-05	2.79	4.50E+01	1.62E+01
ENSMUSG00000037552	Plekhg2	2.77E-06	2.48E-05	2.12	6.75E+01	3.19E+01
ENSMUSG00000022033	Pbk	3.01E-06	2.68E-05	-2.74	2.67E+01	7.30E+01
ENSMUSG00000030559	Rab38	3.02E-06	2.69E-05	3.32	3.28E+01	9.86E+00
ENSMUSG00000018861	Fdxr	3.15E-06	2.80E-05	-2.06	1.31E+01	2.69E+01
ENSMUSG00000036019	Tmtc2	3.21E-06	2.85E-05	3.44	2.57E+01	7.48E+00
ENSMUSG00000023832	Acat2	3.22E-06	2.86E-05	-2.14	7.51E+01	1.60E+02
ENSMUSG00000024891	Slc29a2	3.36E-06	2.97E-05	-2.90	4.37E+00	1.27E+01
ENSMUSG00000044197	Gpr146	3.53E-06	3.11E-05	2.50	4.85E+02	1.94E+02
ENSMUSG00000039865	Slc44a3	3.70E-06	3.25E-05	12.53	2.79E+00	2.23E-01
ENSMUSG00000022554	Hgh1	3.71E-06	3.25E-05	-2.04	1.21E+01	2.47E+01
ENSMUSG00000020656	Grhl1	3.74E-06	3.28E-05	3.43	1.88E+01	5.49E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000024118	Tedc2	3.78E-06	3.31E-05	-2.62	8.36E+00	2.19E+01
ENSMUSG00000031558	Slit2	3.79E-06	3.31E-05	2.94	1.96E+01	6.66E+00
ENSMUSG00000073434	Wdr90	3.84E-06	3.36E-05	-5.42	1.83E+00	9.92E+00
ENSMUSG00000024056	Ndc80	3.88E-06	3.39E-05	-2.07	5.56E+01	1.15E+02
ENSMUSG00000001053	N4bp3	4.03E-06	3.51E-05	-2.61	7.11E+00	1.86E+01
ENSMUSG00000110500	Gm32568	4.03E-06	3.51E-05	22.52	3.90E+00	1.73E-01
ENSMUSG00000029283	Cdc7	4.04E-06	3.52E-05	-3.26	7.69E+00	2.50E+01
ENSMUSG00000041773	Enc1	4.13E-06	3.59E-05	2.46	9.38E+02	3.81E+02
ENSMUSG00000018809	Smyd4	4.19E-06	3.64E-05	-2.45	1.16E+01	2.84E+01
ENSMUSG00000066191	Anks6	4.35E-06	3.76E-05	-2.68	6.46E+00	1.73E+01
ENSMUSG00000020032	Nuak1	4.39E-06	3.79E-05	-2.79	4.10E+01	1.15E+02
ENSMUSG00000049001	Ndnf	4.42E-06	3.82E-05	5.59	1.16E+01	2.08E+00
ENSMUSG00000061414	Cracr2a	4.74E-06	4.08E-05	-2.29	1.93E+01	4.41E+01
ENSMUSG00000098176	Ccdc166	4.89E-06	4.20E-05	-4.35	2.79E+00	1.21E+01
ENSMUSG00000073179	Gm10478	4.99E-06	4.27E-05	-2.58	7.59E+00	1.96E+01
ENSMUSG00000022718	Dgcr8	5.03E-06	4.30E-05	-2.17	4.64E+01	1.01E+02
ENSMUSG00000031762	Mt2	5.04E-06	4.31E-05	3.09	4.08E+03	1.32E+03
ENSMUSG00000054855	Rnd1	5.07E-06	4.33E-05	4.29	6.92E+01	1.61E+01
ENSMUSG00000045382	Cxcr4	5.13E-06	4.37E-05	-3.10	3.62E+02	1.12E+03
ENSMUSG00000045287	Rtn4rl1	5.16E-06	4.40E-05	-2.66	1.43E+01	3.80E+01
ENSMUSG00000042978	Sbk1	5.20E-06	4.43E-05	-3.15	6.34E+00	2.00E+01
ENSMUSG00000086564	Cd101	5.32E-06	4.51E-05	-3.64	3.52E+00	1.28E+01
ENSMUSG00000020492	Ska2	5.37E-06	4.56E-05	-2.23	2.41E+01	5.37E+01
ENSMUSG00000015316	Slamf1	5.43E-06	4.60E-05	10.28	5.39E+00	5.24E-01
ENSMUSG00000049811	Fam161a	5.52E-06	4.66E-05	-4.72	2.82E+00	1.33E+01

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ENSMUSG00000022479	Vdr	5.52E-06	4.67E-05	3.05	2.82E+01	9.23E+00
ENSMUSG00000035560	Wdr20rt	5.57E-06	4.70E-05	21.10	3.23E+00	1.53E-01
ENSMUSG00000038295	Atg9b	5.69E-06	4.79E-05	-3.66	4.09E+00	1.49E+01
ENSMUSG00000072066	6720489N17Rik	5.73E-06	4.81E-05	-4.36	2.64E+00	1.15E+01
ENSMUSG00000052934	Fbxo31	5.75E-06	4.82E-05	-2.92	4.34E+01	1.27E+02
ENSMUSG00000041642	Kif21b	5.77E-06	4.84E-05	-2.25	7.10E+01	1.60E+02
ENSMUSG00000030717	Nupr1	5.86E-06	4.91E-05	2.60	4.96E+02	1.90E+02
ENSMUSG00000038126	Mphosph9	5.87E-06	4.92E-05	-2.22	1.41E+01	3.13E+01
ENSMUSG00000038437	Mllt6	5.96E-06	4.99E-05	2.26	6.70E+02	2.96E+02
ENSMUSG00000098292	Gm27194	6.09E-06	5.08E-05	15.85	5.82E+00	3.67E-01
ENSMUSG00000029406	Pitpnm2	6.23E-06	5.18E-05	-3.53	3.86E+00	1.36E+01
ENSMUSG00000072572	Slc39a2	6.24E-06	5.18E-05	4.66	7.68E+00	1.65E+00
ENSMUSG00000107586	Gm44283	6.28E-06	5.21E-05	2.52	5.97E+01	2.37E+01
ENSMUSG00000015880	Ncapg	6.35E-06	5.26E-05	-2.32	4.76E+01	1.10E+02
ENSMUSG00000050751	Pgbd5	6.45E-06	5.34E-05	-5.29	2.56E+00	1.35E+01
ENSMUSG00000006678	Pola1	6.57E-06	5.43E-05	-2.48	9.91E+01	2.46E+02
ENSMUSG00000028517	Plpp3	6.64E-06	5.48E-05	2.35	1.62E+02	6.91E+01
ENSMUSG00000111133	Gm5831	6.70E-06	5.52E-05	7.25	3.01E+00	4.15E-01
ENSMUSG00000035458	Tnni3	6.70E-06	5.52E-05	3.20	1.38E+01	4.32E+00
ENSMUSG00000030882	Dnhd1	6.81E-06	5.60E-05	3.33	7.80E+00	2.35E+00
ENSMUSG00000035448	Ccr3	6.86E-06	5.63E-05	-2.74	1.28E+01	3.50E+01
ENSMUSG00000030871	Ears2	6.86E-06	5.64E-05	-2.16	1.11E+01	2.40E+01
ENSMUSG00000039783	Kmo	6.95E-06	5.70E-05	4.37	1.61E+01	3.69E+00
ENSMUSG00000007080	Pole	7.28E-06	5.95E-05	-2.40	2.53E+01	6.07E+01
ENSMUSG00000044469	Tnfaip8l1	7.44E-06	6.06E-05	-2.08	1.22E+01	2.53E+01

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ENSMUSG00000035735	Dagla	7.72E-06	6.27E-05	-2.74	1.30E+01	3.56E+01
ENSMUSG00000014164	Klhl3	7.92E-06	6.43E-05	-4.01	4.27E+00	1.71E+01
ENSMUSG00000108238	Gm43984	7.94E-06	6.44E-05	3.41	1.39E+01	4.07E+00
ENSMUSG00000074361	C5ar2	8.15E-06	6.59E-05	-3.57	3.77E+00	1.34E+01
ENSMUSG00000027860	Vangl1	8.22E-06	6.65E-05	-2.15	1.66E+01	3.58E+01
ENSMUSG00000031697	Orc6	8.31E-06	6.71E-05	-2.07	3.81E+01	7.87E+01
ENSMUSG00000054321	Taf4b	8.43E-06	6.80E-05	2.80	1.20E+02	4.27E+01
ENSMUSG00000007379	Dennd2c	8.63E-06	6.94E-05	-3.18	4.08E+00	1.30E+01
ENSMUSG00000044674	Fzd1	8.69E-06	6.98E-05	4.29	5.81E+01	1.35E+01
ENSMUSG00000042129	Rassf4	8.93E-06	7.16E-05	2.23	4.64E+03	2.08E+03
ENSMUSG00000045411	2410002F23Rik	9.19E-06	7.33E-05	-2.06	2.18E+01	4.49E+01
ENSMUSG00000021765	Fst	9.29E-06	7.40E-05	3.41	2.18E+01	6.38E+00
ENSMUSG00000008734	Gprc5b	1.00E-05	7.96E-05	-2.32	3.63E+01	8.42E+01
ENSMUSG00000034271	Jdp2	1.03E-05	8.20E-05	3.62	1.68E+03	4.63E+02
ENSMUSG00000116673	A630089N07Rik	1.04E-05	8.22E-05	-2.47	8.36E+00	2.06E+01
ENSMUSG00000026077	Npas2	1.05E-05	8.34E-05	-3.22	4.73E+00	1.52E+01
ENSMUSG00000064289	Tank	1.06E-05	8.40E-05	2.29	7.94E+02	3.47E+02
ENSMUSG00000057346	Apol9a	1.08E-05	8.55E-05	10.14	3.28E+00	3.24E-01
ENSMUSG00000001630	Stk38l	1.13E-05	8.88E-05	2.31	1.17E+02	5.08E+01
ENSMUSG00000024043	Arhgap28	1.15E-05	9.03E-05	3.13	2.50E+01	8.00E+00
ENSMUSG00000085327	Gm16104	1.15E-05	9.05E-05	-3.03	5.22E+00	1.58E+01
ENSMUSG00000058290	Espl1	1.20E-05	9.36E-05	-2.08	2.56E+01	5.31E+01
ENSMUSG00000044072	Eml6	1.20E-05	9.38E-05	3.68	1.98E+01	5.39E+00
ENSMUSG00000000957	Mmp14	1.23E-05	9.60E-05	2.29	4.39E+02	1.92E+02
ENSMUSG00000021572	Cep72	1.28E-05	9.93E-05	-2.97	5.13E+00	1.52E+01

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ENSMUSG00000029591	Ung	1.29E-05	1.00E-04	-2.94	2.34E+01	6.87E+01
ENSMUSG00000024235	Map3k8	1.33E-05	1.03E-04	2.29	2.27E+02	9.91E+01
ENSMUSG00000022900	Ildr1	1.35E-05	1.04E-04	16.37	3.22E+00	1.96E-01
ENSMUSG00000020732	Rab37	1.36E-05	1.05E-04	2.47	1.53E+01	6.18E+00
ENSMUSG00000019214	Chtf18	1.37E-05	1.06E-04	-2.77	9.69E+00	2.68E+01
ENSMUSG00000024975	Pdcd4	1.37E-05	1.06E-04	-2.39	7.70E+01	1.84E+02
ENSMUSG00000025804	Ccr1	1.38E-05	1.06E-04	3.08	4.46E+02	1.45E+02
ENSMUSG00000095930	Nim1k	1.41E-05	1.09E-04	-3.33	4.64E+00	1.55E+01
ENSMUSG00000074671	Tspyl3	1.47E-05	1.12E-04	-2.16	1.43E+01	3.09E+01
ENSMUSG00000031756	Cenpn	1.47E-05	1.13E-04	-2.13	2.35E+01	5.00E+01
ENSMUSG00000086247	Gm15787	1.48E-05	1.13E-04	4.36	6.13E+00	1.41E+00
ENSMUSG00000117239	Gpr31c	1.49E-05	1.13E-04	3.30	2.96E+01	8.98E+00
ENSMUSG00000025747	Tyms	1.52E-05	1.16E-04	-2.30	3.71E+01	8.52E+01
ENSMUSG00000055994	Nod2	1.55E-05	1.18E-04	4.43	1.86E+02	4.19E+01
ENSMUSG00000020381	Mrnip	1.57E-05	1.19E-04	-2.92	9.02E+00	2.64E+01
ENSMUSG00000024121	Atp6v0c	1.58E-05	1.20E-04	2.66	1.39E+01	5.22E+00
ENSMUSG00000032593	Amigo3	1.63E-05	1.23E-04	2.44	1.30E+01	5.33E+00
ENSMUSG00000105962	Gm42432	1.70E-05	1.28E-04	2.94	1.03E+01	3.52E+00
ENSMUSG00000026473	Glul	1.76E-05	1.32E-04	-2.00	4.66E+02	9.33E+02
ENSMUSG00000015217	Hmgb3	1.80E-05	1.35E-04	-2.51	1.85E+01	4.65E+01
ENSMUSG00000038047	Haus6	1.84E-05	1.38E-04	-2.12	4.97E+01	1.06E+02
ENSMUSG00000052609	Plekhg3	1.84E-05	1.38E-04	-2.27	6.94E+01	1.57E+02
ENSMUSG00000104272	Gm38297	1.88E-05	1.40E-04	7.33	8.61E+00	1.18E+00
ENSMUSG00000035107	Dcbld2	2.00E-05	1.48E-04	2.84	2.51E+02	8.82E+01
ENSMUSG00000020620	Abca8b	2.03E-05	1.50E-04	2.31	2.11E+01	9.17E+00

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ENSMUSG00000071324	Armc2	2.04E-05	1.51E-04	-2.41	1.36E+01	3.28E+01
ENSMUSG00000043487	Acot6	2.06E-05	1.52E-04	-4.15	2.75E+00	1.14E+01
ENSMUSG00000033316	Galnt9	2.19E-05	1.61E-04	-5.57	2.25E+00	1.25E+01
ENSMUSG00000036995	Asap3	2.23E-05	1.64E-04	5.07	9.16E+00	1.81E+00
ENSMUSG00000017499	Cdc6	2.23E-05	1.64E-04	-3.56	1.31E+01	4.67E+01
ENSMUSG00000006930	Hap1	2.24E-05	1.64E-04	8.02	3.31E+00	4.13E-01
ENSMUSG00000034883	Lrr1	2.25E-05	1.65E-04	-3.09	6.19E+00	1.91E+01
ENSMUSG00000049119	Fam110b	2.30E-05	1.69E-04	-2.10	4.81E+01	1.01E+02
ENSMUSG00000032487	Ptgs2	2.35E-05	1.72E-04	11.90	5.33E+03	4.48E+02
ENSMUSG00000048486	Fitm2	2.36E-05	1.72E-04	-2.84	5.72E+00	1.63E+01
ENSMUSG00000042213	Zfand4	2.43E-05	1.77E-04	-3.07	4.68E+00	1.44E+01
ENSMUSG00000045312	Lhfpl2	2.52E-05	1.83E-04	-2.35	7.21E+02	1.70E+03
ENSMUSG00000023991	Foxp4	2.55E-05	1.85E-04	3.14	3.53E+02	1.12E+02
ENSMUSG00000035064	Eef2k	2.57E-05	1.86E-04	-2.55	4.55E+01	1.16E+02
ENSMUSG00000042389	Tsen2	2.60E-05	1.88E-04	-2.29	1.52E+01	3.48E+01
ENSMUSG00000035376	Hacd2	2.70E-05	1.94E-04	2.22	3.16E+02	1.42E+02
ENSMUSG00000025934	Gsta3	2.74E-05	1.97E-04	-2.07	2.19E+01	4.54E+01
ENSMUSG00000038521	C1s1	2.76E-05	1.99E-04	11.24	1.02E+01	9.09E-01
ENSMUSG00000032578	Cish	2.78E-05	2.00E-04	6.01	2.66E+02	4.43E+01
ENSMUSG00000032221	Mns1	2.81E-05	2.01E-04	-2.70	1.39E+01	3.74E+01
ENSMUSG00000056749	Nfil3	2.89E-05	2.07E-04	3.25	2.43E+02	7.48E+01
ENSMUSG00000047003	Zfp41	2.93E-05	2.10E-04	-2.44	1.04E+01	2.53E+01
ENSMUSG00000090319	Gm4462	2.97E-05	2.12E-04	9.48	2.11E+00	2.23E-01
ENSMUSG00000038175	Mylip	2.98E-05	2.12E-04	2.33	4.06E+02	1.74E+02
ENSMUSG00000064338	mt-Tv	3.05E-05	2.17E-04	2.11	2.35E+02	1.12E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000031896	Ctrl	3.07E-05	2.18E-04	4.99	4.92E+00	9.86E-01
ENSMUSG00000114689	Gm9465	3.10E-05	2.20E-04	2.59	3.26E+01	1.26E+01
ENSMUSG00000042842	Serpinb6b	3.10E-05	2.20E-04	2.48	4.86E+02	1.96E+02
ENSMUSG00000040829	Zmynd15	3.10E-05	2.20E-04	2.36	3.59E+01	1.52E+01
ENSMUSG00000026039	Sgo2a	3.10E-05	2.20E-04	-2.25	5.53E+01	1.24E+02
ENSMUSG00000067049	Unc93a	3.12E-05	2.21E-04	14.70	2.55E+00	1.73E-01
ENSMUSG00000052270	Fpr2	3.14E-05	2.22E-04	6.22	5.94E+01	9.56E+00
ENSMUSG00000100018	Gm7776	3.19E-05	2.25E-04	3.30	8.73E+00	2.64E+00
ENSMUSG00000028709	Mob3c	3.20E-05	2.26E-04	2.00	1.54E+02	7.68E+01
ENSMUSG00000036223	Ska1	3.24E-05	2.28E-04	-2.61	2.93E+01	7.63E+01
ENSMUSG00000032392	Parp16	3.29E-05	2.31E-04	-2.84	5.15E+00	1.46E+01
ENSMUSG00000048706	Lurap1l	3.34E-05	2.34E-04	-3.19	4.72E+00	1.51E+01
ENSMUSG00000025154	Arhgap19	3.37E-05	2.36E-04	-2.64	3.34E+01	8.83E+01
ENSMUSG00000044551	9930012K11Rik	3.47E-05	2.43E-04	-4.41	2.07E+00	9.15E+00
ENSMUSG00000094595	Fsbp	3.59E-05	2.50E-04	-7.02	1.13E+00	7.94E+00
ENSMUSG00000042066	Tmcc2	3.63E-05	2.53E-04	-2.61	9.40E+00	2.46E+01
ENSMUSG00000030595	Nfkbib	3.64E-05	2.53E-04	2.40	2.50E+03	1.04E+03
ENSMUSG00000027254	Map1a	3.68E-05	2.55E-04	-2.44	6.15E+00	1.50E+01
ENSMUSG00000029246	Ppat	3.72E-05	2.58E-04	-2.06	3.29E+01	6.77E+01
ENSMUSG00000050014	Apol10b	3.74E-05	2.59E-04	25.75	7.36E+00	2.86E-01
ENSMUSG00000101585	1600010M07Rik	3.74E-05	2.59E-04	-2.04	1.17E+01	2.38E+01
ENSMUSG00000034872	Gipc3	3.76E-05	2.60E-04	9.09	2.94E+00	3.24E-01
ENSMUSG00000031652	N4bp1	3.90E-05	2.69E-04	2.01	7.73E+02	3.84E+02
ENSMUSG00000056091	St3gal5	3.92E-05	2.70E-04	2.36	2.27E+03	9.61E+02
ENSMUSG00000017861	Mybl2	4.04E-05	2.77E-04	-4.00	4.55E+00	1.82E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000066687	Zbtb16	4.29E-05	2.94E-04	-4.18	2.08E+00	8.69E+00
ENSMUSG00000099974	Bcl2a1d	4.39E-05	2.99E-04	7.16	1.43E+01	2.00E+00
ENSMUSG00000041220	Elovl6	4.39E-05	2.99E-04	-2.40	2.20E+01	5.29E+01
ENSMUSG00000026134	Prim2	4.44E-05	3.02E-04	-2.05	3.85E+01	7.87E+01
ENSMUSG00000072980	Oip5	4.50E-05	3.06E-04	-2.02	2.20E+01	4.45E+01
ENSMUSG00000022422	Dscc1	4.52E-05	3.07E-04	-3.50	5.79E+00	2.03E+01
ENSMUSG00000105008	Gm43652	4.60E-05	3.13E-04	2.72	1.96E+01	7.20E+00
ENSMUSG00000020300	Cpeb4	4.70E-05	3.18E-04	2.12	2.09E+03	9.86E+02
ENSMUSG00000054675	Tmem119	4.74E-05	3.21E-04	-3.05	5.22E+00	1.59E+01
ENSMUSG00000104867	Gm43728	4.89E-05	3.30E-04	2.67	1.65E+01	6.18E+00
ENSMUSG00000032113	Chek1	4.91E-05	3.31E-04	-3.16	1.25E+01	3.95E+01
ENSMUSG00000063851	Rnf183	4.95E-05	3.34E-04	-12.16	2.71E-01	3.30E+00
ENSMUSG00000060275	Nrg2	5.01E-05	3.37E-04	9.68	3.55E+00	3.67E-01
ENSMUSG00000030344	Akap3	5.04E-05	3.39E-04	-2.60	5.08E+00	1.32E+01
ENSMUSG00000117079	Gm41611	5.08E-05	3.42E-04	3.25	1.15E+01	3.53E+00
ENSMUSG00000020589	Cyria	5.08E-05	3.42E-04	2.17	4.20E+02	1.93E+02
ENSMUSG00000022802	Lmln	5.38E-05	3.60E-04	-2.36	9.06E+00	2.14E+01
ENSMUSG00000035165	Kcne3	5.41E-05	3.62E-04	-11.94	4.47E-01	5.34E+00
ENSMUSG00000025050	Pcgf6	5.44E-05	3.63E-04	-2.39	1.49E+01	3.56E+01
ENSMUSG00000079553	Kifc1	5.48E-05	3.65E-04	-2.40	1.58E+01	3.78E+01
ENSMUSG00000062991	Nrg1	5.49E-05	3.65E-04	6.95	1.62E+01	2.33E+00
ENSMUSG00000021215	Net1	5.54E-05	3.68E-04	-2.10	1.29E+01	2.72E+01
ENSMUSG00000030055	Rab43	5.66E-05	3.75E-04	2.25	4.54E+01	2.02E+01
ENSMUSG00000097494	4933406C10Rik	5.70E-05	3.77E-04	-12.77	2.11E-01	2.70E+00
ENSMUSG00000017146	Brca1	5.81E-05	3.84E-04	-2.47	2.20E+01	5.43E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000104728	Gm42462	5.85E-05	3.86E-04	3.45	1.28E+01	3.70E+00
ENSMUSG00000040034	Nup43	5.89E-05	3.88E-04	-2.37	1.11E+01	2.63E+01
ENSMUSG00000085882	2610507I01Rik	6.05E-05	3.98E-04	-3.57	2.86E+00	1.02E+01
ENSMUSG00000051235	Gen1	6.18E-05	4.06E-04	-2.11	2.63E+01	5.54E+01
ENSMUSG00000001036	Epn2	6.19E-05	4.06E-04	-2.93	4.16E+00	1.22E+01
ENSMUSG00000031555	Adam9	6.33E-05	4.15E-04	2.10	4.78E+02	2.28E+02
ENSMUSG00000045868	Gvin1	6.54E-05	4.28E-04	24.05	3.68E+00	1.53E-01
ENSMUSG00000038473	Nos1ap	6.57E-05	4.30E-04	-3.20	2.98E+00	9.56E+00
ENSMUSG00000054517	Trim65	6.72E-05	4.39E-04	-2.03	3.43E+01	6.96E+01
ENSMUSG00000042155	Klhl23	6.80E-05	4.43E-04	-4.37	3.66E+00	1.60E+01
ENSMUSG00000039187	Fanci	6.81E-05	4.43E-04	-2.21	9.33E+00	2.06E+01
ENSMUSG00000097006	9530082P21Rik	6.98E-05	4.54E-04	2.82	1.47E+01	5.20E+00
ENSMUSG00000032815	Fanca	7.04E-05	4.57E-04	-2.62	9.00E+00	2.36E+01
ENSMUSG00000114070	Gm47727	7.04E-05	4.57E-04	4.09	2.19E+01	5.36E+00
ENSMUSG00000002055	Spag5	7.13E-05	4.63E-04	-2.28	4.48E+01	1.02E+02
ENSMUSG00000030207	Fam234b	7.21E-05	4.67E-04	-2.39	1.25E+01	2.99E+01
ENSMUSG00000037913	Tmem156	7.25E-05	4.69E-04	-2.22	8.72E+00	1.93E+01
ENSMUSG00000074345	Tnfaip8l3	7.35E-05	4.75E-04	4.17	6.38E+00	1.53E+00
ENSMUSG00000038173	Enpp6	7.51E-05	4.84E-04	3.80	4.72E+00	1.24E+00
ENSMUSG00000090192	Gm16556	7.75E-05	4.97E-04	-3.68	2.09E+00	7.67E+00
ENSMUSG00000072949	Acot1	7.84E-05	5.02E-04	-5.06	1.84E+00	9.29E+00
ENSMUSG00000090556	Olfr753-ps1	7.85E-05	5.03E-04	13.02	2.26E+00	1.73E-01
ENSMUSG00000062007	Hsh2d	8.14E-05	5.20E-04	7.83	2.24E+00	2.86E-01
ENSMUSG00000025026	Add3	8.79E-05	5.58E-04	-2.04	1.45E+02	2.96E+02
ENSMUSG00000032035	Ets1	8.80E-05	5.58E-04	-2.61	7.49E+00	1.95E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000049555	Tmie	8.92E-05	5.65E-04	3.38	1.25E+01	3.70E+00
ENSMUSG00000054115	Skp2	9.35E-05	5.91E-04	-2.41	2.01E+01	4.84E+01
ENSMUSG00000106825	2510016D11Rik	9.41E-05	5.94E-04	-2.02	1.92E+01	3.88E+01
ENSMUSG00000003575	Crtc1	9.42E-05	5.94E-04	-2.24	1.70E+01	3.82E+01
ENSMUSG00000022146	Osmr	9.44E-05	5.95E-04	3.28	9.24E+00	2.82E+00
ENSMUSG00000036862	Dchs1	9.46E-05	5.96E-04	-3.06	2.79E+00	8.54E+00
ENSMUSG00000028163	Nfkb1	9.53E-05	6.00E-04	2.31	1.02E+03	4.42E+02
ENSMUSG00000073529	F830208F22Rik	1.01E-04	6.33E-04	5.66	1.29E+01	2.27E+00
ENSMUSG00000103291	Gm38235	1.02E-04	6.37E-04	3.49	9.38E+00	2.69E+00
ENSMUSG00000108732	2310043P16Rik	1.02E-04	6.39E-04	2.42	1.02E+01	4.21E+00
ENSMUSG00000026031	Cflar	1.07E-04	6.65E-04	3.21	3.45E+03	1.07E+03
ENSMUSG00000020717	Pecam1	1.07E-04	6.65E-04	2.66	9.27E+00	3.49E+00
ENSMUSG00000109861	4930458B22Rik	1.08E-04	6.69E-04	18.56	2.84E+00	1.53E-01
ENSMUSG00000027692	Tnik	1.09E-04	6.72E-04	3.36	2.58E+01	7.68E+00
ENSMUSG00000018925	Heatr9	1.12E-04	6.90E-04	12.72	2.50E+00	1.96E-01
ENSMUSG00000062906	Hdac10	1.13E-04	6.95E-04	-2.11	1.75E+01	3.71E+01
ENSMUSG00000043740	B430306N03Rik	1.17E-04	7.19E-04	-2.08	5.71E+01	1.19E+02
ENSMUSG00000112276	5033421B08Rik	1.17E-04	7.21E-04	-2.73	3.65E+00	9.97E+00
ENSMUSG00000112980	D430020J02Rik	1.21E-04	7.39E-04	-3.25	5.48E+00	1.78E+01
ENSMUSG00000049823	Zbtb12	1.24E-04	7.54E-04	-2.13	1.15E+01	2.44E+01
ENSMUSG00000103688	Gm6321	1.25E-04	7.60E-04	8.28	2.09E+00	2.52E-01
ENSMUSG00000073700	Klhl21	1.27E-04	7.72E-04	-2.11	1.28E+02	2.70E+02
ENSMUSG00000038252	Ncapd2	1.31E-04	7.92E-04	-2.09	2.14E+02	4.49E+02
ENSMUSG00000045231	BC106179	1.32E-04	7.98E-04	-11.24	2.71E-01	3.05E+00
ENSMUSG00000038204	Asb10	1.32E-04	7.98E-04	-9.63	4.47E-01	4.30E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000023473	Celsr3	1.32E-04	8.00E-04	-2.03	8.30E+00	1.69E+01
ENSMUSG00000074863	Platr25	1.33E-04	8.00E-04	-2.42	1.02E+01	2.46E+01
ENSMUSG00000115543	B230362B09Rik	1.33E-04	8.00E-04	-3.84	2.32E+00	8.94E+00
ENSMUSG00000000730	Dnmt3l	1.33E-04	8.00E-04	-4.35	1.74E+00	7.57E+00
ENSMUSG00000104088	Gm38275	1.35E-04	8.15E-04	3.37	4.89E+00	1.45E+00
ENSMUSG00000102964	9430034N14Rik	1.36E-04	8.18E-04	2.17	3.71E+01	1.71E+01
ENSMUSG00000090659	Zfp493	1.37E-04	8.25E-04	-3.95	2.22E+00	8.77E+00
ENSMUSG00000058470	Gm8369	1.39E-04	8.31E-04	2.24	1.93E+01	8.61E+00
ENSMUSG00000081650	Gm16181	1.46E-04	8.69E-04	7.26	7.33E+00	1.01E+00
ENSMUSG00000026873	Phf19	1.46E-04	8.69E-04	-2.17	1.63E+01	3.55E+01
ENSMUSG00000051969	Tlr11	1.47E-04	8.75E-04	10.17	2.26E+00	2.23E-01
ENSMUSG00000066090	Insl5	1.48E-04	8.79E-04	21.10	3.23E+00	1.53E-01
ENSMUSG00000005124	Ccn4	1.49E-04	8.84E-04	-2.47	1.67E+01	4.13E+01
ENSMUSG00000048058	Ldlrad3	1.49E-04	8.86E-04	-2.30	2.50E+01	5.74E+01
ENSMUSG00000027324	Rpusd2	1.50E-04	8.92E-04	-2.98	2.95E+00	8.81E+00
ENSMUSG00000042498	Radx	1.51E-04	8.95E-04	-3.95	2.19E+00	8.66E+00
ENSMUSG00000111361	Gm47445	1.52E-04	8.98E-04	2.02	7.86E+01	3.90E+01
ENSMUSG00000036777	Anln	1.52E-04	8.99E-04	-2.10	3.78E+01	7.95E+01
ENSMUSG00000086527	Gm15856	1.54E-04	9.08E-04	5.42	4.56E+00	8.41E-01
ENSMUSG00000021846	Peli2	1.54E-04	9.09E-04	-2.25	4.57E+01	1.03E+02
ENSMUSG00000044162	Tnip3	1.54E-04	9.11E-04	3.33	2.61E+03	7.84E+02
ENSMUSG00000025225	Nfkb2	1.55E-04	9.12E-04	2.10	6.81E+02	3.24E+02
ENSMUSG00000044968	Napepld	1.59E-04	9.32E-04	-2.51	1.32E+01	3.32E+01
ENSMUSG00000046441	Cmtr2	1.60E-04	9.38E-04	-2.03	1.39E+01	2.83E+01
ENSMUSG00000027326	Knl1	1.62E-04	9.50E-04	-2.02	4.10E+01	8.27E+01

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ENSMUSG00000100235	Gm28557	1.67E-04	9.72E-04	-4.85	1.25E+00	6.08E+00
ENSMUSG00000063568	Jazf1	1.67E-04	9.75E-04	3.08	9.56E+00	3.10E+00
ENSMUSG00000029490	Mfsd7a	1.69E-04	9.87E-04	2.54	7.66E+01	3.02E+01
ENSMUSG00000035364	nan	1.71E-04	9.93E-04	-2.37	9.42E+00	2.23E+01
ENSMUSG00000072889	Nfxl1	1.71E-04	9.95E-04	2.14	1.12E+02	5.23E+01
ENSMUSG00000060923	Acyp2	1.73E-04	1.00E-03	3.69	7.87E+00	2.13E+00
ENSMUSG00000043939	A530064D06Rik	1.76E-04	1.02E-03	-2.67	9.72E+00	2.59E+01
ENSMUSG00000073176	Zfp449	1.76E-04	1.02E-03	-3.24	2.44E+00	7.90E+00
ENSMUSG00000022584	Ly6c2	1.80E-04	1.04E-03	3.26	1.26E+01	3.86E+00
ENSMUSG00000084883	Ccdc85c	1.80E-04	1.04E-03	-9.89	2.71E-01	2.68E+00
ENSMUSG00000056367	Actr3b	1.83E-04	1.05E-03	2.45	2.08E+01	8.51E+00
ENSMUSG00000029861	Fam131b	1.84E-04	1.06E-03	11.95	2.35E+00	1.96E-01
ENSMUSG00000021367	Edn1	1.89E-04	1.08E-03	10.16	1.45E+02	1.43E+01
ENSMUSG00000027387	Zc3h8	1.91E-04	1.09E-03	-2.17	1.13E+01	2.44E+01
ENSMUSG00000048924	Ccdc125	1.92E-04	1.10E-03	-3.37	6.64E+00	2.24E+01
ENSMUSG00000074796	Slc4a11	1.95E-04	1.11E-03	3.07	7.56E+00	2.46E+00
ENSMUSG00000026955	Sapcd2	2.02E-04	1.15E-03	-3.58	3.06E+00	1.09E+01
ENSMUSG00000015709	Arnt2	2.04E-04	1.16E-03	4.50	1.11E+01	2.46E+00
ENSMUSG00000020648	Dus4l	2.05E-04	1.16E-03	-2.70	4.99E+00	1.35E+01
ENSMUSG00000060301	2610008E11Rik	2.09E-04	1.18E-03	-2.02	1.33E+01	2.69E+01
ENSMUSG00000108291	Gm44292	2.10E-04	1.19E-03	3.39	2.82E+02	8.32E+01
ENSMUSG00000055240	Zfp101	2.13E-04	1.20E-03	-2.50	9.34E+00	2.33E+01
ENSMUSG00000040606	Kazn	2.15E-04	1.21E-03	4.52	6.91E+00	1.53E+00
ENSMUSG00000039384	Dusp10	2.16E-04	1.22E-03	3.14	5.38E+01	1.71E+01
ENSMUSG00000026622	Nek2	2.23E-04	1.25E-03	-2.28	2.02E+01	4.62E+01

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ENSMUSG00000004347	Pde1c	2.25E-04	1.26E-03	-2.01	1.02E+01	2.04E+01
ENSMUSG00000038046	Mrm3	2.26E-04	1.26E-03	-2.25	8.90E+00	2.00E+01
ENSMUSG00000047604	Frat2	2.31E-04	1.29E-03	-2.26	5.08E+01	1.15E+02
ENSMUSG00000028636	Ppcs	2.32E-04	1.30E-03	-2.01	2.84E+01	5.71E+01
ENSMUSG00000024334	H2-Oa	2.33E-04	1.30E-03	3.56	8.88E+00	2.49E+00
ENSMUSG00000006362	Cbfa2t3	2.38E-04	1.32E-03	-2.05	6.18E+01	1.27E+02
ENSMUSG00000031548	Sfrp1	2.45E-04	1.36E-03	6.30	4.34E+00	6.89E-01
ENSMUSG00000034842	Art3	2.47E-04	1.37E-03	12.24	2.12E+00	1.73E-01
ENSMUSG00000115902	D730005E14Rik	2.50E-04	1.38E-03	5.64	5.51E+00	9.77E-01
ENSMUSG00000111375	Btbd8	2.54E-04	1.41E-03	-2.22	6.95E+00	1.54E+01
ENSMUSG00000027243	Harbi1	2.57E-04	1.42E-03	-2.15	8.84E+00	1.90E+01
ENSMUSG00000106951	5930430L01Rik	2.60E-04	1.43E-03	-4.78	1.40E+00	6.71E+00
ENSMUSG00000105541	Gm43136	2.65E-04	1.46E-03	3.90	4.23E+00	1.08E+00
ENSMUSG00000097365	C030034L19Rik	2.65E-04	1.46E-03	-3.47	2.83E+00	9.85E+00
ENSMUSG00000020599	Rgs9	2.67E-04	1.47E-03	9.19	5.71E+00	6.21E-01
ENSMUSG00000093765	Gm20658	2.68E-04	1.47E-03	-2.67	5.37E+00	1.43E+01
ENSMUSG00000032946	Rasgrp2	2.68E-04	1.47E-03	-2.51	9.80E+00	2.46E+01
ENSMUSG00000041396	Mettl18	2.70E-04	1.48E-03	-2.53	6.58E+00	1.67E+01
ENSMUSG00000036882	Arhgap33	2.72E-04	1.49E-03	-3.90	2.01E+00	7.82E+00
ENSMUSG00000084760	Gm15472	2.76E-04	1.51E-03	-5.11	1.22E+00	6.21E+00
ENSMUSG00000016283	H2-M2	2.77E-04	1.51E-03	5.49	3.90E+02	7.11E+01
ENSMUSG00000042351	Grap2	2.88E-04	1.57E-03	2.31	2.28E+01	9.88E+00
ENSMUSG00000023066	Rttn	2.95E-04	1.60E-03	-2.22	1.41E+01	3.13E+01
ENSMUSG00000037640	Zfp60	2.98E-04	1.61E-03	-2.00	1.09E+01	2.18E+01
ENSMUSG00000000915	Hip1r	3.03E-04	1.64E-03	3.29	9.81E+00	2.98E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000028678	Kif2c	3.09E-04	1.67E-03	-2.54	2.07E+01	5.26E+01
ENSMUSG00000031613	Hpgd	3.16E-04	1.70E-03	-3.69	3.52E+00	1.30E+01
ENSMUSG00000109685	Gvin-ps1	3.19E-04	1.71E-03	8.77	2.51E+00	2.86E-01
ENSMUSG00000025324	Atp10a	3.19E-04	1.71E-03	2.25	2.67E+01	1.19E+01
ENSMUSG00000019845	Tube1	3.22E-04	1.72E-03	-2.68	6.59E+00	1.77E+01
ENSMUSG00000075232	Amd1	3.23E-04	1.73E-03	-2.31	6.00E+00	1.39E+01
ENSMUSG00000028031	Dkk2	3.36E-04	1.79E-03	-8.84	4.47E-01	3.95E+00
ENSMUSG00000044854	1700056E22Rik	3.38E-04	1.80E-03	2.79	6.95E+00	2.49E+00
ENSMUSG00000030691	Fchsd2	3.39E-04	1.80E-03	2.58	7.29E+02	2.83E+02
ENSMUSG00000021994	Wnt5a	3.41E-04	1.81E-03	-2.56	3.37E+00	8.64E+00
ENSMUSG00000112892	Gm8613	3.44E-04	1.83E-03	9.66	1.48E+00	1.53E-01
ENSMUSG00000032530	Lyzl4	3.45E-04	1.83E-03	-2.38	1.04E+01	2.49E+01
ENSMUSG00000055546	Timd4	3.45E-04	1.83E-03	7.70	3.56E+00	4.63E-01
ENSMUSG00000052632	Asap2	3.45E-04	1.83E-03	-2.33	1.34E+01	3.11E+01
ENSMUSG00000113918	Gm6566	3.58E-04	1.89E-03	2.99	6.41E+00	2.15E+00
ENSMUSG00000039942	Ptger4	3.60E-04	1.90E-03	3.07	1.08E+03	3.51E+02
ENSMUSG00000031383	Dusp9	3.68E-04	1.94E-03	-2.15	6.18E+00	1.33E+01
ENSMUSG00000022661	Cd200	3.69E-04	1.95E-03	3.34	1.07E+02	3.21E+01
ENSMUSG00000074743	Thbd	3.69E-04	1.95E-03	-2.29	1.53E+01	3.50E+01
ENSMUSG00000022512	Cldn1	3.71E-04	1.95E-03	15.27	2.65E+00	1.73E-01
ENSMUSG00000053411	Cbx7	3.75E-04	1.97E-03	-2.21	1.26E+01	2.80E+01
ENSMUSG00000084399	Gm15666	3.86E-04	2.03E-03	5.84	1.80E+01	3.09E+00
ENSMUSG00000028587	Orc1	3.88E-04	2.03E-03	-2.59	7.95E+00	2.06E+01
ENSMUSG00000099746	Ppnr	3.92E-04	2.05E-03	3.31	5.54E+00	1.67E+00
ENSMUSG00000022419	Deptor	3.94E-04	2.06E-03	-2.40	9.87E+01	2.37E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000020897	Aurkb	4.01E-04	2.09E-03	-2.08	2.44E+01	5.08E+01
ENSMUSG00000092626	9130230N09Rik	4.06E-04	2.12E-03	2.28	1.27E+01	5.57E+00
ENSMUSG00000093622	Gm20703	4.07E-04	2.12E-03	-2.04	1.11E+01	2.26E+01
ENSMUSG00000078954	Arhgap8	4.16E-04	2.16E-03	6.70	2.78E+00	4.16E-01
ENSMUSG00000102037	Bcl2a1a	4.18E-04	2.17E-03	4.68	2.61E+01	5.56E+00
ENSMUSG00000064336	mt-Tf	4.27E-04	2.22E-03	3.34	1.19E+01	3.55E+00
ENSMUSG00000104654	Gm43814	4.30E-04	2.23E-03	5.33	2.17E+02	4.08E+01
ENSMUSG00000092118	Fancf	4.32E-04	2.24E-03	-2.34	6.02E+00	1.41E+01
ENSMUSG00000054580	Pla2r1	4.32E-04	2.24E-03	2.37	1.22E+01	5.16E+00
ENSMUSG00000043903	Zfp469	4.36E-04	2.26E-03	-3.01	5.34E+00	1.61E+01
ENSMUSG00000022534	Mefv	4.36E-04	2.26E-03	4.93	2.74E+01	5.55E+00
ENSMUSG00000031342	Gpm6b	4.41E-04	2.28E-03	2.26	1.45E+01	6.42E+00
ENSMUSG00000097705	Gm26740	4.42E-04	2.29E-03	-2.27	1.97E+01	4.47E+01
ENSMUSG00000083678	Gm12989	4.42E-04	2.29E-03	4.32	4.48E+00	1.04E+00
ENSMUSG00000104436	Gm37423	4.43E-04	2.29E-03	2.08	2.67E+01	1.28E+01
ENSMUSG00000107792	Gm43914	4.44E-04	2.29E-03	17.58	2.69E+00	1.53E-01
ENSMUSG00000037466	Tedc1	4.44E-04	2.29E-03	-2.75	6.22E+00	1.71E+01
ENSMUSG00000112391	Gm48230	4.50E-04	2.32E-03	3.91	5.63E+00	1.44E+00
ENSMUSG00000051246	Msantd1	4.51E-04	2.32E-03	3.25	8.04E+00	2.47E+00
ENSMUSG00000022218	Tgm1	4.55E-04	2.34E-03	9.62	2.43E+00	2.52E-01
ENSMUSG00000072844	G530011O06Rik	4.59E-04	2.35E-03	6.10	2.82E+01	4.62E+00
ENSMUSG00000107741	Gm2011	4.59E-04	2.36E-03	2.60	1.69E+01	6.50E+00
ENSMUSG00000026274	Pask	4.59E-04	2.36E-03	-2.93	5.04E+00	1.48E+01
ENSMUSG00000113587	Gm36287	4.61E-04	2.37E-03	5.38	5.58E+00	1.04E+00
ENSMUSG00000112067	Gm48015	4.62E-04	2.37E-03	3.12	8.02E+00	2.57E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000060550	H2-Q7	4.90E-04	2.50E-03	3.76	9.42E+00	2.51E+00
ENSMUSG00000089643	Gm16301	4.96E-04	2.53E-03	10.73	1.64E+00	1.53E-01
ENSMUSG00000053175	Bcl3	4.99E-04	2.54E-03	2.16	1.68E+03	7.80E+02
ENSMUSG00000033083	Tbc1d4	5.14E-04	2.61E-03	-2.06	6.64E+01	1.37E+02
ENSMUSG00000108064	Gm44423	5.28E-04	2.67E-03	2.32	2.97E+01	1.28E+01
ENSMUSG00000042784	Muc1	5.33E-04	2.70E-03	7.73	3.22E+00	4.16E-01
ENSMUSG00000097523	1700022N22Rik	5.38E-04	2.71E-03	-9.55	2.11E-01	2.02E+00
ENSMUSG00000029372	Ppbp	5.40E-04	2.72E-03	-4.18	1.73E+00	7.21E+00
ENSMUSG00000021759	Plpp1	5.43E-04	2.73E-03	2.01	2.93E+01	1.46E+01
ENSMUSG00000048806	Ifnb1	5.46E-04	2.75E-03	21.63	1.17E+01	5.39E-01
ENSMUSG00000062545	Tlr12	5.47E-04	2.75E-03	118.47	1.81E+01	1.53E-01
ENSMUSG00000027715	Ccna2	5.49E-04	2.76E-03	-2.04	1.12E+02	2.29E+02
ENSMUSG00000043015	Nemp2	5.50E-04	2.76E-03	-2.15	7.52E+00	1.62E+01
ENSMUSG00000022791	Tnk2	5.56E-04	2.79E-03	-2.00	1.06E+01	2.12E+01
ENSMUSG00000020988	L2hgdh	5.67E-04	2.84E-03	-3.14	2.27E+00	7.13E+00
ENSMUSG00000095253	Zfp799	5.68E-04	2.84E-03	-2.10	8.04E+00	1.69E+01
ENSMUSG00000051378	Kif18b	5.69E-04	2.84E-03	-2.30	9.31E+00	2.14E+01
ENSMUSG00000042249	Grk3	5.77E-04	2.88E-03	2.45	1.06E+02	4.35E+01
ENSMUSG00000023947	Nfkbie	5.93E-04	2.95E-03	3.67	6.84E+02	1.86E+02
ENSMUSG00000029095	Ablim2	6.02E-04	2.99E-03	2.33	1.23E+01	5.28E+00
ENSMUSG00000024301	Kifc5b	6.11E-04	3.03E-03	-2.37	5.94E+00	1.41E+01
ENSMUSG00000044636	Csrnp2	6.13E-04	3.04E-03	-2.41	6.15E+00	1.48E+01
ENSMUSG00000037991	Rmi2	6.16E-04	3.05E-03	2.29	3.88E+01	1.70E+01
ENSMUSG00000034206	Polq	6.26E-04	3.09E-03	-2.26	1.10E+01	2.48E+01
ENSMUSG00000000562	Adora3	6.34E-04	3.13E-03	4.21	1.04E+01	2.47E+00

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ENSMUSG00000097000	Gm17435	6.40E-04	3.15E-03	3.04	7.84E+00	2.58E+00
ENSMUSG00000083822	Hmgb1-ps5	6.40E-04	3.15E-03	2.14	2.15E+01	1.01E+01
ENSMUSG00000079737	3110001I22Rik	6.46E-04	3.18E-03	2.09	7.34E+01	3.52E+01
ENSMUSG00000003617	Cp	6.51E-04	3.20E-03	2.27	3.04E+01	1.34E+01
ENSMUSG00000024544	Ldlrad4	6.67E-04	3.27E-03	2.07	2.06E+01	9.99E+00
ENSMUSG00000016984	Etaa1	6.68E-04	3.27E-03	-2.02	1.88E+01	3.79E+01
ENSMUSG00000000126	Wnt9a	6.71E-04	3.28E-03	2.87	1.44E+01	5.04E+00
ENSMUSG00000031906	Smpd3	6.74E-04	3.29E-03	-5.86	1.12E+00	6.56E+00
ENSMUSG00000028957	Per3	6.79E-04	3.31E-03	-2.04	1.47E+01	3.00E+01
ENSMUSG00000000320	Alox12	6.87E-04	3.35E-03	12.02	2.08E+00	1.73E-01
ENSMUSG00000104917	Gm43289	6.88E-04	3.35E-03	-7.12	3.48E-01	2.48E+00
ENSMUSG00000049608	Gpr55	6.89E-04	3.35E-03	7.05	3.68E+00	5.22E-01
ENSMUSG00000091906	1700099I09Rik	6.93E-04	3.36E-03	2.31	1.02E+01	4.42E+00
ENSMUSG00000055900	Tmem69	7.31E-04	3.53E-03	-2.09	8.88E+00	1.86E+01
ENSMUSG00000116927	Gm30881	7.54E-04	3.63E-03	2.37	7.79E+00	3.29E+00
ENSMUSG00000115355	4930445E18Rik	7.73E-04	3.71E-03	8.79	2.22E+00	2.52E-01
ENSMUSG00000097023	Mir9-3hg	7.86E-04	3.76E-03	11.47	2.55E+00	2.23E-01
ENSMUSG00000024462	Gabbr1	7.88E-04	3.77E-03	2.49	1.01E+01	4.06E+00
ENSMUSG00000006398	Cdc20	7.88E-04	3.77E-03	-2.18	8.03E+01	1.75E+02
ENSMUSG00000000884	Gnb1l	7.89E-04	3.77E-03	-2.23	8.17E+00	1.82E+01
ENSMUSG00000074738	Fndc10	7.93E-04	3.79E-03	-2.38	7.40E+00	1.76E+01
ENSMUSG00000051817	Sox12	7.96E-04	3.80E-03	-8.54	3.48E-01	2.97E+00
ENSMUSG00000106962	Gm43633	7.98E-04	3.81E-03	4.21	3.50E+00	8.31E-01
ENSMUSG00000039410	Prdm16	7.99E-04	3.81E-03	-2.36	9.07E+00	2.14E+01
ENSMUSG00000073415	Gm10501	8.11E-04	3.86E-03	-5.64	7.04E-01	3.98E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000046223	Plaur	8.17E-04	3.89E-03	2.03	9.72E+02	4.78E+02
ENSMUSG00000041429	Nthl1	8.18E-04	3.89E-03	-2.16	7.66E+00	1.66E+01
ENSMUSG00000025255	Zfhx4	8.19E-04	3.89E-03	2.81	7.70E+00	2.74E+00
ENSMUSG00000040289	Hey1	8.20E-04	3.90E-03	-5.75	8.39E-01	4.82E+00
ENSMUSG00000017009	Sdc4	8.36E-04	3.97E-03	2.44	3.45E+03	1.41E+03
ENSMUSG00000106254	Gm42907	8.38E-04	3.97E-03	3.54	7.61E+00	2.15E+00
ENSMUSG00000109560	Gm8463	8.42E-04	3.99E-03	3.45	5.04E+00	1.46E+00
ENSMUSG00000026646	Suv39h2	8.48E-04	4.01E-03	-2.15	9.37E+00	2.01E+01
ENSMUSG00000102246	9430037O13Rik	8.50E-04	4.02E-03	-6.28	1.48E+00	9.30E+00
ENSMUSG00000045381	Olfr433	8.59E-04	4.06E-03	4.89	5.27E+00	1.08E+00
ENSMUSG00000114169	Gm47075	8.70E-04	4.10E-03	11.54	2.27E+00	1.96E-01
ENSMUSG00000097636	Mirt1	8.71E-04	4.10E-03	-3.21	3.64E+00	1.17E+01
ENSMUSG00000037279	Ovol2	8.75E-04	4.11E-03	23.57	3.61E+00	1.53E-01
ENSMUSG00000021594	Srd5a1	8.82E-04	4.15E-03	-3.34	1.70E+00	5.67E+00
ENSMUSG00000108030	9530062K07Rik	8.82E-04	4.15E-03	-3.57	1.42E+00	5.06E+00
ENSMUSG00000026556	Vangl2	8.94E-04	4.19E-03	-2.80	2.43E+00	6.82E+00
ENSMUSG00000039781	Cep131	9.22E-04	4.31E-03	-2.00	1.44E+01	2.88E+01
ENSMUSG00000113440	Gm46404	9.24E-04	4.31E-03	2.84	6.51E+00	2.29E+00
ENSMUSG00000097378	B230208H11Rik	9.65E-04	4.49E-03	5.05	3.66E+00	7.25E-01
ENSMUSG00000114835	Gm48194	9.72E-04	4.52E-03	2.53	8.88E+00	3.51E+00
ENSMUSG00000085213	Gm13091	9.73E-04	4.52E-03	2.33	1.57E+01	6.71E+00
ENSMUSG00000107529	Gm44291	9.75E-04	4.53E-03	2.17	5.45E+01	2.51E+01
ENSMUSG00000030677	Kif22	9.77E-04	4.54E-03	-2.09	4.33E+01	9.06E+01
ENSMUSG00000020974	Pole2	9.87E-04	4.58E-03	-2.55	1.03E+01	2.63E+01
ENSMUSG00000030393	Zik1	9.94E-04	4.60E-03	-5.93	8.69E-01	5.16E+00

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ENSMUSG00000020808	Pimreg	1.00E-03	4.64E-03	-2.23	3.85E+01	8.57E+01
ENSMUSG00000036053	Fmnl2	1.00E-03	4.64E-03	2.35	2.43E+02	1.03E+02
ENSMUSG00000051029	Serpinb1b	1.02E-03	4.71E-03	2.83	1.23E+01	4.35E+00
ENSMUSG00000058492	Scp2-ps2	1.02E-03	4.72E-03	3.62	4.62E+00	1.28E+00
ENSMUSG00000054843	Atrnl1	1.05E-03	4.83E-03	2.00	4.44E+01	2.22E+01
ENSMUSG00000074607	Tox2	1.05E-03	4.83E-03	-2.67	8.24E+01	2.20E+02
ENSMUSG00000105950	Gm43679	1.06E-03	4.88E-03	2.71	6.13E+00	2.26E+00
ENSMUSG00000035279	Ssc5d	1.07E-03	4.93E-03	2.36	1.19E+01	5.06E+00
ENSMUSG00000028773	Fabp3	1.08E-03	4.94E-03	2.07	2.65E+02	1.28E+02
ENSMUSG00000035246	Pcyt1b	1.08E-03	4.96E-03	-3.03	3.32E+00	1.01E+01
ENSMUSG00000104897	Gm43203	1.09E-03	5.00E-03	4.63	4.10E+00	8.85E-01
ENSMUSG00000050578	Mmp13	1.10E-03	5.04E-03	2.72	9.59E+02	3.53E+02
ENSMUSG00000102437	nan	1.11E-03	5.08E-03	3.15	4.38E+00	1.39E+00
ENSMUSG00000106115	Gm43420	1.14E-03	5.17E-03	2.54	1.11E+01	4.35E+00
ENSMUSG00000026429	Ube2t	1.16E-03	5.25E-03	-2.22	1.26E+01	2.80E+01
ENSMUSG00000115116	Gm46496	1.18E-03	5.36E-03	5.34	2.79E+00	5.22E-01
ENSMUSG00000032515	Csrnp1	1.22E-03	5.51E-03	4.87	1.85E+03	3.80E+02
ENSMUSG00000031898	Dpep3	1.23E-03	5.57E-03	-3.60	2.04E+00	7.35E+00
ENSMUSG00000002100	Mybpc3	1.24E-03	5.58E-03	2.13	2.97E+01	1.39E+01
ENSMUSG00000022122	Ednrb	1.24E-03	5.59E-03	2.45	2.41E+02	9.82E+01
ENSMUSG00000055210	Foxd2	1.25E-03	5.63E-03	-2.32	6.07E+00	1.41E+01
ENSMUSG00000103546	Gm37666	1.25E-03	5.64E-03	3.22	2.40E+01	7.46E+00
ENSMUSG00000007279	Scube2	1.28E-03	5.74E-03	9.83	4.60E+00	4.68E-01
ENSMUSG00000024421	Lama3	1.29E-03	5.76E-03	-2.84	4.57E+00	1.30E+01
ENSMUSG00000053113	Socs3	1.32E-03	5.89E-03	5.99	1.09E+04	1.82E+03

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000048445	Ccdc57	1.32E-03	5.89E-03	-2.52	4.64E+00	1.17E+01
ENSMUSG00000082088	Gm15753	1.33E-03	5.91E-03	4.86	2.79E+00	5.73E-01
ENSMUSG00000020546	Stxbp4	1.33E-03	5.92E-03	-2.15	8.35E+00	1.79E+01
ENSMUSG00000111212	5330432J10Rik	1.33E-03	5.92E-03	2.25	1.01E+01	4.48E+00
ENSMUSG00000021280	Exoc3l4	1.42E-03	6.27E-03	2.09	9.44E+01	4.51E+01
ENSMUSG00000043953	Ccrl2	1.43E-03	6.31E-03	3.83	4.55E+03	1.19E+03
ENSMUSG00000028634	Hivep3	1.46E-03	6.42E-03	2.86	1.39E+03	4.87E+02
ENSMUSG00000016498	Pdcd1lg2	1.48E-03	6.50E-03	4.70	2.73E+00	5.80E-01
ENSMUSG00000001444	Tbx21	1.49E-03	6.52E-03	17.86	3.10E+00	1.73E-01
ENSMUSG00000036898	Zfp157	1.50E-03	6.55E-03	-2.07	1.52E+01	3.15E+01
ENSMUSG00000037904	Ankrd9	1.50E-03	6.57E-03	-2.27	7.24E+00	1.64E+01
ENSMUSG00000066838	Zfp772	1.51E-03	6.62E-03	-2.27	5.52E+00	1.25E+01
ENSMUSG00000086119	Gm2415	1.53E-03	6.67E-03	-2.68	4.79E+00	1.28E+01
ENSMUSG00000027670	Ocstamp	1.54E-03	6.73E-03	6.36	9.26E+00	1.46E+00
ENSMUSG00000026090	Cracdl	1.56E-03	6.80E-03	6.88	4.29E+00	6.23E-01
ENSMUSG00000027463	Slc52a3	1.60E-03	6.95E-03	5.22	4.05E+00	7.77E-01
ENSMUSG00000098065	Gm5177	1.60E-03	6.95E-03	2.89	5.04E+00	1.74E+00
ENSMUSG00000106209	Gm42918	1.62E-03	7.00E-03	2.61	6.87E+00	2.63E+00
ENSMUSG00000084846	A730011C13Rik	1.62E-03	7.00E-03	2.98	4.63E+00	1.55E+00
ENSMUSG00000000078	Klf6	1.62E-03	7.01E-03	2.66	1.98E+04	7.43E+03
ENSMUSG00000034957	Cebpa	1.63E-03	7.06E-03	-2.18	8.00E+02	1.75E+03
ENSMUSG00000050138	Kcnk12	1.63E-03	7.07E-03	-3.19	2.29E+00	7.32E+00
ENSMUSG00000030725	Lipt2	1.64E-03	7.08E-03	-2.09	6.62E+00	1.38E+01
ENSMUSG00000097028	Ptgs2os	1.64E-03	7.08E-03	7.83	4.62E+00	5.90E-01
ENSMUSG00000014773	Dll1	1.69E-03	7.26E-03	6.81	1.51E+00	2.23E-01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000020696	Rffl	1.69E-03	7.26E-03	2.18	1.75E+02	8.03E+01
ENSMUSG00000071335	Mfsd4b3-ps	1.71E-03	7.33E-03	-2.06	7.61E+00	1.57E+01
ENSMUSG00000027456	Sdcbp2	1.72E-03	7.37E-03	2.69	1.09E+01	4.05E+00
ENSMUSG00000027811	4930579G24Rik	1.72E-03	7.38E-03	-2.31	7.13E+00	1.65E+01
ENSMUSG00000000673	Haao	1.73E-03	7.41E-03	2.04	9.31E+00	4.57E+00
ENSMUSG00000116165	Pdxp	1.74E-03	7.43E-03	-2.15	5.96E+00	1.28E+01
ENSMUSG00000035121	Neil2	1.74E-03	7.45E-03	-2.02	7.77E+00	1.57E+01
ENSMUSG00000074892	B3galt5	1.75E-03	7.48E-03	-3.58	3.97E+00	1.42E+01
ENSMUSG00000041907	Gpr45	1.78E-03	7.58E-03	2.91	5.00E+00	1.72E+00
ENSMUSG00000049999	Ppp1r3d	1.78E-03	7.61E-03	2.12	4.38E+01	2.07E+01
ENSMUSG00000026546	Cfap45	1.79E-03	7.65E-03	2.21	1.61E+01	7.27E+00
ENSMUSG00000049916	2610318N02Rik	1.81E-03	7.70E-03	-2.37	8.05E+00	1.91E+01
ENSMUSG00000019874	Fabp7	1.84E-03	7.83E-03	-2.38	8.85E+00	2.10E+01
ENSMUSG00000024049	Myom1	1.90E-03	8.04E-03	-2.85	2.81E+00	8.02E+00
ENSMUSG00000073409	H2-Q6	1.90E-03	8.05E-03	5.13	3.99E+00	7.78E-01
ENSMUSG00000103408	Gm37933	1.91E-03	8.08E-03	-3.48	1.56E+00	5.43E+00
ENSMUSG00000053062	Jam2	1.92E-03	8.11E-03	3.67	7.25E+00	1.98E+00
ENSMUSG00000010021	Kif19a	1.92E-03	8.11E-03	4.15	5.97E+00	1.44E+00
ENSMUSG00000044231	Nhlrc1	1.93E-03	8.15E-03	-2.84	6.71E+00	1.91E+01
ENSMUSG00000037568	Vash2	1.95E-03	8.21E-03	-2.20	7.88E+00	1.73E+01
ENSMUSG00000030206	Gsg1	1.96E-03	8.26E-03	-2.64	3.08E+00	8.14E+00
ENSMUSG00000042010	Acacb	1.99E-03	8.38E-03	3.17	4.65E+00	1.47E+00
ENSMUSG00000102059	Gm20257	2.00E-03	8.40E-03	2.27	1.25E+01	5.48E+00
ENSMUSG00000036478	Btg1	2.05E-03	8.59E-03	2.12	1.36E+03	6.40E+02
ENSMUSG00000033762	Recql4	2.07E-03	8.65E-03	-2.43	3.39E+00	8.24E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000043419	Rnf227	2.09E-03	8.74E-03	-3.06	3.65E+00	1.12E+01
ENSMUSG00000005718	Tfap4	2.09E-03	8.75E-03	-2.65	1.33E+01	3.53E+01
ENSMUSG00000030895	Hpx	2.11E-03	8.81E-03	2.73	8.23E+00	3.02E+00
ENSMUSG00000090626	Tex9	2.12E-03	8.83E-03	-2.03	7.07E+00	1.44E+01
ENSMUSG00000067928	Zfp760	2.14E-03	8.92E-03	-2.60	3.09E+00	8.02E+00
ENSMUSG00000085334	Gm12940	2.14E-03	8.93E-03	2.90	1.22E+01	4.23E+00
ENSMUSG00000066000	Zfp979	2.16E-03	8.99E-03	-2.46	3.85E+00	9.47E+00
ENSMUSG00000028780	Sema3c	2.17E-03	9.04E-03	2.07	1.45E+01	7.00E+00
ENSMUSG00000102662	Gm38377	2.18E-03	9.06E-03	2.82	2.43E+01	8.63E+00
ENSMUSG00000099843	Gm7160	2.20E-03	9.11E-03	2.16	1.35E+01	6.27E+00
ENSMUSG00000048498	Cd300e	2.21E-03	9.15E-03	-3.14	2.11E+00	6.63E+00
ENSMUSG00000114784	Gm47754	2.22E-03	9.18E-03	2.04	8.05E+00	3.94E+00
ENSMUSG00000026303	Mlph	2.29E-03	9.43E-03	-8.58	3.48E-01	2.99E+00
ENSMUSG00000029334	Prkg2	2.29E-03	9.44E-03	-2.74	3.37E+00	9.22E+00
ENSMUSG00000039648	Kyat1	2.32E-03	9.52E-03	-2.10	7.56E+00	1.59E+01
ENSMUSG00000037784	Dzip1l	2.33E-03	9.57E-03	-7.41	2.71E-01	2.01E+00
ENSMUSG00000009614	Sardh	2.45E-03	1.00E-02	-3.00	2.64E+00	7.92E+00
ENSMUSG00000038456	Dennd2a	2.46E-03	1.01E-02	-2.19	7.16E+00	1.56E+01
ENSMUSG00000015652	Steap1	2.54E-03	1.04E-02	3.43	4.44E+00	1.29E+00
ENSMUSG00000102672	Gm37105	2.54E-03	1.04E-02	-2.27	4.26E+00	9.66E+00
ENSMUSG00000036537	Rnf113a1	2.55E-03	1.04E-02	-2.24	5.49E+00	1.23E+01
ENSMUSG00000033900	Map9	2.60E-03	1.06E-02	-2.94	2.86E+00	8.42E+00
ENSMUSG00000116796	Gm49784	2.66E-03	1.08E-02	2.45	1.13E+01	4.61E+00
ENSMUSG00000112883	Gm48023	2.67E-03	1.08E-02	6.98	1.99E+00	2.86E-01
ENSMUSG00000097597	Gm26674	2.71E-03	1.10E-02	-2.97	2.12E+00	6.30E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000097287	D130017N08Rik	2.73E-03	1.10E-02	-2.17	4.34E+00	9.43E+00
ENSMUSG00000067206	Lrrc66	2.76E-03	1.12E-02	3.57	5.99E+00	1.68E+00
ENSMUSG00000030029	Lrig1	2.82E-03	1.14E-02	-2.55	3.43E+00	8.74E+00
ENSMUSG00000032911	Cspg4	2.93E-03	1.17E-02	-2.14	2.32E+01	4.95E+01
ENSMUSG00000089687	Rab42	2.96E-03	1.18E-02	-2.56	2.68E+00	6.84E+00
ENSMUSG00000024014	Pim1	2.97E-03	1.19E-02	2.22	4.48E+03	2.02E+03
ENSMUSG00000078794	Dact3	2.98E-03	1.19E-02	-3.58	1.42E+00	5.08E+00
ENSMUSG00000036634	Mag	3.00E-03	1.20E-02	2.08	1.06E+01	5.11E+00
ENSMUSG00000101903	Gm29291	3.08E-03	1.23E-02	-9.54	2.71E-01	2.59E+00
ENSMUSG00000004864	Mapk13	3.11E-03	1.24E-02	4.70	6.74E+00	1.43E+00
ENSMUSG00000050592	Fam78a	3.14E-03	1.25E-02	-2.47	1.01E+01	2.48E+01
ENSMUSG00000103734	Gm37651	3.16E-03	1.26E-02	2.82	2.99E+01	1.06E+01
ENSMUSG00000043687	1190005I06Rik	3.21E-03	1.27E-02	-2.70	3.45E+00	9.30E+00
ENSMUSG00000065331	Gm24927	3.21E-03	1.27E-02	2.97	6.34E+00	2.14E+00
ENSMUSG00000065494	Mir28a	3.22E-03	1.27E-02	5.79	4.18E+00	7.22E-01
ENSMUSG00000097493	9930014A18Rik	3.24E-03	1.28E-02	-2.74	2.40E+00	6.56E+00
ENSMUSG00000039131	Gipc2	3.24E-03	1.28E-02	-2.23	4.12E+00	9.20E+00
ENSMUSG00000115384	Gm49205	3.28E-03	1.29E-02	8.63	2.47E+00	2.86E-01
ENSMUSG00000021061	Sptb	3.32E-03	1.31E-02	-5.03	7.29E-01	3.67E+00
ENSMUSG00000041949	Tango6	3.33E-03	1.31E-02	-2.32	3.95E+00	9.15E+00
ENSMUSG00000049904	Tmem17	3.35E-03	1.32E-02	-2.04	6.85E+00	1.40E+01
ENSMUSG00000105270	Gm42863	3.36E-03	1.32E-02	4.39	2.52E+00	5.74E-01
ENSMUSG00000110388	Gm30329	3.37E-03	1.32E-02	-2.11	1.38E+01	2.91E+01
ENSMUSG00000028933	Xrcc2	3.37E-03	1.32E-02	-2.22	7.54E+00	1.67E+01
ENSMUSG00000035459	Stab2	3.41E-03	1.33E-02	-2.24	5.70E+00	1.28E+01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000074682	Zcchc3	3.42E-03	1.34E-02	-2.00	9.72E+00	1.95E+01
ENSMUSG00000101462	Gm3052	3.44E-03	1.35E-02	-2.70	2.49E+00	6.73E+00
ENSMUSG00000021281	Tnfaip2	3.47E-03	1.35E-02	2.35	1.65E+04	7.02E+03
ENSMUSG00000031927	1700012B09Rik	3.51E-03	1.37E-02	3.69	3.63E+00	9.83E-01
ENSMUSG00000109428	Gm45698	3.53E-03	1.38E-02	3.57	7.46E+00	2.09E+00
ENSMUSG00000108120	9930120I10Rik	3.53E-03	1.38E-02	2.33	1.10E+01	4.72E+00
ENSMUSG00000021278	Amn	3.56E-03	1.39E-02	4.06	5.52E+00	1.36E+00
ENSMUSG00000020623	Map2k6	3.62E-03	1.41E-02	-2.57	4.30E+00	1.10E+01
ENSMUSG00000032420	Nt5e	3.63E-03	1.41E-02	-6.38	3.48E-01	2.22E+00
ENSMUSG00000027654	Fam83d	3.67E-03	1.42E-02	-2.29	1.31E+01	2.99E+01
ENSMUSG00000085295	4930430E12Rik	3.73E-03	1.45E-02	2.04	1.08E+02	5.29E+01
ENSMUSG00000107604	Gm44041	3.75E-03	1.45E-02	-8.59	2.71E-01	2.33E+00
ENSMUSG00000034800	Zfp661	3.76E-03	1.45E-02	-2.07	5.42E+00	1.12E+01
ENSMUSG00000035283	Adrb1	3.77E-03	1.46E-02	-4.16	1.01E+00	4.19E+00
ENSMUSG00000028807	Zbtb8a	3.85E-03	1.48E-02	-2.07	7.05E+00	1.46E+01
ENSMUSG00000056458	Mok	3.87E-03	1.49E-02	-3.14	1.42E+00	4.48E+00
ENSMUSG00000109836	nan	3.89E-03	1.50E-02	-2.04	5.84E+00	1.19E+01
ENSMUSG00000037548	H2-DMb2	3.94E-03	1.51E-02	2.06	1.27E+01	6.13E+00
ENSMUSG00000097519	4930558J18Rik	4.04E-03	1.54E-02	-2.68	3.11E+00	8.33E+00
ENSMUSG00000074634	Tmem267	4.07E-03	1.56E-02	-2.03	6.31E+00	1.28E+01
ENSMUSG00000015467	Egfl8	4.10E-03	1.56E-02	-2.10	4.19E+00	8.78E+00
ENSMUSG00000021391	Cenpp	4.11E-03	1.57E-02	-2.03	1.35E+01	2.73E+01
ENSMUSG00000115252	Gm48996	4.12E-03	1.57E-02	2.26	4.38E+01	1.94E+01
ENSMUSG00000084866	A930006K02Rik	4.18E-03	1.59E-02	-2.24	4.02E+00	8.98E+00
ENSMUSG00000103284	3110080O07Rik	4.22E-03	1.60E-02	-4.10	1.01E+00	4.13E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000022885	St6gal1	4.23E-03	1.60E-02	-2.22	1.28E+02	2.83E+02
ENSMUSG00000049539	H1f1	4.24E-03	1.61E-02	-7.64	3.48E-01	2.66E+00
ENSMUSG00000017144	Rnd3	4.27E-03	1.62E-02	3.38	3.49E+02	1.03E+02
ENSMUSG00000027977	Ndst3	4.41E-03	1.66E-02	10.01	1.97E+00	1.96E-01
ENSMUSG00000072919	Noxred1	4.43E-03	1.67E-02	2.42	1.18E+01	4.87E+00
ENSMUSG00000105322	Gm43751	4.44E-03	1.67E-02	7.58	3.14E+00	4.14E-01
ENSMUSG00000002578	Ikzf4	4.45E-03	1.67E-02	5.69	4.75E+00	8.34E-01
ENSMUSG00000020491	2810021J22Rik	4.48E-03	1.68E-02	-2.57	3.29E+00	8.47E+00
ENSMUSG00000114019	Gm47155	4.49E-03	1.68E-02	2.37	8.80E+00	3.72E+00
ENSMUSG00000040270	Bach2	4.50E-03	1.69E-02	-2.80	7.26E+00	2.03E+01
ENSMUSG00000070997	1700055D18Rik	4.54E-03	1.70E-02	2.35	8.28E+00	3.52E+00
ENSMUSG00000033949	Trim36	4.54E-03	1.70E-02	2.25	5.27E+01	2.34E+01
ENSMUSG00000025746	Il6	4.54E-03	1.70E-02	8.53	3.32E+01	3.89E+00
ENSMUSG00000097295	Hmgb1-ps8	4.55E-03	1.70E-02	-2.01	1.31E+01	2.63E+01
ENSMUSG00000004748	Mtfp1	4.58E-03	1.71E-02	-7.31	3.48E-01	2.55E+00
ENSMUSG00000090290	Tarbp1	4.64E-03	1.73E-02	-2.77	1.99E+00	5.52E+00
ENSMUSG00000085030	2810455O05Rik	4.70E-03	1.75E-02	-2.75	2.99E+00	8.23E+00
ENSMUSG00000106391	Gm42690	4.71E-03	1.75E-02	-8.68	2.11E-01	1.83E+00
ENSMUSG00000018849	Wwc1	4.71E-03	1.75E-02	-2.78	3.57E+00	9.92E+00
ENSMUSG00000087017	4930417H01Rik	4.72E-03	1.76E-02	7.56	3.12E+00	4.13E-01
ENSMUSG00000097558	Gm26902	4.75E-03	1.77E-02	4.67	2.68E+00	5.74E-01
ENSMUSG00000109408	A930037H05Rik	4.75E-03	1.77E-02	-5.73	5.68E-01	3.25E+00
ENSMUSG00000074807	Gm10762	4.77E-03	1.77E-02	-2.01	5.62E+00	1.13E+01
ENSMUSG00000031377	Bmx	4.83E-03	1.79E-02	-7.45	2.71E-01	2.02E+00
ENSMUSG00000070691	Runx3	4.85E-03	1.79E-02	2.14	3.33E+02	1.56E+02

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000047143	Dmrta2	4.85E-03	1.79E-02	-2.84	1.92E+00	5.47E+00
ENSMUSG00000020363	Gfpt2	4.90E-03	1.81E-02	2.84	7.28E+00	2.56E+00
ENSMUSG00000027317	Ppp1r14d	4.97E-03	1.83E-02	6.53	1.13E+00	1.73E-01
ENSMUSG00000100121	1700025N23Rik	4.97E-03	1.83E-02	9.77	1.69E+00	1.73E-01
ENSMUSG00000020123	Avpr1a	4.99E-03	1.84E-02	-5.64	4.47E-01	2.52E+00
ENSMUSG00000024575	Pde6a	4.99E-03	1.84E-02	4.71	2.24E+00	4.76E-01
ENSMUSG00000084411	Gm11510	5.03E-03	1.85E-02	3.46	4.97E+00	1.44E+00
ENSMUSG00000025010	Ccnj	5.07E-03	1.87E-02	2.05	1.16E+01	5.69E+00
ENSMUSG00000082998	Gm11221	5.08E-03	1.87E-02	-2.61	1.87E+00	4.87E+00
ENSMUSG00000008129	Brme1	5.15E-03	1.89E-02	-5.84	3.48E-01	2.03E+00
ENSMUSG00000059305	Vpreb1	5.15E-03	1.89E-02	-6.78	3.48E-01	2.36E+00
ENSMUSG00000110405	Gm45534	5.18E-03	1.90E-02	3.87	3.38E+00	8.73E-01
ENSMUSG00000046169	Adamts6	5.24E-03	1.92E-02	2.22	8.40E+00	3.78E+00
ENSMUSG00000037725	Ckap2	5.30E-03	1.93E-02	-2.11	2.38E+01	5.04E+01
ENSMUSG00000102556	Gm37569	5.34E-03	1.95E-02	2.12	1.68E+01	7.95E+00
ENSMUSG00000106858	Gm43844	5.35E-03	1.95E-02	2.66	6.27E+00	2.36E+00
ENSMUSG00000012017	Scarf2	5.36E-03	1.95E-02	-2.66	2.77E+00	7.37E+00
ENSMUSG00000102425	Gm26616	5.42E-03	1.97E-02	4.19	3.78E+00	9.03E-01
ENSMUSG00000097572	Gm26797	5.42E-03	1.97E-02	2.33	5.76E+00	2.47E+00
ENSMUSG00000115480	Gm49249	5.47E-03	1.99E-02	-3.25	1.54E+00	5.02E+00
ENSMUSG00000037035	Inhbb	5.52E-03	2.00E-02	2.14	1.24E+01	5.76E+00
ENSMUSG00000087659	Gm12606	5.56E-03	2.01E-02	7.64	3.89E+00	5.09E-01
ENSMUSG00000050605	Zfp61	5.56E-03	2.01E-02	-2.22	8.46E+00	1.88E+01
ENSMUSG00000024502	Jakmip2	5.59E-03	2.02E-02	3.99	2.74E+00	6.86E-01
ENSMUSG00000021640	Naip1	5.69E-03	2.06E-02	-3.81	1.31E+00	5.00E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000103174	Gm37168	5.70E-03	2.06E-02	-2.57	3.54E+00	9.09E+00
ENSMUSG00000041064	Pif1	5.71E-03	2.06E-02	-2.55	8.68E+00	2.21E+01
ENSMUSG00000030577	Cd22	5.84E-03	2.10E-02	-2.01	6.49E+00	1.30E+01
ENSMUSG00000032281	Acsbg1	5.88E-03	2.12E-02	-3.35	2.03E+00	6.82E+00
ENSMUSG00000043415	Otud1	5.95E-03	2.14E-02	2.81	5.25E+02	1.87E+02
ENSMUSG00000016918	Sulf1	6.01E-03	2.16E-02	2.78	8.65E+00	3.11E+00
ENSMUSG00000022149	C9	6.02E-03	2.16E-02	4.00	5.81E+00	1.45E+00
ENSMUSG00000104262	Gm37747	6.02E-03	2.16E-02	3.13	5.96E+01	1.91E+01
ENSMUSG00000059395	Nkapl	6.03E-03	2.17E-02	-6.41	4.47E-01	2.87E+00
ENSMUSG00000031150	Ccdc120	6.06E-03	2.17E-02	-2.90	1.81E+00	5.25E+00
ENSMUSG00000102423	Gm37465	6.10E-03	2.18E-02	-6.31	3.48E-01	2.20E+00
ENSMUSG00000030708	Dnajb13	6.14E-03	2.20E-02	-3.39	1.27E+00	4.31E+00
ENSMUSG00000044702	Palb2	6.20E-03	2.22E-02	-2.10	9.73E+00	2.04E+01
ENSMUSG00000045664	Cdc42ep2	6.28E-03	2.24E-02	3.22	6.80E+02	2.11E+02
ENSMUSG00000107009	6720475M21Rik	6.29E-03	2.25E-02	-3.82	1.45E+00	5.52E+00
ENSMUSG00000039137	Whrn	6.33E-03	2.26E-02	-2.37	2.43E+00	5.75E+00
ENSMUSG00000078773	Rad54b	6.34E-03	2.26E-02	-2.15	1.10E+01	2.37E+01
ENSMUSG00000049670	Morn4	6.35E-03	2.26E-02	-2.09	5.61E+00	1.17E+01
ENSMUSG00000022519	Srl	6.35E-03	2.26E-02	-2.66	3.11E+00	8.27E+00
ENSMUSG00000028755	Cda	6.52E-03	2.32E-02	-5.97	3.48E-01	2.08E+00
ENSMUSG00000006784	Odad4	6.62E-03	2.35E-02	3.50	3.59E+00	1.03E+00
ENSMUSG00000090698	Apold1	6.69E-03	2.37E-02	-4.40	8.34E-01	3.67E+00
ENSMUSG00000098789	Jmjd7	6.74E-03	2.38E-02	-2.34	3.64E+00	8.50E+00
ENSMUSG00000084964	Gm15503	6.75E-03	2.38E-02	-2.01	1.14E+01	2.29E+01
ENSMUSG00000109764	Klkb1	6.76E-03	2.39E-02	3.38	8.05E+00	2.38E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000020332	Meikin	6.81E-03	2.40E-02	6.42	9.83E-01	1.53E-01
ENSMUSG00000099759	1700030C10Rik	6.84E-03	2.41E-02	-7.21	4.47E-01	3.22E+00
ENSMUSG00000041538	H2-Ob	6.86E-03	2.42E-02	2.54	9.04E+00	3.56E+00
ENSMUSG00000037855	Zfp365	6.89E-03	2.43E-02	-2.46	3.18E+00	7.83E+00
ENSMUSG00000006435	Neurl1a	6.92E-03	2.43E-02	-4.31	8.41E-01	3.63E+00
ENSMUSG00000060380	C030014I23Rik	6.94E-03	2.44E-02	-4.47	8.88E-01	3.97E+00
ENSMUSG00000102474	2610012C04Rik	7.04E-03	2.47E-02	-3.98	1.12E+00	4.47E+00
ENSMUSG00000039814	Xkr5	7.12E-03	2.49E-02	-2.56	7.38E+00	1.89E+01
ENSMUSG00000006586	Runx1t1	7.14E-03	2.50E-02	2.50	5.34E+00	2.14E+00
ENSMUSG00000024530	Prelid3a	7.23E-03	2.52E-02	-2.10	5.89E+00	1.24E+01
ENSMUSG00000015468	Notch4	7.27E-03	2.54E-02	-3.36	1.15E+00	3.86E+00
ENSMUSG00000009633	G0s2	7.28E-03	2.54E-02	-4.10	1.10E+00	4.52E+00
ENSMUSG00000021127	Zfp36l1	7.30E-03	2.54E-02	-2.02	3.37E+02	6.82E+02
ENSMUSG00000032558	Nphp3	7.31E-03	2.55E-02	-2.03	6.59E+00	1.34E+01
ENSMUSG00000060044	Tmem26	7.38E-03	2.57E-02	-2.80	1.73E+00	4.86E+00
ENSMUSG00000043572	Pars2	7.48E-03	2.60E-02	-2.14	5.41E+00	1.16E+01
ENSMUSG00000047115	Fam221a	7.48E-03	2.60E-02	-2.54	2.40E+00	6.10E+00
ENSMUSG00000063605	Ccdc102a	7.52E-03	2.61E-02	-3.57	1.27E+00	4.54E+00
ENSMUSG00000025330	Padi4	7.54E-03	2.62E-02	-4.99	4.47E-01	2.23E+00
ENSMUSG00000025738	Fbxl16	7.54E-03	2.62E-02	-2.43	2.69E+00	6.55E+00
ENSMUSG00000051920	Rspo2	7.55E-03	2.62E-02	-2.56	2.37E+00	6.05E+00
ENSMUSG00000022178	Ajuba	7.57E-03	2.62E-02	-2.71	2.76E+00	7.47E+00
ENSMUSG00000026778	Prkcq	7.59E-03	2.63E-02	5.60	1.41E+00	2.52E-01
ENSMUSG00000035373	Ccl7	7.63E-03	2.64E-02	3.32	1.52E+03	4.58E+02
ENSMUSG00000037995	Igsf9	7.75E-03	2.68E-02	2.15	2.15E+01	9.98E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000017639	Rab11fip4	7.79E-03	2.69E-02	-2.51	2.01E+00	5.03E+00
ENSMUSG00000085169	Gm10785	7.85E-03	2.71E-02	-6.81	2.71E-01	1.85E+00
ENSMUSG00000096959	4930509G22Rik	7.96E-03	2.74E-02	6.13	2.25E+00	3.67E-01
ENSMUSG00000042821	Snai1	7.99E-03	2.75E-02	-2.33	2.96E+00	6.90E+00
ENSMUSG00000086150	Bach2os	8.00E-03	2.75E-02	-3.75	1.47E+00	5.51E+00
ENSMUSG00000001014	Icam4	8.04E-03	2.76E-02	2.12	9.81E+00	4.62E+00
ENSMUSG00000025141	Myadml2	8.07E-03	2.77E-02	-5.90	3.48E-01	2.05E+00
ENSMUSG00000022773	Ypel1	8.25E-03	2.83E-02	-2.27	3.25E+00	7.37E+00
ENSMUSG00000056014	A430033K04Rik	8.29E-03	2.83E-02	-2.10	5.50E+00	1.16E+01
ENSMUSG00000047945	Marcksl1	8.31E-03	2.84E-02	2.84	1.34E+03	4.73E+02
ENSMUSG00000044433	Camsap3	8.33E-03	2.84E-02	-3.24	1.40E+00	4.56E+00
ENSMUSG00000110018	5430437J10Rik	8.38E-03	2.86E-02	2.21	3.31E+01	1.50E+01
ENSMUSG00000033060	Lmo7	8.38E-03	2.86E-02	-5.35	4.47E-01	2.39E+00
ENSMUSG00000036617	Etl4	8.41E-03	2.87E-02	2.15	6.97E+01	3.24E+01
ENSMUSG00000111116	Gm48065	8.43E-03	2.87E-02	-5.54	3.48E-01	1.93E+00
ENSMUSG00000050395	Tnfsf15	8.47E-03	2.88E-02	3.87	4.27E+01	1.10E+01
ENSMUSG00000044026	Slc35g1	8.49E-03	2.89E-02	-2.08	6.37E+00	1.32E+01
ENSMUSG00000085360	Arhgap27os2	8.55E-03	2.90E-02	2.32	1.30E+01	5.63E+00
ENSMUSG00000073590	3222401L13Rik	8.69E-03	2.94E-02	-2.62	3.14E+00	8.23E+00
ENSMUSG00000080772	Gm12543	8.74E-03	2.95E-02	-2.37	2.80E+00	6.64E+00
ENSMUSG00000099492	Gm5525	8.76E-03	2.96E-02	3.36	3.11E+00	9.24E-01
ENSMUSG00000107756	Gm44164	8.77E-03	2.96E-02	-2.10	9.29E+00	1.95E+01
ENSMUSG00000033460	Armcx1	8.81E-03	2.97E-02	-4.66	5.75E-01	2.68E+00
ENSMUSG00000030283	St8sia1	8.83E-03	2.98E-02	4.61	1.69E+00	3.67E-01
ENSMUSG00000035000	Dpp4	9.23E-03	3.10E-02	4.89	1.80E+00	3.67E-01

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000058979	Hdhd5	9.24E-03	3.10E-02	-2.27	2.68E+00	6.08E+00
ENSMUSG00000034538	Zfp418	9.39E-03	3.15E-02	-2.88	1.54E+00	4.43E+00
ENSMUSG00000029553	Tfec	9.41E-03	3.15E-02	2.15	5.21E+02	2.42E+02
ENSMUSG00000075271	Ttc30a1	9.45E-03	3.16E-02	-2.86	2.31E+00	6.62E+00
ENSMUSG00000024486	Hbegf	9.65E-03	3.22E-02	2.94	2.21E+02	7.51E+01
ENSMUSG00000029096	Htra3	9.72E-03	3.24E-02	-3.35	1.44E+00	4.83E+00
ENSMUSG00000050671	Ism2	9.72E-03	3.24E-02	4.73	2.76E+00	5.83E-01
ENSMUSG00000049588	Ccdc69	9.77E-03	3.25E-02	-2.09	6.55E+00	1.37E+01
ENSMUSG00000014602	Kif1a	9.82E-03	3.26E-02	2.34	9.33E+00	3.99E+00
ENSMUSG00000078653	Cntd1	9.87E-03	3.28E-02	-4.26	8.56E-01	3.64E+00
ENSMUSG00000097325	Gm16897	9.94E-03	3.30E-02	4.82	1.99E+00	4.12E-01
ENSMUSG00000103749	Pcdhgb5	9.97E-03	3.30E-02	2.41	4.50E+00	1.87E+00
ENSMUSG00000032845	Alpk2	1.02E-02	3.37E-02	4.68	3.48E+00	7.44E-01
ENSMUSG00000067199	Frat1	1.02E-02	3.37E-02	-2.34	1.43E+01	3.36E+01
ENSMUSG00000028909	Ptpru	1.04E-02	3.43E-02	-2.83	1.92E+00	5.42E+00
ENSMUSG00000088989	nan	1.05E-02	3.44E-02	4.48	3.09E+00	6.90E-01
ENSMUSG00000022235	Cmbl	1.05E-02	3.47E-02	-2.10	9.15E+00	1.92E+01
ENSMUSG00000083344	Gm7363	1.06E-02	3.48E-02	2.35	6.93E+00	2.94E+00
ENSMUSG00000049038	Mterf2	1.06E-02	3.49E-02	-2.13	3.66E+00	7.80E+00
ENSMUSG00000055866	Per2	1.07E-02	3.51E-02	-2.31	7.10E+00	1.64E+01
ENSMUSG00000021485	Mxd3	1.07E-02	3.51E-02	-2.59	2.58E+00	6.68E+00
ENSMUSG00000102630	Gm37289	1.07E-02	3.51E-02	2.13	1.27E+01	5.95E+00
ENSMUSG00000043833	2900005J15Rik	1.07E-02	3.52E-02	-2.50	3.83E+00	9.58E+00
ENSMUSG00000068957	4930589L23Rik	1.08E-02	3.55E-02	2.98	4.05E+00	1.36E+00
ENSMUSG00000084154	Gm15644	1.09E-02	3.55E-02	2.21	1.17E+01	5.32E+00

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ENSMUSG00000036928	Stag3	1.09E-02	3.56E-02	-2.35	3.92E+00	9.22E+00
ENSMUSG00000102841	Gm38036	1.09E-02	3.56E-02	-2.52	4.06E+00	1.02E+01
ENSMUSG00000020953	Coch	1.09E-02	3.57E-02	4.64	7.10E-01	1.53E-01
ENSMUSG00000051727	Kctd14	1.10E-02	3.58E-02	3.83	2.97E+00	7.75E-01
ENSMUSG00000097216	4932441J04Rik	1.10E-02	3.58E-02	-2.66	1.53E+00	4.07E+00
ENSMUSG00000056592	Zfp658	1.11E-02	3.60E-02	-2.16	7.23E+00	1.56E+01
ENSMUSG00000026700	Tnfsf4	1.11E-02	3.62E-02	2.75	1.71E+01	6.21E+00
ENSMUSG00000031327	Chic1	1.12E-02	3.63E-02	3.87	1.80E+00	4.65E-01
ENSMUSG00000084081	Gm12057	1.12E-02	3.64E-02	5.84	1.89E+00	3.24E-01
ENSMUSG00000030747	Dgat2	1.13E-02	3.65E-02	2.23	1.22E+01	5.46E+00
ENSMUSG00000109708	Gm45809	1.13E-02	3.68E-02	-6.29	2.71E-01	1.71E+00
ENSMUSG00000019437	Tlcd1	1.14E-02	3.70E-02	-2.29	4.63E+00	1.06E+01
ENSMUSG00000050677	Ccdc96	1.15E-02	3.72E-02	-6.69	2.71E-01	1.81E+00
ENSMUSG00000086773	Gm16192	1.16E-02	3.73E-02	-4.73	5.57E-01	2.64E+00
ENSMUSG00000068587	Mgam	1.16E-02	3.75E-02	-5.65	4.47E-01	2.53E+00
ENSMUSG00000045672	Col27a1	1.16E-02	3.75E-02	2.25	2.21E+01	9.82E+00
ENSMUSG00000072618	Gm10384	1.17E-02	3.76E-02	-2.96	1.98E+00	5.86E+00
ENSMUSG00000110393	Gm36445	1.17E-02	3.77E-02	-2.82	1.86E+00	5.23E+00
ENSMUSG00000064365	mt-Ts2	1.17E-02	3.77E-02	2.80	6.49E+00	2.32E+00
ENSMUSG00000104018	4833412K13Rik	1.19E-02	3.82E-02	-2.27	7.45E+00	1.70E+01
ENSMUSG00000020193	Zpbp	1.19E-02	3.84E-02	-4.97	4.47E-01	2.22E+00
ENSMUSG00000021364	Elovl2	1.20E-02	3.85E-02	4.89	1.58E+00	3.24E-01
ENSMUSG00000065808	nan	1.20E-02	3.85E-02	4.62	4.17E+00	9.02E-01
ENSMUSG00000105568	Gm42971	1.20E-02	3.85E-02	4.54	5.01E+00	1.10E+00
ENSMUSG00000097083	D930019O06Rik	1.21E-02	3.88E-02	-2.21	4.35E+00	9.62E+00

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ENSMUSG00000035594	Chrna5	1.22E-02	3.91E-02	5.83	1.30E+00	2.23E-01
ENSMUSG00000117315	1600022D10Rik	1.22E-02	3.91E-02	2.96	5.57E+00	1.88E+00
ENSMUSG00000003585	Sec14l2	1.23E-02	3.92E-02	-5.60	4.47E-01	2.50E+00
ENSMUSG00000015665	Awat1	1.23E-02	3.93E-02	2.13	5.15E+00	2.42E+00
ENSMUSG00000042417	Ccno	1.23E-02	3.94E-02	2.33	6.51E+00	2.80E+00
ENSMUSG00000026875	Traf1	1.23E-02	3.95E-02	3.28	4.13E+02	1.26E+02
ENSMUSG00000024402	Lta	1.25E-02	3.98E-02	4.08	4.04E+00	9.90E-01
ENSMUSG00000051314	Ffar2	1.26E-02	4.01E-02	4.37	5.94E+00	1.36E+00
ENSMUSG00000061654	nan	1.26E-02	4.01E-02	-5.47	2.71E-01	1.48E+00
ENSMUSG00000086922	Gm13835	1.27E-02	4.04E-02	2.21	5.39E+00	2.44E+00
ENSMUSG00000025481	Urah	1.27E-02	4.04E-02	-6.12	3.48E-01	2.13E+00
ENSMUSG00000111740	Gm49783	1.28E-02	4.06E-02	-2.23	2.30E+00	5.12E+00
ENSMUSG00000058022	Adtrp	1.28E-02	4.07E-02	9.89	2.49E+00	2.52E-01
ENSMUSG00000022240	Ctnnd2	1.28E-02	4.07E-02	2.04	2.94E+01	1.44E+01
ENSMUSG00000106961	Gm43128	1.28E-02	4.07E-02	-2.56	2.71E+00	6.92E+00
ENSMUSG00000024772	Ehd1	1.28E-02	4.08E-02	2.06	3.52E+03	1.70E+03
ENSMUSG00000021587	Pcsk1	1.29E-02	4.10E-02	3.47	2.70E+00	7.77E-01
ENSMUSG00000087252	Gm14379	1.30E-02	4.11E-02	2.13	6.06E+00	2.84E+00
ENSMUSG00000052565	H1f3	1.30E-02	4.12E-02	-2.21	8.78E+00	1.94E+01
ENSMUSG00000080873	Rpl30-ps3	1.31E-02	4.15E-02	2.64	3.80E+00	1.44E+00
ENSMUSG00000036136	Fam110c	1.32E-02	4.16E-02	-2.73	2.60E+00	7.09E+00
ENSMUSG00000046323	Dppa3	1.32E-02	4.18E-02	-3.30	8.60E-01	2.84E+00
ENSMUSG00000031382	Asb11	1.33E-02	4.19E-02	7.62	1.32E+00	1.73E-01
ENSMUSG00000048349	Pou4f1	1.33E-02	4.19E-02	3.95	2.47E+00	6.25E-01
ENSMUSG00000036304	Zdhhc23	1.34E-02	4.22E-02	2.91	9.25E+00	3.18E+00

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ENSMUSG00000090027	Gm15740	1.35E-02	4.25E-02	-5.94	3.48E-01	2.07E+00
ENSMUSG00000050556	Kcnb1	1.35E-02	4.26E-02	-4.33	5.75E-01	2.49E+00
ENSMUSG00000108593	Gm44581	1.35E-02	4.26E-02	4.57	3.35E+00	7.32E-01
ENSMUSG00000101662	Gm28499	1.37E-02	4.30E-02	-4.81	4.47E-01	2.15E+00
ENSMUSG00000034336	Ina	1.37E-02	4.32E-02	-2.29	3.11E+00	7.10E+00
ENSMUSG00000112767	Gm47532	1.39E-02	4.37E-02	7.74	1.18E+00	1.53E-01
ENSMUSG00000074344	Tmigd3	1.40E-02	4.40E-02	2.42	6.65E+00	2.75E+00
ENSMUSG00000045103	Dmd	1.42E-02	4.45E-02	2.55	7.42E+00	2.91E+00
ENSMUSG00000004296	Il12b	1.43E-02	4.47E-02	9.35	2.22E+02	2.38E+01
ENSMUSG00000042439	Zfp532	1.45E-02	4.52E-02	-2.18	3.72E+00	8.09E+00
ENSMUSG00000021363	Mak	1.47E-02	4.59E-02	-2.46	2.38E+00	5.86E+00
ENSMUSG00000038180	Spag4	1.48E-02	4.60E-02	-2.98	1.40E+00	4.17E+00
ENSMUSG00000009108	Gnat2	1.48E-02	4.60E-02	-6.24	2.11E-01	1.32E+00
ENSMUSG00000045662	Henmt1	1.49E-02	4.63E-02	5.09	1.65E+00	3.24E-01
ENSMUSG00000085129	5031425F14Rik	1.49E-02	4.63E-02	-2.83	1.42E+00	4.03E+00
ENSMUSG00000094786	Gm14403	1.50E-02	4.66E-02	-3.77	7.03E-01	2.65E+00
ENSMUSG00000103596	Gm37354	1.50E-02	4.67E-02	3.12	6.93E+00	2.22E+00
ENSMUSG00000105607	Gm43513	1.52E-02	4.70E-02	-5.91	4.47E-01	2.64E+00
ENSMUSG00000037944	Ccr7	1.52E-02	4.71E-02	7.78	1.13E+01	1.46E+00
ENSMUSG00000050545	Fam228b	1.53E-02	4.73E-02	-5.03	3.48E-01	1.75E+00
ENSMUSG00000113128	Gm47813	1.54E-02	4.75E-02	-3.84	8.49E-01	3.26E+00
ENSMUSG00000112637	Gm48225	1.54E-02	4.77E-02	2.29	1.18E+01	5.16E+00
ENSMUSG00000105957	Gm43254	1.55E-02	4.77E-02	-4.46	5.62E-01	2.51E+00
ENSMUSG00000102935	Gm38355	1.55E-02	4.79E-02	-5.79	4.47E-01	2.59E+00
ENSMUSG00000055413	H2-Q5	1.57E-02	4.82E-02	3.18	4.20E+00	1.32E+00

Gene ID	Gene name	P-value	FDR	Fold change	LSMean (IFN-γ)	LSMean (unstimulated)
ENSMUSG00000043340	6530409C15Rik	1.57E-02	4.84E-02	5.71	3.54E+00	6.21E-01
ENSMUSG00000004552	Ctse	1.58E-02	4.86E-02	2.32	6.00E+00	2.59E+00
ENSMUSG00000047963	Stbd1	1.58E-02	4.86E-02	2.07	9.87E+00	4.78E+00
ENSMUSG00000053358	Gm9905	1.60E-02	4.89E-02	2.84	2.78E+00	9.81E-01
ENSMUSG00000026576	Atp1b1	1.61E-02	4.93E-02	3.21	3.72E+00	1.16E+00
ENSMUSG00000040533	Matn1	1.61E-02	4.94E-02	-6.12	2.71E-01	1.66E+00
ENSMUSG00000102863	Gm37639	1.62E-02	4.96E-02	2.12	7.16E+00	3.38E+00

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Review Article

Interferon-induced GTPases orchestrate host cell-autonomous defence against bacterial pathogens

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Interferon (IFN)-induced guanosine triphosphate hydrolysing enzymes (GTPases) have been identified as cornerstones of IFN-mediated cell-autonomous defence. Upon IFN stimulation, these GTPases are highly expressed in various host cells, where they orchestrate anti-microbial activities against a diverse range of pathogens such as bacteria, protozoan and viruses. IFN-induced GTPases have been shown to interact with various host pathways and proteins mediating pathogen control via inflammasome activation, destabilising pathogen compartments and membranes, orchestrating destruction via autophagy and the production of reactive oxygen species as well as inhibiting pathogen mobility. In this mini-review, we provide an update on how the IFN-induced GTPases target pathogens and mediate host defence, emphasising findings on protection against bacterial pathogens.

IFN signalling and induction of IFN-stimulated genes

Exposure of cells to interferons (IFN) results in the induction of a network of genes that combat infections, leading to so-called IFN-mediated cell-autonomous defence [1–5]. This network is a finely tuned mechanism to balance launching an efficient pathogen control while preventing collateral tissue damage. In the last two decades, IFN-induced GTPases have become a focus of attention as key mediators of IFN-mediated host defence.

There is abundant evidence for the vital role of IFN in combating an array of pathogens, including key roles in defence against bacteria [2,6–22]. Ten mammalian IFNs are known, with seven found in humans [23,24]. Based on genetic loci, homology in amino acid sequence and receptor binding, IFNs are currently divided into three groups, namely type I, II and III [1,25].

Upon binding their specific receptors, IFNs activate signal transduction via the JAK/STAT pathway which leads to the formation of the transcription factor complex IFN-stimulated gene factor 3 (ISGF3), consisting of phosphorylated STAT1/STAT2 and IRF9, for type I and type III IFNs and the transcription factor gamma-activated factor (GAF), a homodimer of phosphorylated STAT1, for type 2 IFN-specific signalling [26–28]. These activated transcription factors translocate into the nucleus and bind to their specific promotor elements, IFN-stimulated response element (ISRE) and gamma-activated sequence (GAS) for type I/III and type II, respectively [26–28]. The binding of these transcription factors can modulate the transcription of up to 2000 IFN-stimulated genes (ISGs) [1–3], resulting in immunomodulatory, anti-proliferative and anti-pathogenic consequences [2,29]. Even though these IFNs possess distinct receptors, transcription factors and promotor binding sites, the activation of ISGs via IFNs is complex. All types of IFN show non-canonical signalling, some ISGs are also controlled by IFN regulatory factors (IRFs); which in turn are also ISGs; other ISGs are constitutively expressed at low levels in addition to being IFN-inducible and another portion ISGs are also induced by NF-κB signalling [28,30–35].

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Families of IFN-induced GTPases

GTPases induced by IFN have been identified as crucial effectors in IFN-mediated pathogen control [36–56]. These large GTPases can be divided into four subfamilies based on their paralogy and molecular mass [57]. The four subfamilies are the 21–47 kDa immunity-related GTPases (IRGs), the 65–73 kDa guanylate-binding proteins (GBPs), the 72–82 kDa myxoma (MX) resistance proteins and the 200–285 kDa very large inducible GTPases (VLIGs/GVINs) [58–60]. In the following, we will mainly focus on IRG and GBP GTPases and their functions in cell-autonomous defence against bacteria.

Mice have 23 IRGs and this family of genes has been mostly lost in humans, apart from IRGM1 and IRGC [61,62]. The IRGs can be divided into two classes; the primarily cytosolic 'GKS' IRGs which possess a conserved canonical GX4GKS sequence in the first nucleotide-binding motif (G1) and the predominantly membrane-bound 'GMS' IRGs which possess the non-canonical GX4GMS sequence in their G1 nucleotide-binding motif [60,61]. The 'GMS' IRGs control the activity of 'GKS' IRGs by controlling the GDP to GTP switch, thus acting as guanosine dissociation inhibitors (GDIs) [59,63]. In the absence of 'GMS' IRGs, 'GKS' IRGs are constitutively active, form cytoplasmic aggregates and fail to localise to their respective cellular compartment, *Toxoplasma gondii* parasitophorous vacuole and *Chlamydia trachomatis* inclusions [59,63,64].

Thus far, 7 human GBP (hGBP) genes (*GBP1-GBP7*) located on chromosome 1 and 11 mouse GBPs (mGBPs) (*Gbp2b-Gbp11*) have been identified [49,65–67]. The mGBPs are organised in clusters on chromosome 3 (*Gbp2b*, *Gbp2*, *Gbp3*, *Gbp5*, *Gbp7* and a pseudo*mGbp2b*) and chromosome 5 (*Gbp4*, *Gbp6*, *Gbp8*, *Gbp9*, *Gbp10*, *Gbp11* and a pseudo*mGbp2*) [68]. Transcription of human and mGBPs can be triggered by type 1 and 2 IFN as well as other inflammatory cytokines and TLR ligands, although the quantitative responses vary substantially between the different GBPs and cytokines [49,69,70].

IFN-induced GTPases belong to the dynamin-protein family as judged by structural similarities and shared biochemical characteristics [57,71,72]. As members of the dynamin protein family, they possess a large GTPase domain (~300 amino acids), a middle domain and a GTPase effector domain (GED) [73]. In addition to these three domains, many IFN-induced GTPases also possess other domains and motifs for protein–protein and protein–membrane interactions [44,73–75]. In contrast with dynamin, at least some IFN-induced GBPs can hydrolyse GTP to GDP and GDP to GMP, though their GTPase activation is still dependent on oligomerisation [73,76,77]. These dynamin-related characteristics enable IFN-induced GTPases to operate either as mechanoenzymes or as an assembly platform to co-ordinate diverse functions [57]. For instance, they govern vesicular trafficking and the coordination of protein complex assembly to stimulate autophagic, membranolytic, oxidative and inflammasome-related anti-microbial activities upon cytosolic bacteria as well as on pathogen containing vacuoles [2,57,78–81].

Mechanisms of host defence by IFN-induced GTPases

Targeting of specific pathogens by GBPs and IRGs

To execute anti-microbial functions, GBPs and IRGs co-localise with pathogens invading the host cell. GBPs and IRGs are typically found in the cytosol, in vesicle-like structures and on endomembranes, but translocate to pathogen compartments and cytosolic bacteria which have escaped from the phagosome (Figure 1) [70,75,82,83]. Bacteria shown to interact with GBPs and IRGs include *Listeria monocytogenes*, *Legionella pneumophila*, *Shigella flexneri*, *Mycobacterium bovis* BCG, *Chlamydia trachomatis, Francisella novicida, Salmonella typhimurium, Brucella abortus, Yersinia pseudotuberculosis* and *Burkholderia thailandensis* [2,38–40,42–44,47,56,65,69,84–96].

Even though the exact molecular mechanism which enables them to target and destroy pathogens is not fully understood, it has been shown that human and mGBPs form homo- and hetero- and polymers to fulfil their anti-microbial function [50,97]. Kravets et al. [50] showed that mGBPs accumulate on *T. gondii* vacuoles in densely packed multimers consisting of several thousand monomers. Furthermore, these proteins seem to locate to the pathogens and associated membranes in a hierarchical manner, with GBP1, GBP2 and GBP5 leading the way due to a CaaX prenylation motif at the C-terminus of the protein, which enables them to bind to membranes and to recruit non-prenylated GBPs to their location [50,82]. In addition to targeting various pathogens and their vacuoles directly, in mouse cells 'GMS' IRGs have been suggested to influence the localisation and activation of GBPs and 'GKS' IRGs on target membranes via a 'missing-self' signal [64]. This control of GBP and IRG activation and aggregation on host membranes via the 'GMS' IRG family proteins (IRGM), is further supported by the targeting of GBPs and IRGs onto lipid droplets from which IRGM1 and IRGM3 have been removed independently of infection [64]. Based on this observation, it was suggested that a lack of IRGM proteins and therefore the mistargeting of self-membranes through activated GBPs and IRGs as well as the

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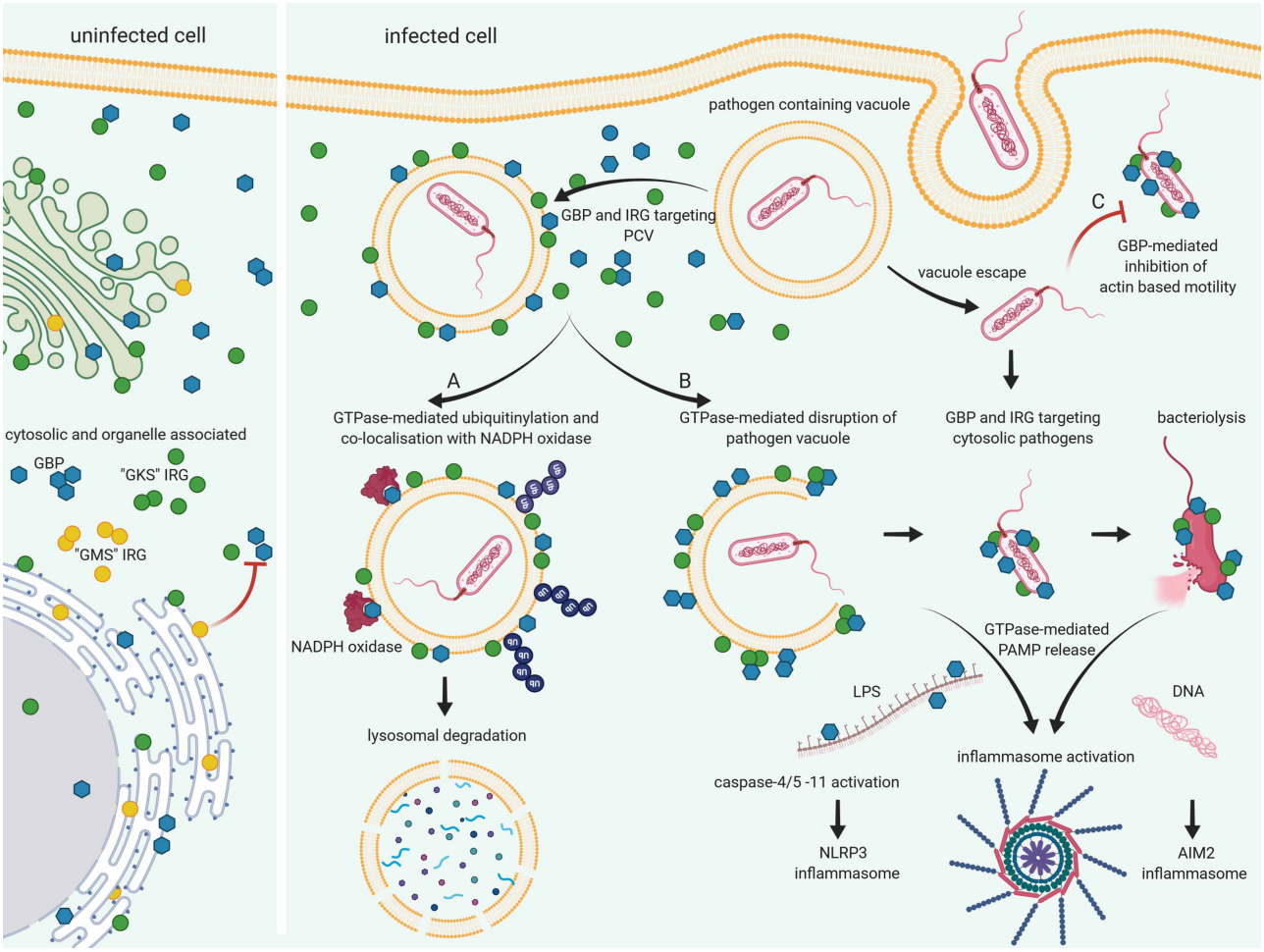

Figure 1. Mechanisms of pathogen clearance by IFN-induced GTPases.

In uninfected cells, GBPs and IRGs are found in the cytosol, in vesicle-like clusters, associated with endomembranes and the nucleus. 'GMS' IRGs control the activation of GBPs and host membrane located 'GKS' IRGs act as guanosine dissociation inhibitors. During infection GBPs and IRGs co-localise with pathogen containing vacuoles (PCV) and cytosolic pathogens within minutes of pathogen entry. (**A**) GBP association with PCV may lead to the accumulation of ubiquitin and subsequent destruction of the invading pathogen. GBP7 is essential for NADPH oxidase holoenzyme assembly on PCV. (**B**) GBP and IRG co-localisation with the PCV and cytosolic bacteria leads to the disruption of vacuole and membrane integrity, releasing PAMPS into the cytosol. GBP^{chrom3}, GBP1, GBP2, GBP3, GBP4 mediate activation of caspase4/5 or 11 during *Salmonella*, *Legionella* or *Chlamydia* infection by cytosolic LPS release leading to pyroptosis. Association with GBPs and IRGB10 leads to loss of membrane integrity and bacteriolysis with subsequent AIM2 activation during *Francisella* infection. (**C**) In addition to disrupting PCV and bacterial membrane integrity, GBPs also mediate host defence via the inhibition of actin-based motility of *Burkholderia* and *Shigella* pathogens. Created with BioRender.com.

formation of cytosolic clusters leads to a diminished pool of available GBPs and IRGs which could effectively target *C. trachomatis* and *T. gondii* [64]. It should be noted that there is some data that is not consistent with the 'missing-self' hypothesis [37,44,67], although some of this was refuted in later publications [98,99].

Park et al. [100] proposed a 'triple check' model for targeting of mGBPs and IRGs to pathogen vacuoles. This model suggests that pathogen vacuoles are targeted by the autophagy conjugation system by depositing microtubule-associated protein light chain 3 (LC3) and its homologues on the pathogen vacuole. IFN-γ stimulation would 'trigger' LC3 on these membranes, either via posttranslational modifications or via the addition of factors such as ubiquitin, to act as a guanine nucleotide exchange factor (GEF) for GBPs and IRGs and activate them. Misguiding of GBPs to endomembranes would be avoided through the protective function of IRGM proteins, which act as GDIs for GBPs and IRGs [63,101]. How the LC3 conjugation system recognises pathogen vacuoles remains unknown. However, Brown et al. [102] have suggested that the autophagy conjugation

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complex or some upstream sensor of this complex recognises changes to the membranes occupied by pathogens, such as missing-self (e.g. lack of IRGM proteins), changed-self (e.g. rearranged protein and lipid composition) and non-self (e.g. pathogen effectors and secretion systems). It was also suggested that the binding of this complex to membranes might be facilitated via autophagy related-protein ATG5 [103], as ATG5 from the autophagy conjugation complex can bind membranes via an unknown lipid moiety [104]. This model is supported by the observations that ATG5 and LC3 are found on murine norovirus (MNV) membranous replication complexes [105] and also *T. gondii* vacuoles without prior IFN-γ stimulation in mouse macrophages [100,106]. Furthermore, GBPs and IRGs are unable to target pathogen containing vacuoles and aggregate in the cytosol in cells lacking all ATG5 or all LC3 homologues [102,106,107]. Whether this model applies to other pathogens and host species, especially with humans which lack most IRGs, remains to be investigated.

To what extent IRGs and GBPs co-operate in targeted co-localisation to pathogens or pathogen vacuoles remains unclear, as reciprocal dependence has been observed. For example, IRGM1 and 3 are needed for targeting of mGBPs to *T. gondii* vacuoles and pathogen control in MEFs, whereas they are dispensable for *Leishmania donovani* control [41,52]. On the other hand, the localisation of IRGs can also be dependent on GBPs, as the targeting of IRGB10 and IRGB6, to *F. novicida*, *T. gondii* and *E. coli* are dependent on GBPs from chromosome 3, as these IRGs failed to co-localise with pathogen inclusions in cells lacking GBPs on mouse chromosome 3 [39,108].

Different GBPs and IRGs have been shown to target specific pathogens, though the underlying mechanisms for this specificity is only now being uncovered [42,52,65,94,109]. Kohler et al. [89] have suggested that changes in the C-terminal polybasic motif (PBM) in primate GBP1s are responsible for the pathogen specificity towards *S. flexneri*. In line with this, it was shown that the unique triple-arginine cassette in the PBM of hGBP1 is responsible for targeting *S. flexneri* [43]. The highly divergent C-terminal amino acid sequence in mGBPs might also indicate a non-redundant function in determining pathogen specificity [49]. In addition, alternative splicing variants of GBPs might play a role in specific pathogen targeting, since a splicing variant of mGBP5, mGBP5a, was present in *L. monocytogenes* infected mouse liver but absent from *T. gondii* infected liver [49]. Besides the co-localisation of GBPs and IRGs with particular pathogens, differences in GBP targeting of the same pathogens have also been observed in distinct cell types of the same host species. For example, hGBP1 co-localises with *T. gondii* in mesenchymal stromal cells and THP1 but not A549 cells [69,96,110,111]. This remarkable diversity of targeting strategies for specific pathogens might be due to the diverse genetic backgrounds and proteomes of different host species and cell types as well as pathogen-specific virulence factors and intracellular life cycles.

Mechanisms of pathogen clearance by IFN-induced GTPases

The anti-microbial mechanisms of IFN-induced GTPases that are discussed below are represented in Figure 1.

Ubiquitination and lysosomal destruction mediated by GBPs and IRGs

GBPs and IRGs can mediate pathogen control by induction of autophagy and ubiquitin-mediated destruction of pathogen vacuoles [112–114]. mGBP7 interacts with and recruits the autophagy protein ATG4B to *Mycobacterium*-containing vacuoles [65], which promotes the expansion of autophagic membranes around the bacteria and damaged bacterial compartments [2,57], leading to degradation of the pathogen via lysosome fusion [65]. Haldar et al. [41] demonstrated that IFN-γ-induced IRGM1 and IRGM3 control the recruitment of the E3 ligase tumour necrosis factor receptor-associated factor 6 (TRAF6) and subsequent ubiquitination of vacuoles of *T. gondii* and *C. trachomatis*. Following ubiquitination, GBPs co-localise with vacuoles in a sequestosome 1 (SQSTM1/p62)-dependent manner and mark these vacuoles for destruction [41]. IRGM-dependent autophagy was also shown for *Mycobacterium* infections though the exact mechanism remains unclear [45,114]. It seems likely that 'GMS' proteins IRGM1 and IRGM3 co-ordinate the localisation of other GKS IRGs to pathogen vacuoles, as virulent *T. gondii* strains and *C. muridarum* inhibit 'GKS' IRG activity and vacuole co-localisation of these IRG proteins thereby avoiding ubiquitination of the replicative niche [41,115-117].

In addition to mediating the ubiquitination of pathogen compartments and the subsequent lysosomal destruction via controlling the 'GKS' IRGs activity, IRGM1 has been shown to target *M. tuberculosis* vacuoles directly [37,65]. The recruitment of IRGM1 to pathogen containing vacuoles appears to facilitate fusion with lysosomes, as lysosomal fusion of *M. tuberculosis* vacuoles is impaired in *Irgm1*-deficient mutants [37]. The C-terminal amphipathic helix (αK) of IRGM1 binds to *Mycobacterium* vacuoles by interaction with phosphoinositide-3,4-bisphosphate (PtdIns[3,4]P_2) and PtdIns[3,4,5]P_3[44].

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For protection against the lung pathogen *L. pneumophila*, IRG-dependent as well as IRG-independent pathways have been described. Both IRGM1 and IRGM3, have been implicated in IFN-mediated control of *L. pneumophila* [9,36]. The binding of IRGM1 to the intracellular replicative niche of *L. pneumophila*, the *Legionella*-containing vacuole (LCV), results in the co-localisation of other IRG proteins and subsequent ubiquitination of the LCV, thereby leading to LCV degradation through autophagy [4]. GBP1 and GBP2 are involved in an IRGM-independent resistance against *L. pneumophila*, as the bacterial protein secretion system on the LCV is recognised as a PAMP, leading to binding of the cytosolic carbohydrate-binding protein galectin-3. The binding of galectin-3 to the LCV recruits GBP1 and GBP2 to the LCV, as well as subsequent ubiquitination and targeting by p62, which leads to the degradation of the bacteria via autophagy [93]. This IRGM-independent and GBP-dependent ubiquitination during *Legionella* infection is in contrast with the previously mentioned IRGM-dependent and GBP-independent ubiquitination of *T. gondii* vacuoles as well as *C. trachomatis* inclusions [41].

In most cases, the ubiquitination of pathogens and their compartments is a host-derived response which favours host survival and promotes pathogen control. In contrast with this, it was shown that the hGBP1-mediated, poly-ubiquitin coat on *S. flexneri* is not host-derived but mediated by a bacterial-derived E3 ubiquitin ligase IpaH9.8, which recognises, binds and ubiquitinates GBP1, GBP2 and GBP4 but not GBP3 and labels them for proteasome-mediated degradation [42,43,90]. This poly-ubiquitination reverses the GBP-mediated restriction and enables the bacteria to form actin tails and spread efficiently from cell to cell [42,43,90].

GBP-mediated production of reactive oxygen species (ROS)

Another host resistance pathway that mediates IFN-induced pathogen control is the production of ROS. NOX2 is an NADPH oxidase that is able to generate superoxide, which has microbicidal properties [118]. During *L. monocytogenes* and *M. bovis* BCG infection, mGBP7 binds the membrane-bound heterodimer $gp91^{phox}$-$p22^{phox}$ (cytochrome b558) and cytosolic $p67^{phox}$ [65]. Thus, GBP7 acts as a linker between membrane-bound and cytosolic NOX2 components to assemble and activate the NOX2 holoenzyme on pathogen compartments after IFN-γ stimulation [65].

GBP-mediated inflammasome activation

Recent work has linked IFN-induced GTPases with inflammasome activation in various host cells and in response to a diverse range of pathogens. IFN-induced GTPases appear to influence inflammasome activation by promoting inflammasome complex assembly and targeting pathogens and their compartments to increase the access of PAMPs to cytosolic inflammasome components. These two mechanisms of inflammasome activation can work in concert to achieve adequate inflammasome activation and thus host defence.

GBP5 is involved in the assembly of the NOD-, LRR- and pyrin domain-containing 3 (NLRP3) inflammasome during *Listeria* or *Salmonella* spp. infections via tetramerisation of GBP5 [119-121]. Assembly of the NLRP3 inflammasome leads to the induction of pyroptosis in order to control bacterial infections. Deletion of single mGBPs from chromosome 3 revealed unique functions for GBPs; namely, GBP5 binding to the pyrin domain of NLRP3 and GBP2 binding of apoptosis-associated speck-like protein containing a CARD (ASC) [121]. Due to their ability to form heterodimers, GBP2 and GBP5 thus facilitate the assembly of the NLRP3 inflammasome to activate caspase-1 [121].

Several observations have shown that GBPs activate inflammasomes by either directly sensing bacterial products or facilitating access to bacterial PAMPs. The induction of inflammasomes via GBPs and IRGs can result in canonical (caspase-1) or non-canonical (caspase-11, human caspase-4/5) mediated pyroptosis. It was shown that GBPs from mouse chromosome 3, namely GBP2, GBP5, as well as IRGB10 are essential for the activation of the AIM2 inflammasome in *F. novicida* infected macrophages, as cells lacking these IFN-induced GTPases showed decreased inflammasome activation [39,87,88]. GBPs from chromosome 3 also control the non-canonical activation of caspase-11 in response to *L. pneumophila* as well as pathogenic and non-pathogenic *E. coli* outer membrane vesicles and free LPS injected into the cytosol [36,122,123]. GBPs from chromosome 3 were also essential for caspase-1 activation and IL1-α as well as IL-1ß release in response to *B. abortus* and *Y. pseudotuberculosis* infections [47,92]. It has been suggested that GBPs might be influencing the membrane dynamics of outer membrane vesicles and the integrity of pathogen membranes due to their dynamin-like activities thus exposing lipid A of LPS and other PAMPS to the cytosol, hence making them accessible for inflammasome activation [39,122,124].

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In line with these previous observations suggesting GBPs mediate LPS release and/or recognition by the inflammasome, hGBP1 was recently identified as a novel cytosolic LPS sensor [69,94-96]. hGBP1 binds to LPS via electrostatic interactions between the negatively charged LPS and positively charged amino acid residues of hGBP1 [94,97]. Detection of LPS via hGBP1 results in the recruitment of hGBP2-4 to cytosolic *Salmonella*, this GBP coat in turn recruits and activates caspase-4 [69,94,95]. Based on these observations and their own, Kutsch et al. [97] presented a model of hGBP1 acting as a detergent on the bacterial LPS layer. hGBP1 was identified as a LPS sensing and binding protein, which disrupts the O-antigen barrier of Gram-negative bacteria through the insertion of the farnesyl tail of hGBP1 molecules into this layer, thereby disrupting the interactions between LPS molecules mediated by the O-antigens [97]. A triple-arginine motif in the C-terminal end of GBP1 mediates the binding of hGBP1 to the pathogen LPS O-antigen [43]. The insertion of hGBP1 into the LPS layer seemingly changes the membrane stiffness and fluidity, thus making the bacteria more accessible to caspase-4 activation and more susceptible to the anti-microbial activity of polymyxin B, as well as potentially influencing the function of other pathogen proteins inserted into the outer membrane such as *Shigella* IcsA [97].

Using different GBP1 catalytic mutants, Xavier et al. [125] identified a novel pathway of NLRP3 activation mediated by hGBP1. This group discovered that hGBP1 recruitment to *C. trachomatis* inclusions activates GTP hydrolysis to GMP and the subsequent generation of uric acid activates the NLRP3 inflammasome [125]. This novel pathway suggests that, in contrast with previous findings [69,94–97], inflammasome activation can be independent of PAMP release in human cells, relying only on the hydrolytic activity of hGBP1 [125]. Whether this activation is unique to the *Chlamydia* inclusion or represents a more general response towards other pathogens, remains to be investigated.

IFN-induced GTPases and actin-based motility

Recent findings have demonstrated that IFN-induced GBPs can inhibit the actin-based motility of intracellular bacteria. hGBPs target cytosolic *S. flexneri* after IFN-γ exposure and interfere with actin tail formation, which is required for cytosolic mobility and cell to cell spread [42,43]. GBP1 is essential for IFN-γ mediated inhibition of actin tail formation as well as recruitment of GBP2, 3 and 4 to the pathogen [42]. GBP-mediated inhibition of actin tails hindered the bacteria from spreading efficiently from cell to cell and resulted in large microcolonies forming in infected cells but significantly fewer cells becoming infected [42]. In addition to *S. flexneri,* hGBP1 also targets *B. thailandensis* through a C-terminal triple-arginine motif that binds O-antigen [43].

mGBPs also inhibit the formation of actin tails and the formation of multinucleated giant cells (MNGCs) during *B. thailandensis* infection by interfering with Arp2/3-mediated actin nucleation and cytoskeletal remodelling [86]. Cells lacking multiple GBPs from chromosome 3 as well as *Gbp2*$^{-/-}$ and *Gbp5*$^{-/-}$ cells showed an increased number of MNGCs and increased bacterial load [86].

Perspectives

Importance of the field: IFN-induced GTPases play a significant role in cell-autonomous defence against a wide variety of pathogens. They initiate and regulate a diverse range of host defence pathways and an appreciation of the roles of IFN-induced GTPases in host defence could lead to more effective anti-microbial treatments.

Current thinking: Individual IFN-induced GTPases possess unique functions that tailor the response to different pathogens and mediate their anti-microbial function by compromising the integrity of pathogen-related membranes, releasing PAMPS into the cytosol, inducing bactericidal small molecules, marking pathogens for destruction or inhibiting pathogen mobility.

Future directions: Identifying GTPase binding partners that mediate their specific function and regulate their activities, will be crucial in enhancing our understanding of how these GTPases mediate IFN-induced cell-autonomous defence against various pathogens.

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Conflicts of interest
The authors have no conflicts of interest.

Competing Interests
The authors declare that there are no competing interests associated with the manuscript.

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Abbreviations
GBPs, guanylate-binding proteins; GDIs, guanosine dissociation inhibitors; hGBP, human GBP; IFN, interferon; IRGs, immunity-related GTPases; ISGs, IFN-stimulated genes; LC3, microtubule-associated protein light chain 3; LCV, *Legionella*-containing vacuole; mGBPs, mouse GBP; MNGCs, multinucleated giant cells; PBM, polybasic motif; ROS, reactive oxygen species.

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