Role of biofilm formation, its triggered immune responses and potential new treatments for bacterial eye infections

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**NANYANG
TECHNOLOGICAL
UNIVERSITY**

SINGAPORE

**ROLE OF BIOFILM FORMATION,
ITS TRIGGERED IMMUNE RESPONSES
AND POTENTIAL NEW TREATMENTS FOR
BACTERIAL EYE INFECTIONS**

**THET TUN AUNG
SCHOOL OF BIOLOGICAL SCIENCES**

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SCHOOL OF BIOLOGICAL SCIENCES

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Table of Contents

TABLE OF CONTENTS.....	I
LIST OF FIGURES.....	VIII
LIST OF TABLES.....	XII
LIST OF ABBREVIATIONS.....	XIII
ABSTRACT.....	XV
Chapter 1.INTRODUCTION.....	1
1.1 <i>Pseudomonas aeruginosa</i>	6
1.1.1 Virulence factors and enzymes.....	6
1.1.1.1 Specific Virulence factors.....	6
1.1.1.2 Bacteria Surface-Associated factors.....	6
1.1.1.3 Glycocalyx.....	7
1.1.1.4 Toxins and Proteases.....	8
1.1.1.4.1 Exotoxin A.....	8
1.1.1.4.2 Exoenzyme S.....	8
1.1.1.4.3 Proteolytic Enzymes.....	9
1.1.1.4.4 Haemolytic Toxin.....	9
1.1.2 Biofilm lifestyles.....	9
1.1.3 eDNA in biofilm matrix.....	10
1.1.4 Exopolysaccharides in biofilm matrix.....	11
1.1.5 Extracellular proteins in biofilm matrix.....	12
1.1.6 Cyclic-di-GMP and biofilm formation mechanisms.....	13
1.1.6.1 <i>Alginate</i> , <i>Pel</i> and <i>Psl</i> polysaccharides.....	14
1.1.6.2 Cup fimbriae.....	15
1.1.6.3 Type IV pili	15

1.1.7	Cyclic-di-GMP as an immunomodulator.....	15
1.1.8	Cyclic-di-GMP manipulation as a biofilm dispersal approach.....	16
1.1.9	Research Gap and scope of thesis work.....	18
1.1.10	Objectives.....	22
1.2	Atypical Mycobacteria.....	23
1.2.1	Colony Characteristics.....	23
1.2.2	Extracellular DNA in biofilm formation.....	24
1.2.2.1	Importance of eDNA in bacterial biofilm.....	24
1.2.2.2	eDNA in cell adhesin.....	27
1.2.2.3	eDNA and structural integrity of biofilm.....	28
1.2.2.4	eDNA and horizontal gene transfer.....	30
1.2.2.5	eDNA and defense from host immune system and antibiotics.....	30
1.2.3	Research Gap and scope of thesis work.....	32
1.2.3.1	Mycobacterial infections around the eye.....	32
1.2.3.2	Mycobacterial biofilm.....	33
1.2.3.3	Mycobacterial biofilm matrix and eDNA.....	33
1.2.3.4	Therapeutic options for mycobacterial keratitis.....	35
1.2.4	Objectives.....	39
1.3	Study Flow Chart.....	40
	Chapter 2. Materials and Methods.....	41
2.1	<i>Pseudomonas aeruginosa</i>	42
2.1.1	Bacterial strains and culture media.....	42
2.1.2	Animals.....	43

2.1.3	Biofilm dispersal agent and Colistin treatment on <i>P. aeruginosa</i> biofilms in continuous-culture flow cell system.....	44
2.1.4	<i>P. aeruginosa</i> biofilm formation on mouse keratitis model.....	45
2.1.5	Colonizing pattern and immune response characterization.....	46
2.1.6	Transcriptomic analysis.....	47
2.1.6.1	RNA preparation.....	47
2.1.6.2	RNA sequencing and data analysis.....	47
2.1.7	Evaluation of host responses to different <i>P. aeruginosa</i> strains.....	48
2.1.8	Chemical toxicity test on rabbit cornea.....	48
2.1.9	Biofilm dispersal agent and Colistin treatment on <i>P. aeruginosa</i> keratitis mouse model.....	49
2.1.10	Quantification of viable <i>P. aeruginosa</i> cells in mouse cornea.....	49
2.2	Atypical mycobacteria.....	51
2.2.1	Bacteria Strains.....	51
2.2.2	Animals.....	51
2.2.3	Growth testing for suitable medium for biofilm work.....	51
2.2.4	Establishment of continuous flow cell system for atypical mycobacterial biofilm.....	52
2.2.5	Establishment of 8 well chamber slide model for atypical mycobacterial biofilm (High through-put screening).....	52
2.2.6	Synthesis of AM-228.....	53
2.2.7	Haemolytic activity of AM-228.....	53
2.2.8	Determination of antimicrobial activity.....	54
2.2.9	Time-kill kinetics.....	55
2.2.10	Synergy experiment by checkerboard method.....	55

2.2.11 Exogenous Extracellular DNA and biofilm formation.....	56
2.2.12 Evolution of resistance to AM-228 or Gatifloxacin.....	57
2.2.13 Biofilm treatment with AM-228 and antibiotics	57
2.2.13.1 For live measurement of biovolume.....	58
2.2.13.2 For Colony Forming Units measurement.....	58
2.2.14 Preparation of AM-228, Gatifloxacin, Amikacin, Besifloxacin and DNase for animal study.....	59
2.2.15 Chemical toxicity testing on rabbit corneal wound healing model.....	59
2.2.16 Mycobacterial keratitis mouse model.....	60
2.2.17 Slit lamp microscopy imaging for disease progress.....	60
2.2.18 Confocal laser scanning microscopy imaging for infected cornea.....	60
2.2.19 AM-228, Gatifloxacin, Amikacin, Besifloxacin and combination of DNase in <i>in vivo</i> efficacy study.....	61
Chapter 3. <i>Pseudomonas aeruginosa</i> part of results.....	62
3.1 <i>P. aeruginosa</i> biofilm formation on mouse keratitis model.....	62
3.1.1 <i>cdrA</i> gene expression on mouse cornea of murine keratitis model.....	63
3.1.2 pyoverdine gene expression on mouse cornea of murine keratitis model.....	65
3.1.3 Discussion.....	67
3.2 C-di-GMP induction leads to establishment of microcolonies and modulates the innate immune response during <i>P. aeruginosa</i> corneal infections.....	68
3.2.1 Phagocyte tolerant microcolonies formation of <i>P. aeruginosa</i> on infected cornea.....	69
3.2.2 Colonization patterns of different c-di-GMP regulated strains on mouse cornea.....	70

3.2.3	Clinical Disease response to different c-di-GMP regulated <i>P. aeruginosa</i> strains	72
3.2.4	C-di-GMP induction of <i>P. aeruginosa</i> modulates the host immune response..	73
3.2.5	Discussion.....	77
3.3	Lowering the c-di-GMP content intracellularly enhances <i>P. aeruginosa</i> <i>in vitro</i> and <i>in vivo</i> biofilms susceptibility to Colistin treatment.....	79
3.3.1	Combination of SNP and Colistin is superior to monotherapy in killing <i>in vitro</i> PAO1/ <i>p_{lac}-gfp</i> biofilms.....	80
3.3.2	Chemical Toxicity Test in <i>in vivo</i>	81
3.3.3	Combination of SNP and Colistin is superior to monotherapy in eliminating PAO1/ <i>p_{lac}-gfp</i> infections in mouse keratitis model.....	82
3.3.4	Discussion.....	84
	Chapter 4. Atypical Mycobacteria part of results.....	85
4.1	Extracellular DNA is important for mycobacterial biofilm matrix maintenance.....	85
4.1.1	Growth testing of <i>Mycobacterium fortuitum</i> ATCC 49404 and <i>Mycobacterium chelonae</i> ATCC 35752.....	86
4.1.2	Establishment of varying degree of biofilm architectures in dynamic flow cell model and 8-well chamber slide model.....	87
4.1.3	Exogenous extracellular DNA enhance biofilm mass in Mycobacterial biofilm.....	91
4.1.4	DNase treatment leads to disruption of Mycobacterial biofilm matrix assembly	92
4.1.5	Discussion.....	94

4.2 Potential Novel anti-mycobacterial drug.....	95
4.2.1 Synthesis diagram of AM-228.....	96
4.2.2 Hemolytic activity and antimicrobial activity of AM-228.....	98
4.2.3 Fast killing kinetics of AM-228 towards Mycobacterial infections	99
4.2.4 AM-228 did not evolve resistance against Mycobacterial infections in multi passage studies.....	101
4.2.5 Outstanding anti-biofilm properties of AM-228 comparable against Gatifloxacin in Mycobacterial biofilms.....	103
4.2.6 Biocompatibility test for AM-228.....	105
4.2.7 Discussion.....	106
4.3 Targeting eDNA can increase efficacy of antibiotics in mycobacterial biofilms.....	108
4.3.1 Combination of DNase and antibiotic is better than antibiotic alone in <i>in vitro</i> biofilm experiment.....	109
4.3.2 Synergistic reactions between Amikacin and Fluoroquinolones for <i>mycobacterium fortuitum</i> and potential DNase treatment.....	113
4.3.3 Besifloxacin for mycobacterial keratitis.....	119
4.3.4 Discussion.....	120
4.4 Mycobacterial keratitis is biofilm mode of infection and novel combination of Fluoroquinolones, Aminoglycoside and DNase is an ideal treatment.....	122
4.4.1 Development of mycobacterial keratitis model.....	123
4.4.2 Mycobacteria biofilm formation on mouse cornea.....	124
4.4.3 Novel treatment strategies for mycobacterial keratitis.....	125
4.4.4 Discussion.....	129
Chapter 5 Conclusions and Future Work	131
Appendix I.....	138

Appendix II.....	139
Appendix III.....	140
Appendix IV.....	141
Appendix V.....	180
Appendix VI.....	224
Author's Publications.....	227
Posters and Talks.....	228
Reference.....	229

List of Figures

Figure 1	Diagram depicting five stages of biofilm development.....	4
Figure 1.1.6	Structure and Function of cyclic-di-GMP.....	13
Figure 1.2.2	eDNA involvement in the biofilm formation and its properties.....	28
Figure 3.1.1	Induction of the <i>p_{cdrA}-gfp</i> (c-di-GMP reporter fusion) in the progress of mouse cornea infection.....	64
Figure 3.1.2.1	PAO1/<i>p_{pydA}-gfp</i> infection on mouse cornea.....	66
Figure 3.1.2.2	PAO1 infection on mouse cornea.....	66
Figure 3.2.1	Distribution of phagocytes among the PAO1/ <i>p_{cdrA}-gfp</i> infected mouse corneas after 1 dpi (A), 2 dpi (B), 4 dpi (C) and 7 dpi (D)	70
Figure 3.2.2	Colonization patterns of the PAO1-<i>gfp</i>, <i>ΔwspF-gfp</i> and PAO1/<i>p_{lac}-yhjH-gfp</i> infected mouse corneas after 2 dpi (A,B,C) and 7 dpi (D,E,F)	71
Figure 3.2.3	Slit Lamp microscopy images of mouse eyes infected with different c-di- GMP mutant strains.....	72
Figure 3.2.4A	PCA of transcriptomes of mouse corneal cells from 2 dpi and 7 dpi caused by <i>P. aeruginosa</i> PAO1, <i>ΔwspF</i> and PAO1/<i>p_{lac}-yhjH</i>	76
Figure 3.2.4B	Production of cytokines of mouse corneal cells after 2 dpi and 7 dpi of infections caused by <i>P. aeruginosa</i> <i>ΔwspF</i> and PAO1/<i>p_{lac}-yhjH</i> strains....	76
Figure 3.3.1	Antimicrobial treatments on PAO1/<i>p_{lac}-gfp</i> biofilm in continuous-culture flow cell system.....	80
Figure 3.3.2	Chemical toxicity test on rabbit corneal wound.....	82

Figure 3.3.4 Slit-lamp microscopy images and quantification of viable PAO1/ <i>p_{lac}-gfp</i> in mouse cornea over the period of 4 days.....	83
Figure 4.1.1.1 Growth testing of <i>M. fortuitum</i> in Luria Broth (LB), Tryptic Soy Broth (TSB), Middle Brook (MB) and Minimal 63.....	86
Figure 4.1.1.2 Growth testing of <i>M. chelonae</i> in Luria Broth (LB), Tryptic Soy Broth (TSB), Middle Brook (MB) and Minimal 63.	87
Figure 4.1.2.1 Confocal laser scanning images of <i>Mycobacterium fortuitum</i> biofilm grown in continuous-culture flow cell system.....	88
Figure 4.1.2.2 Confocal laser scanning images of <i>Mycobacterium chelonae</i> biofilm grown in continuous-culture flow cell system.....	89
Figure 4.1.2.3 Confocal laser scanning images of <i>Mycobacterium fortuitum</i> biofilm grown in 8 well chambers slide model.....	90
Figure 4.1.2.4 Confocal laser scanning images of <i>Mycobacterium chelonae</i> biofilm grown in 8 well chambers slide model.....	91
Figure 4.1.3 Exogenous DNA enhances Mycobacterial biofilm formation.	92
Figure 4.1.4 Effect of DNase on mycobacterial biofilms.....	93
Figure 4.2.1 General synthetic routes for AM-228.....	96
Figure 4.2.3.1 Time-kill curves of <i>Mycobacterium fortuitum</i> against A) AM-228 and B) Gatifloxacin.....	100
Figure 4.2.3.2 Time-kill curves of <i>Mycobacterium chelonae</i> against A) AM-228 and B) Gatifloxacin.....	101
Figure 4.2.4.1 Evolution of <i>M. fortuitum</i> resistance towards Gatifloxacin or AM-228...	102
Figure 4.2.4.2 Evolution of <i>M. chelonae</i> resistance towards Gatifloxacin or AM-228...	102

Figure 4.2.5.1 Anti biofilm effects of AM-228 and Gatifloxacin on <i>M. fortuitum</i> biofilm	103
Figure 4.2.5.2 Anti biofilm effects of AM-228 and Gatifloxacin on <i>M. chelonae</i> biofilm	104
Figure 4.2.6 Chemical toxicity testing of AM-228 on rabbit corneal wound healing model.....	105
Figure 4.3.1.1 Combination treatment of AM-228 (10xMIC) and DNase (12.5µg/ml) on <i>M. fortuitum</i> biofilm.....	110
Figure 4.3.1.2 Combination treatment of Gatifloxacin (10xMIC) and DNase (12.5µg/ml) on <i>M. fortuitum</i> biofilm.....	111
Figure 4.3.1.3 Combination treatment of AM-228 (10xMIC) and DNase (12.5µg/ml) on <i>M. chelonae</i> biofilm.....	112
Figure 4.3.1.4 Combination treatment of Gatifloxacin (10xMIC) and DNase (12.5µg/ml) on <i>M. chelonae</i> biofilm.....	113
Figure 4.3.2.1 Synergistic reactions of Amikacin and Fluoroquinolones and potential adjuvant DNase treatment on <i>M. fortuitum</i> biofilms.....	116
Figure 4.3.2.2 Amikacin, Fluoroquinolones and potential adjuvant DNase treatment on <i>M. chelonae</i> biofilms.....	117
Figure 4.3.2.3 Viable bacteria in colony forming units after synergistic reactions of Amikacin and Fluoroquinolones and potential adjuvant DNase treatment on Mycobacterial biofilms.....	118
Figure 4.4.3.1 Besifloxacin on <i>M. fortuitum</i> biofilm.....	119
Figure 4.4.3.2 Besifloxacin on <i>M. chelonae</i> biofilm.....	120
Figure 4.4.1 Murine model of mycobacterial keratitis.....	123

Figure 4.4.2	Confocal microscopy images of mouse cornea from murine keratitis model at day 3 and day 7 post infection.....	125
Figure 4.4.3.1	Slit lamp and confocal microscopy images of mouse cornea from murine keratitis for different treatments.....	128
Figure 4.4.3.2	Viable bacteria in colony log forming units of different treatments.....	129

List of Tables

Table 1	Common causes of bacterial keratitis in United States.....	2
Table 1.2.1	Classification of non-tuberculous mycobacteria.	23
Table 1.2.2	Importance of eDNA in different bacterial biofilms.....	25
Table 1.2.3.4.1	<i>In vitro</i> activity of anti microbial against <i>Mycobacterium fortuitum</i>.....	35
Table 1.2.3.4.2	<i>In vitro</i> activity of anti microbial against <i>Mycobacterium chelonae</i>.....	36
Table 2.1.1	<i>P. aeruginosa</i> strains used in this study.....	42
Table 2.1.2	Parameters for each fluorescent dye and strain (<i>Pseudomonas</i> <i>aeruginosa</i>).....	43
Table 2.2.1	Parameters for each fluorescent dyes and strains (atypical <i>Mycobacteria</i>).....	51
Table 4.2.2	HC50 of AM-228 and minimum inhibitory concentrations of AM-228 and commercially available antibiotics.....	99
Table 5.2.2	Minimum inhibitory concentration of Levofloxacin, Gatifloxacin and Besifloxacin and their Fractional Inhibitory concentration index (FIC) with Amikacin on <i>M. fortuitum</i> (<i>M. neworleansense</i>) ATCC 49404 and <i>M.</i> <i>chelonae</i> ATCC 35752.....	115

List of abbreviations

ARVO	The Association for Research in Vision and Ophthalmology
SNP	Sodium nitroprusside
<i>M. marinum</i>	<i>Mycobacterium marinum</i>
<i>M. simiae</i>	<i>Mycobacterium simiae</i>
<i>M. asiaticum</i>	<i>Mycobacterium asiaticum</i>
<i>M. scrofulaceum</i>	<i>Mycobacterium scrofulaceum</i>
<i>M. szulgai</i>	<i>Mycobacterium szulgai</i>
<i>M. xenopi</i>	<i>Mycobacterium xenopi</i>
<i>M. avium</i>	<i>Mycobacterium avium</i>
<i>M. intracellulare</i>	<i>Mycobacterium intracellulare</i>
<i>M. haemophilum</i>	<i>Mycobacterium haemophilum</i>
<i>M. gastri</i>	<i>Mycobacterium gastri</i>
<i>M. malmoense</i>	<i>Mycobacterium malmoense</i>
<i>M. nonchromogenicum</i>	<i>Mycobacterium nonchromogenicum</i>
<i>M. terrae</i>	<i>Mycobacterium terrae</i>
<i>M. triviale</i>	<i>Mycobacterium triviale</i>
<i>M. peregrinum</i>	<i>Mycobacterium peregrinum</i>
<i>M. mucogenicum</i>	<i>Mycobacterium mucogenicum</i>
<i>M. senegalese</i>	<i>Mycobacterium Senegalese</i>
<i>M. septicum</i>	<i>Mycobacterium septicum</i>
<i>M. mageritense</i>	<i>Mycobacterium mageritense</i>
<i>M. immunogenum</i>	<i>Mycobacterium immunogenum</i>
<i>M. smegmatis</i>	<i>Mycobacterium smegmatis</i>
<i>M. goodii</i>	<i>Mycobacterium goodii</i>
<i>M. wolinskyi</i>	<i>Mycobacterium wolinskyi</i>
<i>M. abscessus</i>	<i>Mycobacterium abscessus</i>
<i>M. terrae</i>	<i>Mycobacterium terrae</i>
<i>M. flavescens</i>	<i>Mycobacterium flavescens</i>
<i>M. kansasii</i>	<i>Mycobacterium kansasii</i>
<i>M. fortuitum</i>	<i>Mycobacterium fortuitum</i>
<i>M. gordonae</i>	<i>Mycobacterium gordonae</i>
<i>M. ulcerans</i>	<i>Mycobacterium ulcerans</i>
<i>M. chelonae</i>	<i>Mycobacterium chelonae</i>
<i>S. enterica</i>	<i>Salmonella Enterica</i>
<i>E. coli</i>	<i>Escherichia Coli</i>
<i>G. xylinus</i>	<i>Gluconacetobacter xylinus</i>
<i>S. epidermidis</i>	<i>Staphylococcus epidermidis</i>
<i>H. influenzae</i>	<i>Haemophilus influenzae</i>
<i>N. meningitidis</i>	<i>Neisseria meningitidis</i>
<i>Y. pestis</i>	<i>Yersinia Pestis</i>
<i>S. aureus</i>	<i>Staphylococcus aureus</i>
<i>S. pneumoniae</i>	<i>Streptococcus pneumoniae</i>
<i>K. pneumoniae</i>	<i>Klebsiella Pneumoniae</i>
<i>B. cereus</i>	<i>Bacillus cereus</i>
<i>L. pneumophila</i>	<i>Legionella pneumophila</i>
<i>B. subtilis</i>	<i>Bacillus subtilis</i>
<i>P. putida</i>	<i>Pseudomonas putida</i>
<i>P. aeruginosa</i>	<i>Pseudomonas aeruginosa</i>

PI	Propidium Iodide
CLSM	Confocal Laser Scanning Microscope
Dpi	Days post infection
TSB	Tryptic Soy Broth Medium
MB	Middle Brook Broth Medium
LB	Luria Bertani Broth Medium
NaHCO ₃	Sodium hydrogen carbonate
Na ₂ SO ₄	Sodium Sulphate
DMF	N-N-dimethylformamide
DMSO	Dimethyl Sulfoxide
ETOAc	Ethyl Acetate
MeOH	Methanol
IACUC	The Institutional Animal Care and Use Committee
CLSI	Clinical and Laboratory Standards Institute
MIC	Minimum Inhibitory Concentration
DMF	N-N-dimethylformamide
FIC	Fractional inhibitory concentration index
eDNA	Extracellular DNA
CFU	Colony Forming Units
ADC	Albumin Dextrose Catalase
OADC	Oleic Albumin Dextrose Catalase
BSA	Bovine Serum Albumin
EPS	Extracellular polymeric substances
NETs	Neutrophil extracellular traps
PMNs	polymorphonuclear neutrophils
NaCl	Sodium Chloride
PBS	Phosphate Buffered Saline
c-di-GMP	Cyclic-Di-GMP
IL-2	Interleukin 2
IL-6	Interleukin 6
IFN λ 1	Interferon Lambda receptor 1
IL-23a	Interleukin 23- alpha subunit
IL-10	Interleukin 10
TNF- α	Tumor Necrosis Factor-alpha
INF- γ	Interferon Gamma
NTM	Non Tuberculous Mycobacteria
SEM	Scanning Electron Microscope
AFM	Atomic Force Microscopy
TEM	Transmission Electron Microscope
EPS	Extracellular Polymeric substance
DGC	Diguanylate cyclase
PDE	Phosphodiesterase
PAG	Poly- β -1,6- <i>N</i> -acetylglucosamine
NO	Nitric Oxide
MDR	Multidrug-resistant
Hpi	Hours post infection
Dpi	Days post infection
LPS	Lipopolysaccharide
LASIK	Laser-assisted in situ keratomileusis
Th1	T helper 1-type immune response
Th2	T helper 2-type immune response

Abstract

Bacterial keratitis is the most important leading cause of corneal opacification and blindness around the world. Mycobacterial keratitis is very hard to eradicate while *Pseudomonas* keratitis is very common and prone to drug resistance problems. In this study, we investigated the *Pseudomonas* keratitis as a biofilm mode of infection that induces cyclic-di-GMP signaling and forms phagocyte-tolerant microcolonies on mouse cornea. The increased c-di-GMP content in *P. aeruginosa* was responsible for decreased levels in cytokine production. C-di-GMP reducing agent (Sodium Nitroprusside) was shown to enhance the efficacy of Colistin treatment in *Pseudomonas* keratitis. Mycobacteria readily formed biofilms on mouse cornea comprising of large amounts of extracellular DNA. A strong synergism between Amikacin and Fluoroquinolones against *Mycobacterium fortuitum* has been observed. DNase addition further enhanced the efficacy of anti-mycobacterial drugs by breaking the mycobacterial biofilm matrix. New treatment strategy (combination of Amikacin, Fluoroquinolones and DNase) showed the best efficacy for converting mycobacterial infections.

Chapter 1

Introduction

Several types of pathology will lead to keratitis, inflammation of the cornea of the eye. It is characterized by growing of bacteria and the recruitment of polymorphonuclear leukocytes (PMNs) in the cornea which can lead to damage of cornea or blindness in worst cases. Keratitis can affect vision to various levels ultimately leading to blindness. Causal organisms for keratitis include bacteria, fungus, virus, protozoa and parasites. The common risk factors for infectious keratitis include ocular trauma, contact lens wear, recent ocular surgery, preexisting ocular surface disease, dry eyes, lid deformity, corneal sensation impairment, chronic use of topical steroids, and systemic immunosuppression[1, 2]. Among them, bacterial keratitis, mainly *Pseudomonas aeruginosa* keratitis is one of the most important causes of corneal opacifications, which is the second most common cause of legal blindness worldwide after cataracts[3]. Table (1) shows that the most common strain causing bacterial keratitis is by *Staphylococcus aureus* (45.5%) followed by *P.aeruginosa* (33%) in United States at 2013[4].

Class/Organism	Common Isolates*	Cases (%)
Gram-Positive Isolates		29-75.1
Gram-positive cocci	<i>Staphylococcus aureus</i>	4-27.6
	MRSA	1.3
	Coagulase negative <i>Staphylococci</i>	1-45.5
	MRSE	43.1
	<i>Streptococcus pneumoniae</i>	0-3.4
	<i>Streptococcus viridans</i> group	1-6.9
Gram-positive bacilli	<i>Propionibacterium</i> species	4-7
	<i>Mycobacterium</i> species	3
Gram-Negative Isolates		31-50
Gram-negative bacilli	<i>Pseudomonas aeruginosa</i>	3-33
	<i>Serratia marcescens</i>	3-13.5
	<i>Proteus mirabilis</i>	3.4-4
	<i>Moraxella</i> species and related species	1-20.7
	Enteric and other gram-negative bacilli	1-10
Gram-negative coccobacillary organisms	<i>Haemophilus influenzae</i> , other <i>Haemophilus</i> species	2.5

Table 1. Common causes of bacterial keratitis in United States. (Figure was adapted from **American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. Bacterial Keratitis. San Francisco, CA: American Academy Of Ophthalmology;2013. www.aao.org/ppp**)[4].

Erie JC and colleagues reported that the USA has an incidence of 11 per 100,000 persons for microbial keratitis[5]. Contact lens related corneal ulcers in the general population have increased from almost 0% in the 1960s to 52% in 1990[5]. In Minnesota, USA, there is an incidence of ulcerative keratitis of 5.3 per 100,000 people per year, revealing an increase in incidence of 435% from the 1950s to the 1980s[5]. Pathophysiology of bacterial keratitis depend on the characteristic of the particular organism infected. Fibrillae in Gram-positive organisms, glycocalyx and fimbriae in Gram-negative bacteria enhance the bacteria's adherence to the damaged tissue site[6]. Such organisms can invade the corneal stroma easily and cause bacterial keratitis. During the bacterial infections, plasminogen is activated to plasmin, which is proteolytically active. Protease, chymase and typtase released by bacteria cause lesion of the epithelium and dealayed wound healing. Exotoxins produced by live bacteria, endotoxin produced by dead bacteria, proteases, coagulases, lipases and fribrinolysin cause degradation of the corneal matrix[7].

Bacterial pathogens are able to form surface-attached complex multicellular biofilm communities and biofilms can cause 80% of the bacterial infections, including conditions such as gingivitis, infectious kidney stones, bacterial endocarditis, and inner ear infections, along with many hospital-acquired infections from catheters and ports[8-10]. Bacterial cells within biofilms are surrounded by large amounts of extracellular polymeric substances (EPS) consisting of extracellular proteins, exopolysaccharides and extracellular DNA (eDNA), and have distinct physiology compared to their free-living counterparts[11]. Formation of biofilms noticeably increases the bacterial cells' tolerance towards various kinds of antimicrobials as well as to the host immune attack[12, 13]. Biofilm formation is responsible for a large

percentage of treatment failures for infections and causing a huge economic burden for our health care system[12, 13]. There are increasing evidences and reports suggesting that different ocular infections involve biofilm infection as a major contribution. Biofilms presence has been reported on many ocular devices including intraocular lens, contact lens, suture material and scleral buckles. Ocular infections usually result from the secondary infection of these biofilms on biomaterials. Therefore, it is suggested that bacterial biofilms may contribute as a vital component for ocular infections via biofilm formation on ocular tissues or persisting bacteria on abiotic substances, which are using as implants for the eye. Moreover, biofilm formation on ocular tissues is important in several ways that are

1. Bacterial biofilms serve as reservoir which can release the bacteria into the surrounding, leading to the secondary infection
2. They are quite resistant to conventional therapeutic options, making them hard to eliminate.
3. Failure of conventional antibiotics and host immune responses to eliminate the infection lead to chronic infection, which in turn produces the chronic inflammatory responses leading to the tissue damage apart from damage by bacteria directly[14].

Nature Reviews | Drug Discovery

Figure 1 Diagram depicting five stages of biofilm development. A) Reversible attachment to the surface. B) Irreversible attachment to the surface. C) Formation of microcolonies. D) Development of mature biofilm. E) Dispersal of single cells from the biofilms. The bottom panel shows each of the five stages of development represented by a photomicrograph of *P. aeruginosa* when grown under continuous flow condition on a glass substratum.(Figure was adapted from **Davies, D.,** *Understanding biofilm resistance to antibacterial agents.* **Nature Reviews Drug Discovery**, 2003. 2(2): p. 114-122 with permission[15])

1.1 Pseudomonas aeruginosa

Pseudomonas aeruginosa is a gram-negative motile opportunistic pathogen that can cause a wide range of infections in relation to its biofilm formation capacity[16-18]. It is well recognized as the most important and prevalent organism causing severe keratitis. Certain predisposing factors such as trauma, contact lens wear, and pre-existing ocular disease are known to be aggregating keratitis.

1.1.1 Virulence factors and enzymes

1.1.1.1 Specific Virulence factors

Extra-cellular and cell-associated compounds are normally produced by *P. aeruginosa* for its virulence property. Both pili and glycocalyx, cell-associated products, are critical for the bacterial attachment to host cells[19]. Moreover, *P. aeruginosa* produces extracellular enzymes such as exotoxin A and S, which suppress the host's protein synthesis. Toxins produced by *P. aeruginosa* such as proteases, leukocidin and haemolysins promote the bacterial invasion and degrade the host-infected tissues.

1.1.1.2 Bacterial Surface-Associated factors

The reports have been investigated that traumatized cornea serve as a good medium for the bacteria attachment but not to normal cornea. The reports showed that *P. aeruginosa* attached to the injured cornea and stroma by electron microscopy[7, 20]. *P. aeruginosa* was rarely seen on the injured cornea but invaded into the corneal stroma within one hour and some bacteria were present intracellularly[7]. Invasion of *P. aeruginosa* has occurred as early as 7.5 minutes after infection in the damaged epithelial cells followed by corneal stroma invasion[21].

Proteins, lipopolysaccharide and lipids containing *P. aeruginosa*'s cell wall has abundant pili. Pili were found to assist in adherence in various body parts such as cornea[22], mouth[23, 24] and skin[25]. Flexible 60 angstrom in diameter and 2500 nm length pili are present in the *P. aeruginosa*[24]. It was found that there was a strong inhibition of bacterial adherence via the anti-pilus antibody and purified pili, confirming the importance of pili in bacterial adhesion[23, 24]. Flagella have been reported less important in adhesion compared with pili[25]. However, non-flagellate bacteria mutants caused less infectious compared with normal wild type bacteria in experimental burn wound model of rats and mice[26]. Vaccination with flagella antigens protected from lethal infection directing that anti-flagella antibody stimulated phagocytosis[26].

1.1.1.3 Glycocalyx

P. aeruginosa provides slime, which is an extra-cellular glycocalyx, comprised of glycolipoprotein and two polysaccharides (high molecular weight polysaccharide and lipopolysaccharide)[27]. It has been shown that the slime can impair the *in vitro* motility, phagocytosis of human polymorphonuclear neutrophils (PMNs) and endocytosis by promoting the organism's virulence and viability[28]. It was reported that the isolates from cystic fibrosis patient produced a mucoid exopolysaccharide similar to seaweed alginate[28]. Studies have been shown that *P. aeruginosa* can attach easily to inert surfaces and form biofilm containing micro colonies[29]. It has been documented for *P. aeruginosa* biofilm formation on different parts of the body such as mucosal surfaces[30], osteomyelitis bone[29] and the surface of prostheses[29]. It naturally exhibits as a mobile or planktonic swarmer or as a glycocalyx-enclosed microcolony, however, the latter mode is the dominant lifestyle providing protection from phagocytosis and environmental stress[31]. With the aid of scanning electron microscopy, it has been reported a well-established polysaccharide

containing biofilm formation in extended contact lens wears[32]. *In vivo*, there was a study showing formation of *P. aeruginosa* biofilm formation on hydrogel contact lens after 3 days on rabbit corneas[33].

1.1.1.4 Toxins and proteases

Tissue necrosis is mainly mediated by the production of exotoxins, proteolytic enzymes and haemolysins from *P. aeruginosa*. Generally, most of the tissues have a property to resist the toxins; however, corneal stromas lack these criteria because of the absence of a vascular network which is contributing for the PMNs release and opsonization within minutes after infection.

1.1.1.4.1 Exotoxin A

Studies have been investigated that antitoxin immunoglobulin titers were significantly high in recovered patients from *P.aeruginosa* infection, contributing to the most lethal toxin in mice studies, while the survival rate of bacteremia patients was corresponding to an elevated serum antitoxin levels[34]. This toxin's mechanism of action is like diphtheria toxin contributing ADP-ribosylating elongation factor 2 which in turn inhibits the protein synthesis. Inactive form is excreted from *P. aeruginosa* which has a molecular weight of 66,000 Daltons. However, its inactive form is extremely toxic to tissues and animals. It is encoded chromosomally and produced by majorities of *P. aeruginosa* strains approximately 90%[35]. Growth conditions affect the synthesis and excretion while high levels of iron and other toxin can inhibit their synthesis[35].

1.1.1.4.2 Exoenzyme S

40% of the isolates produce this ADP-ribosyltransferase , which interacts with elongation factor 2 at an altered position on mammalian cells[34]. Exoenzyme is an another vital component in contributing *P. aeruginosa*'s virulence and has been evaluated for decades.

1.1.1.4.3 Proteolytic enzymes

P. aeruginosa produces two major proteases, based on the pH activity of the medium, called alkaline and neutral[34]. Their action is to breakdown the host proteins and interfere phagocytosis by breaking immunoglobulin. Neutral protease and lactase can degrade proteoglycans and elastin.

There was a study investigated that the proteases production was highly correlated with the severity of corneal infections in rodents[36]. Exotoxin A played a critical role in establishment of mice corneal while elastase was found to be not important[37]. Moreover, alkaline protease is also an important factor for the severities of corneal infections and survival of bacteria on mouse cornea[38]. Both proteases can lead to the corneal tissue damage by degrading corneal proteoglycans, which can cause collagen fibrils dispersal[39].

1.1.1.4.4 Haemolytic toxin

Two haemolysins are produced by *P. aeruginosa*, heat liable haemolytic toxin, 78,0000 Daltons with phospholipase C activity and glycolipid. Both are actively secreted in phosphate-limiting growth conditions[35]. Their mechanism of action is to lyse red blood cells, which have phosphatidyl choline membranes.

1.1.2 Biofilm lifestyles

Biofilm formation is an endless cycle, which is mainly contributed by a extracellular polymeric substances (EPS) matrix which holds the biofilm cells to a surface[40, 41]. They are known to be the main lifestyles accounting for 65-80% of all microbial infections[14, 42, 43]. Metaphorically, Biofilms are termed as a city of microbes including EPS[10, 44, 45], which in turn result for 85% of total biofilm mass[45]. EPS is mainly contributed by a mixture of extracellular DNA, biomolecules, exopolysaccharides and polypeptides forming a hydrated polar mixture, which contributes to the architecture and scaffold of the biofilm[46-48].

In *P. aeruginosa*, the three main polysaccharides (alginate, *Psl* and *Pel*) have been identified to be responsible for the biofilm stability[49, 50]. There were reports showing that qualitative composition of alginate or *Psl/Pel* differed in mucoid and nonmucoid *P. aeruginosa* strains[51-53]. Alginate, a linear unbranched polymer, is found to contribute the protection, structural stability of the biofilm matrix and retention of water and nutrients[54]. Glucose-rich matrix material, *Pel* and a repeating pentasaccharide of D-mannose, L-rhamnose and D-glucose, *Psl*, are found to be the essential scaffolds for the biofilm development in the early stages[52, 55, 56].

1.1.3 eDNA in biofilm matrix

Another important factor of *P. aeruginosa* biofilm is eDNA. There have been reports showing the essentiality of eDNA in biofilm formation by

1. Exposition to DNase I prevented the biofilm formation[57].
2. Biofilms without eDNA were found to be more sensitive to sodium dofecyl sulfate[58].
3. eDNA stimulated the twitching motility-mediated biofilm expansion[59].
4. Initial and early biofilm development stages required eDNA as a cell-to-cell interconnecting compound[60, 61].
5. eDNA functioned a nutrient stock for starved bacteria during biofilm formation[62].

Immune cells and neutrophils can form neutrophil extracellular traps (NETs) containing large quantities of eDNA[63]. Antimicrobial effect is contributed by the activity of histone presence in the NETs[64]. In *P. aeruginosa*, extracellular DNA was found abundantly in the extracellular matrix, 18 times and 6 times higher than carbohydrates and proteins respectively[65]. Numerous studies have been studied to identify the origin of eDNA and the majority noted for the similarity of eDNA to genomic DNA[66]. In *P. aeruginosa*, intracellular genomic DNA and eDNA are similar by the analysis of randomly amplified polymorphic DNA. The similarity of genomic DNA and eDNA has also been shown by methods such as Southern analysis and polymerase chain reaction[60]. However, there was a report showing in cystic fibrotic patients, the origin of eDNA were from the human neutrophils instead of bacterial genomic DNA[67]. *P. aeruginosa* biofilm matrix can facilitate the bacteria biofilm formation by the help of human neutrophils matrix[68]. Another report was shown that eDNA's source was not directly related to its function by showing addition of either prokaryotic or eukaryotic DNA promoted biofilm formation[69].

1.1.4 Exopolysaccharides in biofilm matrix

Exopolysaccharides are long linear or branched molecules and play a major fraction of the biofilm matrix[70, 71]. Most exopolysaccharides are a mixture containing neutral and charged sugar residues heteropolysaccharides, however, several exopolysaccharides are homopolysaccharides containing fructans and sucrose-derived glucans[71]. There are three distinct exopolysaccharides present in *P.aeruginosa* biofilm matrix; alginate, Pel and Psl[50]. Mucoid strains of *P.aeruginosa* exhibit alginate overproduction as a result of mutations in the gene encoding the MucA. Alginate is a major factor for the microcolonies formation in the early stage of biofilm formation and the mechanical stability of the mature biofilm. However, Pel and Psl polysaccharides play a vital role in the biofilm establishment evidenced in non-mucoid strains. Psl is involved in the bacterial adherence to biotic or abiotic surfaces and in

the biofilm architecture integrity. Psl is anchored to the cell surface in a helical pattern in the attachment phase, promoting cell-cell interactions[51]. Antimatrix agents have been discovered to disrupt matrix components by the enzymes or chelating agents. N-acetyl-D-glucosamine-1-phosphate acetyltransferase (GlmU) is an essential peptidoglycan and lipopolysaccharide (LPS) precursor in Gram-positive and Gram-negative pathogens. GlmU inhibitors, N-ethyl maleimide (NEM) and its analogs showed antibiofilm activity against *E.coli*, *P.aeruginosa* and *E.faecalis*[72]. Moreover, chelating agents can be useful in destroying biofilm matrix. Sodium Citrate inhibits *Staphylococci* species biofilm formation *in vitro*[73]. Disodium-EDTA, in combination with antibiotics, reduced the *Staphylococci* and *P.aeruginosa* biofilm formation *in vitro*[74].

1.1.5 Extracellular proteins in biofilm matrix

A large number of extracellular proteins are present in the biofilm matrix, including enzymatic proteins and non-enzymatic proteins[70]. A variety of extracellular enzymes have been discovered in biofilms, promoting the degradation of biopolymers. The role of the enzymes which degrade the EPS components resembles the matrix an external digestive system which breaks down biopolymers to low-molecular-mass products in the environmental biofilms. Some of these enzymes have a role in the detachment of bacteria from biofilms. Others act as virulence factors in infectious diseases biofilms. The cell surface-associated and extracellular carbohydrate-binding proteins, lectins, are involved not only in a link between the extracellular EPS and the bacterial surface but also in the stabilization and formation of the polysaccharide matrix network[75]. Synthetic high-affinity multivalent ligands which target Lectin inhibit *P.aeruginosa* biofilm formation and stimulate the dispersion of mature biofilms[76].

1.1.6 Cyclic-di-GMP and biofilm formation mechanisms

Figure 1.1.6 Structure and Function of cyclic-di-GMP (Figure was adapted from Hengge, R., *Principles of c-di-GMP signalling in bacteria*. Nat Rev Microbiol, 2009. 7(4): p. 263-73 with permission[77])

First discovery of cyclic-di-GMP showed that it is a soluble second messenger which can allosterically activate the membrane bound cellulose synthase of *Gluconacetobacter xylinus*[77]. C-di-GMP can promote the adhesion production, exopolysaccharides matrix components secretion and inhibition of its motility[78], (Figure 1.1.6). It was reported that c-di-GMP played a pivotal role between sessile and motile lifestyles and its molecular pathways on a variety of gram-Negative bacteria such as *S.enterica*, *E.coli*, *G.xylinus* and *P.aeruginosa*[79-83]. It is involved not only in settling down the bacteria colonies on a surface but also building up of three-dimensional (3D) biofilms. It is a vital component for switching of bacterial lifestyle i.e., planktonic to biofilm or vice versa[84]. Biofilm formation and dispersal of *P. aeruginosa* is regulated by its intracellular content of the secondary messenger c-di-GMP, which is synthesized by a set of diguanylate cyclase (DGC) enzymes and degraded

by phosphodiesterase (PDE) enzymes encoded by its genome[77]. Muroid and small-colony variants from cystic fibrosis represent for the high biofilm formation and c-di-GMP[85]. A high intracellular content of c-di-GMP causes the down regulation of *P. aeruginosa* cell motility and induction of synthesis of two major polysaccharides (*Pel* and *Psl*) resulting in biofilm formation[86, 87]. Biofilm containing diverse exopolysaccharides, adhesive pili, extracellular DNA and non firmbrial adhesions are regulated by c-di-GMP pathway[88]. C-di-GMP controls the biofilm formation at transcriptional, posttranscriptional and posttranslational levels. Lowering the intracellular content of c-di-GMP of biofilm cells by inducing expression of PDE enzymes is able to disperse biofilms both *in vitro*[89] and *in vivo*[90].

1.1.6.1 Alginate, *Pel* and *Psl* polysaccharides

The *Pel* and *Psl* Polysaccharides are present as major constituents for the most bacterial biofilms and it has been studied extensively in *P. aeruginosa* biofilm. It was noted that they are present as major biofilm matrix components of non-muroid *P. aeruginosa* biofilms. However, not all the *P. aeruginosa* (*P. aeruginosa* PA14) do not possess *Psl* operon[91]. C-di-GMP regulate the *Pel* and *Psl* exopolysaccharides on the transcriptional level, by constitutive activation of the REC-GGDEF response regulator-DGC WspR[91]. Moreover, *Pel* exopolysaccharide biosynthesis is regulated by c-di-GMP on posttranslational level[78]. Moreover, *Psl* exopolysaccharide plays a positive feedback loop on c-di-GMP and which in turns increases biofilm formation and expression of biofilm components[92]. It was noted that rugose small-colony variants from the cystic fibrosis patients possessed the high expressions of *Pel* and *Psl* exopolysaccharides[85, 93]. High Alginate expression was observed in muroid *P. aeruginosa* strains in chronic cystic fibrosis lungs[94].

1.1.6.2 Cup fimbriae

It has been investigated for five fimbrial gene clusters of the chaperon/usher pathway (Cup) in *P. aeruginosa*[95]. All of those cup fimbriae contribute towards bacteria adhesion, biofilm progression and are regulated by c-di-GMP at their transcriptional level. It was reported that a small-colony variant from cystic fibrosis patients demonstrated c-di-GMP dependent enhanced CupA fimbriae expression[96]. CupA fimbriae expression was also increased through the c-di-GMP up regulation in the detergent stress[96].

1.1.6.3 Type IV pili

Type IV pili are known to be important for twitching ability through polymerizing and retracting[96, 97]. It was shown that type IV pili and twitching are contributing towards the biofilm formation[98, 99] and reported that Type IV pilus biogenesis and twitching ability is controlled by c-di-GMP in *P. aeruginosa*[100].

1.1.7 Cyclic-di-GMP as an immunomodulator

C-di-GMP acts as an immunomodulator by its previous experiment showing addition of 50 μ M suppressed the tumor cell lines' growth including the human T-cell lymphoblastoid CD4+ Jurkat cell line and the human acute lymphoblastic leukemia cell line Molt 4[101, 102]. C-di-GMP also showed that it can inhibit human colon cancer cells' proliferation and proposed towards for the potential anti cancer target[103].

In *S.aureus* and *K.pneumonia* infection, c-di-GMP has been shown its immunomodulatory effects[104, 105]. They showed that c-di-GMP administration increased cytokines and chemokines secretion, comprising of interferons and interleukins[105, 106]. It also noticed that c-di-GMP stimulated the innate immune response by recruiting neutrophils, granulocytes and monocytes[103, 105]. As a consequence, c-di-GMP demonstrated its beneficial effect by

increase bacterial clearance from the body[104]. It also showed that c-di-GMP increased the immune response by working as an adjuvant with mutant staphylococcal enterotoxin, pneumococcal surface protein A and *S.aureus* clumping factor A[105, 106]. Therefore, it has been proposed that c-di-GMP can be used as an immunomodulator clinically. Unlike other body systems, increase expression of innate immune response such as increase cytokine expression, recruitment of neutrophils and chemokine secretion can lead to further damage of the cornea and vision impair[107]. However, there have been no studies of the role of c-di-GMP in eyes particularly with the most common pathogen, *P. aeruginosa*, for bacterial keratitis.

1.1.8 Cyclic-di-GMP manipulation as a biofilm dispersal approach

Almost 80 percent of bacterial infections are biofilm type of infections and this can lead to drug resistance problems for medical care. In order to address this, future antimicrobials should focus on compounds, which can prevent biofilm formation or destroy biofilm matrix. Therefore, people proposed to use c-di-GMP as a controllable messenger to control biofilm. There was a report showing that lowering of c-di-GMP by inducing *E.coli* PDE YhjH caused biofilm dispersal in *Shewanella oneidensis*[108]. It also showed the same mechanism of c-di-GMP in *P. putida* biofilm dispersal[109]. Controlling biofilm formation via c-di-GMP by manipulating external stimuli, which can inhibit DGCs or stimulate PDE is an important topic for future health care. Firstly, extracellular c-di-GMP could be the potential target to control the biofilm formation. The 200 μ M c-di-GMP inhibited the bacterial adhesion to the mammalian cells and reduced the biofilm formation while did not affect on bacterial growth in *S.aureus*[110]. The c-di-GMP inhibitory effects on biofilm formation have been validated in a human methicillin-resistant *S.aureus* and a bovine mastitis isolate of *S.aureus*. Intercalators have also been discovered which can transform c-di-GMP to a higher order aggregates[111].

Moreover, DGC inhibitors have also been recently discovered to control biofilm formations by high through put screening. These small molecules, which can inhibit DGC at their nanomolar concentrations, hold the potential hopes for controlling biofilm yet more studies are warranted for clinical usage[112]. Finally, a promising signal which can be used for biofilm dispersal is nitric oxide(NO). It has been shown that NO can trigger the biofilm dispersal in a wide range of microorganism at their nanomolar levels[113]. It has been reported that NO can lead to biofilm dispersal in *P. aeruginosa* via c-di-GMP specific PDE directly[114] or indirectly[115]. NO modulation of c-di-GMP was also investigated in other bacteria such as *L.pneumophila* and *Shewanella woodyi*[116] . It has been well noted that NO controls not only c-di-GMP but also c-di-AMP via c-di-AMP specific PDE in *B.subtilis*[117]. It was reported that intermediate NO level was required for biofilm upregulation via c-di-GMP[118]. Thus, Nitric oxide, freely diffusible molecule is a promising signal that can control and modulate the biofilm formation. There was a study reporting the successful usage of Sodium Nitroprusside (SNP) (NO-donor agent) as a biofilm dispersal agent with its low, sub lethal concentrations[119].

1.1.9 Research Gap and scope of thesis work

Recent reports suggest the *P. aeruginosa* biofilms evidence on mucosa of the lungs in cystic fibrosis[18] and on cornea[104]. They reported the classical stages of biofilm formation on experimental mouse cornea and showed the preliminary evidence of biofilm formation using EPS as a marker for biofilm[120]. They employed SEM and TEM images showing the aggregates of biofilm resembled cells embedded along the cells[120]. This report shows the evidence of *P. aeruginosa* biofilm formation on cornea, however, in depth knowledge of *P. aeruginosa* biofilm pathogenesis mechanism, host immune responses, the regulatory pathways governing corneal *P. aeruginosa* biofilms and treatment options are missing.

Moreover, there was a report showing the evidence of biofilm formation on corneal biopsy specimens from infectious crystalline keratopathy patients[121]. To date, this is a first report showing biofilm formation on human keratitis samples. They reported the detection of corneal biofilms employed by TEM[121]. TEM studies had been evaluated for eight chronic microbial keratitis cases. Ruthenium red was employed to detect EPS and three patients have found to be positive[121]. On the other hand, it was noted that the treatment compliance to these three patients was low, contributing the drug tolerance property of biofilms.

Biofilm formation has been proposed as the main cause of a wide range of persistent infections, including the well-characterized cystic fibrosis lung infections[122], dental plaque-induced gingival diseases[123] and urinary tract infections[124]. However, there is a lack of physiological characterization for the presence and/or impact of biofilms in a number of infections. One example is ocular infection, which continues to be the main cause of ocular disease and visual loss[125]. Even though there are growing findings and evidences for the importance of bacterial biofilm in ocular infections, most of these studies are based on *in vitro* characterization of the biofilm formation capacity of ocular bacterial isolates[16]. Studying the

bacterial physiology and host-pathogen interactions within the ocular tissue might provide insights into the pathogenesis mechanisms of bacterial ocular infections. Overall, corneal infection study, targeting the bacterial biofilm pathogenesis is still in initial stage. Most of the studies are still preliminary and lacking the detailed biofilm pathogenesis mechanisms. However, these preliminary reports confirm for the biofilm's critical role in corneal bacterial infections. Moreover, tissues damage is mediated not only by bacteria itself but also by host response against the biofilms. Therefore, greater understanding of the biofilm role in corneal infections and their successful eradications are urgently required for future ophthalmology.

The increasing incidence of multidrug-resistant (MDR) *P. aeruginosa* infections is a global and top-priority problem especially in critically ill patients, and cancer patients[126, 127]. In ophthalmology, it is the major leading cause of keratitis in United States[4]. It is noted that the annual estimated burden is US\$330million /year in United States at 2010[128]. Colistin is considered to be last resort to treat *P. aeruginosa* infection due to its excellent biophysical activity[129, 130]. They are considered to be under antimicrobial peptides category[131, 132], which confer various advantages over other antibiotics such as rare resistance formation and their ability to modulate innate immune response[133]. However, there were reports showing that the Colistin was ineffective in eradicating *P. aeruginosa* biofilm[134]. They have shown that the bacteria strains did not get genetically resistant to Colistin but phenotypically resistant to Colistin when they resident at the top layer of biofilm[134]. In contrast, mature *P. aeruginosa* biofilms contain at least two subpopulations that confer resistance towards different types of antimicrobials[135]. The non-motile cells from inside part of *P. aeruginosa* biofilms are tolerant to antimicrobial targeting cells with low metabolic activity such as ciprofloxacin and tetracycline[134]. In contrast, the motile cells from the outer layer of *P. aeruginosa* biofilms are tolerant to antimicrobial targeting cells with low metabolic activity such as Colistin[134]. Therefore, there is an urgent requirement of new treatment strategy to

replace or boost the current last antibiotic resort for *P. aeruginosa*. Since reducing the intracellular c-di-GMP content can induce cell motility and cause dispersal, we hypothesized in this study that the remaining cells from *P. aeruginosa* biofilms after dispersal are more susceptible to Colistin treatment.

P. aeruginosa keratitis can lead to rapid recruitment of polymorphonuclear neutrophils (PMNs), corneal stromal destruction and corneal ulceration. These effects are contributed by the rapid influx of PMNs to eradicate infection and host immune response via releasing the enzymes[107]. Although influx of PMNs is critical for disease response, it can lead to the severe inflammation resulting in corneal damage and scarring[107]. Pro-inflammatory cytokines induced by the *P. aeruginosa* such as Interleukin-1 β , Interleukin-6 and tumor necrosis factor alpha (TNF- α) can result direct damage to cornea or indirect damage by stimulating PMNs influx and tissue-destruction enzymes production[136, 137]. Phagocytosis, lysosomal degranulation and bacterial killing inside the phagolysosome are the steps required for bacteria killing by PMN. It can usually produce toxic oxygen metabolites leading to the phagocyte's respiratory burst, release of superoxide anions, hydrogen peroxide and peroxynitrite. Phagocytosis often leads to release of extracellular lysosomal enzymes such as elastase, collagenase and myeloperoxidase. All these components can cause corneal stromal damage by breaking collagen strands, killing stromal keratocytes and glycosaminoglycans. In contrast, the bacteria govern initial pathogenesis of *P. aeruginosa* keratitis and progressive tissue destruction is mainly due to the resident corneal cells and stimulated leukocytes[137]. From the described facts, it is a vital task to study immune responses of *P. aeruginosa* keratitis. Current evidence indicates that induction of the T helper 1 (Th1)-type immune response of the C57BL/6 mice is unable to eradicate *P. aeruginosa* during corneal infections, and contributes to corneal destruction and perforation associated with the mouse keratitis model[138]. The inability of the corneal innate immune response to clear *P. aeruginosa*

infections leads to the hypothesis that biofilm formation protects the *P. aeruginosa* cells against immune clearance during corneal infections. As a model organism for biofilm research, the biofilm formation mechanism of *P. aeruginosa* is well characterized[135]. Biofilm formation and dispersal of *P. aeruginosa* is regulated by the intracellular secondary messenger c-di-GMP, and it was reported for its immunomodulatory effect in other systemic infections[104-106]. However, it is unclear whether c-di-GMP regulates *P. aeruginosa* biofilm formation and host-pathogen interactions during ocular infections.

1.1.10 Objectives

1. To study the *Pseudomonas aeruginosa* biofilm pathogenesis in mouse keratitis model
2. To study the roles of c-di-GMP and innate immune responses during *Pseudomonas aeruginosa* corneal infection using a mouse keratitis model
3. To investigate the new treatment strategies for *Pseudomonas aeruginosa* biofilm in *in vitro* and *in vivo* mouse model

1.2 Atypical Mycobacteria

1.2.1 Colony Characteristics

Atypical mycobacteria or non-tuberculous mycobacteria (NTM) are frequently found in the environment such as soil, water and dust and there are mycobacteria other than *mycobacterium tuberculosis*. Runyon classified NTM into four groups, I-IV, (Table 1.2.1) [139-141]. Group I, photochromogens, consists of *M. kansasii* and etc, which usually grow slowly about 2-4 weeks and become yellow when exposed to light. Group II, scotochromogens, consist mainly of *M. gordonae*, and grow in yellow colonies 2-4 weeks in agar plates when cultured in dark. Group III that are nonphotochromogens grow slowly in 2-4 weeks. The rapid growers, group IV, which are the most pathogenic and important for human. They are divided into three subgroups: *Mycobacterium fortuitum* group, *Mycobacterium chelonae/abscessus* group and *Mycobacterium smegmatis* group. According to the literatures, they are susceptible to various antibiotics such as sulfonamide, polymixin B, the third and fourth generation fluoroquinolones[141]. Group IV organism are most important and prevalent strains for eye infections[141].

Runyon Group	Phenotype	Colony Characteristics	<i>Mycobacterium</i> species
I	Photochromogens	Produce yellow pigment when exposed to light	<i>M. marinum</i> , <i>M. kansasii</i> , <i>M. simiae</i> , <i>M. asiaticum</i>
II	Scotochromogens	Produce yellow-orange pigment when exposed to light or in the dark	<i>M. scrofulaceum</i> , <i>M. szulgai</i> , <i>M. gordonae</i> , <i>M. xenopi</i> , <i>M. flavescens</i>

III	Nonchromogenis	Slow growers. Do not produce pigment	<i>M. avium</i> , <i>M. intracellulare</i> , <i>M. haemophilum</i> , <i>M. paratuberculosis</i> , <i>M. gastri</i> , <i>M. malmoeense</i> , <i>M. nonchromogenicum</i> , <i>M. terrae</i> , <i>M. triviale</i>
IV	Rapid Growers	Colonies in 5 days. Do not produce pigment	<p><i>M. fortuitum</i> Group</p> <p><i>M. fortuitum</i>, <i>M. peregrinum</i>, <i>M. mucogenicum</i>, <i>M. Senegalese</i>, <i>M. septicum</i>, <i>M. mageritense</i></p> <p><i>M. chelonae-abscessus</i> Group</p> <p><i>M. chelonae</i>, <i>M. abscessus</i>, <i>M. immunogenum</i></p> <p><i>M. smegmatis</i> Group</p> <p><i>M. smegmatis</i>, <i>M. goodii</i>, <i>M. wolinskyi</i></p>

Table 1.2.1 Classification of non-tuberculous mycobacteria

1.2.2 Extracellular DNA in biofilm formation

1.2.2.1 Important of eDNA in bacterial biofilm

Old studies believed that the main component of the biofilm matrix is exopolysaccharides (EPS), however they are not alone in the biofilm matrix but with extracellular DNA presence. The presence of eDNA was investigated, however the functional importance in the biofilm was known by the pioneer report which showed the requirement of eDNA for biofilm

formation[61]. There have been several reports showing the importance of eDNA in different bacteria species' biofilms (Table 1.2.2)[142].

Bacteria	Findings
Gram-negative	
<i>Pseudomonas aeruginosa</i>	Younger biofilms dispersed by DNase treatment[61, 143]
<i>Acinetobacter baumannii</i>	60 percent of biofilms dispersed by DNase treatment[144]
<i>Haemophilus influenzae</i>	Decreased biofilm formation in DNase presence culture[145]
<i>Klebsiella pneumonia</i>	24-h-old biofilm was depleted by DNase treatment[146]
<i>Bdellobacter bacteriovorus</i>	DNase treatment depleted pre-formed biofilm[147]
<i>Schewanella oneidensis</i>	Static and flow biofilms were disrupted by DNase treatment[148]
<i>Vibrio cholera</i>	DNase destroyed 24-h-old biofilm but not 72-h-old biofilm[149]
<i>Bordetella pertussis and bronchiseptica</i>	DNase disrupted the established biofilms[150]
<i>Neisseria meningitidis</i>	DNase application disrupted biofilm assembly[151]
<i>Comamonas denitrificans</i>	DNase inhibited formation of biofilm[152]

<i>Compylobacter jejuni</i>	2-day-old biofilms were disrupted by DNase[153]
<i>Gram-positive bacteria</i>	
<i>Listeria monocytogenes</i>	Initial attachment of biofilm was inhibited by DNase[154]
<i>Streptococcus pyogenes</i>	DNase treatment destroyed the 24 hour old biofilms[146]
<i>Enterococcus faecalis</i>	Young biofilms were dispersed by DNase treatment[155]
<i>Staphylococcus haemolyticus</i>	Detachment of biofilms were seen after DNase treatment[156]
<i>Staphylococcus aureus</i>	Decreased biofilm phenotype was seen in the medium containing DNase[157]
<i>Staphylococcus epidermidis</i>	DNase treatment dispersed the 6 hour old biofilms[158]
<i>Streptococcus intermedius</i>	Decrease biofilm phenotypes were observed in cultures containing DNase[159]
<i>Streptococcus mutans</i>	Decrease biofilm phenotypes were observed in cultures containing DNase[160]
<i>Streptococcus pneumonia</i>	DNase treatment depleted 6-h-old biofilms[161]
<i>Aggregatibacter actinomycetemcomitans</i>	Disorganization of 18-h-old biofilms was seen after DNase treatment[162]

Table 1.2.2 Importance of eDNA in different bacterial biofilms

1.2.2.2 eDNA in cell adhesion

The first stage of biofilm formation is the attachment of single bacteria on to a surface. Basically, it is comprised of two major stages, in which the bacteria contact to the surfaces via their physio-chemical properties, followed by anchoring of the surfaces by biologically active adhesions[163]. The first stage comprises reversible Liftshitz-van der Waal interactions between the substratum and cell layer[164]. The second stage is composed of more specific and strong interactions at a very close range[165]. It was noted that eDNA is a major constituent contributing for both phases and playing a more important role in a second phase[166].

Smaller cells are easier to overcome an energy barrier compared with bigger cells in order to adhere to a surface. Therefore, it is believed that in smaller cells, eDNA, can bridge the connections between the cells and surfaces and facilitate the stronger and irreversible attraction in the second phase, (Figure 1.2.2) [163, 167-169]. Extracellular DNA may adhere to the bacterial cell's surface in long loop structures, a distance enough to bridge the cells and surfaces[166, 170]. In the second phase, the interaction has been made within nanometers between basic electron donation and acidic electron accepting groups, mediated by eDNA[166, 170].

Another important factor of eDNA presence in biofilm is because of its effect of hydrophobicity towards the bacterial cell surface, which increases bacterial attachment. Several reports have been already reported its impact on hydrophobicity including one report which showed that eDNA increased bacterial attachment to surfaces by using AFM force spectroscopy[171]. This observation was further supported by the measurements of water

contact angle and assessing surface free energy of cells[172]. For *S.epidermidis*, eDNA assisted adhesions on glass or polystyrene surfaces[158] and eDNA assisted adhesions on glass wool in *Acidovorax temperans*[173].

Figure 1.2.2 eDNA involvement in the biofilm formation and its properties (Figure was adapted from Okshevsky M, M.R., *The role of extracellular DNA in the establishment, maintenance and perpetuation of bacterial biofilms*. Critical Reviews in Microbiology, 2015. 41: p. 341-352 with permission [142])

1.2.2.3 eDNA and structural integrity of biofilm

The structural integrity of biofilms is very important depending on cell-cell interactions and cell-matrix interactions. A variety of matrix components and extracellular adhesions

contribute the biofilm's structural integrity via specific and non-specific interactions. As discussed above, disintegration of biofilm components have been observed in different bacterial species by DNase treatment. Moreover, there was a study showing the direct correlation between the biofilm stability and concentration of DNA added in *E.coli*[174]. However, there is a varying amount of eDNA concentration in different strains. *S.aureus* biofilm contains eDNA as a major component[175] but it is a minor component in *S.epidermidis*[176]. However, biofilm stability requires eDNA in these species, indicating that the eDNA concentrations and biofilm development are not directly related. Concerning about the eDNA importance in biofilm growth phases, reports showed that the highest concentration of eDNA presence was observed in the early stages of biofilm development by indication of DNase treatment disperse the early biofilms but not mature biofilms[61, 149, 158]. In *Bacillus cereus*, planktonic exponential phase contained a lot of DNA but stationary phase cells did not contain DNA[177]. However, there were opposite observations in other reports[178, 179]. Therefore, eDNA's major involvement in maintaining biofilm stability might be transitory and perhaps it interacts or binds with other extracellular components to maintain the long term stability of biofilm. Only DNase could effect the disintegration of biofilm stability but not Proteinase K or RNase treatment[180, 181]. However, in *N.meningitis*, two DNA-binding proteins were discovered for eDNA assisted biofilm formation[182]. The α -peptide of IgA protease and NhbA were capable of binding DNA and treatment by protease resulted in less biofilm formation. Moreover, there was a report showing that eDNA was associated with membrane vesicles for biofilm formation[183]. Type IV pili with DNA binding capacity was discovered in *P. aeruginosa* which was critical for bacterial attachment and biofilm formation[184]. eDNA was found to be the highest concentration in the stalk structure of mushroom in mature *P. aeruginosas* biofilms, responsible for both biofilm stability and formation of cap structure, contributing by the stalk structure's eDNA concentrations and

activity of Type IV pili migrating cells[173]. The similar Type IV pili protein were found in *H.influenze*, binding to eDNA and formed mesh, indicating that these protein might act together with eDNA towards biofilm stability[181].

1.2.2.4 eDNA and horizontal gene transfer

Horizontal gene transfer between bacteria is an important factor for bacteria resistance problem in clinical setting and it was first investigated in 1928[185]. It has been noted since its discovery that most bacterial genomes contain horizontally acquired genes and this process is vital for bacterial evolution[186]. Moreover, it has been discovered that eDNA pool in bacterial biofilm provide a rich medium for genetic transformation naturally, other than bacteriophage induced gene transfer and mobile genetic elements[187]. In *P. aeruginosa*, chromosomal markers were transported by its eDNA at a frequency of 10^{-7} and 10^{-8} [188]. These observations suggested that horizontal gene transfer via eDNA occurred in environment and human setting. It was also shown that most of the bacteria actively secreted eDNA which facilitated natural transformation[179].

1.2.2.5 eDNA and defense from host immune system and antibiotics

Bacterial biofilms are very resistant to antibiotics comparing against their planktonic cultures enabling to treat them very difficult. However, this resistance is not only because of their genetic but also resulting from their metabolic diversity states, protected from their matrix components. As mentioned above, eDNA facilitated genetic transformation play a vital role in genetic transformation in biofilm. The number of antibiotic resistant biofilm bacteria is highly expanding, increasing requirement of new antimicrobial drug or strategies development[189].

The antibiotic resistance in bacterial biofilm is thought due to impair transport of antibiotics through the extracellular matrix because of protein and exopolysaccharides interaction[48]. eDNA play a major role in antibiotic resistance due to its ability to bind cation by chelating cationic host antimicrobial peptides, (Figure 1.2.2). There was a report showing that non-typeable *H.influenza*(NTHI) eDNA bound the antimicrobial defense protein β -defensin to abolish its antimicrobial effects[190]. In *P. aeruginosa*, eDNA acted as a protective barrier against aminoglycosides[191].

There were a lot of studies reporting for eDNA's capabilities of increasing genes expressions which could lead to antimicrobial resistance genes[62]. DNA can chelate the ions, such as Magnesium, Manganese, Calcium and zinc[62]. There was a report showing that lack of Magnesium ions stimulated the genes responsible for the modification of cell surface lipopolysaccharides, (Figure 1.2.2), that in turn increased the bacterial outer membrane's negative charge to become resistant to the antimicrobial peptides from the host and the antibiotics, aminoglycosides.

In real scenarios, eDNA can promote bacterial infections or demote bacterial infections. High amount of eDNA can cause membrane disruption of bacteria by stripping Magnesium and Calcium ions from bacterial surface[62] and the eDNA presence protect the bacteria from cationic peptides and antibiotics by providing a shield against them.

1.2.3 Research Gap and scope of thesis work

Although gram-positive and gram-negative bacteria are the most common strains accounting for keratitis in past years, the emerging increasing trends of atypical mycobacterial infections are seen in recent decades because of the rising use of biomaterials, increasing number of ocular surgeries (LASIK, endothelial keratoplasty) and the expanded use of fluoroquinolones prophylaxis[192]. However, there is no strategic study of atypical mycobacterial eye infections.

1.2.3.1 Mycobacterial infections around the eye

After Runyon classified mycobacterium in 1959[193], NTM have become increasingly recognized as important cause of ocular morbidity[194]. NTM can cause periocular, cutaneous, adnexal, orbital,[195-197] conjunctival[139, 198], scleral[199, 200], corneal[201-203] infections. Among the NTM isolates, the most prevalent pathogenic strains for the eye are *M. chelonae* and *M. fortuitum*[192]. There was a report showing that a total of 183 non-tuberculous mycobacteria isolates from 142 eyes were identified, with a fourfold increase in the number of eyes infected with non- tuberculous mycobacteria from 1980–1989 (13.4%) to 2000–2007 (56.3%)[192]. Among them, keratitis was standing (36.6%) among diagnoses followed by scleral buckle infections (14.8%) and socket/implant infections (14.8%)[192]. Identifiable risk factors were the presence of biomaterials (63.1%), ocular surgery (24.1%) and steroid exposure (77%)[192].

1.2.3.2 Mycobacterial biofilm

Biofilm infections display phenotypic resistance to antimicrobials, are resistant to antibiotics and show a property to modulate the host immune system[9, 204-206]. Mycobacteria readily form biofilms and, because of their hydrophobicity and metal-resistance, may be pioneers of biofilm formation. There are growing studies for the biofilm's vital roles in eye infections. Bacterial evolution in a biofilm can lead to a variety of changes not only genetically but also phenotypically. One of the most important significant developments is tolerance to antibiotic therapy[207]. However, biofilm studies in eye infections are still in early stages. There was a report showing that *M. chelonae* recovered from cornea of post-Lasik patients and *M. fortuitum* from blood of bone marrow transplant patients had shown remarkable biofilm formation[208]. *M. chelonae* and *M. fortuitum* showed biofilms under both high and low nutrient conditions on both silastic (material used in medical setting) and high density polyethylene (material used in water distribution system)[209]. Nevertheless, atypical mycobacterial biofilm studies are still in the early stages and there are no reports studying about *M. fortuitum* and *M. chelonae* biofilms.

1.2.3.3 Mycobacterial biofilm matrix and eDNA

Exopolysaccharides remain the major components in most of the bacterial species including gram-positive and gram-negative bacteria. However, there are lacking of genes responsible for producing exopolysaccharides in mycobacteria species[210]. Acetylated derivative of glycopeptidolipids (GPL) play a critical role in surface attachment, sliding motility and biofilm formation in *M. smegmatis*[211]. There was also an another report showing GPL synthesis was required in multicellular growth of *M. Avium* sharing the same physiological process with *M. smegmatis*[212]. Moreover, there were several reports showing the

importance of free mycolic acids and mycolyl-diacylglycerol involvement in mycobacterial biofilm particularly in *M. smegmatis*[213-215]. According to these above reports, lipids play a major and critical component in mycobacterial biofilm in terms of intercellular and cell to substratum interactions. Lsr2, nucleoid associated protein, regulate the free mycolic acid synthesis in the mycobacterial biofilm maturation phase through a GroEL1-dependent modulation of type II fatty acid synthases[213, 214, 216, 217]. Biofilm formation process of *M. smegmatis* is distinct from its planktonic cultures in terms of interaction between GroEL1 and β -keto-acyl ACP synthases (KasA and KasB), the enzymes of FASII[216]. Development of mycobacterial biofilm has been shown to be efficient in iron-rich environment by inducing siderophore synthesis which is a common and important feature in other gram-negative bacterial biofilms[217]. There genetic loci, pks16, helY and pks1 are important for mycobacterial biofilm formation in mycobacteria tuberculosis and mutants of these three loci are unable to form mature biofilm[214, 218].

Reports were shown that *M. ulcerans* and *M. avium* were seen as multicellular communities in *in vivo* [219, 220] . *M. ulcerans* provided a well-organized multicellular structure biofilms by an extracellular matrix in an aquatic insect, *Naucoris cimicoides*[220]. Moreover, the matrix of *M. ulcerans* had abundance of mycolactone, which led to virulence of the pathogens to the host[220, 221]. Therefore, there is a direct stimulation of virulence factors by the mycobacterial biofilm matrix in *M. ulcerans*. There was a report showing the vesicles carrying toxin involvement in extracellular matrix of *M. ulcerans* biofilm, which in turn led to increase virulence of bacteria, resistance to the antibiotics and better colonization of bacteria to the host[222]. However, there have been no research reports studying *M. fortuitum* and *M. chelonae* biofilms.

Although there are so many studies investigating the effects and involvement of eDNA in different bacteria, there was only one study investigating about eDNA involvement in

mycobacterial biofilm[223]. The author stressed that there were presence of varying amounts of eDNA in biofilms grown by *M. avium*[223]. They also investigated that extracellular DNA was genomic origin. They suggested that eDNA could be a new potential target for the future treatment strategies for *M. avium* strains[223]. However, there is no study of eDNA in the particular mycobacterial biofilms formed by *M. fortuitum* and *M. chelonae*. Therefore, we hypothesized here that extracellular DNA plays a major component for biofilm assembly and a major barrier against antibiotic penetration for *M. fortuitum* and *M. chelonae* biofilms.

1.2.3.4 Therapeutic options for mycobacterial keratitis

There are several reports showing the variation of MIC susceptibilities on *M. fortuitum* and *M. chelonae* against different antimicrobials.

Antimicrobial	No of Strains	MIC90 (µg/ml)	MIC range (µg/ml)
Amikacin	13	3	0.25-4[224]
	6	-	4-16[225]
	23	≤16	-[226]
Moxifloxacin	10	1.6	-[227]
	23	≤1	-[226]
Ofloxacin	37	≥8	4-8[228]
	20	50	-[229]
	4	-	0.25-8[230]

Ciprofloxacin	64	≥ 8	0.5->8[231]
	6	-	0.5-8[225]
	23	81% ≤ 1	-[226]
Levofloxacin	4	48% ≤ 2	0.125-4[230]
	23	52% > 2	-[226]
Gatifloxacin	10	3.2	-[227]
	20	6.25	-[229]
Clarithromycin	25	≥ 8	0.5->8[232]
	23	≤ 2	-[226]

Table 1.2.3.4.1 *In vitro* activity of anti microbial against *Mycobacterium fortuitum*

Antimicrobial	No of Strains	MIC ₉₀ (µg/ml)	MIC range (µg/ml)
Amikacin	18	1	0.25-1[224]
	5	-	0.5-8[225]
	13	≤ 16	-[226]
Moxifloxacin	12	0.2	-[227]
	13	≤ 1	-[226]
Ofloxacin	88	0.5	≤ 0.06 -0.5[228]

	20	3.13	-[229]
	3	-	0.25-0.5[230]
Ciprofloxacin	24	170	0.1[231]
	5	-	0.125[225]
	13	≤ 1	-[226]
Levofloxacin	3	-	0.125-0.2[230]
	13	≤ 2	-[226]
Gatifloxacin	12	0.2	-[227]
	20	0.78	-[229]
Clarithromycin	25	≥ 8	0.25->8[232]
	23	≤ 2	-[226]

Table 1.2.3.4.2 *In vitro* activity of antimicrobials against *Mycobacterium chelonae*

According to the literatures reviewed, *in vitro* activity of various antibiotics showed a quite huge range of antimicrobial sensitiveness, (Table 1.2.3.4.1 and 1.2.3.4.2) which enabling to treat effectively for *M. fortuitum* and *M. chelonae*. On the other hand, Non-tuberculous infections in and around the eye are clinically recalcitrant to treatment, recur after cessation of therapy, and require long-term therapy to eradicate infection. There is currently lacking of antibiotics that can efficiently eradicate the atypical mycobacterium infections. Therefore, urgent requirement of effective new antibiotic or treatment strategies is warranted. Here in this

report, we identified a new antimicrobial, AM-228, which has outstanding antimicrobial properties in planktonic cells and biofilm cells.

From the above described facts, we hypothesized here that poor response to mycobacterial keratitis is due to their biofilm formations, and disrupting the biofilm matrix component particularly eDNA or new treatment strategies can facilitate the clinical treatment success.

1.2.4 Objectives

1. To study the biofilm pathogenesis of ocular pathogens, *Mycobacterium fortuitum* and *chelonae*, in *in vitro* and *in vivo* mouse keratitis model
2. To investigate the importance of mycobacterial biofilm matrix component, extracellular DNA, for biofilm formation
3. To study the novel new antibiotic, AM-228, in the treatment of mycobacterial infections comparable against the most successful fourth generation fluoroquinolone, Gatifloxacin, in *in vitro* and *in vivo*
4. To investigate the new treatment strategies in order to replace the current treatment for better clinical outcomes

1.3 Study Flow chart

Chapter 2

Materials and methods

2.1 *Pseudomonas aeruginosa*

2.1.1 Bacterial strains and culture media

Bacterial strains used in this project are listed in Table (2.1.1). Bacterial strains were cultured overnight in Luria-Bertani medium with shaking (200rpm) at 37°C and supplemented with 30 $\mu\text{g m}^{-1}$ of gentamicin (Gm) ml^{-1} from 1 mg m^{-1} stock solution or 30 $\mu\text{g m}^{-1}$ of tetracycline (Tc) from 12.5 mg m^{-1} stock solution . Stock solution were kept at -20°C. Overnight cultures were adjusted to $\text{OD}_{600} = 0.1$ prior inoculation into 3-channel flow cell. Biofilms grown in continuous-culture flow cell biofilms experiments were carried out in 37°C in ABT minimal medium supplemented with glucose, 0.4 g l^{-1} (ABTG). Overnight cultures were adjusted to about 1×10^6 bacterial cells with PBS for mouse corneal infection. SNP stock solution (50 μM) was prepared in normal saline and kept in dark at 4°C. Solutions of the nitric oxide donor SNP were freshly prepared from the SNP stock solution for each biofilm experiment.

Strain(s) or plasmid	Relevant characteristic(s)	Source or reference
<i>P. aeruginosa</i> strains		
PAO1	Prototypic wild-type strain	[233]
$\Delta wspF$	<i>wspF</i> derivative of PAO1 constructed by allelic exchange ('locked' high c-di-GMP strain)	[234]
PAO1/ <i>p_{lac}-yhjH</i>	Tc ^r ; PAO1 containing the <i>p_{lac}-yhjH</i> vector ('locked low c-d-GMP strain')	[89]
PAO1/ <i>p_{cdrA}-gfp</i>	Gm ^r ; PAO1 carrying the <i>p_{cdrA}-gfp</i> reporter (c-di-GMP reporter fusion strain)	[234]
PAO1-miniTn7- <i>gfp</i>	Gm ^r ; PAO1 tagged by the miniTn7- <i>gfp</i> (GFP tagged Prototypic wild-type strain)	[89]
$\Delta wspF$ -miniTn7- <i>gfp</i>	Gm ^r ; $\Delta wspF$ tagged by the miniTn7- <i>gfp</i> (GFP tagged 'locked' high c-di-GMP strain)	[89]
PAO1/ <i>p_{lac}-yhjH</i> -	Gm ^r ;Tc ^r ; PAO1/ <i>p_{lac}-yhjH</i> tagged by the miniTn7- <i>gfp</i> (GFP	[89]

miniTn7- <i>gfp</i>	tagged 'locked' low c-di-GMP strain)	
PAO1/ <i>p_{pvdA}-gfp</i>	PAO1 containing the <i>p_{pvdA}-gfp</i> fusion reporter, Tc ^r (GFP tagged c-di-GMP reporter fusion strain)	[235]

Table 2.1.1 *P. aeruginosa* strains used in this study

Fluorescent	Excitation/emission (nm)	Manufacturer
SYTO®9, Live stain (green)	480/500	Invitrogen, Carlsbad, California
Propidium Iodide, dead stain (red)	490/635	Invitrogen, Carlsbad, California
SYTO®62, Red nucleic acid stain (red)	649/680	Invitrogen, Carlsbad, California
LysoTracker® Red DND-99 (red)	577/590	Invitrogen, Carlsbad, California
Alexa Fluor® 635 Phalloidin	633/647	ThermoFisher Scientific, Waltham, MA
PAO1/ <i>p_{lac}-gfp</i>	485/535	NA
PAO1/ <i>p_{cdrA}-gfp</i>	485/535	NA
PAO1/ <i>p_{pvdA}-gfp</i>	485/535	NA
PAO1- <i>gfp</i>	485/535	NA
Δ <i>wspF-gfp</i>	485/535	NA
and PAO1/ <i>p_{lac-yhjH}-gfp</i>	485/535	NA

Table 2.1.2 Parameters for each fluorescent dye and strain (*Pseudomonas aeruginosa*)

2.1.2 Animals

New Zealand White Rabbits (3-4 months old, 2-3 kg) and wild type C57BL6 (6-8 weeks old, 20-30 g) mice purchased from the National University of Singapore were used for this study. All animal experiments were conducted in compliance with the ARVO statement for the Use of Animals in Ophthalmic and Vision Research, the guide for the Care and Use of

laboratory animals (National Research Council) and under the supervision of Singhealth Experimental Medical Centre (SEMC).

2.1.3 Biofilm dispersal agent and Colistin treatment on *P. aeruginosa* biofilms in continuous-culture flow cell system

Fluorescently tagged bacterial strains were cultured overnight in Luria-Bertani medium with shaking at 37°C and supplemented with respective antibiotic. Overnight cultures were adjusted to $OD_{600nm} = 0.1$ prior inoculation into 3-channel flow cell. Biofilms grown in continuous-culture flow cell biofilms experiments were carried out in 37°C in ABT minimal medium supplemented with glucose, 0.4 g l⁻¹ (ABTG). Solutions of the nitric oxide donor, SNP, were freshly prepared for each biofilm experiment. 500 µl diluted overnight culture of gfp-tagged *P. aeruginosa* strains of $OD_{600nm} = 0.1$ were inoculated into each flow cell chamber. The flow cells were left without flow in an inverted position for 1 h after inoculation. The flow cells were then returned to an upright position and medium was fed into the flow cells using Watson Marlow 205s peristaltic pump at the flow rate of 4 ml h⁻¹. For the chemically induced biofilm dispersal, four groups of treatment were tested on 72 h old PAO1/*plac*-gfp biofilms. SNP (Sigma-Alrich, Germany) was added into the medium bottle to the final concentration of 5 µM. Colistin sulphate (Sigma-Alrich, Germany) was introduced to the biofilms at the final concentration of 10 µg ml⁻¹ and both SNP (5 µM) and Colistin sulphate (10 µg ml⁻¹) were applied to the biofilms in the combination treatment group. Treatment was carried out for 24 h and results were compared to the untreated controls. To determine the viability of the cells in the biofilm, the biofilms were stained with 20 µM Propidium Iodide (PI) (Molecular Probes, US). Live and dead Propidium Iodide-stained cells in the biofilms were observed using CLSM at 20x objective lens using an argon laser (488 nm, emission 535 nm) and helium laser (561 nm, emission 617 nm) respectively. Confocal images

were analyzed using IMARIS™ 7.6 (Bitplane AG) to obtain Live/Dead ratio of the cells in the biofilms. One-way ANOVA and student's T-test statistical analysis methods were used to determine the significance of the treatment groups compared to control group. A probability value of $p \leq 0.05$ was considered statistically significant.

2.1.4 *P. aeruginosa* biofilm formation on mouse keratitis model

P. aeruginosa PAO1/*p_{cdrA}-gfp*, PAO1/*p_{pvdA}-gfp* and PAO1 wild type strains (PAO1-miniTn7-*gfp*) were cultured overnight in Luria-Bertani medium with shaking at 37°C and supplemented with respective antibiotics. The mice were anesthetized intra-peritoneally by 0.2 ml of ketamine (100 mg/ml) (Ceva Animal Health, US) and 0.1 ml of xylazil (20 mg/ml)(Troy Laboratories, AUS), mixed with 0.7 ml of normal saline (0.08 ml/mice). A sterile miniblade (BD-Beaver) was used to make corneal scratches (n=3, each 1 mm long), which did not breach beyond the superficial stroma on the right eye whereas the left eye remained untouched[236, 237]. Topical application of 10 µl ($\sim 1 \times 10^6$) of the overnight bacteria suspension was used to infect the scratched cornea. For PAO1/*p_{cdrA}-gfp* strains, the infected corneas were dissected on 2 hour, 4 hour, 8 hour, 2 day, 4 day and 7 day post infection (dpi) and stained by Propidium iodide for dead cells staining. The corneas were viewed using Zeiss LSM780 Confocal Laser Scanning Microscope, CLSM (Carl Zeiss, Jena, Germany) at 63x objective lens using an argon laser (488 nm, emission 535 nm) and helium laser (561 nm, emission 617 nm). The planktonic form of PAO1/*p_{cdrA}-gfp* strain and wild type PAO1 strain (PAO1-miniTn7-*gfp*) were used as a negative control. For the planktonic state, the bacterial cells were cultured in LB media for 6 hour (mid-log phase) with shaking in 37°C and supplemented with respective antibiotics and were then viewed under CLSM.

For PAO1/*p_{pvdA}-gfp* strain, corneas were dissected at 2 dpi and 4 dpi and corneas were viewed with LSM780 Confocal Laser Scanning Microscope, CLSM (Carl Zeiss, Jena, Germany) at 63x objective lens using an argon laser (405 nm, emission 450 nm) for the presence of pyoverdine expression. The planktonic form of the strain acts as a control.

2.1.5 Colonizing pattern and immune response characterization

Female C57BL6 (6-8 weeks old, 20-30 g) mice were infected by the *P. aeruginosa* PAO1/*p_{cdrA}-gfp*, PAO1 wild-type, Δ *wspF* mutant or the PAO1/*p_{lac}-yhjH* strain as above described. For phagocyte tolerant microcolonies formation, PAO1/*p_{cdrA}-gfp* infected cornea at 1 dpi, 2 dpi, 4 dpi, 7 dpi were dissected and stained with 1 μ M of LysoTracker® Red DND-99 stain (Molecular Probes, Invitrogen) to visualize the eukaryotic cells under CLSM.

For visualizing the presence of bacteria and characterizing the colonization patterns and recruitment of phagocytes, the control scratched corneas and infected corneas (infected with PAO1 wild-type, Δ *wspF* mutant or the PAO1/*p_{lac}-yhjH* strain) were dissected after 2 dpi and 7 dpi and stained for 15 min with 20 μ l of solution consisting 1 μ M of LysoTracker® Red DND-99 and approximately 0.165 μ M Alexa Fluor® 635 phalloidin (Life Technologies) (633 nm, emission 647), which stain phagocytes and F-actin of the eukaryotic cells respectively, prior to CLSM imaging.

For measuring the cytokines, the infected corneas at 2 dpi and 7 dpi were dissected and followed by homogenization using VCX 750 probe sonicator (Sonics & Materials, US). The cell debris was removed by centrifugation at 13,000 g for 5 min and the supernatants were used for innate immune response characterization. The amount of cytokines were normalized against the total proteins using Qubit® 2.0 Fluorometer (Invitrogen) prior characterization of

pro-inflammatory response using Bio-Plex ProTM Mouse Cytokine 8-plex Assay (Bio-Rad) with Bio-Plex[®] 200 systems (Bio-Rad).

2.1.6 Transcriptomic analysis

2.1.6.1 RNA preparation

Female C57BL6 (6-8 weeks old, 20-30 g) mice were infected by the *P. aeruginosa* PAO1 wild type, $\Delta wspF$ and PAO1/p_{lac}-*yhjH* mutants as above described. The infected corneas were dissected on 2 dpi and 7 dpi and total RNA was extracted using MiRNeasy mini kit (Qiagen). A Turbo DNA-free vigorous protocol was used for DNase treatment (Ambion). The integrity of the total RNA and the level of DNA contamination were assessed with an Agilent 2200 TapeStation (Agilent Technologies) and a Qubit 2.0 Fluorometer (Invitrogen). Three biological replicates were used for the transcriptomic analysis of 2 dpi and 7 dpi, respectively.

2.1.6.2 RNA sequencing and data analysis

Gene expression analysis was conducted via Illumina RNA sequencing (RNA-Seq technology). RNA-Seq was conducted for three biological replicates of each sample. Libraries were produced using an Illumina TruSeq Stranded messenger RNA Sample Prep Kit. The libraries were sequenced using the Illumina HiSeq2500 platform with a paired-end protocol and read lengths of 100 nt.

A total of ~ 20 million reads were obtained for each sample. Raw reads were trimmed; adaptor sequences removed and any reads below 50bp were discarded. Quality trimming was done by the trimming quality limit set at 0.05. RNA seq analysis pipeline within CLC genomics Workbench 9.0 (CLC Bio, Aarhus, Denmark) was used for aligning. Trimmed reads were then mapped onto the mouse reference genome, which is available for download from the ensembl database (<ftp.ensembl.org>), using the 'RNA-Seq and expression analysis' application of the

CLC genomics Workbench 9.0 (CLC Bio, Aarhus, Denmark) by using the following parameters: maximum number of hits for a read of 1, minimum length fraction of 0.9, minimum similarity fraction of 0.8 and maximum number of two mismatches.

The raw count table of transcripts was then used as an input of Deseq2 R package for differential expression analysis[238]. First, raw counts were normalized according to sample library size. Then, a negative binomial test was fit for each gene and a Wald's test was performed to identify the differentially expressed genes. Transcripts were determined as differentially expressed among pairwise comparisons when their absolute fold-change value was greater than five and the associated adjusted P-value (Benjamin-Hochberg method) was smaller than 0.05. The normalized transcripts were then $\log_2(N+1)$ transformed prior Principal Component Analysis and UPGMA hierarchical clustering for sample dendrogram on the heatmap.

2.1.7 Evaluation of host response to different *Pseudomonas aeruginosa* strains

Slit-lamp microscopy imaging had been taken for the infected animals at day 2 and day 7 for their host responses by using slit lamp biomicroscopy using direct diffuse illumination mode (New-generation Zoom clinical Slit Lamp, NS-2D, Righton).

2.1.8 Chemical toxicity test on rabbit cornea

Twelve rabbits (3-4 months old, 2-3 kg) were randomly grouped into three groups of four rabbits each, comprised of the PBS control treated group, 50 μM SNP treated group and 2 mg ml^{-1} Colistin treated group. Intramuscular injection of 1 ml of ketamine (100 mg ml^{-1}) and 0.5 ml of xylazil (20 mg ml^{-1}) had been used to anesthetize the rabbits. Corneas were anesthetized by topical administration of 1 % xylocaine. A corneal wound had been made by

using a 5 mm trephine and mechanical removal of epithelial cells was carried out using a sterile mini blade (BD-Beaver) leaving the basal lamina intact[239]. All the three groups were treated by topical administration of respective drug three times per day. The corneal wound was visualized with the aid of cobalt-blue filter equipped slit lamp biomicroscopy (New-generation Zoom clinical Slit Lamp, NS-2D, Righton), staining with Minims fluorescein sodium eye drops (Bausch and lomb, 2 % w/v), which is used in ophthalmology clinic for visualization of the wound on the ocular surface[240, 241]. Residual wound area (pixel square) was measured during the wound healing process by Image-J 1.44o version. The Mann-Whitney U Test was employed to determine difference in re-epithelialization existed among the different groups by using PASW statistic 18. A probability value of $p \leq 0.05$ was considered statistically significant.

2.1.9 Biofilm dispersal agent and Colistin treatment on *P. aeruginosa* keratitis mouse model

Healthy and good corneal clarity mice were chosen for this study through careful monitoring with slit-lamp photography. The mice were anesthetized for corneas to be scratched. For chemically induced biofilm dispersal, topical application of 10 μ l of PAO1/*p_{lac}-gfp* suspension ($\sim 1 \times 10^6$ cells) was used to infect the scratched mouse cornea. The animals were divided into 4 groups; PBS as control, SNP (10 μ l of 50 μ M), Colistin (10 μ l of 2 mg ml⁻¹), SNP (10 μ l of 50 μ M) and Colistin (10 μ l of 2 mg ml⁻¹). The groups were treated with the respective drug treatment 3 times each day starting from 1 d post infection. The experiments were carried out over a period of four days.

2.1.10 Quantification of viable *P. aeruginosa* cells in mouse cornea

At each time point of treatment, four animals from each group were euthanized. The infected corneas were dissected and processed to quantify the numbers of viable bacteria present. The corneas were homogenized separately in sterile 0.9% NaCl containing 0.25% BSA[237, 242, 243] and serially diluted and plated in triplicate on LB agar plates. The plates were incubated for 24-48 h at 37°C for bacterial growth. Results are expressed as log₁₀ number of CFU of bacteria[237]. One-way ANOVA and post-hoc analysis (Bonferoni test) were carried out. A probability value of $p \leq 0.05$ was considered statistically significant.

2.2 Atypical Mycobacteria

2.2.1 Bacteria Strains

Mycobacterium Chelonae ATCC 35752 and *Mycobacterium fortuitum* (*M. neworleansense*) ATCC 49404 were used in this study. The bacteria were grown in Middle Brook Broth supplemented with ADC enrichment medium with shaking at 37°C. The liquid cultures were incubated for 3-5 days in order to get the desired growth.

Fluorescent	Excitation/emission (nm)	Manufacturer
SYTO®9, Live stain (green)	480/500	Invitrogen, Carlsbad, California
Propidium Iodide, dead stain (red)	490/635	Invitrogen, Carlsbad, California
Alexa Fluor® 635 Phalloidin	633/647	ThermoFisher Scientific, Waltham, MA

Table 2.2.1 Parameters for each fluorescent dyes and strains (atypical Mycobacteria)

2.2.2 Animals

Wild type (C57BL6) female mice (6-8 weeks old, 20-30 g) and New Zealand White Rabbits (NZW) (3-4 months old, 2-3 kg) were purchased from National University of Singapore for the experiment. The experiment was conducted in accordance with the Association for Research in Vision and Ophthalmology (ARVO) statement and Singhealth Institutional Animal Care and Use Committee approved the protocol.

2.2.3 Growth testing for suitable medium for Biofilm work

Growths testing in different medias (Luria Broth, Trytic Soy Broth, Middle Brook Broth and minimal 63 medium) were done until day 7. The liquid cultures were adjusted to OD₆₀₀=0.05 in different mediums prior experiments. The cultures were incubated at 37°C in rotary shaker (200 RPM). A small portion of culture was taken out to check the growth with spectrometer OD₆₀₀ at different time points; 12, 24, 48, 72, 96 and 120 hours respectively.

2.2.4 Establishment of continuous flow cell system for atypical mycobacterial biofilm

Mycobacterial biofilms were cultivated in flow chambers of three channels with dimensions of 40 mm x 4 mm x 1 mm. The flow chamber was set up as previously described[244] and used Luria Broth medium at 37°C. 500µl diluted culture of *M. fortuitum* and *M. chelonae* of OD_{600nm} = 0.1 were inoculated into each flow cell chamber. The flow cells were inverted without flow for 2 hour after inoculation. After which, the flow cells were changed back to upright position and medium were fed into the flow cells using Watson Marlow 205s peristaltic pump at the flow rate of 7.7ml h⁻¹, incubated at 37°C for 10 days. Luria Broth was used. Syto-9 (Green Fluorescence) from LIVE/DEAD BacLight kit were added into each channel and viewed with Zeiss LSM780 Confocal Laser Scanning Microscope, CLSM (Carl Zeiss, Jena, Germany) at (Excitation: 488nm, Emission 535nm). Confocal Laser Scanning Microscopy images were taken at day3, day5, day7 and day10 post experiment.

2.2.5 Establishment of 8 well chamber slide model for atypical mycobacterial biofilm **(High through-put screening)**

Mycobacterial cells are cultivated in µ-Slide 8 well glass bottom (*ibdi*) for high through put biofilm analysis to screen potential antimicrobials. The mid-log growth cultures were made OD₆₀₀ in Luria Broth Medium prior to inoculations. 200 µl of the dilutions was put into the each well of an 8-well chamber slide and incubate at 37°C for 5 days. Fresh pre-warmed medium was put along the wall of chamber without disrupting the biofilm every 24 hours time interval[245]. At each different time point, aspirate the medium from the well and wash resident biofilm twice gently with sterile PBS. Syto-9 (Green Fluorescence) from LIVE/DEAD BacLight kit was added into each well and viewed with Zeiss LSM780 Confocal

Laser Scanning Microscope, CLSM (Carl Zeiss, Jena, Germany) at (Excitation: 488nm, Emission 535nm). The images were taken at day1, day3 and day5 post experiment.

2.2.6 Synthesis of AM-228

α -Mangostin (500 mg, 1.22 mmol) was dissolved in 10 mL of acetone. Potassium carbonate (7.5 equiv) and 1,4-diiodobutane (15.0 equiv) were added. The reaction mixture was refluxed for 24 h. After the reaction was complete, the solvent was removed under reduced pressure. The oil residue was diluted with EtOAc and washed twice with saturated brine and once with water. The organic phase was dried over anhydrous Na_2SO_4 , then purified via silica gel column chromatography (petroleum ether/EtOAc, 15/1, v/v) to obtain intermediate **AM-227**. Afterward, diethylamine (4 mL) was added to a solution of **AM-227** (100 mg, 0.11 mmol) in DMSO (4 mL). The mixture was stirred at room temperature for 4 h. After completion of the reaction, the mixture was diluted with 50 mL of ethyl acetate, then washed with aqueous NaHCO_3 and saturated brine (each three times). The organic phase was dried over anhydrous Na_2SO_4 and concentrated under vacuum. **AM-228** was achieved by purifying the residual crude oil in silica gel column chromatography (EtOAc/MeOH/ Et_3N , 100/2/1, v/v).

2.2.7 Hemolytic activity of AM-228

Hemolytic assay with fresh rabbit red blood cells (RBCs) was performed for the compound. The study was done under supervision of Singhealth IACUC and according to the Association for the Research in Vision and Ophthalmology (ARVO). Freshly isolated rabbit red blood cells were centrifuged at 3,000 rpm for 10 min and thoroughly washed with sterile PBS for two times to get the serum. The compound was mixed with RBCs for desired concentration

(final v/v of RBCs=45) and incubated at 37°C for 1 hour in a 96-well plate (SPL life science). 100 µL of supernatant was transferred for measuring absorbance (576 nm) with a TECAN infinite 200-microplate reader. Triton X-100 (2%) was set up as a positive control and PBS and DMSO (1%) were used as a negative control. This equation had been used to calculate the percentage of hemolysis.

$$\% \text{ of haemolysis} = \frac{(\text{mixture abs } 576\text{nm} - \text{negative control abs } 576\text{nm})}{(\text{positive control abs } 576\text{nm} - \text{negative control abs } 576\text{nm})} [239]$$

2.2.8 Determination of antimicrobial activity

Susceptibility testing of all compounds was performed in Luria Broth (LB) using broth micro-dilution in accord to the CLSI guidelines with minor modifications[246]. Minimum inhibitory concentrations (MIC) were determined by broth micro dilution using Luria Broth (LB). Briefly, AM-228 was dissolved in N-N-dimethylformamide (DMF) to make 1,000 µg/mL stock solutions. Thereafter, Luria Broth (LB) was used to prepare serial twofold dilutions of the compounds in the wells. The cultured suspensions were prepared in sterile PBS to a density of 0.5 Mac Farland standard (OD₆₀₀=0.1). One hundred microlitres of this culture suspension was transferred into 15 millilitres of Luria Broth to make approximately 10⁶ CFU/mL. 100 µl of the bacterial suspension in Luria Broth was transferred to each well of the compounds. After inoculation, each well contained approximately 5 × 10⁵ CFU/mL. The dilutions were tested in duplicate. Bacteria were incubated with the compounds for 5 days at 35 °C prior to reading with Infinite M200 microplate reader (Tecan Group Ltd, Switzerland). The MIC was accessed by both measuring OD₆₀₀ and visible growth[228, 247, 248].

2.2.9 Time-kill kinetics

The culture was suspended and adjusted in LB Broth to obtain the bacterial suspension with 10^5 to 10^6 CFU/ml. Then, the inoculum was treated with various concentrations of Gatifloxacin and AM-228. The mixtures were incubated at 35°C. Culture aliquots were removed at 6hr, 1 Day, 2 Day, 3 Day, 4 Day and 5 Day for viable plate counts. The aliquots were 10-fold serially diluted and plated on LB agar plates. The plates were incubated at 35 °C for 3-5 days. Enumerating the colonies grown on the plates accessed cell viability. Bactericidal activity was defined as 3-log reduction of viable count in culture treated with antimicrobial compared with the untreated control at different time point.

2.2.10 Synergy experiment by Checkerboard method

The synergy experiment was carried out between the commercial antibiotics particularly between Amikacin and different Fluoroquinolones. All the commercial available antibiotics stock solutions were dissolved in sterile water. Two fold dilutions of each drug to double the MIC was prepared in Luria broth with accordance to CLSI recommendations[246]. 50 µl of drug 1 dissolved in Luria Broth was distributed along the ordinates and 50 µl of drug 2 in Luria Broth was dispensed along the abscissa. Bacteria suspension was made in Luria Broth containing 0.05% Tween 80 to get the final cell density of approximately 10^6 CFU/ml and 100 µl of the bacterial suspension was mixed with the combinations of two drugs. The plates were incubated at 35°C for 5 days and the optical density at 600 nm (OD_{600}) was used to determine the bacterial growth. Fractional inhibitory concentration index (FIC) was calculated by the following formula.

$$\Sigma FIC = FIC A + FIC B,$$

where FIC A is the MIC of drug A in the combination/MIC of drug A alone, and

FIC B is the MIC of drug B in the combination/MIC of drug B alone.

The combination is reflected synergistic if the Σ FIC is ≤ 0.5 , indifferent if the Σ FIC is > 0.5 to < 2 , and antagonistic if the Σ FIC is ≥ 2 [249].

2.2.11 Exogenous Extracellular DNA and biofilm formation

Effect of exogenous extracellular DNA and biofilm formation was investigated. In brief, eDNA from salmon testes (D1626, Sigma) was cut into the small fibers, sonicated at 37 freq, 50 power (a minute each) for several times in order to get a less viscous solution. It was then put in a heat block at 100°C for 15 minutes. *M. fortuitum* and *M. chelonae* were grown in 8 well chamber slide model as described earlier. In short, bacteria were grown in a μ -Slide 8 well glass bottom (ibidi, Germany) in Luria Broth medium with starting inoculum size, $OD_{600}=0.1$. The 8 well chamber slide was incubated at 35°C for 5 days. Fresh medium was replaced every 24 hours without disturbing biofilm while at day 2-post experiment; the medium was replaced with the medium containing eDNA 50 μ g/ml. At the end of experiment, which is day 5 after the experiment, medium was removed from the well. Luria Broth containing Syto-9 (Green Fluorescence) from LIVE/DEAD BacLight kit (L-7007, Molecular Probes) was added into each well, viewed with Zeiss LSM780 Confocal Laser Scanning Microscope, (Carl Zeiss, Jena, Germany) at (Excitation: 480nm, Emission 500nm). Confocal images were analyzed using IMARIS™ 7.6 (Bitplane AG) to obtain the total biovolume of the cells in exogenous DNA added wells and control wells. Surface mode was used to reconstruct the 3D biofilm images with the aid of IMARIS™ 7.6 (Bitplane AG). Respective surface was created for Syto-9 (green fluorescence) channel to achieve the biovolume [250, 251]. The average of the total biovolume was exported and used for further analysis. Non-parametric test Mann-Whitney U test was applied using PASW statistisc 18. P values (≤ 0.05) were taken as statistically significant

2.2.12 Evolution of resistance to AM-228 or Gatifloxacin

Multi-passage resistance studies have been carried out using *M. fortuitum* and *M. chelonae* with AM-228 or Gatifloxacin. Dilution series of eight concentrations of each drug was prepared. The progressive increase in the MIC of the bacteria over the passages determined the resistance of the strains against AM-228 or Gatifloxacin. The incubation time is 5 days at 35°C. Bacteria growth in 0.5X MIC of either Gatifloxacin or AM-228 was passaged again for the next passage. The total numbers of passages of each antibiotic for *M. fortuitum* is 12 and *M. chelonae* is 11. The resistance was defined as an increase of 4 times against the initial MIC[252].

2.2.13 Biofilm Treatment with AM-228 and antibiotics)

M. fortuitum and *M. chelonae* were grown in an 8 well chamber slide as detailed above. The optimal DNase concentration that led to a significant reduction of biomass was determined by serial two-fold dilutions of DNase1 RQ1 RNase-Free DNase (M6101, Promega) using Luria Broth. To evaluate the effects of antibiotics alone and in combination with DNase on NTM biofilm, AM-228 and commercially available antibiotics were tested individually at 10 X MIC or combination with DNase at its optimal concentrations. To determine DNase action in synergistic antibiotics, cocktail of synergistic antibiotics at 10xMIC as well combination with DNase at an optimal concentration were diluted in LB. All the above respective compounds were added to day 4 mycobacterial biofilms. The medium was untouched in the control well and 24 hour treatment of each compound was carried out.

2.2.13.1 For live measurement of biovolume

At the end of the experiment, the medium was withdrawn from the wells and replaced with Luria Broth containing Syto-9 (Green Fluorescence) and 20 μ M Propidium Iodide (PI) from LIVE/DEAD BacLight kit (Molecular Probes). Images for the stained biofilms were taken under CLSM using argon laser (480nm, emission 500nm) and helium laser (490nm, emission 635nm) respectively. Confocal images were analyzed using IMARIS™ 7.6 (Bitplane AG) to obtain the Live/Dead cell ratio of the cells in antibiotic treated wells and Live Biovolume in the eDNA added wells. Surface mode was used to reconstruct the 3D biofilm images with the aid of IMARIS™ 7.6 (Bitplane AG). Respective surface was created for Syto-9 (green fluorescence) and Propidium Iodide (red fluorescence) channels to achieve the biovolume[250, 251]. The average of the total biovolume was exported and used for further analysis. Non-parametric test Mann-Whitney U test was applied using PASW statistic 18. P values (≤ 0.05) were taken as statistically significant.

2.2.13.2 For Colony forming units (CFU) measurement

The medium was aspirated at the end of experiment and sterile PBS was used to wash the wells thoroughly 2 times. Sterile 3 mm glass beads were utilized to disperse the biofilm mass. The aliquots were serially 10-fold diluted, plated on LB agar and incubated at 35 °C for 3-5 days. Bacterial viability was achieved by enumerating colonies growing on the plates[250]. Non-parametric test, Mann-Whitney U test was employed by using PASW statistic 18. P values (≤ 0.05) were taken as statistically significant.

2.2.14 Preparation of AM-228, Gatifloxacin, Amikacin, Besifloxacin and DNase for animal study

Gatifloxacin, Amikacin, Besifloxacin, AM-228 and DNase were dissolved in PBS for desired concentrations, which is 5 mg/ml for Amikacin, 6 mg/ml for Besifloxacin and 3mg/ml for the rest to be used for animal testing.

2.2.15 Chemical toxicity testing on Rabbit corneal wound healing model

Nine New Zealand Rabbits (3-4 months old, 2-3 kg) were purchased from the National University of Singapore. All animal experiments were conducted in compliance with the ARVO statement for the Use of Animals in Ophthalmic and Vision Research and the guide for the Care and Use of Laboratory Animals (National Research Council) and under the supervision of the SingHealth Experimental Medical Centre (SEMC). Ethics approval was obtained from SingHealth IACUC. Six New Zealand White rabbits were chosen randomly into three groups, control treated with PBS, group treated with DNase 3 mg/ml and group treated with AM-228 3 mg/ml. Rabbits were anesthetized and corneas received xylocaine 1%. A corneal wound was made by using a 5-mm trephine and mechanical removal of epithelial cells was carried out by sterile mini blade (BD-Beaver) leaving the basal lamina intact[248]. Topical application of the respective drug was made 3 times/day. Cornea wound was visualized every day until closure by the aid of cobalt-blue filter equipped slit lamp biomicroscopy, staining with Minims fluorescein sodium eye drops which was routinely used in ophthalmic clinic to check cornea damage. Fluorescein stained images were analyzed for wound area by Image-J 1.44o. The Mann-Whitney U Test was employed to determine difference in re-epithelialization existed among the different groups by using PASW statistic 18. A probability value of $p \leq 0.05$ was considered statistically significant.

2.2.16 *Mycobacterial keratitis mouse model*

The animals were immunosuppressed by standard systemic immunosuppression with minor modifications used for rodents[253]. In brief, animals were immunosuppressed by cyclophosphamide (sigma) 250 mg/kg intra-peritoneally and cortisone acetate (sigma) 250 mg/kg subcutaneously at day 2 before infection experiment. In order to promote local immunosuppression, Dexamethasone 0.1% (Alcon) eye drops were given 3 times/day for 10 days prior to infection. All the mice had been screened through slit-lamp examination before infection procedure in order to get good clarity cornea and free from infection. Three corneal scratches, each 1 mm long, had made on right eye of the animal which did not penetrate beyond the superficial stroma with a sterile mini blade (BD-Beaver) with the aid of the dissecting microscope while the other eye remain untouched[237, 254]. The bacterial concentration of 12×10^8 CFU/ml was used for the animal study. The scratched eye received 10 μ l of prepared bacterial suspension.

2.2.17 *Slit-lamp microscopy imaging for disease progression*

Slit-lamp microscopy imaging had been taken for the infected animal by using slit lamp biomicroscopy (New-generation Zoom clinical Slit Lamp, NS-2D, Righton) for all the groups at before treatment (day3 post infection) and after treatment (day7 post infection).

2.2.18 *Confocal Laser Scanning Microscopy imaging for infected cornea*

Infected mouse corneas from the respective group were excised with the aid of dissecting microscopes at before treatment (day3 post infection) and after treatment (day7 post infection). The cornea was flattened by small cuts at the four edges for the confocal imaging. Sterile PBS containing Syto-9 (Green Fluorescence) and 20 μ M Propidium Iodide (PI) from LIVE/DEAD BacLight kit (Molecular Probes) was used to stain the cornea. Stained corneas

were observed under CLSM using argon laser (480nm, emission 500nm) and helium laser (490nm, emission 635nm) respectively.

2.2.19 AM-228, Gatifloxacin, Amikacin, Besifloxacin and combination with DNase in In-vivo efficacy study

All the treatments started at day 3 post infection. Four animals (n=4) were used for each group. All the respective drugs were given 3 times/day for 4 days. At day4 post treatment, the corneas were dissected, homogenized in sterile 0.9% NaCl containing 0.25% BSA[242, 243] serially diluted, plated in duplicates on Middle Brook Agar supplemented with OADC enrichment media. The plates were incubated at 35 °C for 5 days. Counting individual colonies from various dilutions at the end of incubation and multiplying with the dilution factors was carried out. Results are reported as log₁₀ number of CFU/cornea[237]. Data were analyzed by non-parametric test (Mac-Whitney U test) and P value ($p \leq 0.05$) was considered as statistically significant.

Chapter 3

***Pseudomonas aeruginosa* part of results**

Chapter 3.1

***P. aeruginosa* biofilm formation on mouse**

keratitis model

3.1.1 *cdrA* gene expression on mouse cornea of murine keratitis model

PAO1/*p_{cdrA}-gfp* was used as a reporter strain for the presence of intracellular c-di-GMP[234]. We examined the kinetic of *P. aeruginosa*'s c-di-GMP level during corneal infections by using a *P. aeruginosa* PAO1 strain carrying the *p_{cdrA}-gfp* c-di-GMP reporter fusion to establish infections[234]. The *cdrA* gene encodes a large extracellular matrix adhesion, and its expression is up-regulated in the presence of high intracellular c-di-GMP content[87]. Planktonic PAO1/*p_{cdrA}-gfp* cells showed an extremely low expression level of the *p_{cdrA}-gfp* fusion (below the detection threshold) compared to a planktonic PAO1 control cells tagged by the *p_{lac}-gfp* (Figure 3.1.1A and 3.1.1B), implying that the level of intracellular c-di-GMP content is low. This result correlates well with the previous study showing that expression of the *p_{cdrA}-gfp* fusion can only be detected in the planktonic *P. aeruginosa* cells with high intracellular c-di-GMP content such as the $\Delta wspF$ mutant[89, 234]. A *p_{lac}-gfp* tagged PAO1 strain showed a clear biofilm-like aggregation morphology 8 hour-post-infection (8 hpi) (Figure 3.1.1C). To capture the transition stage of *p_{cdrA}-gfp* expression, we monitored the expression of the *p_{cdrA}-gfp* fusion in the PAO1/*p_{cdrA}-gfp* strain after 2 hpi, 4 hpi and 8 hpi, and found that around half of the PAO1/*p_{cdrA}-gfp* cells had induced *gfp* expression after 2 hpi (Figure 3.1.1D), suggesting that c-di-GMP synthesis in *P. aeruginosa* might be induced shortly after establishment of corneal infections. After 4 hpi, only *gfp*-expressing cells were visualized in the PAO1/*p_{cdrA}-gfp* infected corneas (Figure 3.1.1E), suggesting that the host immune system might eradicate the bacteria expressing low c-di-GMP level due to their low fitness. After 8 hpi, small biofilm-like aggregations were visualized in the PAO1/*p_{cdrA}-gfp* infected corneas with bright *gfp* fluorescent signal (Figure 3.1.1F). The expression of the *p_{cdrA}-gfp* fusion was maintained at a high level in mouse cornea samples after 2 dpi and 4 dpi, suggesting a constitutively increased *P. aeruginosa*'s c-di-GMP level through the corneal

infection progression (Figure 3.1.1G and 3.1.1H). Interestingly, the expression of the *p_{cdrA}-gfp* fusion was reduced in PAO1 cells after 7 dpi (Figure 3.1.1I). No background *gfp* fluorescence could be detected in the control scratched mouse corneas (Appendix 1C). Confocal images from individual channel has been attached at Appendix 2, showing the single channel image from mouse cornea infected with PAO1/*p_{cdrA}-gfp* 2 hour, 4 hour, 8 hour post infection and PAO1/*p_{lac}-gfp* 8 hour post infection. The induction of c-di-GMP signaling in PAO1 cells during the corneal infection strongly suggests that the corneal infection caused by *P. aeruginosa* is a biofilm-associated infection. Hence, this first indication suggests that *P. aeruginosa* biofilm can be formed on the mouse cornea.

Figure 3.1.1 Induction of the *p_{cdrA}-gfp* (c-di-GMP reporter fusion) in the progress of mouse corneal infection. A: confocal image of planktonic PAO1/*p_{lac}-gfp* cells; B: confocal image of

planktonic PAO1/*p_{cdrA}-gfp* cells; C: confocal image of PAO1/*p_{lac}-gfp* infected mouse cornea 8 hour post infection D-H: confocal images of PAO1/*p_{cdrA}-gfp* infected mouse corneas (D) 2 hour post infection, (E) 4 hour post infection, (F) 8 hour post infection, (G) 2 day post infection, (H) 4 day post infection and (I) 7 day post infection. Green fluorescence represents expression of the *p_{cdrA}-gfp* fusion. The red fluorescence represents the staining of all cells by Syto-62. Representative images are shown for each condition. Scale bars, 10 μ m. (This image is equally contributed by Yam Kuok Hoong Joey, PhD student, SCELSE)

3.1.2 Pyoverdine gene expression on mouse cornea of murine keratitis model

Another biomarker for PAO1 biofilms, *p_{pvdA}-gfp* was used to observe the presence of biofilms. PAO1/*p_{pvdA}-gfp* is the reporter for the expression of pyoverdine in *P. aeruginosa*. Pyoverdine, a siderophore, plays an important role in the development of biofilm and virulence factors[255]. Similar to PAO1/*p_{cdrA}-gfp* infection, PAO1/*p_{pvdA}-gfp* showed bright GFP fluorescence on 2 dpi (Figure 3.1.2.1C) and 4 dpi (Figure 3.1.2.1D) on mouse cornea whereas planktonic PAO1/*p_{pvdA}-gfp* showed little expression of green fluorescence (Figure 3.1.2.1A). Other than transcriptional observation of pyoverdine, phenotypic observation was also carried out. Pyoverdine fluorescence in PAO1 wild type was observed under CLSM. Pyoverdine was highly expressed in 2 dpi (Figure 3.1.2.2C) and 4 dpi (Figure 3.1.2.2D) on the mouse cornea as depicted by the blue fluorescence whereas low pyoverdine expression was observed in planktonic cells (Figure 3.1.2.2A and 3.1.2.2B). Hence, the results from both reporter strains suggested the presence of *P. aeruginosa* biofilm in the mouse cornea.

Figure 3.1.2.1 PAO1/*p_{vdA}-gfp* infection on mouse cornea. A) Confocal image of planktonic cells .B) Bright-field image of planktonic cells. C) Confocal image of 2 dpi. D) Confocal image of 4 dpi. Green fluorescence represents the expression of *pvdA*. Scale bar, 10 μ m.

Figure 3.1.2.2 PAO1 infection on mouse cornea. A) Confocal image of planktonic cells. B) Bright-field image of planktonic cells. C) Confocal image of 2 dpi. D) Confocal image of 4 dpi. The blue fluorescence represents presence of pyoverdine, which has an excitation wavelength of 405 nm and emission wavelength of 450 nm. Scale bar, 10 μ m

3.1.3 Discussion

Current investigations on the mechanisms of how *P. aeruginosa* causes microbial keratitis revealed that an elevated immune response of the C57BL/6 mice likely contributes to corneal destruction and perforation[138]. In addition, microbial keratitis is associated with the production and secretion of *P. aeruginosa* virulence factors that are required for the establishment of the corneal infections[256, 257]. It has also been recently suggested that the formation of a biofilm by *P. aeruginosa* biofilms is an important contributor to the etiology of microbial keratitis[258, 259] and this might explain the failure of the host immune system to clear the infecting pathogen. In support of this hypothesis, a recent study has provided the first evidence for the existence of biofilm-like structures of *P. aeruginosa* cells in the mouse corneal infection.

Here, we monitored the P_{cdrA} -*gfp* (c-di-GMP reporter fusion) expression patterns on the *P. aeruginosa* mouse keratitis model and showed that the c-di-GMP signaling was evoked during the course of establishing mouse corneal infections (Figure 3.1.1). We observed that a large amount of pyoverdine is produced by *P. aeruginosa* in the mouse keratitis model (Figure 3.1.2.1). Pyoverdine can disrupt the iron homeostasis of host cells and is also involved in the regulation of other virulence factors such as the *PrpL* protease and rhamnolipids[260-262].

Chapter 3.2

**C-di-GMP induction leads to
establishment of microcolonies and
modulates the innate immune response
during *P. aeruginosa* corneal infections**

3.2.1 Phagocyte tolerant microcolonies formation of *P. aeruginosa* on infected cornea

P. aeruginosa corneal infection is well known to lead to neutrophil recruitment[263]. However, these recruited neutrophils are unable to eradicate *P. aeruginosa* during corneal infection and this is likely due to the high level of tolerance towards the phagocytic cells from the host immune system of *P. aeruginosa* biofilms. Both *in vitro* and *in vivo* experiments provide evidence that the host phagocytic cells could not penetrate into the biofilms formed by *P. aeruginosa*[264, 265]. To visualize the interaction between the host immune cells and biofilms formed by *P. aeruginosa*, the LysoTracker[®] Red DND-99 stain (Molecular Probes, USA) was used to stain for the immune cells in C57BL6 mouse corneas infected by the *P. aeruginosa* PAO1/*p_{cdrA}-gfp* strain. LysoTracker[®] Red DND-99 is able to stain the acidic lysosomes of host immune cells such as macrophages and neutrophils. We noticed that a large number of host immune cells were recruited towards the biofilm-like microcolonies formed by the *P. aeruginosa* PAO1/*p_{cdrA}-gfp* strain at 1, 2, 4 and 7 dpi, but were unable to penetrate into those microcolonies (Figure 3.2.1A-D). This observation is very similar to the *P. aeruginosa* infection sites at the lungs of cystic fibrosis patients[266], where the formation of *P. aeruginosa* biofilms is believed to be the main cause of persistent infections and destruction of lungs.

Figure 3.2.1 Distribution of phagocytes among the PAO1/ p_{cdrA} - gfp infected mouse corneas after 1 dpi (A), 2 dpi (B), 4 dpi (C) and 7 dpi (D). Green fluorescence represents expression of the p_{cdrA} - gfp fusion. The red fluorescence represents the staining of lysosomes of phagocytes including polymorphonuclear leukocytes by LysoTracker® Red DND-99. Representative confocal images are shown for each condition. Scale bars, 10 μ m.

3.2.2 Colonization patterns of different c-di-GMP regulated strains on mouse cornea

Neutrophil recruitment following *P. aeruginosa* corneal infection is well documented[263]. Since the c-di-GMP reporter fusion p_{cdrA} - gfp assay suggest that c-di-GMP synthesis is induced during *P. aeruginosa* ocular infections, we hypothesized that high c-di-GMP level is required for *P. aeruginosa* colonization in *in vivo*. Therefore, we monitored the colonization patterns of p_{lac} - gfp -tagged *P. aeruginosa* PAO1, the $\Delta wspF$ mutant (with high c-di-GMP content) and the PAO1/ p_{lac} - $yhjH$ mutant (with c-di-GMP depleted) at 2 dpi and 7 dpi of corneal infections. To visualize the interaction between the host immune cells and *P. aeruginosa* biofilms, the

LysoTracker[®] Red DND-99 stain (Molecular Probes, USA) was used to identify immune cells in C57BL6 mouse corneas infected by *P. aeruginosa*. LysoTracker[®] Red DND-99 stains the acidic lysosomes of host immune cells such as macrophages and neutrophils. Alexa Fluor[®] 635 phalloidin was also used to stain the F-actin of the eukaryotic cells. As expected, the *P. aeruginosa* PAO1 and the $\Delta wspF$ mutant formed large and densely packed microcolonies at the infection sites, surrounded by phagocytes after 2 dpi (Figure 3.2.2A, B) and 7 dpi (Figure 3.2.2D, E). The PAO1/ p_{lac} -*yhjH* strain formed irregular smaller cell aggregates at the infection sites at 2 dpi, with phagocytes penetrating into *P. aeruginosa* aggregates (Figure 3.2.2C). As a consequence of phagocyte penetration, there were very few PAO1/ p_{lac} -*yhjH* cells remaining after 2 dpi compared to corneas infected by PAO1 and $\Delta wspF$ (Figure 3.2.2A, B). A large number of phagocytes accumulated at the PAO1/ p_{lac} -*yhjH* infection sites at 7 dpi with very few PAO1/ p_{lac} -*yhjH* cells visible and viable (Figure 3.2.2F).

Figure 3.2.2 Colonization patterns of the PAO1-*gfp*, $\Delta wspF$ -*gfp* and PAO1/*p_{lac}-yhjH-gfp* infected mouse corneas after 2 dpi (A,B,C) and 7 dpi (D,E,F). Green fluorescence represents expression of bacteria colony formation. The red fluorescence represents the staining of lysosomes of phagocytes including polymorphonuclear leukocytes by LysoTracker[®] Red DND-99. The yellow fluorescence represents the staining of Eukaryotic cells by F-actin. Representative confocal images are shown for each condition. Scale bars, 20 μ m.

3.2.3 Clinical Disease response to different c-di-GMP regulated *P. aeruginosa* strains

In order to further prove this, we used slit lamp microscopy to monitor the cornea responses to different c-di-GMP releasing strains. We observed that there was presence of corneal inflammation and cloudiness in the mouse eyes infected with either strain on 2 dpi (Figure 3.2.3). However, there was clearness of central cornea and less inflammation in mouse infected with PAO1/*p_{lac}-yhjH* compared to others (Figure 3.2.3).

Figure 3.2.3 Slit Lamp microscopy images of mouse eyes infected with different c-di-GMP mutant strains. Corneal edema and inflammation are present at eyes infected with either strain on 2dpi while there is presence of less inflammation and central cornea clearness in eyes infected with PAO1/p_{lac}-*yhjH* compared with other strains infected eyes. (Magnification- 40X)

3.2.4 C-di-GMP induction of *P. aeruginosa* modulates the host immune response

Biofilm formation is proposed to shift bacterial infections from the acute phase to the chronic phase since biofilm cells can evade host immune attack and produce less acute virulence factors compared to planktonic cells[267-269]. To examine the host responses of mouse cornea towards *P. aeruginosa* infection, we examined the host-associated RNA reads of the dual RNA-seq dataset to perform a comparative transcriptomic analysis of the mouse corneas at 2 dpi and 7 dpi infected by the *P. aeruginosa* PAO1, $\Delta wspF$ and PAO1/p_{lac}-*yhjH* mutants. Between 25,457,626 and 32,332,158 reads were mapped to the mouse genome (Appendix 3).

Projection of the host transcriptomes by principal component analysis (PCA) revealed that *P. aeruginosa* infections affected the host gene expression in a time-dependent manner, where 8 out of 9 host transcriptomes after 2 dpi were grouped together, independent of the c-di-GMP content of the *P. aeruginosa* cells (Figure 3.2.4A). Interestingly, c-di-GMP was shown to affect host gene expression after 7 dpi, where the high intracellular c-di-GMP strain significantly affected PC1 genes (Figure 3.2.4A).

To further examine the role of c-di-GMP signaling in modulating the host immune responses, we compared the host transcriptomes after being infected by the two c-di-GMP ‘locked’ strains: $\Delta wspF$ and PAO1/p_{lac}-*yhjH*. We excluded the host transcriptome of the *P. aeruginosa* PAO1 infected corneas as there might be a fluctuation of c-di-GMP content of PAO1 during the infection (Figure 3.1.1I), which is due to the dynamic activities of different DGCs and PDEs.

We analyzed the data by using cut-off values, (P-value, 0.05) and (Fold-change, 5), 1385 host genes (Appendix 4) were up regulated and 507 host genes (Appendix 5) were down-regulated in corneal cells at 7 dpi compared to corneal cells at 2 dpi after infection caused by the $\Delta wspF$ mutant while not the PAO1/ $p_{lac-yhjH}$ mutant. Thus expression of these host genes is specifically associated with increased c-di-GMP content in *P. aeruginosa*, and analysis of these genes might reveal important mechanisms how high intracellular c-di-GMP containing clinic isolates (such as the small colony variant, SCV) are evolved during chronic infections.

Several well-known genes involved in the host immune response towards bacterial infections were down-regulated, including *il10* (encoding interleukin 10) by 21.4-fold, *il23a* (encoding interleukin 23, alpha subunit) by 20.4-fold, *tnf* (encoding tumor necrosis factor) by 18.4-fold, *Ifnlr1* (encoding interferon lambda receptor 1) by 9.8 fold, in the corneal cells at 7 dpi compared to the corneal cells at 2 dpi (Appendix 5) after being infected by the $\Delta wspF$ mutant while not the PAO1/ $p_{lac-yhjH}$ mutant. This suggests components of Th1 and Th2 mediated immune responses were down regulated at the late stage of corneal infection due to *P. aeruginosa*'s high c-di-GMP content.

To validate the transcriptomic analysis, the C57BL6 mouse corneas were infected with the *P. aeruginosa* $\Delta wspF$ mutant and the PAO1/ $p_{lac-yhjH}$ mutant. Infected mouse corneas were harvested at 2 dpi and 7 dpi to compare their cytokine levels. In accordance with the transcriptomic analysis, the production of cytokines Interleukin-10 (IL-10), Interferon-gamma (IFN- γ) and tumor necrosis factor- α (TNF- α) were all induced at 2 dpi for both *P. aeruginosa* strains (Figure 3.2.4B), and the production of these cytokines was reduced at 7 dpi in corneas infected by $\Delta wspF$ mutant (Figure 3.2.4B), while it remained at the same levels or was increased at 7 dpi in corneas infected by the PAO1/ $p_{lac-yhjH}$ strain (Figure 3.2.4B). The reduced cytokine levels in mouse corneas infected by the *P. aeruginosa* $\Delta wspF$ mutant at 7 dpi compared to 2 dpi corresponds well with the very few phagocytes associated with the

$\Delta wspF$ microcolonies at 7 dpi (Figure 3.2.2E). In contrast, the high cytokine levels in mouse corneas infected by the PAO1/*p_{lac}-yhjH* strain (*P. aeruginosa* c-di-GMP depleted strain) at 7 dpi compared to 2 dpi corresponds well with the large numbers of live phagocytes at the infection sites at 7 dpi (Figure 3.2.2F). Levels of the cytokine have been previously reported to peak at the early stages (1-3 d) of *P. aeruginosa* mouse corneal infections and reduce to baseline levels in the BALB/c mice and remain at lower levels in the C57BL/6 mice at the late stage of corneal infections (5-7 d)[107]. However, more frequent sampling of cytokines (5 dpi and 10 dpi) would be warranted for future studies since cytokines levels changed drastically within the first two days.

Figure 3.2.4 A. PCA of transcriptomes of mouse corneal cells from 2 dpi and 7 dpi caused by *P. aeruginosa* PAO1, $\Delta wsfF$ and PAO1/ $p_{lac-yhjH}$. Raw data of RNA-Seq were normalized using the

DESeq package before PCA analysis. Dotted line was used to indicate separation of transcriptomes of 2 dpi cells and 7 dpi cells by PCA analysis. **B. Production of cytokines of mouse corneal cells after 2 dpi and 7 dpi of infections caused by *P. aeruginosa* $\Delta wspF$ and PAO1/ p_{lac} -*yhjH* strains.** Black bars represent 2 dpi and gray bars represent 7 dpi. Means and s.d. from triplicate experiments are shown. * $P \leq 0.05$, ** $P \leq 0.01$, ANOVA test.

3.2.5 Discussion

Large biofilm-like aggregations were observed in the mouse corneas infected by *P. aeruginosa* PAO1 and the high c-di-GMP containing $\Delta wspF$ mutant (Figure 3.2.2). In contrast, the PAO1/ p_{lac} -*yhjH* strain (*P. aeruginosa* c-di-GMP depleted strain) was unable to form phagocyte tolerant microcolonies during corneal infections and was cleared at the late stage of infection (Figure 3.2.2). These results strongly suggest that *P. aeruginosa* is able to establish chronic corneal infection by inducing c-di-GMP and establishing phagocyte tolerant biofilms. Similar to our study, a recent report showed that c-di-GMP is also required for establish *in vivo* *P. aeruginosa* biofilms during the catheter-associated urinary tract infection[270].

C-di-GMP plays an essential role in establishment of the *P. aeruginosa* *in vitro* biofilms by increasing the production of *Pel*, *Psl* exopolysaccharides, *CdrA* adhesion, iron siderophore pyoverdine and decreasing bacterial motility[87, 271, 272]. These biofilm-associated properties are well known to confer resistance against the host immune system clearance. The production of the *Psl* polysaccharide and reduction of motility of *P. aeruginosa* is linked to a reduction in neutrophil opsonophagocytosis[273, 274]. In accordance with biofilm formation, we showed that phagocytic cells accumulated around the *P. aeruginosa* microcolonies, while being unable to penetrate into these microcolonies in the infected mouse corneas (Figure 3.2.1), which is similar to the *P. aeruginosa* microcolonies shown by Bjarnsholt et al. in the infected lung of cystic fibrosis patients[266]. Phagocytic cells that are recruited to the site of

infection are likely to cause severe damage through the host's inflammatory response[107]. While it is clear that elevated c-di-GMP concentrations and biofilm formation are important causative steps in microbial keratitis, it currently remains unclear what is triggering in the host-pathogen interaction that leads to induction of the c-di-GMP signaling pathway in *P. aeruginosa* in the mouse keratitis model.

Longitudinal investigation of the mouse corneal transcriptomes during the course of *P. aeruginosa* PAO1 infection revealed that several Th2 immune response genes were down regulated in the later stages of corneal infection (7 dpi) compared to early stage of corneal infection (2 dpi) in response to high c-di-GMP producing strain (Appendix 5). These Th2 mediated immune response cytokines and chemokines are responsible for the recruitment of polymorphonuclear neutrophils and the subsequent tissue damage during corneal infection[107]. Moreover, Th1 immune response cytokines (TNF- α and INF- γ) were downregulated by *P. aeruginosa* $\Delta wspF$ mutant at the late stage of corneal infection (7 dpi) compared to early stage of corneal infection (2 dpi) (Figure 3.2.4). This transcriptome study and cytokine study suggest that c-di-GMP is able to modulate the host immune system by less activation of Th1 and Th2 immune responses in the later infection stages which in turn result in failure of immune clearance and, thus, remain as a chronic corneal infection, leading to the progressive corneal damage.

Chapter 3.3

**Lowering the c-di-GMP content
intracellularly enhances *P. aeruginosa in
vitro* and *in vivo* biofilms susceptibility to
Colistin treatment**

3.3.1 Combination of SNP and Colistin is superior to monotherapy in killing in vitro

PAO1/*p_{lac}-gfp* biofilms

As metabolically active Colistin tolerant cells often emerge from Colistin-treated *P. aeruginosa* biofilms[275], combination of dispersal agent and Colistin was used to eradicate biofilms more effectively. Colistin-tolerant subpopulation was seen in 4 d old PAO1/*p_{lac}-gfp* biofilms after 24 h treatment with Colistin on day 3 (Figure 3.3.1C). PI staining and CLSM imaging showed that SNP single treatment was able to disperse but unable to kill PAO1 biofilms (Figure 3.3.1B). Single Colistin treatment was able to kill approximate 50% of the biofilm cells, leaving behind the tolerant subpopulations (Figure 3.3.1C). Combined treatment with SNP and Colistin significantly reduced the development of Colistin tolerant cells in PAO1 biofilms and was able to kill up to 80% of the cells (Figure 3.3.1D). The Live/Dead biovolume of each treatment is shown in figure 3.3.1E.

Figure 3.3.1 Antimicrobial treatments on PAO1/*p_{lac}-gfp* biofilm in continuous-culture flow cell system. A to D shows confocal images of PAO1-*gfp* after treatment with different antimicrobial compound: A) Control; B) 5 μ M SNP; C) 10 μ g ml⁻¹ Colistin; D) 5 μ M SNP and 10 μ g ml⁻¹ Colistin. Panel E depicts the biovolume of the live and dead cells after respective treatments (n = 3). ** represents (p < 0.01) significant difference.

3.3.2 Chemical Toxicity Test in vivo

The synergistic effect of SNP and Colistin treatment in killing *in vitro* PAO1/p_{lac}-gfp biofilms compared to controls suggest this to be a promising strategy to control the PAO1 infections in animal model. Prior to studying of the killing effect of the combined treatment in mouse keratitis model, chemical toxicity test was carried out for SNP and Colistin using rabbit corneal wound repair model. The wounds were created and treated with 50 µM of SNP and 2 mg ml⁻¹ of Colistin. Compared to the control group, wound treated with SNP or Colistin was able to heal completely on the third day (Figure 3.3.2). The statistical test revealed that there is no statistical significance (P>0.05) in all time points compared with control. These results indicated that both SNP and Colistin did not exert any toxic effect on the rabbit corneal, under the tested conditions. Hence, the feasibility of this treatment strategy was tested on *P. aeruginosa* keratitis mouse model.

Figure 3.3.2 Chemical toxicity test on rabbit corneal wound. A) Images of cornea viewed under cobalt-blue filter-equipped slit lamp biomicroscopy. Presence of fluorescein sodium, a green fluorescence stain, indicates the wound area. (Magnification- 40X) B) The percentage of wound closure. (n = 4).

3.3.3 Combination of SNP and Colistin is superior to monotherapy in eliminating PAO1/*p_{lac}* *gfp* infections in mouse keratitis model.

The feasibility of using SNP and Colistin combination treatment was carried out on *P. aeruginosa* keratitis mouse model. For chemically induced biofilm dispersal, PAO1/*p_{lac}*-*gfp*

was topically applied to the scratched mouse cornea. SNP single treatment had no effect on reducing the *P. aeruginosa* load on the cornea. Colistin single treatment caused a substantial reduction of log₁₀ CFU differences of 1.14, 2.68 and 2.37 on day 2, 3 and 4 respectively, comparing to the control of the *P. aeruginosa* load on the cornea (Figure 3.3.3). Combination of SNP and Colistin treatment had the best effects on reducing the *P. aeruginosa* load on the cornea, which is 2.67, 3.38 and 3.41 log₁₀ differences on day 2, 3 and 4 as compared to the control (Figure 3.3.3). One-way ANOVA and post-hoc analysis (Bonferoni test) were carried out. The data revealed that combination treatment was statistically significant in day 2, 3 and 4 ($P < 0.05$) as compared with Colistin single treatment. Combination treatment was statistically significant ($P < 0.05$) in all days compared with the control.

Figure 3.3.3 Slit-lamp microscopy images and quantification of viable PAO1/*p_{lac}-gfp* in mouse cornea over the period of 4 days. PAO1/*p_{lac}-gfp* was treated with control, SNP single treatment, Colistin single treatment or SNP and Colistin combination treatment. Combination Vs Colistin ($P <$

0.05, all time points) (Combination vs control ($P < 0.05$, all time points) ($P < 0.05$ was considered to be statistically significant) ($n=4$))

3.3.4 Discussion

Reports showed that the most common causal agent for bacterial keratitis was *P. aeruginosa* in contact lens associated keratitis, responsible for one-third of the overall cases[276, 277]. Ten-year review study showed that *P. aeruginosa* was standing the second most common ocular pathogen[278] and a study from Italy showed that the most common causal agent for keratitis was *P. aeruginosa*[279]. A study from Brazil reported that *P. aeruginosa* was the most common organism causing keratitis in elderly among gram-negative bacteria group[280]. Moreover, from our earlier experiments of the biofilm formation of *P. aeruginosa* on murine cornea proposed the new threats of antibiotic resistance problems owing the resistance to antibiotics, easily emergence of mutant bacteria, and low penetration due to biofilm matrix secretion. Our group and other research groups have previously reported for the c-di-GMP signaling's ability to increase the *P. aeruginosa*'s resistance towards antimicrobials *in vitro*[281, 282]. Our results here showed that c-di-GMP enhance the development of Colistin-tolerant subpopulations of *in vitro P. aeruginosa* biofilms (Figure 3.3.1) and increase the resistance of *P. aeruginosa* to Colistin *in vivo* (Figure 3.3.3). We further demonstrated that application of the c-di-GMP reducing agents is able to repress the development of Colistin-tolerant subpopulations of *in vitro P. aeruginosa* biofilms (Figure 3.3.1) and enhance the killing efficiency of Colistin *in vivo* (Figure 3.3.3).

Chapter 4

Atypical Mycobacteria part of results

Chapter 4.1

**Extracellular DNA is important for
mycobacterial biofilm matrix maintenance**

4.1.1 Growth testing of *Mycobacterium fortuitum* ATCC 49404 and *Mycobacterium chelonae* ATCC 35752

Mycobacteria were tested in different media in order to choose a suitable medium for biofilm experiments. The experiments indicated that growth was the best in Middle Brook Medium followed by Tryptic Soy Broth and Luria Broth. However, we chose the Luria Broth because of the reasonable growth medium for both strains.

Figure 4.1.1.1 Growth testing of *M. fortuitum* in Luria Broth (LB), Tryptic Soy Broth (TSB), Middle Brook (MB) and Minimal 63.

Figure 4.1.1.2 Growth testing of *M. chelonae* in Luria Broth (LB), Tryptic Soy Broth (TSB), Middle Brook (MB) and Minimal 63.

4.1.2 Establishment of varying degree of biofilm architectures in dynamic flow cell model and 8-well chamber slide model

As biofilms play the important role in bacterial infections and the treatment regime will fail to resistant forming biofilm phenotypes. Thus, we carried out to develop an *in vitro* biofilm forming potential and architecture in dynamic flow cell model and 8 well chamber slide model. These two models revealed that *M. fortuitum* and *M. chelonae* formed thick biofilm in Luria-Broth. The findings revealed that *M. fortuitum* formed biofilm earlier (1 day)(Figure 4.1.2.1A) than *M. chelonae* (3 day)(Figure 4.1.2.2B). Finger-like projections from base of the structure were formed as early as day3 and the biofilm mass became larger and thicker as the days progress. Biofilm thickness was the highest at day 10 (100 μ m) and biofilm dispersal was observed (Figure 4.1.2.1D).

Figure 4.1.2.1 Confocal laser scanning images of *M. fortuitum* biofilm grown in continuous-culture flow cell system. A to D shows confocal images of *M. fortuitum* biofilm A) 3 day post incubation; B) 5 day post incubation; C) 7 day post incubation D) 10 day post incubation. Green color represents live biomass stained by Syto-9. Representative images are selected out from three replicate experiments. Scale Bar, 50 μm .

M. chelonae biofilm formation was seen starting day 5 as irregular short structures and small microcolonies (Figure 4.1.2.2B). Large diffuse microcolonies had been formed in day 7 (Figure 4.1.2.2C) and day 10 (Figure 4.1.2.2 D).

Figure 4.1.2.2 Confocal laser scanning images of *M. chelonae* biofilm grown in continuous-culture flow cell system. A to D shows confocal images of *M. chelonae* biofilm A) 3 day post incubation; B) 5 day post incubation; C) 7 day post incubation D) 10 day post incubation. Green color represents live biomass stained by Syto-9. Representative images are selected out from three replicate experiments. Scale Bar, 50 μ m.

In 8 well chamber slide model, *M. fortuitum* biofilm formed as Finger-like projections and irregular diffuse structures since day 1. Mature biofilm of irregular diffuse structures had been formed at day 5 (Figure 4.1.2.3).

Figure 4.1.2.3 Confocal laser scanning images of *M. fortuitum* biofilm grown in 8 well chambers slide model. A to D shows confocal images of *M. fortuitum* biofilm A) 1 day post incubation; B) 3 day post incubation; C) 5 day post incubation. Green color represents live biomass stained by Syto-9. Representative images are selected out from three replicate experiments. Scale Bar, 50 μm .

Cord-like structures and mature diffuse microcolonies have been formed at day 5 *M. chelonae* biofilm in 8-well chamber slide model (Figure 4.1.2.4).

Figure 4.1.2.4 Confocal laser scanning images of *M. chelonae* biofilm grown in 8 well chambers slide model. A to D shows confocal images of *M. chelonae* biofilm A) 1 day post incubation; B) 3 day post incubation; C) 5 day post incubation. Green color represents live biomass stained by Syto-9. Representative images are selected out from three replicate experiments. Scale Bar, 50 µm.

4.1.3 Exogenous extracellular DNA enhance biofilm mass in Mycobacterial biofilm

Biofilms are bacterial communities embedded within a secreted matrix of extracellular polymeric substance, EPS. Extracellular DNA played a major role in building biofilm matrix and involved as a major constituent and nutrient reservoir for biofilm matrix[62]. In our studies, exogenous input of extra cellular DNA enhanced biofilm mass compared with wild type non-supplemented biofilm (wild type *M. fortuitum* biofilm Vs exogenous DNA supplemented *M. fortuitum* biofilm, $P=0.009$), (wild type *M. chelonae* biofilm Vs exogenous DNA supplemented *M. chelonae* biofilm, $P=0.002$) (Figure 4.1.3). This results point out that *mycobacterium fortuitum* and *chelonae* could form biofilm easily on *in vivo* compared to their

in vitro growth since the extra cellular DNA could be easily achieved by bacterial cell death[60], formation of neutrophil extracellular traps (NETs) by other immune cells and neutrophils[63].

Figure 4.1.3 Exogenous DNA enhances Mycobacterial biofilm formation. Confocal images of (A) wild type *M. fortuitum* biofilm in normal medium (B) *M. fortuitum* biofilm grown in extracellular DNA Supplemented medium (C) wild type *M. chelonae* biofilm in normal medium (D) *M. chelonae* biofilms in extracellular DNA Supplemented medium. Histograms show the comparison of total biovolume between wild type and exogenous DNA supplemented biofilms. Mean and SD from triplicate experiments are shown. Scale Bar, 50 µm. Non-parameteric test (Mann-Whitney U test) was applied. (A Vs B, P=0.009) and (C Vs D, P=0.002) (*, P≤0.05 was set to be statistically significant).

4.1.4 DNase treatment leads to disruption of mycobacterial biofilm matrix assembly

Biofilms are mainly made up of extracellular polymeric substance, which contains protein,

polysaccharides, lipids and nucleic acids accounting for a barrier for antibiotics penetration[45, 283-287]. It was believed that extra-cellular DNA played an important role in antibiotic resistance and destruction of extracellular DNA increased the efficacy of antibiotic. However, the role of DNA involvement in atypical mycobacterial biofilm has not been well studied.

Firstly, we explored the optimal DNase concentration that could reduce the biomass. Biovolume was compared along different serial dilutions of DNase, employed by Non-parametric test (Kruskal-Wallis test) and post-hoc test (pair-wise comparison), PASW statistic 18. There is significance difference ($P \leq 0.05$) of groups (12.5, 25 and 50 $\mu\text{g/ml}$) of DNase compared against control in both strains (Figure 4.1.4).

Figure 4.1.4 Effect of DNase on mycobacterial biofilms. Comparisons of biovolume with different Dnase treatment on A) *M. fortuitum*; B) *M. chelonae* (n = 3). * represents ($p < 0.05$) significant

difference.

4.1.5 Discussion

NTM infections are complicated for its potential biofilm formation, which play as a vital role in eye infections[288]. NTM bacterial progress in a biofilm community is responsible for changing genetically and phenotypically because of their high hydrophobicity with increased resistance to antibiotic therapy as the result[289]. Mycobacteria can readily form biofilms and, because of their hydrophobicity and metal-resistance, is one of the earliest known biofilm formers[290]. In this study, we attempted to understand the different biofilm architectures for *M. chelonae* and *M. fortuitum*. *M. chelonae* and *M. fortuitum* formed thick biofilms with irregular shapes that could lead to antibiotic resistant problems (Chapter 4.1.2).

Biofilm is made up with the matrix that contains the exopolysaccharides (EPS). In addition to the expolysaccharides for the biofilm matrix's component, extracellular DNA is another critical factor found in the biofilm matrix. It was discovered in bacteria biofilms comprising of many gram-positive bacteria[154, 157, 158, 161, 177, 291] and gram-negative bacteria[61, 149-151, 245, 292]. eDNA has been discovered in *M. avium* biofilm for the first report[223]. The effect of treatment of DNase has been investigated in various gram-positive, gram-negative bacteria and *M. avium* biofilms. However, this is the first report showing the eDNA presence in *Mycobacteria fortuitum* and *chelonae* biofilms(Chapter 4.1.4). In contrast, we showed in our experiments that exogenous addition of DNA could lead to further enhancement of biofilm assembly (Chapter 4.1.3) and DNase disrupted the biofilm matrix maintenance, highlighting the essential role of eDNA in mycobacterial/ biofilm structural integrity (Chapter 4.1.4).

Chapter 4.2

Potential Novel anti-mycobacterial drug

4.2.1 Synthesis diagram of AM-228

Figure 4.2.1 General synthetic routes for AM-228. Reaction conditions: (a) $\text{I}(\text{CH}_2)_4\text{I}$, K_2CO_3 , acetone, reflux, 24 h, 62%; (b) diethylamine, DMSO, rt, 4 h, 34%

1,3,6-Tris(4-iodobutoxy)-7-methoxy-2,8-bis(3-methylbut-2-en-1-yl)-9H-xanthen-9-one (**AM227**) was prepared according to general procedure which was stated in Chapter 2.2.6 from α -mangostin (500 mg, 1.22 mmol) and 1,4-diiodobutane (2.41 mL, 18.3 mmol). **AM227** was obtained as a light yellow solid (723 mg) in 62% yield. ^1H NMR (400 MHz, CDCl_3) δ 13.48 (s, 1H, OH), 6.69 (s, 1H, Ar-H), 6.27 (s, 1H, Ar-H), 5.28 – 5.23 (m, 2H, 2 $\times$ CH), 4.19–4.01 (m, 8H, 4 $\times$ CH₂), 3.80 (s, 3H, OCH₃), 3.37–3.33 (m, 2H, CH₂), 3.32–3.22 (m, 6H, 3 $\times$ CH₂), 2.16–1.92 (m, 12H, 6 $\times$ CH₂), 1.85 (s, 3H, CH₃), 1.80 (s, 3H, CH₃), 1.69 (s, 6H, 2 $\times$ CH₃). ^{13}C NMR (101 MHz, CDCl_3) δ 181.89, 162.48, 159.80, 157.14, 155.14, 155.01, 143.97, 137.20, 131.64, 131.38, 123.23, 122.45, 112.00, 111.44, 103.88, 98.71, 89.15, 67.54 (2 $\times$ CH₂), 67.05, 60.88, 30.03 (2 $\times$ CH₂), 29.99 (2 $\times$ CH₂), 29.81 (2 $\times$ CH₂), 26.14, 25.87, 25.80, 21.41, 18.16, 17.87, 6.03 (2 $\times$ CH₂), 5.94. MS (APCI): calcd for $\text{C}_{36}\text{H}_{48}\text{I}_3\text{O}_6$ $[\text{M} + \text{H}]^+$ 957.1, found 957.0.

1,3,6-Tris(4-(diethylamino)butoxy)-7-methoxy-2,8-bis(3-methylbut-2-en-1-yl)-9H-xanthen-9-one (**AM228**) was prepared according to which was stated in Chapter 2.2.6 from **AM227** (100 mg, 0.11 mmol) and diethylamine (4 mL). **AM228** was obtained as a light yellow oil (28 mg) in 34% yield. ^1H NMR (400 MHz, CDCl_3) δ 6.99 (s, 1H, Ar-H), 6.87 (s, 1H, Ar-H), 5.26

(t, 1H, CH), 5.16 (t, 1H, CH), 4.28-4.17 (m, 4H, 2×CH₂), 4.13-4.07 (m, 2H, CH₂), 3.99-3.93 (m, 2H, CH₂), 3.80 (s, 3H, OCH₃), 3.46-3.38 (m, 4H, 2×CH₂), 3.30-3.18 (m, 16H, 8×CH₂), 2.15-1.92 (m, 12H, 6×CH₂), 1.84 (s, 3H, CH₃), 1.83 (s, 3H, CH₃), 1.69 (s, 3H, CH₃), 1.68 (s, 3H, CH₃), 1.38-1.27 (m, 18H, 9×CH₃). ¹³C NMR (101 MHz, MeOD) δ 178.51, 163.38, 158.21, 157.99, 155.95, 145.59, 137.74, 132.50, 132.03, 125.34, 124.21, 122.17, 115.23, 111.59, 100.16, 96.86, 75.19, 69.44, 69.21, 61.46, 53.67, 52.57, 52.52, 48.49 (2×CH₂), 48.19 (2×CH₂), 48.16 (2×CH₂), 28.71, 27.35, 27.18, 26.96, 26.08, 25.92, 23.57, 22.61, 22.12, 21.89, 18.41, 18.36, 9.14 (2×CH₃), 9.07 (4×CH₃). MS (ESI): calcd for C₄₈H₇₈N₃O₆ [M + H]⁺ 792.6, found 792.4.

The main side-product is AM016 which is two-arms functionalization. The screening and identification of AM228 was initially done via screening against Gram-positive bacteria. AM-228 has been screened and rationalized to choose as a promising compound for further investigation based on the below factors[239].

In general, an amphiphilic xanthone could be structural classified into four parts[293]:

A) Cationic moieties

B) Spacer length

C) Lipophilic chain

D) Tri-arm functionalization

In brief, the cationic moieties have to possess high pK_a so it could be protonated into cationic charge easier. From the screening, cyclic cationic moieties were found to possess higher toxicity issue. Therefore, the linear analogs such as diethylamine was selected. Spacer length screening further shows that n= 4 is the optimized length to exert antibacterial activity. Induction effect from the oxygen atom was found to reduce the cationic charge of the cationic moiety with a short spacer length compound. On the other hand, if n> 6, aggregation dominated and reduced the interaction of amphiphilic xanthenes with the bacteria. Isoprenyl

group (lipophilic chain) is important as an inner membrane probe to permeabilize bacterial cytoplasmic membrane

For the tri-arm functionalization, the 3rd hydroxyl group was further modified to diethylamine. In general, that tri-arm functionalization was found to improve the selectivity compared to their bi-functionalized analog.

4.2.2 Hemolytic activity and antimicrobial activity of AM-228

In clinical practice, the standard regimes for atypical mycobacterial infections contain combination of antibiotics for 2 to 3 months. However, slow response of therapy and poor drug penetration are important barriers for treating atypical mycobacterial infections. Therefore, there is urgent need of new antimicrobial, which can eradicate atypical mycobacterial infections. We successfully identified new antimicrobial, which was synthesized from nature mangosteen pericarp (Figure 4.2.1).

Firstly, AM-228 underwent hemolysis test for safety usage in clinical setting and antibacterial activity compare against commercially available antibiotics. The result showed that AM-228 had a good HC_{50} ($>200 \mu\text{g/ml}$) and outstanding antimicrobial activity (Table 4.2.2). The minimal inhibitory concentration of the AM-228 was $12.5 \mu\text{g/ml}$ for both strains comparable against other commercially available antibiotics (Table 4.2.2). Gatifloxacin, fourth generation fluoroquinolones, was found to be the most sensitive antibiotic against *M. fortuitum* and *M. chelonae*.

	Molecular weight (g/mol)	HC50
AM228	792.1	>200

Antimicrobial	Mycobacterium chelonae (ATCC 35752) MIC (µg/mL)	Mycobacterium fortuitum (ATCC 49404) MIC (µg/mL)
AM228	12.5	12.5
Gatifloxacin	0.195	0.195
Amikacin	25	3.125
Tobramycin	3.125	25
Levofloxacin	0.39	0.78

Table 4.2.2 HC50 of AM-228 and minimum inhibitory concentrations of AM-228 and commercially available antibiotics.

4.2.3 Fast killing kinetics of AM-228 towards Mycobacterial infections

Our time kill studies revealed that AM-228 showed the outstanding antimicrobial activity than the most sensitive commercially available antibiotic, Gatifloxacin. For *M. fortuitum*, 3 log reduction was seen at approximately post 72 hours treatment with 1xMIC AM-228 and reached sterile level at day 4. The solution was completely sterile at 72 hours post treatment with 2xMIC and 4xMIC. Gatifloxacin showed that 3-log reduction was formed at approximately post 48 hours with 1xMIC and 2xMIC, but did not reach sterile level until day 5. 4xMIC treatment reached sterile level after 72 hours treatment (Figure 4.2.3.1).

Figure 4.2.3.1 Time-kill curves of *M. fortuitum* against A) AM-228 and B) Gatifloxacin. MIC against *M. fortuitum*: AM-228=12.5µg/ml , Gatifloxacin=0.195µg/ml. The control is the culture without any antimicrobial treatment.

For *M. chelonae*, 3-log reduction was seen at approximately post 48 hours AM-228 treatment 2xMIC and 4xMIC. Gatifloxacin treatment revealed that 2xMIC and 4xMIC received 3 log reduction at 4 hours post treatment. However, there was bacterial regrowth seen in 1xMIC and 2xMIC of Gatifloxacin in day 5 after treatment (Figure 4.2.3.2).

Figure 4.2.3.2 Time-kill curves of *M. chelonae* against A) AM-228 and B) Gatifloxacin. MIC against *M. fortuitum*: AM-228=12.5µg/ml , Gatifloxacin=0.195µg/ml. The control is the culture without any antimicrobial treatment.

4.2.4 AM-228 did not evolve resistance against Mycobacterial infections in multi passage studies

The major limitation for successful treatment of atypical mycobacterial infection is the formation of resistant mutant. Therefore, we have carried out resistance evolution pattern of new antimicrobial, AM-228, against Gatifloxacin. We have noticed that Gatifloxacin showed 8 fold and 4-fold increase of their initial MIC values in *M. fortuitum* and *M. chelonae* respectively (Figure 4.2.4.1 and 4.2.4.2). However, *M. fortuitum* and *M. chelonae* did not form resistance towards AM-228 (Figure 4.2.4.1 and 4.2.4.2) since 4 fold increase of MIC is required to be termed as resistance[252].

Figure 4.2.4.1 Evolution of *M. fortuitum* resistance towards Gatifloxacin or AM-228. The ability of AM-228 and Gatifloxacin to avoid mutational resistance against *M. fortuitum* was evaluated using multipassage resistance selection studies. Resistance was defined as more than 4-fold increase in the original MIC.

Figure 4.2.4.2 Evolution of *M. chelonae* resistance towards Gatifloxacin or AM-228. The ability of AM-228 and Gatifloxacin to avoid mutational resistance against *M. chelonae* was evaluated using multipassage resistance selection studies. Resistance was defined as more than 4-fold increase in the original MIC.

4.2.5 Outstanding anti-biofilm properties of AM-228 comparable against Gatifloxacin in Mycobacterial biofilms

It is well known that biofilms are resistant to antibiotic and nearly all bacterial infections are related to biofilm. We investigated the resistance formation of mycobacterial biofilms to antimicrobials. It was found that mycobacterial biofilms were very resistant to antimicrobial whilst AM-228 performed better activity than Gatifloxacin in killing biofilms. AM-228 showed the outstanding activity in treating both *M. fortuitum* biofilm (AM-228 vs control) ($P=0.003$, biovolume) ($P=0.021$, CFU) and (gatifloxacin vs control) ($P=0.019$, biovolume) ($P=0.021$, CFU) (Figure 4.2.5.1) and *M. chelonae* biofilm (AM-228 vs control) ($P=0.004$, biovolume) ($P=0.021$, CFU) and (gatifloxacin vs control) ($P=0.005$, biovolume) ($P=0.021$, CFU) (Figure 4.2.5.2), comparable against the commercially available antibiotic, Gatifloxacin. ($P \leq 0.05$ was set to be statistically significant).

Figure 4.2.5.1 Anti biofilm effects of AM-228 and Gatifloxacin on *M. fortuitum* biofilm. Confocal images of (A) control *M. fortuitum* biofilm (day5) and *M. fortuitum* biofilm after treatment with (B) AM-228 or (C) gatifloxacin, at 10xMIC respectively. Green color represents live biomass whereas Red

is dead biomass. Histograms show comparison of Live/Dead ratio and viable bacteria (Colony Forming Units) of treatment effect on *M. fortuitum* biofilm. Scale Bar, 50 μ m. Means and SD from triplicate experiments are shown. Non-parametric tests, (Kruskal-Wallis test), (Man-whitney test) and post-hoc test (pair-wise comparison), were employed by using PASW statistic 18. (AM-228 vs control) (P=0.003,biovolume) (P=0.021, CFU) and (gatifloxacin vs control) (P=0.019,biovolume) (P=0.021, CFU). (*, **, $P \leq 0.05$ was considered to be statistically significant).

Figure 4.2.5.2 Anti biofilm effects of AM-228 and Gatifloxacin on *M. chelonae* biofilm. Confocal images of (A) control *M. chelonae* biofilm (day5) and *M. chelonae* biofilm after treatment with (B) AM-228 or (C) gatifloxacin, at 10xMIC respectively. Green color represents live biomass whereas Red is dead biomass. Histograms shows comparison of Live/Dead ratio and viable bacteria (Colony Forming Units) of treatment effect on *M. chelonae* biofilm. Scale Bar, 50 μ m. Means and SD from triplicate experiments are shown. Non-parametric tests, (Kruskal-Wallis test), (Man-whitney test) and post-hoc test (pair-wise comparison), were employed by using PASW statistic 18. (AM-228 vs control) (P=0.004,biovolume) (P=0.021, CFU) and (gatifloxacin vs control) (P=0.005,biovolume) (P=0.021, CFU). (*, **, $P \leq 0.05$ was set to be statistically significant).

4.2.6 Biocompatibility test for AM-228

The potential new antibiotic (AM-228) showed the promising new treatment option for mycobacterial infections in planktonic and biofilm models. Therefore, the *in vivo* biocompatibility of AM-228 was evaluated using rabbit corneal wound healing model. The results showed that there was no wound healing delay observed in the treatment groups compared with the control. Moreover, there was no toxicity signs and inflammation observed in the treated groups (Figure 4.2.6) The statistical test revealed that there is no statistical significance ($P>0.05$) in all time points compared with control.

Figure 4.2.6 Chemical toxicity testing of AM-228 on rabbit corneal wound healing model. Slit lamp images showed the normal wound healing pattern and rate compared with control. There were no signs of inflammation and toxic effects on rabbit corneas treated with AM-228. (Magnification- 12X) (n=3)

4.2.7 Discussion

Non-tuberculous mycobacteria (NTM), atypical mycobacteria, are non-motile, non-spore forming slender bacilli, aerobic, opportunistic free-living pathogens found in the environment including soil and water sources, food, dust, aerosols and animals[193, 294]. They have also been discovered in drinking water distribution systems and are relatively resistant to chlorine, organomercurials and other routine disinfectants[194, 195, 294]. Moreover, they possess the ability to form biofilms and survive under a wide range of temperature, pH, salinity, oxygen tension and low nutrient conditions[194, 196]. Diagnosis of mycobacterium requires considerable time due to its slow growth and may be misdiagnosed with other bacteria such as *Diphtheroids* or *Nocardia*[197].

The average time taken for the diagnoses of mycobacterial cases was around 4 months in post-surgical cases in South Florida[295]. Non-tuberculous mycobacteria infections in and around the eye are clinically recalcitrant to treatment, recur after cessation of therapy, and require long-term therapy (2 to 3 months) to eradicate infection[296, 297]. The treatment of NTM infections is also complicated because identification and determination of *in vitro* antibiotic sensitivities can be delayed for weeks. These factors and a low index of clinical suspicion, often result in inefficient treatment of NTM infections. Moreover, topical steroid usage prior to a correct diagnosis may worsen the prognosis[298]. Amikacin was an early treatment of choice, but this drug has been shown to have poor penetration through an intact corneal epithelium[299]. Another report showed that Amikacin was not effective in NTM infections of the eye[298]. Combination therapy, clarithromycin and amikacin, of 3 to 4 months duration have been used for treating NTM infections[296, 297]. Recent studies have suggested that the fluoroquinolones are useful for treating NTM infections[300]. Reports on NTM resistance to ciprofloxacin and gatifloxacin have been published[288, 289, 301]. Therefore, there is an urgent need of new antimicrobial targeting the NMT infections. Our data indicated that

gatifloxacin, a fourth generation fluoroquinolone, was currently the most effective antibiotic against NTM (Table 4.2.2). However, our new anti-microbial AM-228 showed outstanding bacterial killing efficiency in time kill studies, low potential for bacteria's resistance evolution and better eradication of mycobacterial biofilms comparable to Gatifloxacin (Chapter 4.2.3, 4.2.4, 4.2.5).

Chapter 4.3

Targeting eDNA can increase efficacy of antibiotics in mycobacterial biofilms

4.3.1 Combination of DNase and antibiotic is better than antibiotic alone in in vitro biofilm experiment

Biofilm architecture is formed, as a fibrous 3-dimensional network comprised of proteins, polysaccharides, lipids and nucleic acids that act as a barrier for the penetration of antibiotics[284, 302]. Extracellular DNA or eDNA has an important role in antibiotic resistance and the destruction of eDNA was found to increase the efficacy of antibiotics[286]. Moreover, the eDNA plays a major role in horizontal gene transfer in biofilm matrix creating an opportunity for fast transmission of virulence factors and antibiotic resistance genes from one bacterial genome to another bacterial genome[223]. The presence of eDNA in biofilm infections reduces the chemokine production, prevents the phagocytosis and conditions the innate immune response for the immune response difficult to eradicate the infections[187]. Therefore, the present study was designed to evaluate the role of eDNA in the treatment of NTM biofilm and a new treatment strategy i.e., combination of DNase and antibiotic. An optimal DNase concentration that could maximally reduce the biomass was found (Figure 4.1.4). The combination treatment (10xMIC AM-228 and optimal DNase concentration) or (10xMIC Gatifloxacin and optimal DNase concentration) for NTM biofilms was tested. The results showed that the combination treatment (10xMIC AM-228 and DNase) and (10xMIC Gatifloxacin and optimal DNase concentration) was better than single use of antibiotic to treat *M. fortuitum* biofilms (combination vs AM-228)($P=0.018$, biovolume) ($P=0.021$, CFU) and (combination vs Gatifloxacin) ($P=0.002$, biovolume) ($P=0.043$, CFU) (Figure 4.3.1.1, 4.3.1.2). For *M. chelonae* biofilm, the results showed that (combination vs AM-228) ($P=0.006$, biovolume) ($P=0.021$, CFU) and (combination vs Gatifloxacin) ($P=0.002$, biovolume) ($P=0.021$, CFU) (Figure 4.3.1.3, 4.3.1.4).

Figure 4.3.1.1 Combination treatment of AM-228 (10xMIC) and DNase (12.5µg/ml) on *M. fortuitum* biofilm. Confocal images of *M. fortuitum* biofilm after treatment with (A) AM-228 at 10xMIC or (B) AM-228 at 10xMIC and DNase 12.5 µg/ml respectively. Green color represents live biomass whereas Red is dead biomass. Histograms show comparison of Live/Dead ratio and viable bacteria (Colony Forming Units) of treatment effect on *M. fortuitum* biofilm. Scale Bar, 50 µm. Means and SD from triplicate experiments are shown. Combination treatment performed somewhat better than AM-228 alone. Live/Dead ratio was compared by using Man-Whitney U Test between two different groups, (combination vs AM-228)(P=0.018,biovolume) (P=0.021, CFU). (*, P≤0.05 was set to be statistically significant).

Figure 4.3.1.2 Combination treatment of Gatifloxacin (10xMIC) and DNase (12.5µg/ml) on *M. fortuitum* biofilm. Confocal images of *M. fortuitum* biofilm after treatment with (A) Gatifloxacin at 10xMIC or (B) Gatifloxacin at 10xMIC and DNase 12.5 µg/ml respectively. Green color represents live biomass whereas Red is dead biomass. Histograms show comparison of Live/Dead ratio and viable bacteria (Colony Forming Units) of treatment effect on *M. fortuitum* biofilm. Scale Bar, 50 µm. Means and SD from triplicate experiments are shown. Combination treatment performed somewhat better than Gatifloxacin alone. Live/Dead ratio was compared by using Man-Whitney U Test between two different groups, (combination vs Gatifloxacin) (P=0.002, biovolume) (P=0.043, CFU). (*, P≤0.05 was set to be statistically significant).

Figure 4.3.1.3 Combination treatment of AM-228 (10xMIC) and DNase (12.5µg/ml) on *M. chelonae* biofilm. Confocal images of *M. chelonae* biofilm after treatment with (A) AM-228 at 10xMIC or (B) AM-228 at 10xMIC and DNase 12.5 µg/ml respectively. Green color represents live biomass whereas Red is dead biomass. Histograms show comparison of Live/Dead ratio and viable bacteria (Colony Forming Units) of treatment effect on *M. chelonae* biofilm. Scale Bar, 50 µm. Means and SD from triplicate experiments are shown. Combination treatment was more efficient than AM-228 treatment. Live/Dead ratio was compared using the Man-Whitney U Test between two different groups, (combination vs AM-228) (P=0.006, biovolume) (P=0.021, CFU). (*, P≤0.05 was set to be statistically significant).

Figure 4.3.1.4 Combination treatment of Gatifloxacin (10xMIC) and DNase (12.5µg/ml) on *M. chelonae* biofilm. Confocal images of *M. chelonae* biofilm after treatment with (A) Gatifloxacin at 10xMIC or (B) AM-228 at 10xMIC and DNase 12.5 µg/ml respectively. Green color represents live biomass whereas Red is dead biomass. Histograms show comparison of Live/Dead ratio and viable bacteria (Colony Forming Units) of treatment effect on *M. chelonae* biofilm. Scale Bar, 50 µm. Means and SD from triplicate experiments are shown. Combination treatment was more efficient than individual treatment. Live/Dead ratio was compared using the Man-Whitney U Test between two different groups, (combination vs Gatifloxacin) (P=0.002, biovolume) (P=0.021, CFU). (*, P≤0.05 was set to be statistically significant).

4.3.2 Synergistic reactions between Amikacin and Fluoroquinolones for mycobacterium fortuitum and potential adjuvant DNase treatment

There are several reports showing the variation of MIC sensitivities on *M. fortuitum* and *M. chelonae* against different antimicrobials[298]. According to the literatures reviewed, *in vitro* activity of various antibiotics showed a quite huge range of antimicrobial sensitiveness, which enabling to treat effectively for *M. fortuitum* and *M. chelonae*[303]. Clinically, the most

common used antibiotic is Amikacin[304] or combination of Amikacin and fluoroquinolones[305] for mycobacterial keratitis. Moreover, there is currently lacking of settled treatment option that can efficiently eradicate the atypical mycobacterium infections. In this report, we showed the strong synergistic reactions between Amikacin and Fluoroquinolones in treating *M. fortuitum* in their planktonic (Table 4.3.2) and biofilm modes of growth (Amikacin Vs Amikacin+Levofloxacin, $P=0.009$ -biovolume) (Levofloxacin Vs Amikacin+Levofloxacin, $P=0.035$ -biovolume) (Amikacin Vs Amikacin+Gatifloxacin, $P=0.003$ -biovolume) (Gatifloxacin Vs Amikacin+Gatifloxacin, $P=0.018$ -biovolume) (Figure 4.3.2.1). The viable CFU for combination treatment are lower than its individual treatment (Figure 4.3.2.3).

Moreover, we proposed a new treatment option, DNase addition, could enhance bacteria killing activity in the treatments. For *M. fortuitum* biofilm, (Amikacin Vs Amikacin+DNase, $P=0.048$ -biovolume, $P=0.021$ -CFU) (Levofloxacin Vs Levofloxacin+DNase, $P=0.013$ -biovolume, $P=0.021$ -CFU), (Gatifloxacin Vs Gatifloxacin+DNase, $P=0.025$ -biovolume, $P=0.021$ -CFU) (Amikacin+Levofloxacin Vs Amikacin+Levofloxacin+DNase, $P=0.018$ -bio volume, $P=0.021$ -CFU), (Amikacin+Gatifloxacin Vs Amikacin+Gatifloxacin+DNase, $P=0.048$ -biovolume, $P=0.021$ -CFU). (Figure 4.3.2.1 and 4.3.2.3)

For *M. chelonae* biofilm, (Amikacin Vs Amikacin+DNase, $P=0.035$ -biovolume, $P=0.021$ -CFU), (Levofloxacin Vs Levofloxacin+DNase, $P=0.013$ -biovolume, $P=0.021$ -CFU) (Figure 4.3.2.2 and 4.3.2.3)

Organism	MIC Amikacin (µg/ml)	MIC Levofloxacin (µg/ml)	FICI (Amikacin +Levofloxacin)	MIC Gatifloxacin(µg/ml)	FICI (Amikacin + Gatifloxacin)	MIC Besifloxacin(µg/ml)	FICI (Amikacin + Besifloxacin)
	Alone	Alone		Alone		Alone	
<i>Mycobacterium fortuitum</i> (ATCC 49404)	3.12	0.78	0.5	0.195	0.5	0.39	1.007
<i>Mycobacterium chelonae</i> (ATCC 35752)	25	0.39	1.01	0.195	1.01	0.39	1.007

Table 4.3.2 Minimum inhibitory concentration of Levofloxacin, Gatifloxacin and Besifloxacin and their Fractional Inhibitory concentration index (FICI) with Amikacin On *M. fortuitum* (*M. neworleansense*) ATCC 49404 and *M. chelonae* ATCC 35752. The combinations that yielded the best synergisms are shown in Bold.

Figure 4.3.2.1 Synergistic reactions of Amikacin and Fluoroquinolones and potential adjuvant DNase treatment on *M. fortuitum* biofilms. Confocal images of (A) control *M. fortuitum* biofilm (day5) and *M. fortuitum* biofilm after treatment with (B) Amikacin 10xMIC (C) Amikacin 10xMIC+DNase 12.5 µg/ml (D) Levofloxacin 10xMIC (E), Levofloxacin 10xMIC+DNase 12.5 µg/ml (F) Gatifloxacin 10xMIC (G), Gatifloxacin 10xMIC+DNase 12.5 µg/ml (H) Amikacin 10xMIC+Levofloxacin 10xMIC (I), Amikacin 10xMIC+Levofloxacin 10xMIC+DNase 12.5 µg/ml (J) Amikacin 10xMIC+Gatifloxacin 10xMIC (K), Amikacin 10xMIC+Gatifloxacin 10xMIC+DNase 12.5 µg/ml respectively. Green color represents live biomass whereas Red is dead biomass. Histograms show comparison of Live/Dead ratio of treatment effects on *M. fortuitum* biofilm. Scale Bar, 50 µm. Means and SDs from triplicate experiments are shown. Non-parametric tests (Mann-Whitney U test) was employed by using PASW statistic 18. (B Vs C, $P=0.048$) (D Vs E, $P=0.013$) (F Vs G, $P=0.025$) (H Vs I, $P=0.018$) (J Vs K, $P=0.048$) (B Vs H, $P=0.009$) (B Vs J, $P=0.003$) (D Vs H, $P=0.035$) (F Vs J, $P=0.018$)

For all the groups against control, $P \leq 0.05$. (*, **, $P \leq 0.05$ was set to be statistically significant).

Figure 4.3.2.2 Amikacin, Fluoroquinolones and potential adjuvant DNase treatment on *M. chelonae* biofilms. Confocal images of (A) control *M. chelonae* biofilm (day5) and *M. chelonae* biofilm after treatment with (B) Amikacin 10xMIC (C) Amikacin 10xMIC+DNase 12.5 µg/ml (D) Levofloxacin 10xMIC (E), Levofloxacin 10xMIC+DNase 12.5 µg/ml respectively. Green color represents live biomass whereas Red is dead biomass. Histograms show comparison of Live/Dead ratio of treatment effects on *M. chelonae* biofilm. Scale Bar, 50 µm. Means and SDs from triplicate experiments are shown. Non-parametric tests (Mann-Whitney U test) was employed by using PASW statistic 18(B Vs C, $P=0.035$) (D Vs E, $P=0.013$)

For all the groups against control, $P \leq 0.05$. (*, **, $P \leq 0.05$ was set to be statistically significant).

Figure 4.3.2.3 Viable bacteria in colony forming units after synergistic reactions of Amikacin and Fluoroquinolones and potential adjuvant DNase treatment on Mycobacterial biofilms. Viable bacteria in colony forming units of (A) control biofilm (day5) and biofilm after treatment with (B) Amikacin 10xMIC (C) Amikacin 10xMIC+DNase 12.5 µg/ml (D) Levofloxacin 10xMIC (E), Levofloxacin 10xMIC+DNase 12.5 µg/ml (F) Gatifloxacin 10xMIC (G) Gatifloxacin 10xMIC+ DNase 12.5 µg/ml (H) Amikacin 10xMIC+ Levofloxacin 10xMIC (I) Amikacin 10xMIC+ Levofloxacin 10xMIC+DNase 12.5 µg/ml (J) Amikacin 10xMIC+ Gatifloxacin 10xMIC (K) Amikacin 10xMIC+ Gatifloxacin 10xMIC+DNase 12.5 µg/ml respectively. Histograms show comparison of Viable bacteria of treatment effects on biofilm. Scale Bar, 50 µm. Means and SDs from triplicate experiments are shown. Non-parametric test (Mann-Whitney U test) was employed by using PASW statistic 18. For *M. fortuitum* biofilm, (B Vs C, P=0.021) (D Vs E, P=0.021) (F Vs G, P=0.021) (H Vs I, P=0.021) (J Vs K, P=0.021) (B Vs H, P=0.021) (B Vs J, P=0.021) (D Vs H, P=1) (F Vs J, P=0.66) For *M. chelonae* biofilm, (B Vs C, P=0.021) (D Vs E, P=0.021) For all the groups against control, P≤0.05. (*, **, P≤0.05 was set to be statistically significant)

4.3.3 Besifloxacin for mycobacterial keratitis

In this study, we investigated the newest FDA approved ophthalmology fluoroquinolone, Besifloxacin, in *in vitro* anti biofilm effects and on mycobacterial keratitis mouse model. The sensitiveness of Besifloxacin against *M. fortuitum* and *M. chelonae* is 0.39 μ g/ml, which is comparable to Gatifloxacin and better than Levofloxacin (Table 4.3.2). *In vitro* anti biofilms studies showed that for *M. fortuitum* biofilm, (Besifloxacin vs control) (P=0.003, biovolume) (P=0.021, CFU) and (Besifloxacin vs Besifloxacin+DNase) (P=0.002, biovolume) (P=0.021, CFU) (Figure 4.3.3.1). For *M. chelonase* biofilm, (Besifloxacin vs control) (P=0.002, biovolume) (P=0.021, CFU) and (Besifloxacin vs Besifloxacin+DNase) (P=0.032, biovolume) (P=0.021, CFU) (Figure 4.3.3.2)

Figure 4.3.3.1 Besifloxacin on *M. fortuitum* biofilm. Confocal images of (A) control *M. fortuitum* biofilm (day5) and *M. fortuitum* biofilm after treatment with (B) Besifloxacin 10xMIC (C) Besifloxacin 10xMIC+DNase 12.5 μ g/ml respectively. Green color represents live biomass whereas Red is dead biomass. Histograms show comparison of Live/Dead ratio and viable Colony Forming Units of treatment effects on *M. fortuitum* biofilm. Scale Bar, 50 μ m. Means and SDs from triplicate experiments are shown. Non-parametric tests (Mann-Whitney U test) was employed by using PASW statistic 18. (Besifloxacin vs control) (P=0.003, biovolume) (P=0.021, CFU) and (Besifloxacin vs

Besifloxacin+DNase) (P=0.002, biovolume) (P=0.021, CFU). (*, **, $P \leq 0.05$ was set to be statistically significant).

Figure 4.3.3.2 Besifloxacin on *M. chelonae* biofilm. Confocal images of (A) control *M. chelonae* biofilm (day5) and *M. chelonae* biofilm after treatment with (B) Besifloxacin 10xMIC (C) Besifloxacin 10xMIC+DNase 12.5 µg/ml respectively. Green color represents live biomass whereas Red is dead biomass. Histograms show comparison of Live/Dead ratio and viable Colony Forming Units of treatment effects on *M. fortuitum* biofilm. Scale Bar, 50 µm. Means and SDs from triplicate experiments are shown. Non-parametric tests (Mann-Whitney U test) was employed by using PASW statistic 18. (Besifloxacin vs control) (P=0.002, biovolume) (P=0.021, CFU) and (Besifloxacin vs Besifloxacin+DNase) (P=0.032, biovolume) (P=0.021, CFU). (*, **, $P \leq 0.05$ was set to be statistically significant).

4.3.4 Discussion

Amikacin was the Gold Standard and treatment of choice for mycobacterial keratitis. Agreement to the previous published reports[304, 306], we have investigated in this report that Amikacin was not as effective as fluoroquinolones particularly fourth generation fluoroquinolones. We have found that there is a strong synergism between Amikacin and fluoroquinolones against *M. fortuitum*, in *in vitro*. To our knowledge, this is the first study

showing the synergism of Amikacin and fluoroquinolones in NTM infections (Chapter 4.3.2) . On the other hand, there have been reports of fluoroquinolones resistant case reports and the sensitiveness of fluoroquinolones could vary among the different clinical strains.

Bacteria within biofilms resist antibiotics more than planktonic bacteria not only because of limitation of antibiotic penetration but also because the biofilm matrix may inactivate antimicrobials[307]. The effect of combination treatment of DNase and antibiotic has been investigated in *mycobacteria avium* biofilms[223]. In this report, DNase treatment of NTM biofilm reduced the biofilm biomass, suggesting that eDNA might be present with a role in the properties of the biofilm (Chapter 4.1). Combination treatment of DNase (12.5 µg/ml) and 10xMIC of conventional antibiotics clearly showed a significant eradication of bacteria in NTM biofilms, suggesting that destruction of eDNA by DNase leads to a decrease in the extracellular matrix, allowing better penetration and efficacy of conventional antibiotics (Chapter 4.3.1, 4.3.2, 4.3.3).

Chapter 4.4

**Mycobacterial keratitis is biofilm mode of
infection and novel combination of
Fluoroquinolones, Aminoglycoside and
DNase is the ideal treatment approach**

4.4.1 Development of mycobacterial keratitis model

In order to be useful for pre clinical screening of new antimicrobials, murine novel mycobacterial keratitis model using *M. fortuitum* was developed. To our knowledge, this model is the first time developed for mycobacterial keratitis. Our results indicated that infection started from day 3 post infection presence of slight opacity on the cornea and there has been increasing opacity and bacteria burden on the mouse cornea (Figure 4.4.1). The results showed that there was bacterial burden of 4.17, 4.2, 4.47 and 4.77 log CFU/cornea at day 3, day 4, day 5 and day 6 post infection respectively. Our results showed that this model is useful for accessing efficacy of potential anti-mycobacterial drugs for pre-clinical testing.

Figure 4.4.1 Murine model of mycobacterial keratitis. Slit lamp microscopy images of mycobacterial keratitis for different days. It was observed that Infection started as early as day 3 post infection as slight haze in the central cornea. Infection progressed along the time course. Line graph showed the revived *M. fortuitum* CFU from infected cornea over time. (Magnification- 40X)

4.4.2 Mycobacteria biofilm formation on mouse cornea

Initiation of a biofilm through attachment followed by microcolonies formation and subsequent formation of heterogeneous biofilm communities are the steps to form a mature biofilm. These bacterial communities develop biomass, which convey an extra measure or therapeutic resistance to an infection[50]. In addition to the expolysachacrides, extracellular DNA is another critical factor found in the biofilm matrix. It was discovered in many gram-positive[154, 155, 157, 158, 161, 177, 291] and gram-negative[61, 149-151, 245, 292] bacteria biofilm. The reports showed that eDNA is critical for surface attachment and colonization[149, 151, 154, 161], biofilm recruitment and structural integrity[149, 150, 155, 157, 158, 245, 291]. Moreover, it has been playing a major factor for Horizontal gene transfer[292] and nutrient acquisition[149]. *In vitro* (Chapter 4.1) results point out that *M. fortuitum* and *chelonae* could form biofilm easily on *in vivo* compared to their *in vitro* growth since the extra cellular DNA could be easily achieved by bacterial cell death[60] or from neutrophil extracellular traps (NETs) formed by other immune cells and neutrophils[63].

Our results showed the abundance of eDNA stained by Propidium Iodide on mouse cornea on day 3 and day 6 post infection (Figure 4.4.2). Moreover, there was evidence of microcolonies formation of mycobacteria on mouse cornea by Syto-9 staining (Figure 4.4.2). Overall, our results showed evidence in the first time that mycobacteria infections on cornea are biofilm mode of growth rather than planktonic mode of growth.

Figure 4.4.2 Confocal microscopy images of mouse cornea from murine keratitis models at day 3 and day 7 post infection. Green fluorescence represents the staining of live bacterial cells by Syto-9 , red represents extracellular DNA staining by Propidium Iodide staining and yellow represents Eukaryotic cells staining by F-actin. Confocal Images showed the evidence of the microcolonies formation both in day 3 and day 7, stained by Syto-9 while F-actin stain was absent. Abundance of extra cellular DNA staining by Propidium Iodide staining was observed suggesting the evidence of biofilm formation in both time points. Scale Bar, 10 μ m.

4.4.3 Novel treatment strategies for mycobacterial keratitis

Medical treatment for atypical mycobacterial keratitis is often unsatisfactory. It might be due to delay diagnosis, inadequate penetration and slow response to therapy because of biofilm formation. Moreover, there is emergence of drug resistant bacteria due to long term exposure of antibiotics and their natural resistant to commercially available antibiotics are potential

barriers for success of medical treatment[305, 308, 309]. Therefore, there is urgent need of potential new antimicrobials or strategies.

In this study, we reported one novel treatment strategies i.e., combination of DNase and antibiotics. From our studies, Combination of commercial antibiotics with DNase was better than antibiotic alone in *in vivo*, (AM228 Vs AM228+DNase, P=0.04) (Amikacin Vs Amikacin+DNase, P=0.001) (Gatifloxacin Vs Gatifloxacin+DNase, P=0.027) (Besifloxacin Vs Besifloxacin+DNase, P=0.001) (Amikacin+Gatifloxacin Vs Amikacin+Gatifloxacin+DNase, P=0.001). For all the antibiotics treated groups against their respective controls, $P \leq 0.05$ except Amikacin Vs control (P=0.059) (Figure 4.4.3.2). The log differences between the DNase combination groups and its respective controls have been calculated. The results are 1.47, 1.55, 2.92, 1.9, 2.93 $\log_{10}$ CFU difference of AM228+DNase, Amikacin+DNase, Gatifloxacin+DNase, Besifloxacin+DNase, Amikacin+Gatifloxacin+DNase compared with their respective control groups (Figure 4.4.3.2). Overall, Combination of three drugs (Amikacin, Gatifloxacin and DNase) showed the most significant reduction of bacteria burden among the different combinations (Figure 4.4.3.2). Slit lamp microscopy images revealed that (Amikacin, Gatifloxacin and DNase) possessed the best clarity of cornea compared against the other treatment options (Figure 4.4.3.1). Moreover, there was ultimately low bacteria survival and no microcolonies formation on mouse cornea by confocal microscopy (Figure 4.4.3.1) in that combination group.

Figure 4.4.3.1 Slit lamp and confocal microscopy images of mouse cornea from murine keratitis for different treatments. Green fluorescence represents the staining of live bacterial cells by Syto-9 , red represents extracellular DNA staining by Propidium Iodide staining and yellow represents Eukaryotic cells staining by F-actin. Good corneal clarity has been observed in the group treated with Besifloxacin or Gatifloxacin with DNase treatment while there is significantly the best corneal clarity observed in the group treated by Amikacin, gatifloxacin and DNase. There were no microcolonies formation observed in this group and there are very few bacteria on mouse cornea. Scale Bar, 10 μ m. (Magnification- 40X).

Figure 4.4.3.2 Viable bacteria in log colony forming units of (D) Amikacin 5mg/ml+DNase 3mg/ml treatment (F) Besifloxacin 6 mg/ml+DNase 3 mg/ml (H) Gatifloxacin 3 mg/ml+DNase 3mg/ml treatment (J) Amikacin 5mg/ml+Gatifloxacin 3mg/ml+DNase 3mg/ml treatment and (L) AM-228 3mg/ml+DNase 3mg/ml treatment respectively in murine keratitis model using *M. fortuitum*. Histograms show comparison of Viable bacteria in log₁₀ CFU after different treatments. Non-parametric tests (Mann-Whitney U test) was employed by using PASW statistic 18. (Amikacin Vs Amikacin+DNase, C Vs D, P=0.001) (Besifloxacin Vs Besifloxacin+DNase, E Vs F, P=0.001) (Gatifloxacin Vs Gatifloxacin+DNase, G Vs H, P=0.027) (Amikacin+Gatifloxacin Vs Amikacin+Gatifloxacin+DNase, I Vs J, P=0.001) (AM-228 Vs AM-228+DNase, K Vs L, P=0.04) For all the groups against control, P≤0.05 except Amikacin Vs control (P=0.059) (*, ** P≤0.05 was set to be statistically significant).

4.4.4 Discussion

Reports have been suggested that it is very hard to produce a mycobacterial keratitis animal model because of its resistance to the pathogens. There have been several reports failing to produce an animal model[310, 311], however, experimental *M. chelonae* rabbit keratitis model has been reported[312]. This is the first report showing the development of mycobacterial

keratitis in mouse models (Chapter 4.4.1). We followed the Turner's suggestion that 2 weeks pre treatment of corticosteroid suppress the local resistance to pathogens in order to develop this model combined with the systemic immunosuppression to reduce the polymorphonuclear leukocytes recruitments to the eye after infections[310]. This model could be useful for pre-clinical screening of potential anti-mycobacterial compounds easily on the eye for the future ophthalmic drugs against NTM.

Besifloxacin, the most recent approved ophthalmic fluoroquinolone, had been tested in this report. It is considered to be an outstanding drug for ocular infections because of its area-under-the-concentration-versus-time curve over 24 hours (AUC_{0-24h}) is over 9.7 and 5.7 times higher than moxifloxacin and gatifloxacin in rabbit eyes[313]. Studies in human indicated for the greater residence times and a longer half-life in the eyes[314]. *In vitro*, it showed the anti-mycobacterial efficacy almost equivalent to Gatifloxacin in planktonic bacteria killing ability (Table 4.3.2) and the outstanding anti biofilm effect (Chapter 4.3.3). It also showed that it is very effective against NTM comparable to other fluoroquinolones in *in vivo* (Figure 4.4.3.2). It is well noted from our studies that all the fluoroquinolones are working effectively against the NTM, better than Amikacin in all cases (Figure 4.4.3.2).

Many reports have been published suggesting that DNase might be the next potential adjuvant treatment in bacterial infections and in the present report, we have expanded more DNase studies comprising more fluoroquinolones and combination of three different compounds, i.e., Aminoglycoside, Fluoroquinolones and DNase *in vitro* and *in vivo*. We have concluded that DNase could essentially help to boost the efficacy of anti mycobacterial treatment strategy by breaking the biofilm matrix barriers in all the treatment combinations *in vitro* (Chapter 4.3) and *in vivo* (Chapter 4.4).

Chapter 5

Conclusion and Future work

It has been proposed for decades that bacterial biofilm formation is responsible for many persistent and chronic infections. *In vitro* experiments already demonstrated that biofilms confer tolerance towards antimicrobials and phagocytosis by immune cells[267]. Numerous chemical biology strategies have also been developed to eradicate biofilms by targeting specific signaling pathways such as quorum sensing and c-di-GMP signaling, which are essential for *in vitro* biofilm formation[8]. However, development of biofilm controlling strategies is largely limited by the lack of characterization of *in vivo* biofilms.

Firstly, by using a mouse keratitis model, we have provided physiological evidence that *in vivo* biofilms formed by *P. aeruginosa* contribute to the establishment of ocular infections (Chapter 3.1). Our studies showed that *Pseudomonas aeruginosa* PAO1 and the $\Delta wspF$ mutant formed biofilms evidenced by densely packed phagocyte tolerant microcolonies (Chapter 3.2.1 and Chapter 3.2.2). Based on our results confirming that keratitis is biofilm type of infection, future studies should be focused on how the clinical isolates from human keratitis samples behave on this murine keratitis model. This could potentially provide the insight why *P. aeruginosa* become resistant to immune response and antibiotics in the real practice.

Importantly and secondly, we demonstrated that the bacterial secondary messenger, c-di-GMP, plays a crucial role in establishment of mouse corneal infections. A p_{cdrA} -*gfp* reporter indicated the kinetics of the *P. aeruginosa*'s c-di-GMP during mouse ocular infections (Chapter 3.1.1), where the intracellular c-di-GMP level was increased after 2 h of infections (Figure 3.1.1D) and reduced after 7 dpi (Figure 3.1.1I). The induction of c-di-GMP content intracellularly is crucial for *P. aeruginosa* persistence in early stage of mouse ocular infections (Figure 3.2.2). The PAO1/ p_{lac} -*yhjH* strain was cleared by the mouse immune system much more efficiently compared to PAO1 wild-type and the $\Delta wspF$ mutant (Figure 3.2.2 and Figure 3.2.3). In contrast, lowering the intracellular c-di-GMP from PAO1/ p_{lac} -*yhjH* (Figure 3.3.1) and PAO1

after 1 dpi had no impact on the survival of these strains during the infection (Figure 3.3.3). Similarly to our observation, a recent report showed that c-di-GMP synthesis is also required to establish *in vivo* *P. aeruginosa* biofilms during catheter-associated urinary tract infection[270]. Our transcriptomic and cytokine studies showed that increased c-di-GMP content in *P. aeruginosa* is associated with down regulation of Th1 and Th2 immune response genes(Appendix 5) and reduction of cytokine levels (Figure 3.2.4) from the infected corneas of C57BL/6 mice. Therefore, we conclude that c-di-GMP is up regulated, induces biofilm formation and modulates the host immune responses during *Pseudomonas* keratitis infection and, the manipulation of *P. aeruginosa*'s c-di-GMP content could be further investigated for improving current therapeutic strategies against biofilms-associated infections.

Third, high c-di-GMP containing *P. aeruginosa* variants (such as the $\Delta wspF$ mutant) are often isolated from chronic *P. aeruginosa* infections[85]. We provide *in vivo* evidence that a high c-di-GMP containing *P. aeruginosa* variant is able to form large microcolonies during ocular infections (Figure 3.2.2). Phagocytic cells accumulated around but were unable to penetrate the *P. aeruginosa* biofilm microcolonies in the infected mouse corneas (Figure 3.2.2), in a similar manner to previously demonstrated *P. aeruginosa* microcolonies in infected lung tissue of cystic fibrosis patients[266]. Phagocytic cells that are recruited to infection sites are likely to cause severe damage during the host's inflammatory response[107]. Therefore, we conclude from our studies that *P. aeruginosa* keratitis can cause phagocyte tolerant infections and future studies should focus on new treatment combinations comprised of new biofilm dispersal therapeutics and conventional antibiotics.

Several groups, including our own group, have demonstrated that *P. aeruginosa*'s c-di-GMP level governs the resistance of the pathogen towards antimicrobials *in vitro* [281, 282]. Our results here demonstrate that c-di-GMP enhances the development of Colistin-tolerant subpopulations of *in vitro* *P. aeruginosa* biofilms and increases their tolerance to Colistin *in*

vivo (Figure 3.3.1 and Figure 3.3.3). Finally for the *Pseudomonas* part of results, we present evidence that C-di-GMP reducing agent, Sodium Nitroprusside (SNP) boosts the Colistin treatment by repressing the development of Colistin-tolerant subpopulation in *in vitro* biofilm model and *in vivo* mouse keratitis model (Figure 3.3.1 and Figure 3.3.3). In a previous study, we showed that artificially lowering intracellular c-di-GMP content produced *P. aeruginosa* biofilm cells with increased virulence[315] and increased resistance towards Colistin by 2 folds[89]. Thus, dispersed biofilm cells could potentially transmit infections to other sites of the body[316]. For example, large numbers of *P. aeruginosa* cells were found in the bloodstream and spleen after they were dispersed from an implant biofilms in an *in vivo* biofilm dispersal study[90]. Here, we have demonstrated ways of reducing the risk of septicemia due to sudden biofilm dispersal. For example, a combination of selected groups of antibiotics and c-di-GMP repressing reagents can effectively control *in vitro* biofilms and biofilm-associated infections, thus result in improved clinical treatments for otherwise recalcitrant, chronic infections associated with biofilm formation. The combination of biofilm dispersal agent and conventional antibiotics should be evaluated on rabbit keratitis model in future for verification since rabbit is the standard model for ophthalmology.

NTM keratitis is relatively rare in clinical scenarios although there is an increasing incidence of mycobacterial keratitis. However, keratitis is the most common clinical presentations among the NTM infections around the eye[310, 317-319]. The increasing incidence of mycobacterial keratitis infections might be due to popularity of LASIK, increasing cataract surgery and high usage of biomaterials[192]. The American Society of Cataract and Refractive Surgery (ASCRS) Cornea Clinical Committee published a post-LASIK infectious keratitis survey, which stressed that NTM is the most leading infection after LASIK (33/69, 48%), standing the majority of culture-positive cases[320]. With high popularity and advances of laser-assisted *in situ* keratomileusis (LASIK) nowadays, NTM is most commonly found in the

post LASIK patients[193, 305, 308]. There have been reports of post-LASIK NTM keratitis outbreak been reported in USA, Japan and Brazil[321-323]. Moreover, biofilm is known to be the most common property that could be formed by NTM infections[209]. Firstly for the mycobacterial part of results, we observed the different biofilm architectures that comprised of irregular finger like projections from *M. fortuitum* biofilm and microcolonies formation from *M. chelonae* biofilm (Chapter 4.1.2) and increase drug resistance patterns while they are in biofilm modes in *in vitro* (Chapter 4.2.5). We conclude that *M. fortuitum* and *M. chelonae* readily form drug resistant biofilm suggesting the main cause of poor treatment compliance to conventional antibiotics. The future studies would be needed to address the nutrient stress and nutritional requirements regarding the mycobacterial biofilms, which would be important for mycobacterial keratitis management clinically.

Biofilm is made up with the matrix that contains the exopolysaccharides. In addition to the exopolysaccharides for the biofilm matrix's component, extracellular DNA is another critical factor found in the biofilm matrix. It was discovered and researched for its different functions in many gram-positive[154, 155, 157, 158, 161, 177, 291] and gram-negative[61, 149-151, 245, 292] bacteria biofilm. In contrast, eDNA is the major factor building the bacterial biofilm matrix. In our report, we have observed that addition of exogenous eDNA can boost the mycobacterial biofilm matrix (Chapter 4.1.3), addition of DNase destroyed the established mycobacterial biofilm(Chapter 4.1.4) and DNase enhanced the efficacy of conventional antibiotics (Chapter 4.3 and Chapter 4.4.3). There was a report showing the presence of eDNA in *M. avium*[223] and our report showed for the first time that there is a significant eDNA releases in *M. fortuitum* and *chelonae* and it is important in protecting against the antibiotics (Chapter 4.1.4 and Chapter 4.3)[250]. Moreover, we have observed the presence of eDNA abundance in infected cornea along with the microcolonies formation(Chapter 4.4.2), suggesting mycobacterial keratitis is biofilm type of infections. To our knowledge, this is the

first report showing that mycobacterial keratitis is biofilm mode of infection. By our observations, we have concluded secondly for the mycobacterial part that eDNA is the major factor responsible for the mycobacterial biofilm structural integrity and protecting against the penetration of antibiotics. Moreover, we have suggested that poor clinical outcomes of NTM infections might be due to its presence of biofilm matrix causing a barrier for antibiotic penetration and resistance. Therefore, future studies should be focused more on other exopolysaccharides and lipids required for formation of mycobacterial biofilm matrix and this could provide insight on new potential therapeutic targets for mycobacterial infections.

NTM infections are very difficult to eradicate, poor response to treatment and requires long-term treatment of combination of two drugs or more[297, 302]. Therefore, there is an urgent need of new antimicrobial treatment options to replace the old treatment plans. The medical treatments of NTM infections are often unsuccessful due to possible biofilm formations[250], variable *in vitro* sensitiveness by the different strains[303]. Although NTM keratitis is increasing and there would be expectations of more post-LASIK NTM keratitis in future, the medical treatment remains ineffective and the optimal treatment option is unsettled. Amikacin has been shown to be the pioneer choice of treatment for the most NTM and gold standard treatment clinically[304]. However, the clinical effect was often unsatisfactory due to poor penetration[300], highly potential to acquire resistance because of its single agent therapy[231] and poor compliance due to its toxic effects[324]. We have also investigated that Amikacin was not as effective as fluoroquinolones, particularly fourth generation fluoroquinolones(Chapter 4.3.2 and Chapter 4.4.3). Fluoroquinolones have variable success on NTM infections[192], however, they are the most effective antibiotics among the others currently[301, 325]. The structural modification of fourth-generation fluoroquinolones, Gatifloxacin, has a methyl group at C8, contribute to the better ocular penetration and superior bactericidal activity[326]. We have found that there is a strong synergism between Amikacin

and fluoroquinolones in *M. fortuitum*, in *in vitro* (Chapter 4.3.2) and *in vivo* (Chapter 4.4.3). Therefore, our studies concluded that the synergism treatment should be the first line treatment option in suspected mycobacterial keratitis cases in order to treat effectively and reduce the resistance formation. Moreover, we have observed that DNase enhance the anti mycobacterial treatment in *in vitro* (Chapter 4.3) and *in vivo* (Chapter 4.4.3). Finally, we have concluded that combination of three drugs (Amikacin, Fluoroquinolones and DNase) could replace the current anti mycobacterial treatment for mycobacterial keratitis (Chapter 4.4.3). However, future studies should be focused on validation of this strategy in keratitis model using other NTM strains or clinical isolates in *in vivo* and discovery of specific antibodies against eDNA for better treatment outcomes.

Appendix (1)

Appendix (1) confocal image of (A) planktonic PAO1/p_{cdrA}-gfp cells; B: bright-field image of planktonic PAO1/p_{cdrA}-gfp cells; C: confocal image of control scratched mouse cornea; D: bright-field image of control scratched mouse cornea. Representative images are shown for each condition. Scale bars, 10 μ m

Appendix (2)

Appendix (2) Confocal images of mouse corneas infected with *PAOI/p_{cdrA}-gfp* 2 hour, 4 hour, 8 hour post infection and *PAOI/p_{lac}-gfp* 8 hour post infection. Green fluorescence represents expression of the *p_{cdrA}-gfp* fusion and bacteria expression for *PAOI/p_{cdrA}-gfp* and *PAOI/p_{lac}-gfp* respectively. The red fluorescence represents the staining of all cells by Syto-62. Representative images are shown for each condition. Scale bars, 10 μm

Appendix (3)

	2 dpi_1	2 dpi_2	2 dpi_3	7 dpi_1	7 dpi_2	7 dpi_3
Total fragments	20,446,081	20,239,128	21,051,896	21,291,172	27,074,040	21,948,163
non-rRNA fragments	12,084,954	6,323,790	7,811,760	10,337,454	13,076,972	9,161,384
% of Total fragments non-rRNA	59.11	31.25	37.11	48.55	48.30	41.74
Total fragments map to Mouse	8,748,329	4,017,810	5,038,700	7,375,206	9,399,425	6,369,275
% of Total fragments map to Mouse	42.79	19.85	23.93	34.64	34.72	29.02
Counted fragments map to PA	45,346	51,723	44,850	11,172	6,289	6,356
% of Total fragments map to <i>P. aeruginosa</i>	0.22	0.26	0.21	0.05	0.02	0.03

Appendix (3) Mapping statistics of the RNA sequencing raw reads

Appendix (4)

Feature ID	Fold change	P value	Database identifier	Annotations - GO biological process
Cadm3	43.203154 28	2.24005 E-19	MGI:2137 858	0007157 // heterophilic cell-cell adhesion (MGI:MGI:2675176 PMID:12826663 [IDA]) /// 0008104 // protein localization (MGI:MGI:3582084 PMID:15893517 [IMP]) /// 0007156 // homophilic cell adhesion (MGI:MGI:2675176 PMID:12826663 [IDA]) /// 0008037 // cell recognition (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000589024) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130)
Kcnma1	33.814975 94	5.83485 E-17	MGI:9992 3	0060073 // micturition (MGI:MGI:3053479 PMID:15184377 [IMP] MGI:MGI:3053849) /// 0001666 // response to hypoxia (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620715) /// 0045475 // locomotor rhythm (MGI:MGI:3654773 PMID:16845385 [IMP] MGI:MGI:3053849) /// 0042311 // vasodilation (MGI:MGI:3695011 PMID:15867178 [IMP] MGI:MGI:3050114) /// 0009268 // response to pH (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620715) /// 0046541 // saliva secretion (MGI:MGI:3695228 PMID:16873365 [IGI] MGI:MGI:1277957) /// 0045909 // positive regulation of vasodilation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620715) /// 0007605 // sensory perception of sound (MGI:MGI:3052624 PMID:15328414 [IMP] MGI:MGI:3050114) /// 0007605 // sensory perception of sound (MGI:MGI:3697763 PMID:17135251 [IMP] MGI:MGI:3053849) /// 0042491 // auditory receptor cell differentiation (MGI:MGI:3052624 PMID:15328414 [IMP] MGI:MGI:3050114) /// 0060083 // smooth muscle contraction involved in micturition (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0006813 // potassium ion transport (MGI:MGI:1346192 PMID:10517674 [IDA]) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0001666 // response to hypoxia (MGI:MGI:3611743 PMID:16306267 [IDA]) /// 0006813 // potassium ion transport (MGI:MGI:61591 PMID:7687074 [IDA]) /// 0034465 // response to carbon monoxide (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0031960 // response to corticosteroid stimulus (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620715) /// 0043525 // positive regulation of neuron apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620715) /// 0032344 // regulation of aldosterone metabolic process (MGI:MGI:3693138 PMID:17122062 [IMP] MGI:MGI:3050114) /// 0042491 // auditory receptor cell differentiation (MGI:MGI:3697555 PMID:17074442 [IMP] MGI:MGI:3050114) /// 0042391 // regulation of membrane potential (MGI:MGI:3047034 PMID:15194823 [IMP] MGI:MGI:3050114) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0042391 // regulation of membrane potential (MGI:MGI:61591 PMID:7687074 [IDA]) /// 0051260 // protein homooligomerization (MGI:MGI:3700594 PMID:17303127 [IDA]) /// 0051289 // protein homotetramerization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620715) /// 0007268 // synaptic transmission (MGI:MGI:3047034 PMID:15194823 [IMP] MGI:MGI:3050114) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0043627 // response to estrogen stimulus (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620715) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0050885 // neuromuscular process controlling balance (MGI:MGI:3053479 PMID:15184377 [IMP] MGI:MGI:3053849) /// 0007628 // adult walking behavior (MGI:MGI:3053479 PMID:15184377 [IMP] MGI:MGI:3053849) /// 0042312 // regulation of vasodilation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620715) /// 0042391 // regulation of membrane potential (MGI:MGI:3626129 PMID:16763026 [IMP] MGI:MGI:3050114) /// 0001666 // response to hypoxia (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0007605 // sensory perception of sound (MGI:MGI:3626129 PMID:16763026 [IMP] MGI:MGI:3050114) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0060073 // micturition (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0030007 // cellular potassium ion homeostasis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0045794 // negative regulation of cell volume (MGI:MGI:3695228 PMID:16873365 [IMP] MGI:MGI:3053849) /// 1904348 /// 0051592 // response to calcium ion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0007623 // circadian rhythm (MGI:MGI:3654773 PMID:16845385 [IMP] MGI:MGI:3053849) /// 0006970 // response to osmotic stress (MGI:MGI:4834177 GO_REF:0000096

				[ISO] UniProtKB:Q12791) /// 0051592 // response to calcium ion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620715) /// 0060082 // eye blink reflex (MGI:MGI:3047034 PMID:15194823 [IMP] MGI:MGI:3050114) /// 0007628 // adult walking behavior (MGI:MGI:3047034 PMID:15194823 [IMP] MGI:MGI:3050114) /// 0048469 // cell maturation (MGI:MGI:3052624 PMID:15328414 [IMP] MGI:MGI:3050114) /// 0060083 // smooth muscle contraction involved in micturition (MGI:MGI:3612609 PMID:15827347 [IMP] MGI:MGI:3053849) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0045794 // negative regulation of cell volume (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0019228 // regulation of action potential in neuron (MGI:MGI:3654773 PMID:16845385 [IMP] MGI:MGI:3053849) /// 0006813 // potassium ion transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0042391 // regulation of membrane potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12791) /// 0050885 // neuromuscular process controlling balance (MGI:MGI:3047034 PMID:15194823 [IMP] MGI:MGI:3050114) /// 0060087 // relaxation of vascular smooth muscle (MGI:MGI:3695011 PMID:15867178 [IMP] MGI:MGI:3050114)
Trnp1	33.641733 95	7.6803E -17	MGI:1916 789	0042127 // regulation of cell proliferation (MGI:MGI:5488886 PMID:16792503 [IMP]) /// 0061351 // neural precursor cell proliferation (MGI:MGI:5490679 PMID:23622239 [IMP]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0007399 // nervous system development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0524) /// 0051726 // regulation of cell cycle (MGI:MGI:5488886 PMID:16792503 [IMP]) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0021696 // cerebellar cortex morphogenesis (MGI:MGI:5490679 PMID:23622239 [IMP]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0007049 // cell cycle (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0131)
Gria4	33.105380 28	5.52356 E-13	MGI:9581 1	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0050804 // regulation of synaptic transmission (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61863) /// 0051968 // positive regulation of synaptic transmission, glutamatergic (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61863) /// 0007268 // synaptic transmission (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61863) /// 0035235 // ionotropic glutamate receptor signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61863) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001508)
Scg3	31.388602 62	4.95514 E-13	MGI:1030 32	
Tmem59l	31.289467 09	2.1743E -13	MGI:1915 187	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Slc24a2	30.535764 19	8.61283 E-13	MGI:1923 626	0070588 // calcium ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:628650) /// 0034220 // ion transmembrane transport (MGI:MGI:3775882 PMID:18166528 [ISO] UniProtKB:Q9UI40) /// 0060292 // long term synaptic depression (MGI:MGI:3640012 PMID:16407245 [IMP] MGI:MGI:3663782) /// 0006816 // calcium ion transport (MGI:MGI:3640012 PMID:16407245 [IDA]) /// 0007612 // learning (MGI:MGI:3640012 PMID:16407245 [IMP] MGI:MGI:3663782) /// 0060291 // long-term synaptic potentiation (MGI:MGI:3640012 PMID:16407245 [IMP] MGI:MGI:3663782) /// 0006874 // cellular calcium ion homeostasis (MGI:MGI:3640012 PMID:16407245 [IMP] MGI:MGI:3663782) /// 0007613 // memory (MGI:MGI:3640012 PMID:16407245 [IMP] MGI:MGI:3663782)
Pdlim3	30.451057 77	1.82381 E-20	MGI:1859 274	0007507 // heart development (MGI:MGI:1934048 PMID:11329061 [IMP] MGI:MGI:2388199) /// 0007015 // actin filament organization (MGI:MGI:1934048 PMID:11329061 [IDA]) /// 0007519 // skeletal muscle tissue development (MGI:MGI:1930426 PMID:11238905 [IMP] MGI:MGI:2385940)
Dusp26	30.396321 37	2.98209 E-13	MGI:1914 209	0044387 // negative regulation of protein kinase activity by regulation of protein phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9BV47) /// 0016311 // dephosphorylation

				(MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR016130 InterPro:IPR000387) /// 1902310 /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9BV47) /// 0045785 // positive regulation of cell adhesion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9BV47) /// 0035335 // peptidyl-tyrosine dephosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9BV47) /// 0070373 // negative regulation of ERK1 and ERK2 cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9BV47) /// 0006470 // protein dephosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9BV47)
Slc1a3	30.38929702	7.25244E-29	MGI:99917	0098792 /// 0006536 // glutamate metabolic process (MGI:MGI:1928030 PMID:11102482 [IMP] MGI:MGI:1931872) /// 0043200 // response to amino acid stimulus (MGI:MGI:70531 PMID:7723632 [ISO] UniProtKB:P46411) /// 0002230 // positive regulation of defense response to virus by host (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P43003) /// 0051938 // L-glutamate import (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P43003) /// 0070779 // D-aspartate import (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P43003) /// 0098779 /// 0015813 // L-glutamate transport (MGI:MGI:3041380 PMID:14723703 [IDA]) /// 0015813 // L-glutamate transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3698) /// 0050806 // positive regulation of synaptic transmission (MGI:MGI:1203466 PMID:9539795 [IMP] MGI:MGI:1931872) /// 0048667 // cell morphogenesis involved in neuron differentiation (MGI:MGI:1202024 PMID:9753165 [IMP] MGI:MGI:1931872) /// 0021545 // cranial nerve development (MGI:MGI:1202024 PMID:9753165 [IMP] MGI:MGI:1931872) /// 0007605 // sensory perception of sound (MGI:MGI:1928030 PMID:11102482 [IMP] MGI:MGI:1931872) /// 0050885 // neuromuscular process controlling balance (MGI:MGI:1202024 PMID:9753165 [IMP] MGI:MGI:1931872) /// 0042493 // response to drug (MGI:MGI:1203466 PMID:9539795 [IMP] MGI:MGI:1931872) /// 0010035 // response to inorganic substance (MGI:MGI:70531 PMID:7723632 [ISO] UniProtKB:P46411) /// 0015813 // L-glutamate transport (MGI:MGI:70531 PMID:7723632 [ISO] UniProtKB:P24942) /// 0006537 // glutamate biosynthetic process (MGI:MGI:3613135 PMID:15305132 [IMP] MGI:MGI:1931872) /// 0043490 // malate-aspartate shuttle (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3698) /// 0010035 // response to inorganic substance (MGI:MGI:70531 PMID:7723632 [ISO] UniProtKB:P24942) /// 0015813 // L-glutamate transport (MGI:MGI:70531 PMID:7723632 [ISO] UniProtKB:P46411) /// 0009611 // response to wounding (MGI:MGI:1202024 PMID:9753165 [IMP] MGI:MGI:1931872) /// 0006835 // dicarboxylic acid transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001991) /// 0009416 // response to light stimulus (MGI:MGI:1203466 PMID:9539795 [IMP] MGI:MGI:1931872) /// 0089711 /// 0051938 // L-glutamate import (MGI:MGI:3613117 PMID:15390100 [IMP] MGI:MGI:1931872) /// 0031223 // auditory behavior (MGI:MGI:1928030 PMID:11102482 [IMP] MGI:MGI:1931872) /// 0009449 // gamma-aminobutyric acid biosynthetic process (MGI:MGI:3613135 PMID:15305132 [IMP] MGI:MGI:1931872) /// 0046677 // response to antibiotic (MGI:MGI:3583497 PMID:15862894 [IMP] MGI:MGI:1931872) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Ckb	29.60720956	2.37313E-27	MGI:88407	0030644 // cellular chloride ion homeostasis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2357) /// 0016310 // phosphorylation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0418)
Kcng4	28.70390667	4.2059E-13	MGI:1913983	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006813 // potassium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0633) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8TDN1) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0051260 // protein homooligomerization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003131) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0006813 // potassium ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003968 InterPro:IPR003971 InterPro:IPR028325) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)

Hspa12a	28.222446 94	1.01625 E-22	MGI:1920 692	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
RP24- 267C3.3	28.176859 99	3.01121 E-14		
C130071C03 Rik	28.020073 2	3.63001 E-12	MGI:2443 574	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Sphkap	27.803844 82	1.58749 E-21	MGI:1924 879	0010738 // regulation of protein kinase A signaling cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000027542)
Synpr	27.298721 45	1.27402 E-18	MGI:1919 253	0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001285)
Gpr37	27.157842 08	2.07343 E-15	MGI:1313 297	0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000276 InterPro:IPR003909) /// 0045964 // positive regulation of dopamine metabolic process (MGI:MGI:3046856 PMID:15218106 [IMP] MGI:MGI:3027995) /// 0043410 // positive regulation of MAPK cascade (MGI:MGI:5586790 PMID:23690594 [IMP]) /// 0042416 // dopamine biosynthetic process (MGI:MGI:3046856 PMID:15218106 [IMP] MGI:MGI:3027995) /// 0031987 // locomotion involved in locomotory behavior (MGI:MGI:3046856 PMID:15218106 [IMP] MGI:MGI:3027995) /// 0043410 // positive regulation of MAPK cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15354) /// 1903206 /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297) /// 0007193 // adenylate cyclase-inhibiting G-protein coupled receptor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15354)
Rorb	27.134098 92	5.35062 E-15	MGI:1343 464	0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1306778) /// 0007601 // visual perception (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0844) /// 0042752 // regulation of circadian rhythm (MGI:MGI:3712731 PMID:17303680 [IMP]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:3652638 PMID:16574740 [IDA]) /// 0035881 // amacrine cell differentiation (MGI:MGI:5546314 PMID:23652001 [IMP]) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0046549 // retinal cone cell development (MGI:MGI:3652638 PMID:16574740 [IDA]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0045668 // negative regulation of osteoblast differentiation (MGI:MGI:5554363 PMID:22189870 [IDA]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1306778) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:5546314 PMID:23652001 [IDA]) /// 0060041 // retina development in camera-type eye (MGI:MGI:5546314 PMID:23652001 [IMP]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000536 InterPro:IPR001723 InterPro:IPR003079 InterPro:IPR001628 InterPro:IPR013088) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0046548 // retinal rod cell development (MGI:MGI:4366105 PMID:19805139 [IMP]) /// 0043401 // steroid hormone mediated signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000536) /// 0045892 // negative regulation of transcription, DNA-dependent (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1306778) /// 0046548 // retinal rod cell development (MGI:MGI:3652638 PMID:16574740 [IMP]) /// 0050896 // response to stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0716) /// 0042462 // eye photoreceptor cell development (MGI:MGI:3652638 PMID:16574740 [IMP]) /// 0071300 // cellular response to retinoic acid (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1306778) /// 0048511 // rhythmic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0090)
Snap91	26.694179 52	5.62871 E-16	MGI:1091 32	0048268 // clathrin coat assembly (MGI:MGI:4418638 PMID:11102472 [IMP]) /// 0007163 // establishment or maintenance of cell polarity (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69276) /// 0030100 // regulation of endocytosis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69276) /// 0007268 // synaptic transmission (MGI:MGI:4418638 PMID:11102472 [IMP]) /// 0007409 // axonogenesis

				(MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69276) /// 0048268 // clathrin coat assembly (MGI:MGI:4418645 PMID:9045662 [IDA]) /// 0048268 // clathrin coat assembly (MGI:MGI:4418641 PMID:10428863 [IMP]) /// 2000369 // regulation of clathrin-mediated endocytosis (MGI:MGI:3607441 PMID:16254249 [ISO] UniProtKB:O60641) /// 0051223 // regulation of protein transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69276) /// 0007269 // neurotransmitter secretion (MGI:MGI:4418638 PMID:11102472 [IMP]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0015031 // protein transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0653)
Cadm2	26.595896 42	9.76983 E-13	MGI:2442 722	0007157 // heterophilic cell-cell adhesion (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000589024) /// 0007156 // homophilic cell adhesion (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000589024) /// 0008037 // cell recognition (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000589024) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130)
Cntnap2	26.392756 74	6.24175 E-15	MGI:1914 047	0007612 // learning (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UHC6) /// 0045163 // clustering of voltage-gated potassium channels (MGI:MGI:2675531 PMID:12963709 [IMP]) /// 0071205 // protein localization to juxtaparanode region of axon (MGI:MGI:3829295 PMID:19109503 [IMP] MGI:MGI:2677631) /// 0007155 // cell adhesion (MGI:MGI:4412433 PMID:18987363 [TAS]) /// 0042297 // vocal learning (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UHC6) /// 0008038 // neuron recognition (MGI:MGI:4412433 PMID:18987363 [TAS]) /// 0071205 // protein localization to juxtaparanode region of axon (MGI:MGI:2675531 PMID:12963709 [IMP]) /// 0031175 // neuron projection development (MGI:MGI:4438147 PMID:19458237 [IGI] MGI:MGI:104518) /// 0035176 // social behavior (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UHC6) /// 0030534 // adult behavior (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UHC6) /// 0071625 // vocalization behavior (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UHC6)
Cadps	26.284254 19	1.31127 E-10	MGI:1350 922	0016082 // synaptic vesicle priming (MGI:MGI:4879076 PMID:21040848 [IGI] MGI:MGI:2443963) /// 0050432 // catecholamine secretion (MGI:MGI:3583730 PMID:15820695 [IMP] MGI:MGI:3583931) /// 0006887 // exocytosis (MGI:MGI:3583730 PMID:15820695 [IMP] MGI:MGI:3583931) /// 0045956 // positive regulation of calcium ion-dependent exocytosis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:708573) /// 0016050 // vesicle organization (MGI:MGI:3583730 PMID:15820695 [IMP] MGI:MGI:3583931) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0015031 // protein transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0653)
Astn1	25.700253 85	2.73034 E-11	MGI:1098 567	0001764 // neuron migration (MGI:MGI:5466150 PMID:1821847 [IMP]) /// 0016337 // cell-cell adhesion (MGI:MGI:2159504 PMID:11861479 [IMP] MGI:MGI:2445955) /// 0007158 // neuron cell-cell adhesion (MGI:MGI:893790 PMID:8602532 [IDA]) /// 0016477 // cell migration (MGI:MGI:2159504 PMID:11861479 [IMP] MGI:MGI:2445955) /// 0007626 // locomotory behavior (MGI:MGI:2159504 PMID:11861479 [IMP] MGI:MGI:2445955) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0001764 // neuron migration (MGI:MGI:893790 PMID:8602532 [IDA])
Cntn4	25.526882 16	4.19494 E-13	MGI:1095 737	0045665 // negative regulation of neuron differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8I WV2) /// 0007155 // cell adhesion (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR033007) /// 0007399 // nervous system development (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8I WV2) /// 0031175 // neuron projection development (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621361) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0007411 // axon guidance (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR033007)
Kcnh5	25.524704 97	1.61269 E-12	MGI:3584 508	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006813 // potassium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0633) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0010389 // regulation of G2/M transition of mitotic cell cycle (MGI:MGI:5432821 PMID:22855790 [ISO] UniProtKB:Q8NCM2) ///

				0042391 // regulation of membrane potential (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000025348) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0000160 // phosphorelay signal transduction system (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000700) /// 0006813 // potassium ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003949 InterPro:IPR003938) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0631)
Nrxn3	25.4769917	2.00881E-10	MGI:1096389	0007269 // neurotransmitter secretion (MGI:MGI:3040168 PMID:12827191 [IGI] MGI:MGI:1096391 MGI:MGI:1096362) /// 0001525 // angiogenesis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0037) /// 0007268 // synaptic transmission (MGI:MGI:3040168 PMID:12827191 [IGI] MGI:MGI:1096391 MGI:MGI:1096362) /// 0090129 // positive regulation of synapse maturation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR027158) /// 0051965 // positive regulation of synapse assembly (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR027158) /// 0007416 // synapse assembly (MGI:MGI:3040168 PMID:12827191 [IGI] MGI:MGI:1096391 MGI:MGI:1096362) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130)
Adgral	24.60821795	3.87444E-13	MGI:1277167	0007166 // cell surface receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR017981) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000832 InterPro:IPR017983) /// 0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Gria2	24.13865953	5.03137E-10	MGI:95809	0001919 // regulation of receptor recycling (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61862) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0007268 // synaptic transmission (MGI:MGI:2683829 PMID:14687553 [IDA]) /// 0031623 // receptor internalization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61862) /// 0051262 // protein tetramerization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61862) /// 0007268 // synaptic transmission (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61862) /// 0035235 // ionotropic glutamate receptor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P42262) /// 0045184 // establishment of protein localization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61862) /// 0051966 // regulation of synaptic transmission, glutamatergic (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61862) /// 0050806 // positive regulation of synaptic transmission (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61862) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001508)
Lin7a	23.74451407	4.17889E-13	MGI:2135609	0048839 // inner ear development (MGI:MGI:5140238 PMID:21795542 [IDA]) /// 1903361 /// 0006887 // exocytosis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001019267) /// 0048489 // synaptic vesicle transport (MGI:MGI:2680876 PMID:14622577 [IMP]) /// 0045199 // maintenance of epithelial cell apical/basal polarity (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001019267) /// 0007269 // neurotransmitter secretion (MGI:MGI:3607873 PMID:16186258 [IGI] MGI:MGI:2135609 MGI:MGI:1330839) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0015031 // protein transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0653)
Enpp2	23.46128033	3.0147E-25	MGI:1321390	0048714 // positive regulation of oligodendrocyte differentiation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69298) /// 0010634 // positive regulation of epithelial cell migration (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13822) /// 0008152 // metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR017849 InterPro:IPR017850) /// 0090305 // nucleic acid phosphodiester bond hydrolysis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69298) /// 0006935 // chemotaxis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0145) /// 0051894 // positive regulation of focal adhesion assembly (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69298) /// 0006629 // lipid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0443) /// 0045765 // regulation of angiogenesis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR029881) /// 0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR020436 InterPro:IPR001212) /// 0034638 // phosphatidylcholine

				<p>catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13822) /// 1900026 // positive regulation of substrate adhesion-dependent cell spreading (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69298) /// 0009395 // phospholipid catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13822) /// 0050731 // positive regulation of peptidyl-tyrosine phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13822) /// 0006935 // chemotaxis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR029881) /// 0034638 // phosphatidylcholine catabolic process (MGI:MGI:5050048 PMID:21240269 [IDA]) /// 0001953 // negative regulation of cell-matrix adhesion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69298) /// 0034638 // phosphatidylcholine catabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69298) /// 2000394 // positive regulation of lamellipodium morphogenesis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13822) /// 0030334 // regulation of cell migration (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13822) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69298) /// 0060326 // cell chemotaxis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69298) /// 0016042 // lipid catabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0442)</p>
Ryr3	23.325984 42	1.36724 E-16	MGI:9968 4	<p>0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0006941 // striated muscle contraction (MGI:MGI:1194690 PMID:9384575 [IMP] MGI:MGI:2181794) /// 0051209 // release of sequestered calcium ion into cytosol (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q15413) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000699) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0051209 // release of sequestered calcium ion into cytosol (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68952) /// 0006874 // cellular calcium ion homeostasis (MGI:MGI:1194690 PMID:9384575 [IMP] MGI:MGI:2181794) /// 0006816 // calcium ion transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q15413) /// 0051481 // reduction of cytosolic calcium ion concentration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68952) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0107) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)</p>
Gad1	23.280037 16	2.96799 E-13	MGI:9563 2	<p>0009449 // gamma-aminobutyric acid biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2652) /// 0042136 // neurotransmitter biosynthetic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0530) /// 0019752 // carboxylic acid metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002129) /// 0035176 // social behavior (MGI:MGI:5605217 PMID:24952328 [IMP] MGI:MGI:3762150) /// 0035641 // locomotory exploration behavior (MGI:MGI:5605217 PMID:24952328 [IMP] MGI:MGI:3762150)</p>
Ano5	23.102828 92	7.70629 E-14	MGI:3576 659	<p>0006821 // chloride transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q75V66) /// 1902476</p>
Stmn3	23.040241 83	1.15673 E-10	MGI:1277 137	<p>0035021 // negative regulation of Rac protein signal transduction (MGI:MGI:3706230 PMID:17135267 [IDA]) /// 0031110 // regulation of microtubule polymerization or depolymerization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000956) /// 0043087 // regulation of GTPase activity (MGI:MGI:3706230 PMID:17135267 [IDA]) /// 0007019 // microtubule depolymerization (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000802387) /// 0031175 // neuron projection development (MGI:MGI:3706230 PMID:17135267 [IDA]) /// 0031122 // cytoplasmic microtubule organization (MGI:MGI:3706230 PMID:17135267 [IDA]) /// 0051493 // regulation of cytoskeleton organization (MGI:MGI:3706230 PMID:17135267 [IDA])</p>
Lonrf2	22.998325 3	2.80555 E-16	MGI:1920 209	<p>0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])</p>
Pacsin1	22.981143 93	6.97876 E-17	MGI:1345 181	<p>0097320 // membrane tubulation (MGI:MGI:4454229 PMID:20404169 [IMP]) /// 0097320 // membrane tubulation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3247) /// 0048666 // neuron development (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028518) /// 0048488 // synaptic vesicle endocytosis (MGI:MGI:5304995 PMID:21926968 [IMP]) ///</p>

				0048812 // neuron projection morphogenesis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000102991) // 0006897 // endocytosis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0254) // 0045806 // negative regulation of endocytosis (MGI:MGI:1929303 PMID:11082044 [IDA]) // 0090002 // establishment of protein localization to plasma membrane (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3247) // 1900006 // positive regulation of dendrite development (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3247) // 0072657 // protein localization to membrane (MGI:MGI:5304995 PMID:21926968 [IMP]) // 0007010 // cytoskeleton organization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3247) // 0048812 // neuron projection morphogenesis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3247) // 0097320 // membrane tubulation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9BY11) // 0007015 // actin filament organization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028518) // 0007165 // signal transduction (MGI:MGI:1341470 PMID:9746365 [TAS])
Pde3a	22.949119 73	5.20554 E-36	MGI:1860 764	0071321 // cellular response to cGMP (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q14432) // 0006198 // cAMP catabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61942) // 0043116 // negative regulation of vascular permeability (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q14432) // 0043066 // negative regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61942) // 0019933 // cAMP-mediated signaling (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q14432) // 0060282 // positive regulation of oocyte development (MGI:MGI:4361111 PMID:19474061 [IGI] MGI:MGI:2651499) // 0043117 // positive regulation of vascular permeability (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q14432) // 0042493 // response to drug (MGI:MGI:2136575 PMID:11420239 [IDA]) // 0001556 // oocyte maturation (MGI:MGI:2136575 PMID:11420239 [IDA]) // 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002073) // 0006198 // cAMP catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q14432) // 0019934 // cGMP-mediated signaling (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q14432) // 0040020 // regulation of meiosis (MGI:MGI:2136575 PMID:11420239 [IDA])
Soga3	22.766597 47	3.86406 E-11	MGI:1914 662	0010506 // regulation of autophagy (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR027881) // 0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Syt13	22.549893 65	2.98261 E-12	MGI:1933 945	0048791 // calcium ion-dependent exocytosis of neurotransmitter (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000001285) // 0016192 // vesicle-mediated transport (MGI:MGI:1931671 PMID:11171101 [IPI] UniProtKB:Q9CS84) // 0006906 // vesicle fusion (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000001285)
Lrit2	22.524159 04	2.3914E -10	MGI:2444 885	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Scg2	22.491161 1	3.07162 E-11	MGI:1030 33	2001237 // negative regulation of extrinsic apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13521) // 0000165 // MAPK cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13521) // 0050918 // positive chemotaxis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13521) // 0048245 // eosinophil chemotaxis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13521) // 2000352 // negative regulation of endothelial cell apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13521) // 0001525 // angiogenesis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13521) // 0001938 // positive regulation of endothelial cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13521) // 0035556 // intracellular signal transduction (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13521) // 0000165 // MAPK cascade (MGI:MGI:3688376 PMID:14970115 [ISS] UniProtKB:P13521) // 0001525 // angiogenesis (MGI:MGI:3688376 PMID:14970115 [IDA]) // 0050930 // induction of positive chemotaxis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13521)
Plppr4	22.478522 42	5.26414 E-16	MGI:1065 30	0048839 // inner ear development (MGI:MGI:5140238 PMID:21795542 [IDA]) // 0046839 // phospholipid dephosphorylation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:727806) // 0046839 // phospholipid dephosphorylation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001606015) // 0007409 // axonogenesis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:727806) // 0006644 // phospholipid metabolic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001606015) //

				0007409 // axonogenesis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000018009) /// 0007165 // signal transduction (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001606015)
Dpysl4	22.380134 67	1.04564 E-12	MGI:1349 764	0097485 /// 0070997 // neuron death (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR030612)
Gabra2	22.244457 94	2.69646 E-11	MGI:9561 4	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006821 // chloride transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005432) /// 0007214 // gamma-aminobutyric acid signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P47869) /// 0099565 /// 0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006202) /// 0001505 // regulation of neurotransmitter levels (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P47869) /// 0007268 // synaptic transmission (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P47869) /// 0006836 // neurotransmitter transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P47869) /// 0006821 // chloride transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0869) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006028 InterPro:IPR001390 InterPro:IPR006201 InterPro:IPR006029) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Adcy1	22.025227 07	2.26057 E-11	MGI:9967 7	0006171 // cAMP biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1309318) /// 0007193 // adenylate cyclase-inhibiting G-protein coupled receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001728527) /// 0007189 // adenylate cyclase-activating G-protein coupled receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001728527) /// 0009190 // cyclic nucleotide biosynthetic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) /// 0019933 // cAMP-mediated signaling (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001728527) /// 0035556 // intracellular signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) /// 0042752 // regulation of circadian rhythm (MGI:MGI:5518489 PMID:24048828 [IMP]) /// 0048511 // rhythmic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0090) /// 0006171 // cAMP biosynthetic process (MGI:MGI:1270087 PMID:9662407 [TAS]) /// 0007616 // long-term memory (MGI:MGI:1344240 PMID:10482244 [IGI] MGI:MGI:2176596) /// 0007190 // activation of adenylate cyclase activity (MGI:MGI:1270087 PMID:9662407 [TAS]) /// 0007409 // axonogenesis (MGI:MGI:3699973 PMID:17229090 [IMP] MGI:MGI:1857775)
Kcna5	21.795168 41	1.96311 E-15	MGI:9666 2	0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0006813 // potassium ion transport (MGI:MGI:79064 PMID:8576199 [ISO] UniProtKB:P22460) /// 0042391 // regulation of membrane potential (MGI:MGI:3526601 PMID:15277200 [IGI] MGI:MGI:107231 MGI:MGI:107570) /// 0086014 // regulation of atrial cardiac muscle cell action potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22460) /// 0006813 // potassium ion transport (MGI:MGI:63618 PMID:8226976 [IDA]) /// 0006813 // potassium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2953) /// 0042391 // regulation of membrane potential (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2953) /// 2000288 // positive regulation of myoblast proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2953) /// 0051260 // protein homooligomerization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003131) /// 0086052 // membrane repolarization involved in regulation of SA node cell action potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22460) /// 1900087 // positive regulation of G1/S transition of mitotic cell cycle (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2953) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0060081 // membrane hyperpolarization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22460) /// 0019229 // regulation of vasoconstriction (MGI:MGI:2138011 PMID:11481235 [IMP] MGI:MGI:2384510) /// 0042391 // regulation of membrane potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22460) /// 0055075 // potassium ion homeostasis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2953) /// 0086050 // membrane repolarization involved in regulation of bundle of His cell action potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22460) /// 0007219 // Notch signaling pathway (MGI:MGI:5609934 PMID:23117660 [IDA]) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) ///

				0051481 // reduction of cytosolic calcium ion concentration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2953) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0060372 // regulation of atrial cardiac muscle cell membrane repolarization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22460) /// 0043267 // negative regulation of potassium ion transport (MGI:MGI:63618 PMID:8226976 [IDA]) /// 0071435 // potassium ion export (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22460) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2953) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22460) /// 0051259 // protein oligomerization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2953) /// 0086091 // regulation of heart rate by cardiac conduction (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22460) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0043266 // regulation of potassium ion transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22460)
Amph	21.344246 37	6.6993E -17	MGI:1035 74	0007612 // learning (MGI:MGI:2176305 PMID:11879655 [IMP] MGI:MGI:2388118) /// 0048488 // synaptic vesicle endocytosis (MGI:MGI:2176305 PMID:11879655 [IMP] MGI:MGI:2388118)
Cerkl	21.257389 73	3.84019 E-10	MGI:3037 816	0043066 // negative regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q49MI3)
Syp	21.183013 62	1.58489 E-10	MGI:9846 7	2000474 // regulation of opioid receptor signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3802) /// 0048172 // regulation of short-term neuronal synaptic plasticity (MGI:MGI:1349221 PMID:10595519 [IMP]) /// 0006897 // endocytosis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3802) /// 0071310 // cellular response to organic substance (MGI:MGI:3801567 PMID:18497889 [IDA]) /// 0007268 // synaptic transmission (MGI:MGI:2387907 PMID:12271488 [TAS]) /// 0048168 // regulation of neuronal synaptic plasticity (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028714) /// 0048169 // regulation of long-term neuronal synaptic plasticity (MGI:MGI:1349221 PMID:10595519 [IMP]) /// 0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001285) /// 0006897 // endocytosis (MGI:MGI:2387907 PMID:12271488 [TAS])
Meg3	21.125458 1	5.87175 E-28	MGI:1202 886	0071514 // genetic imprinting (MGI:MGI:4839866 PMID:20610486 [IMP] MGI:MGI:4840060) /// 0001701 // in utero embryonic development (MGI:MGI:4839866 PMID:20610486 [IMP] MGI:MGI:4840060) /// 0007519 // skeletal muscle tissue development (MGI:MGI:4839866 PMID:20610486 [IMP] MGI:MGI:4840060) /// 0001889 // liver development (MGI:MGI:3841506 PMID:19264764 [IMP] MGI:MGI:3842511) /// 0001701 // in utero embryonic development (MGI:MGI:3841506 PMID:19264764 [IMP] MGI:MGI:3842511) /// 0009791 // post-embryonic development (MGI:MGI:3841506 PMID:19264764 [IMP] MGI:MGI:3842511) /// 0048286 // lung alveolus development (MGI:MGI:3841506 PMID:19264764 [IMP] MGI:MGI:3842511) /// 0071514 // genetic imprinting (MGI:MGI:5465388 PMID:23195472 [IDA]) /// 0006306 // DNA methylation (MGI:MGI:4839866 PMID:20610486 [IMP] MGI:MGI:4840060) /// 0008340 // determination of adult lifespan (MGI:MGI:3841506 PMID:19264764 [IMP] MGI:MGI:3842511) /// 0035264 // multicellular organism growth (MGI:MGI:3841506 PMID:19264764 [IMP] MGI:MGI:3842511) /// 0060395 // SMAD protein signal transduction (MGI:MGI:5486383 PMID:23390484 [IDA]) /// 0006306 // DNA methylation (MGI:MGI:5465388 PMID:23195472 [IDA])
Mdga2	21.040517 51	1.39482 E-10	MGI:2444 706	0007389 // pattern specification process (MGI:MGI:50741 PMID:1633717 [IMP])
Scn7a	21.020775	3.60871 E-27	MGI:1029 65	0055078 // sodium ion homeostasis (MGI:MGI:3616303 PMID:16223844 [IMP]) /// 0019228 // regulation of action potential in neuron (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000798901) /// 0086010 // membrane depolarization involved in regulation of action potential (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000004140) /// 0055078 // sodium ion homeostasis (MGI:MGI:3616303 PMID:16223844 [IDA])
Adgrb3	20.775360 73	8.30142 E-11	MGI:2441 837	0007166 // cell surface receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR017981) /// 0007520 // myoblast fusion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O60242) /// 0016525 // negative regulation of angiogenesis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR008077) /// 0051965 // positive regulation of synapse assembly (MGI:MGI:5576449 PMID:24613359 [IDA]) /// 0007186 // G-protein coupled receptor signaling pathway

				(MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000832 InterPro:IPR017983) /// 0016322 // neuron remodeling (MGI:MGI:5629603 PMID:25611509 [IGI] MGI:MGI:1344400) /// 0061743 /// 0099558 /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0048814 // regulation of dendrite morphogenesis (MGI:MGI:5644012 PMID:23628982 [IMP]) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297)
Myt1l	20.573968 17	5.15147 E-10	MGI:1100 511	0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0007399 // nervous system development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0524) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620550) /// 0030154 // cell differentiation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0221) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002515) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804)
Tenm1	20.347636 5	1.68865 E-11	MGI:1345 185	0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR009471) /// 0033138 // positive regulation of peptidyl-serine phosphorylation (MGI:MGI:5465054 PMID:22698694 [IDA]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0006359 // regulation of transcription from RNA polymerase III promoter (MGI:MGI:5487510 PMID:22209827 [IDA]) /// 0030838 // positive regulation of actin filament polymerization (MGI:MGI:5465054 PMID:22698694 [IDA]) /// 0051491 // positive regulation of filopodium assembly (MGI:MGI:5465054 PMID:22698694 [IDA]) /// 0007218 // neuropeptide signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0527) /// 0043406 // positive regulation of MAP kinase activity (MGI:MGI:5465054 PMID:22698694 [IDA]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804)
Gucy1a3	20.308469 56	5.3532E -16	MGI:1926 562	0006182 // cGMP biosynthetic process (MGI:MGI:3640061 PMID:16614755 [IMP] MGI:MGI:3640802) /// 0060087 // relaxation of vascular smooth muscle (MGI:MGI:3640061 PMID:16614755 [IMP] MGI:MGI:3640802) /// 0006182 // cGMP biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q02108) /// 0052565 // response to defense-related host nitric oxide production (MGI:MGI:3640061 PMID:16614755 [IMP] MGI:MGI:3640802) /// 0007165 // signal transduction (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000228924) /// 0009190 // cyclic nucleotide biosynthetic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) /// 0006182 // cGMP biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68436) /// 0006171 // cAMP biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68436) /// 0035556 // intracellular signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) /// 0008217 // regulation of blood pressure (MGI:MGI:3640061 PMID:16614755 [IMP] MGI:MGI:3640802) /// 0030828 // positive regulation of cGMP biosynthetic process (MGI:MGI:3640061 PMID:16614755 [IMP] MGI:MGI:3640802) /// 0007263 // nitric oxide mediated signal transduction (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68436)
Grin2b	20.294512 12	2.9765E -10	MGI:9582 1	0060078 // regulation of postsynaptic membrane potential (MGI:MGI:3689798 PMID:16157280 [IMP]) /// 0050806 // positive regulation of synaptic transmission (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:2677534 PMID:11530236 [IMP]) /// 0010738 // regulation of protein kinase A signaling cascade (MGI:MGI:5529705 PMID:24336715 [IMP]) /// 0035235 // ionotropic glutamate receptor signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 1900273 // positive regulation of long-term synaptic potentiation (MGI:MGI:3770075 PMID:16901514 [IMP]) /// 0050966 // detection of mechanical stimulus involved in sensory perception of pain (MGI:MGI:3604261 PMID:16190898 [IMP]) /// 0001701 // in utero embryonic development (MGI:MGI:894616 PMID:9147327 [IMP] MGI:MGI:1928295) /// 0007613 // memory (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0048168 // regulation of neuronal synaptic plasticity (MGI:MGI:3688374 PMID:14622581 [TAS]) /// 0007423 // sensory organ development (MGI:MGI:79108 PMID:8789948 [IMP] MGI:MGI:1928295) /// 0006816 // calcium ion transport

				<p>(MGI:MGI:3590469 PMID:16045501 [IMP]) /// 0001508 // regulation of action potential (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0001967 // suckling behavior (MGI:MGI:79108 PMID:8789948 [IMP] MGI:MGI:1928295) /// 0048511 // rhythmic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:2682163 PMID:14645471 [IGI] MGI:MGI:95819) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:2667489 PMID:12832518 [IMP]) /// 0007612 // learning (MGI:MGI:3701026 PMID:16710293 [IMP] MGI:MGI:3701351) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3590469 PMID:16045501 [IMP]) /// 0043408 // regulation of MAPK cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0001662 // behavioral fear response (MGI:MGI:3701026 PMID:16710293 [IMP] MGI:MGI:3701351) /// 0007612 // learning (MGI:MGI:1344140 PMID:10485705 [IDA]) /// 0008306 // associative learning (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0043113 // receptor clustering (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0009790 // embryo development (MGI:MGI:1195436 PMID:9458051 [IMP] MGI:MGI:1928293) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3610918 PMID:10634899 [IMP] MGI:MGI:1928295) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0048266 // behavioral response to pain (MGI:MGI:3610653 PMID:11711849 [IMP] MGI:MGI:1928295) /// 0006812 // cation transport (MGI:MGI:69304 PMID:7531804 [IGI] MGI:MGI:95819) /// 0060291 // long-term synaptic potentiation (MGI:MGI:4821029 PMID:20661302 [IGI] MGI:MGI:95820) /// 0007613 // memory (MGI:MGI:3689798 PMID:16157280 [IMP]) /// 0007268 // synaptic transmission (MGI:MGI:79108 PMID:8789948 [IMP] MGI:MGI:1928295) /// 0048167 // regulation of synaptic plasticity (MGI:MGI:3701026 PMID:16710293 [IMP] MGI:MGI:3701351) /// 0034220 // ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0001964 // startle response (MGI:MGI:3040117 PMID:11488959 [IMP] MGI:MGI:1928295) /// 0042596 // fear response (MGI:MGI:3689798 PMID:16157280 [IMP]) /// 0048169 // regulation of long-term neuronal synaptic plasticity (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0045471 // response to ethanol (MGI:MGI:2677534 PMID:11530236 [IMP]) /// 0014049 // positive regulation of glutamate secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0010942 // positive regulation of cell death (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2738) /// 0007613 // memory (MGI:MGI:1344140 PMID:10485705 [IDA]) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3689798 PMID:16157280 [IMP]) /// 0007611 // learning or memory (MGI:MGI:3688374 PMID:14622581 [TAS]) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001508) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0045471 // response to ethanol (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13224) /// 0048167 // regulation of synaptic plasticity (MGI:MGI:3621670 PMID:11719203 [IMP]) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:894616 PMID:9147327 [IMP] MGI:MGI:1928295) /// 0007613 // memory (MGI:MGI:5529705 PMID:24336715 [IMP]) /// 0001964 // startle response (MGI:MGI:3604326 PMID:16221859 [IGI] MGI:MGI:95820) /// 0006816 // calcium ion transport (MGI:MGI:3606996 PMID:12816890 [IMP] MGI:MGI:1928295)</p>
Calb2	20.1606177	9.72324E-10	MGI:101914	<p>0051480 // cytosolic calcium ion homeostasis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001461922) /// 0051480 // cytosolic calcium ion homeostasis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620981)</p>
Unc5d	20.15454288	6.98196E-13	MGI:2389364	<p>0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0098609 // 2001222 // regulation of neuron migration (MGI:MGI:5486433 PMID:21673655 [IGI] MGI:MGI:3603594) /// 0007411 // axon guidance (MGI:MGI:5486433 PMID:21673655 [IGI] MGI:MGI:3603594) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0021859 // pyramidal neuron differentiation (MGI:MGI:5440366 PMID:22726835 [IDA]) /// 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000488)</p>
Ttyh1	20.14987339	3.36083E-13	MGI:1889007	<p>0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0016337 // cell-cell adhesion (MGI:MGI:3702737 PMID:17116230 [IDA]) /// 0044070 // regulation of anion transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H313) /// 0007067 // mitosis (MGI:MGI:4461352 PMID:20568244 [IMP] MGI:MGI:4818475) /// 0007155 // cell adhesion</p>

				(MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0031589 // cell-substrate adhesion (MGI:MGI:3702737 PMID:17116230 [IDA]) /// 0006821 // chloride transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H313) /// 0046847 // filopodium assembly (MGI:MGI:3702737 PMID:17116230 [IDA]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Negr1	20.13484302	3.73739E-13	MGI:2444846	0010976 // positive regulation of neuron projection development (MGI:MGI:5446883 PMID:22844493 [IDA]) /// 0007631 // feeding behavior (MGI:MGI:5446883 PMID:22844493 [IMP] MGI:MGI:5447397) /// 0016337 // cell-cell adhesion (MGI:MGI:5446883 PMID:22844493 [IDA]) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0007626 // locomotory behavior (MGI:MGI:5446883 PMID:22844493 [IMP] MGI:MGI:5447397)
Syt4	20.09269982	1.44389E-14	MGI:101759	0048489 // synaptic vesicle transport (MGI:MGI:68023 PMID:8058779 [TAS]) /// 0006887 // exocytosis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028683) /// 0045955 // negative regulation of calcium ion-dependent exocytosis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68397) /// 0048791 // calcium ion-dependent exocytosis of neurotransmitter (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000001285) /// 0017158 // regulation of calcium ion-dependent exocytosis (MGI:MGI:68023 PMID:8058779 [TAS]) /// 0031339 // negative regulation of vesicle fusion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68397) /// 1903861 // 0007269 // neurotransmitter secretion (MGI:MGI:3047044 PMID:15197251 [IDA]) /// 0030154 // cell differentiation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0221) /// 0006906 // vesicle fusion (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000001285)
Snhg14	20.03679001	6.0988E-14		
Gm3764	20.036445	3.69178E-11	MGI:3781938	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Pak7	19.98393499	1.04589E-10	MGI:1920334	0006468 // protein phosphorylation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000719 InterPro:IPR002290) /// 0007010 // cytoskeleton organization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028754) /// 0007613 // memory (MGI:MGI:3820133 PMID:18675265 [IGI] MGI:MGI:2679420) /// 0016049 // cell growth (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028754) /// 0007612 // learning (MGI:MGI:3820133 PMID:18675265 [IGI] MGI:MGI:2679420) /// 0007626 // locomotory behavior (MGI:MGI:5508869 PMID:23593460 [IGI] MGI:MGI:2679420) /// 0007626 // locomotory behavior (MGI:MGI:3820133 PMID:18675265 [IGI] MGI:MGI:2679420) /// 0007612 // learning (MGI:MGI:5508869 PMID:23593460 [IGI] MGI:MGI:2679420) /// 0006915 // apoptotic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028754) /// 0007613 // memory (MGI:MGI:5508869 PMID:23593460 [IGI] MGI:MGI:2679420) /// 2001237 // negative regulation of extrinsic apoptotic signaling pathway (MGI:MGI:2673247 PMID:12897128 [IDA]) /// 0006950 // response to stress (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000684825) /// 0016310 // phosphorylation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0418) /// 0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053)
Scn8a	19.81071928	1.27886E-13	MGI:103169	0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0007517 // muscle organ development (MGI:MGI:3042517 PMID:15170223 [IMP] MGI:MGI:2429911) /// 0019228 // regulation of action potential in neuron (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3638) /// 0007626 // locomotory behavior (MGI:MGI:2670553 PMID:12920299 [IMP] MGI:MGI:1856079) /// 0009636 // response to toxic substance (MGI:MGI:3590477 PMID:16029194 [IDA]) /// 0035725 // sodium ion transmembrane transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UQD0) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0007628 // adult walking behavior (MGI:MGI:75224 PMID:7670495 [IMP] MGI:MGI:1856078) /// 0019228 // regulation of action potential in neuron (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000798901) /// 0050905 // neuromuscular process (MGI:MGI:57371 PMID:3674018 [IMP] MGI:MGI:1856079) /// 0008344 // adult locomotory behavior (MGI:MGI:57371 PMID:3674018 [IMP] MGI:MGI:1856079)

				<p>/// 0086010 // membrane depolarization involved in regulation of action potential (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000004140) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0035725 // sodium ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3638) /// 0006814 // sodium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3638) /// 0060078 // regulation of postsynaptic membrane potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UQD0) /// 0006814 // sodium ion transport (MGI:MGI:1316579 PMID:9828131 [NAS]) /// 0007605 // sensory perception of sound (MGI:MGI:3625255 PMID:12204355 [IMP] MGI:MGI:1856079) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)</p>
Spock3	19.665815 04	5.00563 E-12	MGI:1920 152	<p>0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR019577) /// 0010466 // negative regulation of peptidase activity (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0646) /// 0010951 // negative regulation of endopeptidase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9BQ16) /// 0019800 // peptide cross-linking via chondroitin 4-sulfate glycosaminoglycan (MGI:MGI:3807344 PMID:18757743 [IDA])</p>
Acsf6	19.584125 58	3.38526 E-14	MGI:8942 91	<p>0001676 // long-chain fatty acid metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69403) /// 0010747 // positive regulation of plasma membrane long-chain fatty acid transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69403) /// 0010976 // positive regulation of neuron projection development (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69403) /// 0001676 // long-chain fatty acid metabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UKU0) /// 0007405 // neuroblast proliferation (MGI:MGI:2664065 PMID:12767919 [IDA]) /// 0008152 // metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000873) /// 0006641 // triglyceride metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69403) /// 0010867 // positive regulation of triglyceride biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69403) /// 0008654 // phospholipid biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69403) /// 0006629 // lipid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0443) /// 0006631 // fatty acid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0276) /// 0015908 // fatty acid transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69403)</p>
5430419D17 Rik	19.527082 08	2.78911 E-09	MGI:1918 645	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
E130218I03 Rik	19.427897 25	8.91622 E-10	MGI:3528 958	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Cygb	19.264920 86	1.46552 E-14	MGI:2149 481	<p>0006979 // response to oxidative stress (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69415) /// 0015671 // oxygen transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0561) /// 0015671 // oxygen transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR013314) /// 0019395 // fatty acid oxidation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69415) /// 2000490 // negative regulation of hepatic stellate cell activation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69415) /// 0010764 // negative regulation of fibroblast migration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69415) /// 0006979 // response to oxidative stress (MGI:MGI:3688067 PMID:11320098 [ISS] UniProtKB:Q921A4) /// 0032966 // negative regulation of collagen biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69415) /// 0098869 /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)</p>
Slc24a4	19.256237 85	1.4774E -09	MGI:2447 362	<p>0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006813 // potassium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0633) /// 0007608 // sensory perception of smell (MGI:MGI:5306100 PMID:22057188 [IMP]) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR004837) /// 0006874 // cellular calcium ion homeostasis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000090975) /// 0006816 // calcium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0109) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR030232) /// 0050896 // response to stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0716) ///</p>

				0097186 // amelogenesis (MGI:MGI:5520028 PMID:23375655 [IMP]) /// 0006814 // sodium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0739) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Nr2e3	19.0589854	2.51294E-10	MGI:1346317	0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003068 InterPro:IPR000536 InterPro:IPR001723 InterPro:IPR001628 InterPro:IPR013088) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:3574255 PMID:15689355 [IGI] MGI:MGI:1194883) /// 0043401 // steroid hormone mediated signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000536) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3574255 PMID:15689355 [IGI] MGI:MGI:1194883) /// 0008285 // negative regulation of cell proliferation (MGI:MGI:3624051 PMID:12407160 [IMP] MGI:MGI:1346317) /// 0042462 // eye photoreceptor cell development (MGI:MGI:4849309 PMID:21052544 [IMP]) /// 0060041 // retina development in camera-type eye (MGI:MGI:4849309 PMID:21052544 [IMP]) /// 0060041 // retina development in camera-type eye (MGI:MGI:3624051 PMID:12407160 [IMP] MGI:MGI:1346317) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0045872 // positive regulation of rhodopsin gene expression (MGI:MGI:3574255 PMID:15689355 [IGI] MGI:MGI:1194883 MGI:MGI:102567)
Ryr2	18.99407916	2.2063E-15	MGI:99685	0060401 // cytosolic calcium ion transport (MGI:MGI:3713015 PMID:17431507 [IMP] MGI:MGI:3713774) /// 0086005 // regulation of ventricular cardiac muscle cell action potential (MGI:MGI:3820489 PMID:17872467 [IMP]) /// 0019722 // calcium-mediated signaling (MGI:MGI:1267127 PMID:9628868 [IMP]) /// 0002027 // regulation of heart rate (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0098735 /// 0060048 // cardiac muscle contraction (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0006816 // calcium ion transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0006816 // calcium ion transport (MGI:MGI:3027171 PMID:14593104 [IDA]) /// 0003220 // left ventricular cardiac muscle tissue morphogenesis (MGI:MGI:3713015 PMID:17431507 [IMP] MGI:MGI:3713774) /// 0030509 // BMP signaling pathway (MGI:MGI:3703823 PMID:17360443 [IDA]) /// 0035994 // response to muscle stretch (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0051775 // response to redox state (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0051284 // positive regulation of sequestering of calcium ion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0010882 // regulation of cardiac muscle contraction by calcium ion signaling (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0001666 // response to hypoxia (MGI:MGI:3836482 PMID:19120137 [IDA]) /// 0035584 // calcium-mediated signaling using intracellular calcium source (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0002027 // regulation of heart rate (MGI:MGI:3820489 PMID:17872467 [IMP]) /// 0051480 // cytosolic calcium ion homeostasis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620314) /// 0032026 // response to magnesium ion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620314) /// 0071313 // cellular response to caffeine (MGI:MGI:5431202 PMID:22406107 [IDA]) /// 0098904 /// 0031000 // response to caffeine (MGI:MGI:1345009 PMID:10473538 [IDA]) /// 0010460 // positive regulation of heart rate (MGI:MGI:2182484 PMID:12089338 [IMP] MGI:MGI:2183509) /// 0006816 // calcium ion transport (MGI:MGI:1345009 PMID:10473538 [IDA]) /// 0070296 // sarcoplasmic reticulum calcium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620314) /// 0014808 // release of sequestered calcium ion into cytosol by sarcoplasmic reticulum (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0006874 // cellular calcium ion homeostasis (MGI:MGI:1267127 PMID:9628868 [IMP]) /// 0051481 // reduction of cytosolic calcium ion concentration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620314) /// 0097050 // type B pancreatic cell apoptotic process (MGI:MGI:3720302 PMID:15044459 [IMP]) /// 0086029 // Purkinje myocyte to ventricular cardiac muscle cell signaling (MGI:MGI:3820489 PMID:17872467 [IMP]) /// 0098910 /// 0003300 // cardiac muscle hypertrophy (MGI:MGI:3713015 PMID:17431507 [IMP] MGI:MGI:3713774) /// 0098911 /// 0031000 // response to caffeine (MGI:MGI:3027171 PMID:14593104 [IDA]) /// 0098907 /// 0071313 // cellular response to caffeine

				(MGI:MGI:2182484 PMID:12089338 [IDA]) /// 0005513 // detection of calcium ion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0014850 // response to muscle activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0010460 // positive regulation of heart rate (MGI:MGI:3713015 PMID:17431507 [IMP] MGI:MGI:3713774) /// 0010881 // regulation of cardiac muscle contraction by regulation of the release of sequestered calcium ion (MGI:MGI:3621834 PMID:12837242 [IGI] UniProtKB:Q9Z212) /// 0034220 // ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620314) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620314) /// 0060402 // calcium ion transport into cytosol (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0014808 // release of sequestered calcium ion into cytosol by sarcoplasmic reticulum (MGI:MGI:4442115 PMID:20226167 [IDA]) /// 0071872 // cellular response to epinephrine stimulus (MGI:MGI:3820489 PMID:17872467 [IMP]) /// 0051209 // release of sequestered calcium ion into cytosol (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0071421 // manganese ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620314) /// 0071313 // cellular response to caffeine (MGI:MGI:1267127 PMID:9628868 [IDA]) /// 0031000 // response to caffeine (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0071313 // cellular response to caffeine (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0014808 // release of sequestered calcium ion into cytosol by sarcoplasmic reticulum (MGI:MGI:2182484 PMID:12089338 [IMP]) /// 0060070 // canonical Wnt receptor signaling pathway (MGI:MGI:3703823 PMID:17360443 [IDA]) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 1901896 // positive regulation of calcium-transporting ATPase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0003143 // embryonic heart tube morphogenesis (MGI:MGI:1267127 PMID:9628868 [IMP]) /// 0010460 // positive regulation of heart rate (MGI:MGI:2182484 PMID:12089338 [IMP]) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0006816 // calcium ion transport (MGI:MGI:3612568 PMID:16204356 [IPI] UniProtKB:Q61144) /// 0006816 // calcium ion transport (MGI:MGI:1267127 PMID:9628868 [IMP]) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:5141561 PMID:21673970 [IMP] MGI:MGI:3641338) /// 0055117 // regulation of cardiac muscle contraction (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0072599 // establishment of protein localization to endoplasmic reticulum (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736) /// 0051209 // release of sequestered calcium ion into cytosol (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620314) /// 0051592 // response to calcium ion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620314) /// 0097050 // type B pancreatic cell apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92736)
Scn1	18.942819 86	5.26259 E-18	MGI:1917 188	0006508 // proteolysis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005322) /// 0006887 // exocytosis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000313101)
Eef1a2	18.910852 93	1.76353 E-09	MGI:1096 317	0006414 // translational elongation (MGI:MGI:1203323 PMID:9588196 [IDA]) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:2158865 PMID:11724805 [IDA]) /// 0006412 // translation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0648) /// 0090218 // positive regulation of lipid kinase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q05639)
Csrnp3	18.901014 67	5.03047 E-12	MGI:1925 021	0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3769171 PMID:17726538 [IDA]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:3785099 PMID:18291095 [IDA]) /// 0010923 // negative regulation of phosphatase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8WYN3) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804)
Vstm2a	18.875660 65	4.97865 E-14	MGI:2384 826	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Nsg2	18.802346 07	2.24877 E-10	MGI:1202 070	0048268 // clathrin coat assembly (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR009431) /// 0007212 // dopamine receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR009431)

Nalcn	18.792054 53	8.93053 E-14	MGI:2444 306	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0006816 // calcium ion transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001295293) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0086010 // membrane depolarization involved in regulation of action potential (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000004140) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0006814 // sodium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0739) /// 0034220 // ion transmembrane transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000004140) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Rtn1	18.578002 58	2.82866 E-17	MGI:1933 947	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Igsf11	18.560213 82	1.18195 E-09	MGI:2388 477	0040008 // regulation of growth (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0341) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130)
Kcnb2	18.558749 48	1.68343 E-09	MGI:9963 2	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0051260 // protein homooligomerization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003131) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621349) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0072661 // protein targeting to plasma membrane (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621349) /// 0006813 // potassium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621349) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Sez6l	18.508380 28	4.47692 E-09	MGI:1935 121	0008344 // adult locomotory behavior (MGI:MGI:3654399 PMID:16814779 [IGI] MGI:MGI:2385295 MGI:MGI:104745) /// 0060074 // synapse maturation (MGI:MGI:3654399 PMID:16814779 [IGI] MGI:MGI:2385295 MGI:MGI:104745) /// 0090036 // regulation of protein kinase C signaling cascade (MGI:MGI:3654399 PMID:16814779 [IGI] MGI:MGI:2385295 MGI:MGI:104745) /// 0021680 // cerebellar Purkinje cell layer development (MGI:MGI:3654399 PMID:16814779 [IGI] MGI:MGI:2385295 MGI:MGI:104745)
Hecw1	18.486484 28	4.00208 E-10	MGI:2444 115	0042787 // protein ubiquitination involved in ubiquitin-dependent protein catabolic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000134256)
Ppfia2	18.463414 63	1.30841 E-10	MGI:2443 834	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Capn6	18.373507 21	4.64488 E-20	MGI:1100 850	0001578 // microtubule bundle formation (MGI:MGI:3709943 PMID:17210638 [IMP]) /// 0006508 // proteolysis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000021568) /// 0051493 // regulation of cytoskeleton organization (MGI:MGI:3709943 PMID:17210638 [IMP])
Dpp6	18.312462	6.53586 E-09	MGI:9492 1	0043266 // regulation of potassium ion transport (MGI:MGI:4459564 PMID:20573902 [IMP]) /// 0072659 // protein localization to plasma membrane (MGI:MGI:5616307 PMID:22311982 [IDA]) /// 1901379 // regulation of potassium ion transmembrane transport (MGI:MGI:5616307 PMID:22311982 [IDA]) /// 0042391 // regulation of membrane potential (MGI:MGI:4459564 PMID:20573902 [IMP]) /// 0090004 // positive regulation of establishment of protein localization to plasma membrane (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68402) /// 0042391 // regulation of membrane potential (MGI:MGI:5299265 PMID:21943606 [IMP] MGI:MGI:5302080) /// 1901381 // positive regulation of potassium ion transmembrane transport (MGI:MGI:5299265 PMID:21943606 [IMP] MGI:MGI:5302080) /// 0043268 // positive regulation of potassium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68402) /// 0006508 // proteolysis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001375 InterPro:IPR002469) /// 0019228 // regulation of action potential in neuron (MGI:MGI:4459564 PMID:20573902 [IMP]) /// 1901379 // regulation of potassium ion transmembrane transport

				(MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P42658) /// 1901379 // regulation of potassium ion transmembrane transport (MGI:MGI:5554959 PMID:24225951 [IGI] MGI:MGI:97769)
Lsmp	18.25040658	2.26662E-10	MGI:1261760	0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0035641 // locomotory exploration behavior (MGI:MGI:3773579 PMID:18199495 [IMP] MGI:MGI:3773703)
Pnmal1	18.22694697	2.90125E-09	MGI:1918941	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Arl6	18.22102645	1.05162E-14	MGI:1927136	0007264 // small GTPase mediated signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR024156) /// 0007420 // brain development (MGI:MGI:5306530 PMID:22139371 [IMP] MGI:MGI:5310744) /// 0046909 // intermembrane transport (MGI:MGI:5306530 PMID:22139371 [IMP] MGI:MGI:5310744) /// 0097499 /// 0007265 // Ras protein signal transduction (MGI:MGI:1858942 PMID:10508919 [ISS]) /// 0010842 // retina layer formation (MGI:MGI:5306530 PMID:22139371 [IMP] MGI:MGI:5310744) /// 0042384 // cilium assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H0F7) /// 0042384 // cilium assembly (MGI:MGI:5306530 PMID:22139371 [IMP] MGI:MGI:5310744) /// 0010842 // retina layer formation (MGI:MGI:4442100 PMID:20333246 [IMP] MGI:MGI:4442928) /// 0030030 // cell projection organization (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0970) /// 1903441 /// 0061512 // protein localization to cilium (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:Q9H0F7) /// 0008589 // regulation of smoothened signaling pathway (MGI:MGI:5306530 PMID:22139371 [IMP] MGI:MGI:5310744) /// 0016055 // Wnt receptor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H0F7) /// 0006471 // protein ADP-ribosylation (MGI:MGI:1858942 PMID:10508919 [ISS]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0015031 // protein transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0653)
Fbln2	18.19544013	3.7981E-72	MGI:95488	0010811 // positive regulation of cell-substrate adhesion (MGI:MGI:3807344 PMID:18757743 [IDA])
Kcna2	18.17701462	1.16839E-15	MGI:96659	0006813 // potassium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0633) /// 0014059 // regulation of dopamine secretion (MGI:MGI:4947004 PMID:21233214 [IMP]) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2950) /// 0019233 // sensory perception of pain (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2950) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0019228 // regulation of action potential in neuron (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2950) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0021633 // optic nerve structural organization (MGI:MGI:3042560 PMID:15102918 [IMP] MGI:MGI:3043422) /// 0051260 // protein homooligomerization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003131) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P16389) /// 0051259 // protein oligomerization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2950) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0045188 // regulation of circadian sleep/wake cycle, non-REM sleep (MGI:MGI:3770734 PMID:17925011 [IMP]) /// 0006813 // potassium ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003968 InterPro:IPR003972 InterPro:IPR004049 InterPro:IPR028325) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:4947004 PMID:21233214 [IDA])
Esrrg	18.13916745	8.32516E-14	MGI:1347056	0006355 // regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P62508) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:3690144 PMID:12715898 [IDA]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:1342114 PMID:10428842 [IDA]) /// 0043401 // steroid hormone mediated signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000536) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:5572884 PMID:15149736 [IMP]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:3690793 PMID:10072763 [NAS]) /// 0048384 // retinoic acid receptor signaling pathway

				(MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003078) /// 0007275 // multicellular organismal development (MGI:MGI:1342114 PMID:10428842 [NAS]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804)
Snhg11	18.099116 93	3.56823 E-10	MGI:2441 845	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Rnf207	18.031461 65	4.50178 E-10	MGI:2684 989	1902261 /// 0010628 // positive regulation of gene expression (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6ZRF8) /// 1903762
Pcdh15	17.840785 3	1.38156 E-08	MGI:1891 428	0060088 // auditory receptor cell stereocilium organization (MGI:MGI:3654702 PMID:16887306 [IMP] MGI:MGI:3505691) /// 0007605 // sensory perception of sound (MGI:MGI:3722521 PMID:14570705 [IMP]) /// 0008344 // adult locomotory behavior (MGI:MGI:76231 [IMP] MGI:MGI:1856394 MGI:MGI:1855958) /// 0045494 // photoreceptor cell maintenance (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96QU1) /// 0002009 // morphogenesis of an epithelium (MGI:MGI:1929046 PMID:11138007 [IMP] MGI:MGI:2151877) /// 0007605 // sensory perception of sound (MGI:MGI:1341448 PMID:10430593 [IMP] MGI:MGI:2151877) /// 0060088 // auditory receptor cell stereocilium organization (MGI:MGI:3526751 PMID:15537665 [IGI] MGI:MGI:1890219) /// 0007605 // sensory perception of sound (MGI:MGI:3616414 PMID:16481439 [IMP] MGI:MGI:1856394) /// 0060088 // auditory receptor cell stereocilium organization (MGI:MGI:1928787 PMID:10978835 [IMP] MGI:MGI:2151877) /// 0035264 // multicellular organism growth (MGI:MGI:1928787 PMID:10978835 [IMP] MGI:MGI:2151877) /// 0007605 // sensory perception of sound (MGI:MGI:76231 [IMP] MGI:MGI:1856394 MGI:MGI:1855958) /// 0007605 // sensory perception of sound (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:Q96QU1) /// 0048839 // inner ear development (MGI:MGI:1928787 PMID:10978835 [IMP] MGI:MGI:2151877 MGI:MGI:1855958) /// 0007015 // actin filament organization (MGI:MGI:3619110 PMID:11124469 [IMP] MGI:MGI:1856396 MGI:MGI:1856394 MGI:MGI:1855958) /// 0007155 // cell adhesion (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR020894 InterPro:IPR030718) /// 0007626 // locomotory behavior (MGI:MGI:1928787 PMID:10978835 [IMP] MGI:MGI:2151877) /// 0007605 // sensory perception of sound (MGI:MGI:3526751 PMID:15537665 [IGI] MGI:MGI:1890219) /// 0007605 // sensory perception of sound (MGI:MGI:53703 PMID:5093631 [IMP] MGI:MGI:1856467) /// 0051017 // actin filament bundle assembly (MGI:MGI:4950645 PMID:21427143 [IMP] MGI:MGI:5697806) /// 0007601 // visual perception (MGI:MGI:3655911 PMID:16799054 [IMP] MGI:MGI:2448714) /// 0007605 // sensory perception of sound (MGI:MGI:3619110 PMID:11124469 [IMP] MGI:MGI:1856396 MGI:MGI:1856394 MGI:MGI:1855958) /// 0060013 // righting reflex (MGI:MGI:1928787 PMID:10978835 [IMP] MGI:MGI:2151877) /// 0048839 // inner ear development (MGI:MGI:3574187 PMID:15811708 [IMP] MGI:MGI:2183469) /// 0051592 // response to calcium ion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1590969) /// 0007628 // adult walking behavior (MGI:MGI:3619110 PMID:11124469 [IMP] MGI:MGI:1856396 MGI:MGI:1856394 MGI:MGI:1855958) /// 0007626 // locomotory behavior (MGI:MGI:3664354 PMID:16962269 [IMP] MGI:MGI:2183469) /// 0060122 // inner ear receptor stereocilium organization (MGI:MGI:3794916 PMID:18339676 [IMP] MGI:MGI:1856394) /// 0007156 // homophilic cell adhesion (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002126) /// 0035058 // nonmotile primary cilium assembly (MGI:MGI:3616414 PMID:16481439 [IMP] MGI:MGI:1856394) /// 0050957 // equilibriumception (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96QU1) /// 0007605 // sensory perception of sound (MGI:MGI:1196061 PMID:9653653 [IMP] MGI:MGI:1856467) /// 0050910 // detection of mechanical stimulus involved in sensory perception of sound (MGI:MGI:3616414 PMID:16481439 [IMP] MGI:MGI:1856394) /// 0060013 // righting reflex (MGI:MGI:3574187 PMID:15811708 [IMP] MGI:MGI:2183469) /// 0060088 // auditory receptor cell stereocilium organization (MGI:MGI:5468200 PMID:23217710 [IMP] MGI:MGI:1856394) /// 0007626 // locomotory behavior (MGI:MGI:3574187 PMID:15811708 [IMP] MGI:MGI:2183469) /// 0042491 // auditory receptor cell differentiation (MGI:MGI:3616414 PMID:16481439 [IMP] MGI:MGI:1856394) /// 0050973 // detection of mechanical stimulus involved in equilibriumception (MGI:MGI:3616414 PMID:16481439 [IMP] MGI:MGI:1856394) /// 0060088 // auditory receptor cell stereocilium organization (MGI:MGI:3619110 PMID:11124469 [IMP] MGI:MGI:1856396 MGI:MGI:1856394 MGI:MGI:1855958) /// 0007605 // sensory perception of sound (MGI:MGI:1928787 PMID:10978835 [IMP] MGI:MGI:2151877) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) ///

				0007626 // locomotory behavior (MGI:MGI:1341448 PMID:10430593 [IMP] MGI:MGI:2151877) /// 0050910 // detection of mechanical stimulus involved in sensory perception of sound (MGI:MGI:4950645 PMID:21427143 [IMP] MGI:MGI:5697806) /// 0050953 // sensory perception of light stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96QU1) /// 0001964 // startle response (MGI:MGI:3574187 PMID:15811708 [IMP] MGI:MGI:2183469)
Car10	17.650670 14	1.51899 E-08	MGI:1919 855	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Slc6a2	17.645044 39	8.97994 E-12	MGI:1270 850	0015844 // monoamine transport (MGI:MGI:3586396 PMID:16024787 [ISO] UniProtKB:P23975) /// 0015874 // norepinephrine transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000178409) /// 0006836 // neurotransmitter transport (MGI:MGI:2157273 PMID:11805341 [IDA]) /// 0015874 // norepinephrine transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621822) /// 0048265 // response to pain (MGI:MGI:2157273 PMID:11805341 [IMP]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Sez6	17.629553 44	2.44363 E-10	MGI:1047 45	0060074 // synapse maturation (MGI:MGI:3654399 PMID:16814779 [IGI] MGI:MGI:1935121 MGI:MGI:2385295) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3776726 PMID:18031681 [IMP] MGI:MGI:3777582) /// 1900006 // positive regulation of dendrite development (MGI:MGI:3776726 PMID:18031681 [IDA]) /// 0090036 // regulation of protein kinase C signaling cascade (MGI:MGI:3654399 PMID:16814779 [IGI] MGI:MGI:1935121 MGI:MGI:2385295) /// 0008344 // adult locomotory behavior (MGI:MGI:3654399 PMID:16814779 [IGI] MGI:MGI:1935121 MGI:MGI:2385295) /// 0050773 // regulation of dendrite development (MGI:MGI:3776726 PMID:18031681 [IMP] MGI:MGI:3777582) /// 0021680 // cerebellar Purkinje cell layer development (MGI:MGI:3654399 PMID:16814779 [IGI] MGI:MGI:1935121 MGI:MGI:2385295) /// 2000171 // negative regulation of dendrite development (MGI:MGI:3776726 PMID:18031681 [IDA])
Hcn1	17.621839 42	1.20389 E-08	MGI:1096 392	0006813 // potassium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0633) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 2001259 // positive regulation of cation channel activity (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620688) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:5520040 PMID:22006928 [IMP]) /// 0042391 // regulation of membrane potential (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000025348) /// 0060078 // regulation of postsynaptic membrane potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O60741) /// 0003254 // regulation of membrane depolarization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620688) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O60741) /// 0046549 // retinal cone cell development (MGI:MGI:4849309 PMID:21052544 [IMP]) /// 0006814 // sodium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0739) /// 0035725 // sodium ion transmembrane transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O60741) /// 0042391 // regulation of membrane potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O60741) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0071320 // cellular response to cAMP (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O60741) /// 0071320 // cellular response to cAMP (MGI:MGI:5520040 PMID:22006928 [IMP]) /// 0045759 // negative regulation of action potential (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620688) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 1902630 /// 0045176 // apical protein localization (MGI:MGI:3531603 PMID:15564593 [IMP] MGI:MGI:2686950) /// 0051592 // response to calcium ion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620688) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0006813 // potassium ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003938)
Chmb3	17.491261	4.27263 E-09	MGI:1062 12	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0007274 // neuromuscular synaptic transmission (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001450363) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006201 InterPro:IPR006029 InterPro:IPR002394) /// 0035094 // response to nicotine (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001450363) /// 0051291 // protein heterooligomerization

				(MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621544) /// 0098655 /// 0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006202) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0007271 // synaptic transmission, cholinergic (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001450363)
Dnm1	17.436723 11	6.61314 E-21	MGI:1073 84	0007032 // endosome organization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q05193) /// 0008344 // adult locomotory behavior (MGI:MGI:4821669 PMID:20700442 [IMP] MGI:MGI:3033341) /// 0031623 // receptor internalization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:71096) /// 0006897 // endocytosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q05193) /// 0006898 // receptor-mediated endocytosis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:71096) /// 0002031 // G-protein coupled receptor internalization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:71096) /// 0051932 // synaptic transmission, GABAergic (MGI:MGI:4821669 PMID:20700442 [IMP] MGI:MGI:3033341) /// 0006897 // endocytosis (MGI:MGI:4821669 PMID:20700442 [IDA]) /// 0051262 // protein tetramerization (MGI:MGI:4821669 PMID:20700442 [IMP] MGI:MGI:3033341) /// 0007605 // sensory perception of sound (MGI:MGI:4821669 PMID:20700442 [IMP] MGI:MGI:3033341) /// 1903423 /// 0072583 // clathrin-mediated endocytosis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR027741) /// 1901998 // toxin transport (MGI:MGI:5492256 PMID:23716698 [IMP]) /// 0006898 // receptor-mediated endocytosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q05193)
Frrs11	17.430049 72	4.39803 E-09	MGI:2442 704	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Tmod2	17.429671 98	1.0536E -32	MGI:1355 335	0030239 // myofibril assembly (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000096564) /// 0007015 // actin filament organization (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000096563) /// 0051694 // pointed-end actin filament capping (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR004934 InterPro:IPR030130) /// 0007270 // neuron-neuron synaptic transmission (MGI:MGI:2663390 PMID:12799133 [IMP] MGI:MGI:2664500 MGI:MGI:2664502) /// 0007611 // learning or memory (MGI:MGI:2663390 PMID:12799133 [IMP] MGI:MGI:2664502) /// 0006936 // muscle contraction (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000096567) /// 0045745 // positive regulation of G-protein coupled receptor protein signaling pathway (MGI:MGI:2663390 PMID:12799133 [IMP] MGI:MGI:2664500)
Dscam	17.420152 76	6.54232 E-10	MGI:1196 281	0048842 // positive regulation of axon extension involved in axon guidance (MGI:MGI:3829111 PMID:18585357 [IDA]) /// 0007162 // negative regulation of cell adhesion (MGI:MGI:4413613 PMID:19945391 [IMP]) /// 0007399 // nervous system development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0524) /// 0007155 // cell adhesion (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR033027) /// 0042327 // positive regulation of phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O60469) /// 0048813 // dendrite morphogenesis (MGI:MGI:3768917 PMID:18216855 [IMP] MGI:MGI:3761008) /// 0048842 // positive regulation of axon extension involved in axon guidance (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O60469) /// 0048842 // positive regulation of axon extension involved in axon guidance (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619992) /// 0007626 // locomotory behavior (MGI:MGI:3768917 PMID:18216855 [IMP] MGI:MGI:3761008) /// 0007399 // nervous system development (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR033027) /// 0070593 // dendrite self-avoidance (MGI:MGI:4413613 PMID:19945391 [IMP]) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0060060 // post-embryonic retina morphogenesis in camera-type eye (MGI:MGI:3768917 PMID:18216855 [IMP] MGI:MGI:3761008)
Snrpn	17.405589 49	4.13666 E-11	MGI:9834 7	0000398 // mRNA splicing, via spliceosome (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000075760)
RP23-54G8.1	17.395574 51	1.37703 E-09		
C1qc	17.297211 86	2.36469 E-33	MGI:8822 5	0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0006958 // complement activation, classical pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0180) /// 0045650 // negative regulation of macrophage differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P02747) /// 0002376 //

				immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0030853 // negative regulation of granulocyte differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P02747)
Rpl_1	17.181299 97	3.31812 E-08		
Fat3	17.181173 83	1.253E- 11	MGI:2444 314	0001764 // neuron migration (MGI:MGI:5292419 PMID:21903076 [IMP] MGI:MGI:5295415) /// 0007155 // cell adhesion (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR020894) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0007156 // homophilic cell adhesion (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002126) /// 0000904 // cell morphogenesis involved in differentiation (MGI:MGI:5292419 PMID:21903076 [IMP] MGI:MGI:5295415) /// 2000171 // negative regulation of dendrite development (MGI:MGI:5292419 PMID:21903076 [IMP] MGI:MGI:5295415) /// 0010842 // retina layer formation (MGI:MGI:5292419 PMID:21903076 [IGI] MGI:MGI:1341907)
Cacna2d4	17.144179 01	9.58599 E-10	MGI:2442 632	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0006816 // calcium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0109) /// 0050908 // detection of light stimulus involved in visual perception (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q7Z3S7) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q7Z3S7) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000018365) /// 0051924 // regulation of calcium ion transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000018365) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Unc80	16.920513 64	3.74096 E-09	MGI:2652 882	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Sv2c	16.734782 66	8.48054 E-11	MGI:1922 459	0007268 // synaptic transmission (MGI:MGI:2657076 PMID:12687700 [TAS]) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR011701 InterPro:IPR005828 InterPro:IPR005829) /// 0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR022308) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0006836 // neurotransmitter transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0532)
Ptpn2	16.722630 51	5.19929 E-09	MGI:1074 18	0035773 // insulin secretion involved in cellular response to glucose stimulus (MGI:MGI:5141326 PMID:21732083 [IMP]) /// 0016311 // dephosphorylation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR016130 InterPro:IPR000387) /// 0034260 // negative regulation of GTPase activity (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61904) /// 0006470 // protein dephosphorylation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000242) /// 0007269 // neurotransmitter secretion (MGI:MGI:3847158 PMID:19361477 [IMP])
Phactr1	16.675956 7	5.991E- 16	MGI:2659 021	0048870 // cell motility (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9C0D0) /// 0043149 // stress fiber assembly (MGI:MGI:5487491 PMID:22976292 [IMP]) /// 0042325 // regulation of phosphorylation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1303187) /// 0031032 // actomyosin structure organization (MGI:MGI:5487491 PMID:22976292 [IMP]) /// 0031032 // actomyosin structure organization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9C0D0) /// 0031532 // actin cytoskeleton reorganization (MGI:MGI:5487491 PMID:22976292 [IMP]) /// 0043149 // stress fiber assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9C0D0)
Cdhr1	16.645519 55	1.45311 E-10	MGI:2157 782	0007155 // cell adhesion (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR020894) /// 0009987 // cellular process (MGI:MGI:2154844 PMID:11738025 [IMP] MGI:MGI:3046299) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0007156 // homophilic cell adhesion (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002126) /// 0045494 // photoreceptor cell maintenance (MGI:MGI:2154844 PMID:11738025 [IMP] MGI:MGI:3046299)

Col6a3	16.629262 42	1.34623 E-41	MGI:8846 1	
Cbln2	16.621101 64	4.65036 E-09	MGI:8828 2	0051965 // positive regulation of synapse assembly (MGI:MGI:5002432 PMID:21356198 [IDA])
Grik2	16.617012 45	5.13837 E-12	MGI:9581 5	0007268 // synaptic transmission (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2733) /// 0042391 // regulation of membrane potential (MGI:MGI:3611088 PMID:16219388 [IMP] MGI:MGI:1857979) /// 0042391 // regulation of membrane potential (MGI:MGI:49230 PMID:1310861 [IDA]) /// 0042391 // regulation of membrane potential (MGI:MGI:1197809 PMID:9490692 [IMP] MGI:MGI:1857979) /// 0048169 // regulation of long-term neuronal synaptic plasticity (MGI:MGI:3050715 PMID:11182092 [IMP] MGI:MGI:1857979) /// 0048169 // regulation of long-term neuronal synaptic plasticity (MGI:MGI:3040774 PMID:12947409 [IMP] MGI:MGI:1857979) /// 0060080 // regulation of inhibitory postsynaptic membrane potential (MGI:MGI:2387276 PMID:12223554 [IMP] MGI:MGI:1857979) /// 0006874 // cellular calcium ion homeostasis (MGI:MGI:3611088 PMID:16219388 [IMP] MGI:MGI:1857979) /// 0042391 // regulation of membrane potential (MGI:MGI:3622023 PMID:15513934 [IMP] MGI:MGI:1857979) /// 0060080 // regulation of inhibitory postsynaptic membrane potential (MGI:MGI:1354133 PMID:10704492 [IMP] MGI:MGI:1857979) /// 0050804 // regulation of synaptic transmission (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13002) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3654423 PMID:11069933 [IMP] MGI:MGI:1857979) /// 0042391 // regulation of membrane potential (MGI:MGI:3531002 PMID:15509753 [IMP] MGI:MGI:1857979) /// 0060080 // regulation of inhibitory postsynaptic membrane potential (MGI:MGI:1927732 PMID:11144357 [IGI] MGI:MGI:95814) /// 0007268 // synaptic transmission (MGI:MGI:3688795 PMID:15928066 [IGI] MGI:MGI:95814) /// 0043113 // receptor clustering (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2733) /// 0048172 // regulation of short-term neuronal synaptic plasticity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13002) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3575241 PMID:11985817 [IGI] MGI:MGI:95814) /// 0043525 // positive regulation of neuron apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2733) /// 0007268 // synaptic transmission (MGI:MGI:3688795 PMID:15928066 [IMP] MGI:MGI:1857979) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3708428 PMID:17428973 [IGI] MGI:MGI:107164) /// 0048169 // regulation of long-term neuronal synaptic plasticity (MGI:MGI:3611088 PMID:16219388 [IMP] MGI:MGI:1857979) /// 0001662 // behavioral fear response (MGI:MGI:3577154 PMID:15673679 [IMP] MGI:MGI:1857979) /// 0051967 // negative regulation of synaptic transmission, glutamatergic (MGI:MGI:3575241 PMID:11985817 [IGI] MGI:MGI:95814) /// 0042391 // regulation of membrane potential (MGI:MGI:49230 PMID:1310861 [IGI] MGI:MGI:95818) /// 0050806 // positive regulation of synaptic transmission (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13002) /// 0051967 // negative regulation of synaptic transmission, glutamatergic (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2733) /// 0035249 // synaptic transmission, glutamatergic (MGI:MGI:3531002 PMID:15509753 [IMP] MGI:MGI:1857979) /// 0042391 // regulation of membrane potential (MGI:MGI:2387276 PMID:12223554 [IMP]) /// 0048172 // regulation of short-term neuronal synaptic plasticity (MGI:MGI:3050715 PMID:11182092 [IMP] MGI:MGI:1857979) /// 0006886 // intracellular protein transport (MGI:MGI:3574145 PMID:15014126 [IDA]) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3708428 PMID:17428973 [IMP] MGI:MGI:1857979) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001508) /// 0035249 // synaptic transmission, glutamatergic (MGI:MGI:1202247 PMID:9580260 [IMP] MGI:MGI:1857979) /// 0042391 // regulation of membrane potential (MGI:MGI:2183350 PMID:12151522 [IDA]) /// 0060080 // regulation of inhibitory postsynaptic membrane potential (MGI:MGI:1354133 PMID:10704492 [IGI] MGI:MGI:99402) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0048169 // regulation of long-term neuronal synaptic plasticity (MGI:MGI:3577154 PMID:15673679 [IMP] MGI:MGI:1857979) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3615737 PMID:14724198 [IMP] MGI:MGI:1857979) /// 0046328 // regulation of JNK cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2733) /// 0051402 // neuron apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2733) /// 0042391 // regulation of membrane potential (MGI:MGI:1354133 PMID:10704492 [IMP] MGI:MGI:1857979) /// 0019228 // regulation of action potential in neuron (MGI:MGI:3622010 PMID:15539395 [IMP] MGI:MGI:1857979) /// 0043524 // negative regulation of neuron apoptotic process

				(MGI:MGI:1344923 PMID:10479699 [IGI] MGI:MGI:95819) /// 0060080 // regulation of inhibitory postsynaptic membrane potential (MGI:MGI:1327732 PMID:9880586 [IMP] MGI:MGI:1857979) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Cend1	16.614132 41	4.35999 E-10	MGI:1929 898	0021549 // cerebellum development (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR020162) /// 0007628 // adult walking behavior (MGI:MGI:4830814 PMID:20153830 [IMP] MGI:MGI:4831137) /// 0021686 // cerebellar granular layer maturation (MGI:MGI:4830814 PMID:20153830 [IMP] MGI:MGI:4831137) /// 0021941 // negative regulation of cerebellar granule cell precursor proliferation (MGI:MGI:4830814 PMID:20153830 [IMP] MGI:MGI:4831137) /// 0030182 // neuron differentiation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR020162) /// 0021702 // cerebellar Purkinje cell differentiation (MGI:MGI:4830814 PMID:20153830 [IMP] MGI:MGI:4831137) /// 0021933 // radial glia guided migration of cerebellar granule cell (MGI:MGI:4830814 PMID:20153830 [IMP] MGI:MGI:4831137)
Disp2	16.607506 07	4.72563 E-16	MGI:2388 733	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Gnb3	16.603994 07	3.80247 E-08	MGI:9578 5	0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:69413 PMID:1543505 [TAS]) /// 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR016346) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807)
Atp6v0e2	16.596016 26	9.78593 E-16	MGI:1923 502	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0016049 // cell growth (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8NHE4) /// 0015991 // ATP hydrolysis coupled proton transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR008389 InterPro:IPR017385) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0015992 // proton transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0375)
Sv2b	16.554619 08	6.69214 E-14	MGI:1927 338	0007268 // synaptic transmission (MGI:MGI:2657076 PMID:12687700 [TAS]) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR011701 InterPro:IPR005828 InterPro:IPR005829) /// 0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR022308) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0006836 // neurotransmitter transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0532)
Adamts3	16.543096 45	2.73796 E-12	MGI:3045 353	0032964 // collagen biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15072) /// 1900748 // positive regulation of vascular endothelial growth factor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15072) /// 0010573 // vascular endothelial growth factor production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15072) /// 0016485 // protein processing (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15072) /// 0016485 // protein processing (MGI:MGI:3621082 PMID:16556917 [IDA])
Slc8a3	16.518180 23	5.59037 E-10	MGI:1079 76	0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR004837) /// 0006816 // calcium ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR004836) /// 0014819 // regulation of skeletal muscle contraction (MGI:MGI:3027331 PMID:14722618 [IMP]) /// 0030001 // metal ion transport (MGI:MGI:83241 PMID:8798769 [IDA]) /// 0002244 // hematopoietic progenitor cell differentiation (MGI:MGI:5520108 PMID:24029230 [IMP]) /// 0006874 // cellular calcium ion homeostasis (MGI:MGI:5013898 PMID:21593315 [IMP]) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:5013898 PMID:21593315 [IMP]) /// 0006814 // sodium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620197) /// 0042552 // myelination (MGI:MGI:5524192 PMID:21959935 [IMP]) /// 0006816 // calcium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0109) /// 0006874 // cellular calcium ion homeostasis (MGI:MGI:3027331 PMID:14722618 [IMP]) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:3027331 PMID:14722618 [IMP]) /// 0060291 // long-term synaptic potentiation (MGI:MGI:5013898 PMID:21593315 [IMP]) /// 0048709 // oligodendrocyte differentiation (MGI:MGI:5524192 PMID:21959935 [IMP]) /// 1990035 // calcium ion import into cell (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620197) /// 0035725 // sodium ion transmembrane transport (MGI:MGI:3027331 PMID:14722618 [IMP]) /// 1990034 // calcium ion export from cell (MGI:MGI:4417868 GO_REF:0000096

				[ISO] RGD:620197) /// 0007612 // learning (MGI:MGI:5013898 PMID:21593315 [IMP]) /// 0051560 // mitochondrial calcium ion homeostasis (MGI:MGI:5693358 PMID:24101730 [IMP]) /// 0071320 // cellular response to cAMP (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620197) /// 0007154 // cell communication (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003644) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0060402 // calcium ion transport into cytosol (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620197) /// 0006851 // mitochondrial calcium ion transport (MGI:MGI:5693358 PMID:24101730 [IMP]) /// 0007613 // memory (MGI:MGI:5013898 PMID:21593315 [IMP]) /// 0071456 // cellular response to hypoxia (MGI:MGI:5693358 PMID:24101730 [IDA]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Cxxc4	16.47245199	6.70502E-12	MGI:2442112	0016055 // Wnt receptor signaling pathway (MGI:MGI:1930830 PMID:11113207 [IPI] UniProtKB:P51141) /// 0030178 // negative regulation of Wnt receptor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H2H0)
Fndc1	16.37127065	1.51819E-24	MGI:1915905	0071456 // cellular response to hypoxia (MGI:MGI:4420359 PMID:19723622 [ISO] UniProtKB:Q2Q0I9) /// 0051223 // regulation of protein transport (MGI:MGI:4420359 PMID:19723622 [ISO] UniProtKB:Q2Q0I9) /// 0001934 // positive regulation of protein phosphorylation (MGI:MGI:4420359 PMID:19723622 [ISO] UniProtKB:Q2Q0I9) /// 0010666 // positive regulation of cardiac muscle cell apoptotic process (MGI:MGI:4420359 PMID:19723622 [ISO] UniProtKB:Q2Q0I9)
Celf4	16.3144366	1.98007E-15	MGI:1932407	0006376 // mRNA splice site selection (MGI:MGI:1930458 PMID:11158314 [IDA]) /// 0048026 // positive regulation of mRNA splicing, via spliceosome (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9BZC1) /// 0048025 // negative regulation of mRNA splicing, via spliceosome (MGI:MGI:5532638 PMID:23636947 [IMP]) /// 0090394 // negative regulation of excitatory postsynaptic membrane potential (MGI:MGI:5313512 PMID:21745337 [IMP] MGI:MGI:5425630) /// 0000381 // regulation of alternative mRNA splicing, via spliceosome (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:Q9BZC1) /// 0006397 // mRNA processing (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0507) /// 0008380 // RNA splicing (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0508) /// 1902866
Fam171b	16.284721	1.93699E-20	MGI:2444579	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Ntng1	16.27817397	9.82456E-13	MGI:1934028	0007399 // nervous system development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0524) /// 0007409 // axonogenesis (MGI:MGI:2158548 PMID:11804778 [IDA]) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0030154 // cell differentiation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0221)
Grin2a	16.27424981	8.24592E-11	MGI:95820	0060078 // regulation of postsynaptic membrane potential (MGI:MGI:3689798 PMID:16157280 [IMP]) /// 0001508 // regulation of action potential (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0051930 // regulation of sensory perception of pain (MGI:MGI:3702825 PMID:10771345 [IMP] MGI:MGI:1928285) /// 0098655 // 0042428 // serotonin metabolic process (MGI:MGI:2384280 PMID:11160454 [IMP] MGI:MGI:1928285) /// 1900273 // positive regulation of long-term synaptic potentiation (MGI:MGI:3770075 PMID:16901514 [IMP]) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:2682163 PMID:14645471 [IMP] MGI:MGI:1928287) /// 0006816 // calcium ion transport (MGI:MGI:2682163 PMID:14645471 [IMP] MGI:MGI:1928287) /// 0007626 // locomotory behavior (MGI:MGI:3687911 PMID:12427824 [TAS]) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:1928500 PMID:8987814 [IGI] MGI:MGI:95822) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:2677534 PMID:11530236 [IMP] MGI:MGI:1928287) /// 0006816 // calcium ion transport (MGI:MGI:3590469 PMID:16045501 [IMP]) /// 0007611 // learning or memory (MGI:MGI:3590469 PMID:16045501 [IMP]) /// 0050804 // regulation of synaptic transmission (MGI:MGI:3687911 PMID:12427824 [IMP]) /// 0071230 // cellular response to amino acid stimulus (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0042177 // negative regulation of protein catabolic process (MGI:MGI:3054180 PMID:15317856 [IGI] MGI:MGI:95822) /// 0042391 // regulation of membrane potential

				<p>(MGI:MGI:1277016 PMID:9712642 [IMP] MGI:MGI:1928285) /// 0034220 // ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0050966 // detection of mechanical stimulus involved in sensory perception of pain (MGI:MGI:3604261 PMID:16190898 [IMP] MGI:MGI:1928285) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3590469 PMID:16045501 [IMP]) /// 0006816 // calcium ion transport (MGI:MGI:65947 PMID:1374164 [IGI] MGI:MGI:95819) /// 0006816 // calcium ion transport (MGI:MGI:2384280 PMID:11160454 [IMP] MGI:MGI:1928285) /// 0035235 // ionotropic glutamate receptor signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0045471 // response to ethanol (MGI:MGI:2677534 PMID:11530236 [IMP] MGI:MGI:1928287) /// 0042493 // response to drug (MGI:MGI:3041713 PMID:14750973 [IMP] MGI:MGI:1928285) /// 0007613 // memory (MGI:MGI:1195436 PMID:9458051 [IMP] MGI:MGI:1928287) /// 0007613 // memory (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0007612 // learning (MGI:MGI:3610666 PMID:9427357 [IMP] MGI:MGI:1928506) /// 0001964 // startle response (MGI:MGI:3040117 PMID:11488959 [IMP] MGI:MGI:1928285) /// 0048169 // regulation of long-term neuronal synaptic plasticity (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0008542 // visual learning (MGI:MGI:70176 PMID:7816096 [IMP] MGI:MGI:1928285) /// 0007611 // learning or memory (MGI:MGI:1277016 PMID:9712642 [IMP] MGI:MGI:1928285) /// 0001964 // startle response (MGI:MGI:1339865 PMID:9718984 [IMP] MGI:MGI:1928285) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0071294 // cellular response to zinc ion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0040011 // locomotion (MGI:MGI:2384280 PMID:11160454 [IMP] MGI:MGI:1928285) /// 0001964 // startle response (MGI:MGI:3605193 PMID:14985927 [IGI] MGI:MGI:95821) /// 0060291 // long-term synaptic potentiation (MGI:MGI:4821029 PMID:20661302 [IGI] MGI:MGI:95821 MGI:MGI:109137 MGI:MGI:1346858) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:81551 PMID:8699248 [IMP] MGI:MGI:1928285) /// 0007612 // learning (MGI:MGI:2384280 PMID:11160454 [IMP] MGI:MGI:1928285) /// 0009611 // response to wounding (MGI:MGI:1314964 PMID:9822733 [IMP] MGI:MGI:1928285) /// 0045471 // response to ethanol (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12879) /// 0051262 // protein tetramerization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0022008 // neurogenesis (MGI:MGI:3607839 PMID:12941447 [IMP] MGI:MGI:1928285) /// 0030431 // sleep (MGI:MGI:3629276 PMID:12754515 [IMP] MGI:MGI:1928285) /// 0009611 // response to wounding (MGI:MGI:1201242 PMID:9512392 [IGI] MGI:MGI:95822) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0019233 // sensory perception of pain (MGI:MGI:1353324 PMID:10694228 [IMP] MGI:MGI:1928285) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:3757796 PMID:17803966 [IGI] MGI:MGI:1096575 MGI:MGI:95819) /// 0048167 // regulation of synaptic plasticity (MGI:MGI:3687911 PMID:12427824 [IMP]) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:3689798 PMID:16157280 [IMP]) /// 0001975 // response to amphetamine (MGI:MGI:3656418 PMID:15731593 [IMP] MGI:MGI:1928285) /// 0040011 // locomotion (MGI:MGI:3041713 PMID:14750973 [IMP] MGI:MGI:1928285) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:1928500 PMID:8987814 [IMP] MGI:MGI:1928506) /// 2000463 // positive regulation of excitatory postsynaptic membrane potential (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001508) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0008104 // protein localization (MGI:MGI:3054180 PMID:15317856 [IMP] MGI:MGI:1928285) /// 0033058 // directional locomotion (MGI:MGI:1928500 PMID:8987814 [IGI] MGI:MGI:95822) /// 0042391 // regulation of membrane potential (MGI:MGI:70176 PMID:7816096 [IMP] MGI:MGI:1928285) /// 0008104 // protein localization (MGI:MGI:3054180 PMID:15317856 [IGI] MGI:MGI:95822) /// 0007268 // synaptic transmission (MGI:MGI:894616 PMID:9147327 [IMP] MGI:MGI:1928506) /// 0042417 // dopamine metabolic process (MGI:MGI:2384280 PMID:11160454 [IMP] MGI:MGI:1928285) /// 0007268 // synaptic transmission (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0010942 // positive regulation of cell death (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0048511 // rhythmic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2737) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:894616 PMID:9147327 [IMP] MGI:MGI:1928506)</p>
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Gucy1b3	16.185160 41	7.96184 E-16	MGI:1860 604	0006182 // cGMP biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q02153) /// 0006182 // cGMP biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2769) /// 0007165 // signal transduction (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000228924) /// 0006171 // cAMP biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2769) /// 0009190 // cyclic nucleotide biosynthetic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) /// 0035556 // intracellular signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) /// 0007263 // nitric oxide mediated signal transduction (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2769)
Runx1t1	16.157314 7	8.2298E -16	MGI:1047 93	0045892 // negative regulation of transcription, DNA-dependent (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000822368) /// 0045599 // negative regulation of fat cell differentiation (MGI:MGI:5751611 PMID:26774823 [IMP]) /// 0045892 // negative regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q06455) /// 0051101 // regulation of DNA binding (MGI:MGI:3511635 PMID:15509789 [IDA]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:3511635 PMID:15509789 [IDA]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0045444 // fat cell differentiation (MGI:MGI:3511635 PMID:15509789 [IDA])
Prune2	16.119346 34	2.04035 E-27	MGI:1925 004	0006915 // apoptotic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000251507)
Apba2	16.045249 26	5.12658 E-09	MGI:1261 791	0007268 // synaptic transmission (MGI:MGI:3691953 PMID:17167098 [IGI] MGI:MGI:1888527 PMID:1860297) /// 0035264 // multicellular organism growth (MGI:MGI:3691953 PMID:17167098 [IGI] MGI:MGI:1860297) /// 0007626 // locomotory behavior (MGI:MGI:3691953 PMID:17167098 [IGI] MGI:MGI:1860297) /// 0010468 // regulation of gene expression (MGI:MGI:3691953 PMID:17167098 [IGI] MGI:MGI:1860297 PMID:1888527) /// 0001701 // in utero embryonic development (MGI:MGI:3691953 PMID:17167098 [IGI] MGI:MGI:1860297) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0015031 // protein transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0653)
Slc4a8	15.930364 32	2.66478 E-21	MGI:1928 745	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0009790 // embryo development (MGI:MGI:5516546 PMID:23677982 [IMP]) /// 0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR016152) /// 0098656 /// 0015701 // bicarbonate transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000894302) /// 0006814 // sodium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0739) /// 0006820 // anion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR013769 InterPro:IPR011531 InterPro:IPR003020 InterPro:IPR003024) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0051453 // regulation of intracellular pH (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000894242)
St18	15.904009 37	3.94734 E-09	MGI:2446 700	0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:708566) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002515) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804)
Wdr17	15.884005 62	4.866E- 08	MGI:1924 662	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Lhx4	15.882411 52	2.25484 E-08	MGI:1017 76	0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:2389279 PMID:12183375 [IMP] MGI:MGI:2385815) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR017970) /// 0021526 // medial motor column neuron differentiation (MGI:MGI:1316601 PMID:9865699 [IGI] MGI:MGI:102673) /// 0009887 // organ morphogenesis (MGI:MGI:2389279 PMID:12183375 [IMP] MGI:MGI:2385815) /// 0001890 // placenta development (MGI:MGI:3789527 PMID:18425848 [IGI])

				MGI:MGI:102673) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0008045 // motor neuron axon guidance (MGI:MGI:1316601 PMID:9865699 [IGI] MGI:MGI:102673)
Zfyve28	15.827814 18	3.24936 E-10	MGI:2684 992	0007175 // negative regulation of epidermal growth factor-activated receptor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9HCC9) /// 0042059 // negative regulation of epidermal growth factor receptor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9HCC9)
Apbb1	15.824005 36	1.31046 E-20	MGI:1077 65	0045739 // positive regulation of DNA repair (MGI:MGI:3698695 PMID:17121854 [IMP]) /// 0030048 // actin filament-based movement (MGI:MGI:3687936 PMID:12089154 [NAS]) /// 0050714 // positive regulation of protein secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2122) /// 0007411 // axon guidance (MGI:MGI:3614238 PMID:16407979 [IGI] MGI:MGI:108405) /// 0006974 // response to DNA damage stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O00213) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:3687936 PMID:12089154 [IDA]) /// 0006302 // double-strand break repair (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2122) /// 0045739 // positive regulation of DNA repair (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2122) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O00213) /// 0001764 // neuron migration (MGI:MGI:3614238 PMID:16407979 [IGI] MGI:MGI:108405) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3589585 PMID:15944124 [IGI] MGI:MGI:88059 MGI:MGI:1932051) /// 0050760 // negative regulation of thymidylate synthase biosynthetic process (MGI:MGI:3687936 PMID:12089154 [IDA]) /// 0006974 // response to DNA damage stimulus (MGI:MGI:3698695 PMID:17121854 [IDA]) /// 0016568 // chromatin modification (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0156) /// 0043967 // histone H4 acetylation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2122) /// 0006302 // double-strand break repair (MGI:MGI:3698695 PMID:17121854 [IMP]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0007050 // cell cycle arrest (MGI:MGI:3687936 PMID:12089154 [IDA]) /// 0010976 // positive regulation of neuron projection development (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2122) /// 0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2122) /// 0030308 // negative regulation of cell growth (MGI:MGI:3687936 PMID:12089154 [IDA]) /// 0030198 // extracellular matrix organization (MGI:MGI:3614238 PMID:16407979 [IGI] MGI:MGI:108405) /// 0008542 // visual learning (MGI:MGI:3522016 PMID:14689444 [IMP] MGI:MGI:3514266) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O00213) /// 0050821 // protein stabilization (MGI:MGI:3688060 PMID:11544248 [NAS]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2122) /// 0045665 // negative regulation of neuron differentiation (MGI:MGI:3835738 PMID:18278038 [IMP] MGI:MGI:3514266)
Rasl11a	15.803895 04	4.46692 E-11	MGI:1916 145	0045943 // positive regulation of transcription from RNA polymerase I promoter (MGI:MGI:4441017 PMID:20168301 [IDA]) /// 0007264 // small GTPase mediated signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001806) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR020849)
Slco1a4	15.728371 37	2.58415 E-11	MGI:1351 896	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0043252 // sodium-independent organic anion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621389) /// 0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR004156) /// 0043252 // sodium-independent organic anion transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001685178) /// 0006820 // anion transport (MGI:MGI:2182694 PMID:12101011 [IDA]) /// 0015721 // bile acid and bile salt transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621389) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0008206 // bile acid metabolic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000147525)

Rlbpl	15.721833 13	8.02188 E-12	MGI:9793 0	0007601 // visual perception (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0844) /// 0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001071) /// 0050896 // response to stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0716) /// 0007601 // visual perception (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR032941) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Gpr162	15.698983 27	5.31205 E-17	MGI:1315 214	0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR022347 InterPro:IPR000276 InterPro:IPR022348) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND]) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297)
Grid2	15.634538 34	2.47207 E-08	MGI:9581 3	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0034613 // cellular protein localization (MGI:MGI:3852309 PMID:15207857 [IDA]) /// 0010975 // regulation of neuron projection development (MGI:MGI:71424 PMID:7891151 [IMP] MGI:MGI:1857337) /// 0035249 // synaptic transmission, glutamatergic (MGI:MGI:72217 PMID:7766857 [IMP] MGI:MGI:2178052) /// 0043523 // regulation of neuron apoptotic process (MGI:MGI:1861056 PMID:10884318 [IGI] MGI:MGI:99702) /// 0007157 // heterophilic cell-cell adhesion (MGI:MGI:4839424 PMID:20537373 [IGI] UniProtKB:Q9R171) /// 0043523 // regulation of neuron apoptotic process (MGI:MGI:1861056 PMID:10884318 [IMP] MGI:MGI:1857337) /// 0021707 // cerebellar granule cell differentiation (MGI:MGI:4839424 PMID:20537373 [IGI] UniProtKB:Q9R171) /// 0060134 // prepulse inhibition (MGI:MGI:3040117 PMID:11488959 [IMP] MGI:MGI:2178052) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001508) /// 0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:72217 PMID:7766857 [IMP] MGI:MGI:2178052)
Dlg2	15.606885 39	2.5757E -19	MGI:1344 351	0007268 // synaptic transmission (MGI:MGI:2669049 PMID:12890763 [IMP] MGI:MGI:2388036) /// 0019233 // sensory perception of pain (MGI:MGI:2669049 PMID:12890763 [IMP] MGI:MGI:2388036) /// 0007399 // nervous system development (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001501163) /// 0010923 // negative regulation of phosphatase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q15700) /// 0043113 // receptor clustering (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001501163) /// 0045161 // neuronal ion channel clustering (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619895) /// 0097120 // receptor localization to synapse (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001501163) /// 0043113 // receptor clustering (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619895)
Nrep	15.540811 6	1.64356 E-16	MGI:9944 4	0017015 // regulation of transforming growth factor beta receptor signaling pathway (MGI:MGI:3034115 PMID:14985127 [IDA]) /// 0045664 // regulation of neuron differentiation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:631411)
Vtn	15.478628 25	4.37428 E-08	MGI:9894 0	0010811 // positive regulation of cell-substrate adhesion (MGI:MGI:3807344 PMID:18757743 [IDA]) /// 0048260 // positive regulation of receptor-mediated endocytosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P04004) /// 0010951 // negative regulation of endopeptidase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P04004) /// 0050731 // positive regulation of peptidyl-tyrosine phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P04004) /// 0097421 // liver regeneration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3967) /// 0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR020436 InterPro:IPR001212) /// 0014911 // positive regulation of smooth muscle cell migration (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P04004) /// 0051258 // protein polymerization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3967) /// 0032092 // positive regulation of protein binding (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P04004) /// 0048709 // oligodendrocyte differentiation (MGI:MGI:5619735 PMID:23155445 [IDA]) /// 0007160 // cell-matrix adhesion (MGI:MGI:3577694 PMID:15728191 [IDA]) /// 0033627 // cell adhesion mediated by integrin (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P04004) /// 0035987 // endodermal cell differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P04004) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0061302 // smooth muscle cell-matrix adhesion

				(MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P04004) /// 0030198 // extracellular matrix organization (MGI:MGI:3807344 PMID:18757743 [IDA]) /// 0007160 // cell-matrix adhesion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P04004)
C230004F18 Rik	15.47031755	8.65735E-09	MGI:3041217	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Crb1	15.43188512	9.4127E-10	MGI:2136343	0042462 // eye photoreceptor cell development (MGI:MGI:2675211 PMID:12915475 [IMP] MGI:MGI:2676366) /// 0007009 // plasma membrane organization (MGI:MGI:3051713 PMID:15316081 [IMP] MGI:MGI:3052072) /// 0042462 // eye photoreceptor cell development (MGI:MGI:4849309 PMID:21052544 [IMP]) /// 0061024 // membrane organization (MGI:MGI:2675211 PMID:12915475 [IMP] MGI:MGI:2676366)
Cacnalf	15.36565469	8.59135E-08	MGI:1859639	0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0006874 // cellular calcium ion homeostasis (MGI:MGI:3608035 PMID:16155113 [IMP] MGI:MGI:3609549) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR030157 InterPro:IPR005446 InterPro:IPR002077) /// 0007601 // visual perception (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O60840) /// 0007409 // axonogenesis (MGI:MGI:3608035 PMID:16155113 [IMP] MGI:MGI:3609549) /// 0060041 // retina development in camera-type eye (MGI:MGI:4849309 PMID:21052544 [IMP] MGI:MGI:3605845) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0107) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0006816 // calcium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0109) /// 0086010 // membrane depolarization involved in regulation of action potential (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000004140) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0050896 // response to stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0716) /// 0050856 // regulation of T cell receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR030157) /// 0007601 // visual perception (MGI:MGI:3608035 PMID:16155113 [IMP] MGI:MGI:3609549) /// 0043029 // T cell homeostasis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR030157) /// 0048813 // dendrite morphogenesis (MGI:MGI:3608035 PMID:16155113 [IMP] MGI:MGI:3609549) /// 0050908 // detection of light stimulus involved in visual perception (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O60840) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Serping1	15.35860803	9.65812E-21	MGI:894696	0010466 // negative regulation of peptidase activity (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0646) /// 0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0010951 // negative regulation of endopeptidase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05155) /// 0006958 // complement activation, classical pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0180) /// 0001869 // negative regulation of complement activation, lectin pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05155) /// 0007599 // hemostasis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0356) /// 0007596 // blood coagulation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0094) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0042730 // fibrinolysis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0280)
AI593442	15.34646054	2.9996E-08	MGI:2143099	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Vsx2	15.33681776	6.49398E-11	MGI:88401	0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3575842 PMID:15767664 [IDA]) /// 0045165 // cell fate commitment (MGI:MGI:3512656 PMID:15576400 [IMP] MGI:MGI:1856112) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0060042 // retina morphogenesis in camera-type eye (MGI:MGI:79586 PMID:8630490 [IMP] MGI:MGI:1856112) /// 0006355 // regulation of transcription, DNA-dependent

				(MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR017970) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0043010 // camera-type eye development (MGI:MGI:3512656 PMID:15576400 [IGI] MGI:MGI:104554) /// 0008285 // negative regulation of cell proliferation (MGI:MGI:3611606 PMID:16384989 [IMP] MGI:MGI:1856112) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:79586 PMID:8630490 [IMP] MGI:MGI:1856112) /// 0060040 // retinal bipolar neuron differentiation (MGI:MGI:79586 PMID:8630490 [IMP] MGI:MGI:1856112) /// 0060042 // retina morphogenesis in camera-type eye (MGI:MGI:3701027 PMID:16854970 [IMP] MGI:MGI:1856112) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804)
Slc38a3	15.327558 51	1.87871 E-08	MGI:1923 507	0051365 // cellular response to potassium ion starvation (MGI:MGI:3851650 PMID:19458124 [IDA]) /// 0006865 // amino acid transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0029) /// 0006868 // glutamine transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:628620) /// 0015817 // histidine transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:628620) /// 2000487 // positive regulation of glutamine transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:628620) /// 0006814 // sodium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0739) /// 0015817 // histidine transport (MGI:MGI:2138068 PMID:10716701 [IDA]) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006867 // asparagine transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:628620) /// 0015808 // L-alanine transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q99624) /// 0015817 // histidine transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q99624) /// 0061402 // positive regulation of transcription from RNA polymerase II promoter in response to acidity (MGI:MGI:3851650 PMID:19458124 [IDA]) /// 0006868 // glutamine transport (MGI:MGI:2138068 PMID:10716701 [IDA]) /// 0006868 // glutamine transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q99624) /// 0006867 // asparagine transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000536413) /// 0089709 // 0006867 // asparagine transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q99624) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Trpc4	15.289896 43	8.33525 E-09	MGI:1095 25	0006828 // manganese ion transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000012230) /// 0006816 // calcium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621276) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0107) /// 0014051 // gamma-aminobutyric acid secretion (MGI:MGI:3029676 PMID:14668438 [IMP] MGI:MGI:2387666) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821 InterPro:IPR004729) /// 0048709 // oligodendrocyte differentiation (MGI:MGI:3836214 PMID:19139271 [IMP]) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0051924 // regulation of calcium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621276) /// 0070509 // calcium ion import (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UBN4) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005460 InterPro:IPR002153) /// 0051480 // cytosolic calcium ion homeostasis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000012230) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Gabrb3	15.274865 07	7.35839 E-12	MGI:9562 1	0043524 // negative regulation of neuron apoptotic process (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0060021 // palate development (MGI:MGI:87150 PMID:9108119 [IMP]) /// 1901215 // negative regulation of neuron death (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0007605 // sensory perception of sound (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006202) /// 0007214 // gamma-aminobutyric acid signaling pathway (MGI:MGI:71434 PMID:7893750 [ISO] RefSeq:NM_017065) /// 0060080 // regulation of inhibitory postsynaptic membrane potential (MGI:MGI:5619469 PMID:19846622 [IMP]) /// 0051932 // synaptic transmission, GABAergic (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2651) /// 0006821 // chloride transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0869) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0071420 // cellular response to histamine (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P28472) /// 0006811 //

				ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006028 InterPro:IPR002289 InterPro:IPR006201 InterPro:IPR006029) /// 0007165 // signal transduction (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2651) /// 1902476 /// 0043523 // regulation of neuron apoptotic process (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0048666 // neuron development (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0060119 // inner ear receptor cell development (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0060384 // innervation (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0090102 // cochlea development (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Calb1	15.264529 55	4.38121 E-10	MGI:8824 8	0051480 // cytosolic calcium ion homeostasis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001461922) /// 0048167 // regulation of synaptic plasticity (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69340) /// 0007614 // short-term memory (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05937) /// 0071310 // cellular response to organic substance (MGI:MGI:3801567 PMID:18497889 [IDA]) /// 0051480 // cytosolic calcium ion homeostasis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69340) /// 0007616 // long-term memory (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05937) /// 0007626 // locomotory behavior (MGI:MGI:2661329 PMID:12716955 [IMP] MGI:MGI:2181196) /// 0055074 // calcium ion homeostasis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR029634)
Adam23	15.132876 15	1.26033 E-13	MGI:1345 162	0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0006508 // proteolysis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006586 InterPro:IPR001590 InterPro:IPR002870)
Egflam	14.999560 73	1.18711 E-09	MGI:2146 149	0010811 // positive regulation of cell-substrate adhesion (MGI:MGI:3807344 PMID:18757743 [IDA]) /// 0019800 // peptide cross-linking via chondroitin 4-sulfate glycosaminoglycan (MGI:MGI:3807344 PMID:18757743 [IDA]) /// 0030198 // extracellular matrix organization (MGI:MGI:3807344 PMID:18757743 [IDA])
Ackr1	14.999498 23	1.37066 E-15	MGI:1097 689	0006954 // inflammatory response (MGI:MGI:1888874 PMID:10961863 [IMP] MGI:MGI:1888977) /// 0070098 // chemokine-mediated signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005384) /// 0032642 // regulation of chemokine production (MGI:MGI:4819434 PMID:20643340 [IMP] MGI:MGI:1888977) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297)
Pde6c	14.998671 02	1.0549E -07	MGI:1059 56	0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002073) /// 0007603 // phototransduction, visible light (MGI:MGI:3655007 PMID:16723493 [IMP] MGI:MGI:2657247) /// 0050896 // response to stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0716) /// 0050953 // sensory perception of light stimulus (MGI:MGI:3655007 PMID:16723493 [IMP] MGI:MGI:2657247) /// 0046549 // retinal cone cell development (MGI:MGI:4849309 PMID:21052544 [IMP]) /// 0007601 // visual perception (MGI:MGI:5462118 PMID:22937111 [IMP] MGI:MGI:2657247)
Gpr158	14.980225 36	1.03673 E-09	MGI:2441 697	0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR017978) /// 0008277 // regulation of G-protein coupled receptor protein signaling pathway (MGI:MGI:5428056 PMID:22689652 [IDA]) /// 0072659 // protein localization to plasma membrane (MGI:MGI:5428056 PMID:22689652 [IDA]) /// 0008277 // regulation of G-protein coupled receptor protein signaling pathway (MGI:MGI:5428056 PMID:22689652 [IGI] MGI:MGI:1346089) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297)
Nrcam	14.865643 25	4.28E- 08	MGI:1047 50	0019227 // neuronal action potential propagation (MGI:MGI:3575364 PMID:14602817 [IMP] MGI:MGI:2387976) /// 0007417 // central nervous system development (MGI:MGI:2447374 PMID:12182881 [IDA]) /// 0031290 // retinal ganglion cell axon guidance (MGI:MGI:3716012 PMID:16701205 [IMP] MGI:MGI:2387976) /// 0034113 // heterotypic cell-cell adhesion (MGI:MGI:4839704 PMID:20188654 [IGI] MGI:MGI:2388361) /// 0045162 // clustering of voltage-gated sodium channels (MGI:MGI:4839704 PMID:20188654 [IMP] MGI:MGI:2387976) /// 0045162 // clustering of voltage-gated sodium channels

				(MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92823) /// 0010975 // regulation of neuron projection development (MGI:MGI:3716012 PMID:16701205 [IMP] MGI:MGI:2387976) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0007411 // axon guidance (MGI:MGI:2447374 PMID:12182881 [IDA]) /// 0008104 // protein localization (MGI:MGI:3654396 PMID:16882004 [IDA]) /// 0016337 // cell-cell adhesion (MGI:MGI:2447374 PMID:12182881 [IDA])
Cacna2d2	14.856961 38	1.90991 E-10	MGI:1929 813	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006816 // calcium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:631360) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0006816 // calcium ion transport (MGI:MGI:2148384 PMID:11487633 [IC] GO:0005245) /// 0040014 // regulation of multicellular organism growth (MGI:MGI:3710069 PMID:17320843 [IMP] MGI:MGI:1856022) /// 0046622 // positive regulation of organ growth (MGI:MGI:1098380 PMID:9349522 [IMP] MGI:MGI:1856022) /// 0007528 // neuromuscular junction development (MGI:MGI:3710069 PMID:17320843 [IMP] MGI:MGI:1856022) /// 0048747 // muscle fiber development (MGI:MGI:3710069 PMID:17320843 [IMP] MGI:MGI:1856022) /// 0060024 // rhythmic synaptic transmission (MGI:MGI:3620292 PMID:16474392 [IMP] MGI:MGI:1856022) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0107) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Slc6a1	14.843489 65	1.39247 E-07	MGI:9562 7	0007268 // synaptic transmission (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000177868) /// 0015812 // gamma-aminobutyric acid transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000177868) /// 0051939 // gamma-aminobutyric acid import (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620533) /// 0014074 // response to purine-containing compound (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620533) /// 0010033 // response to organic substance (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620533) /// 0007612 // learning (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620533) /// 0098779 // 0009636 // response to toxic substance (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620533) /// 0032229 // negative regulation of synaptic transmission, GABAergic (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620533) /// 0014054 // positive regulation of gamma-aminobutyric acid secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620533) /// 0051260 // protein homooligomerization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620533) /// 0006836 // neurotransmitter transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000177868) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Gucy2e	14.778708 48	5.81107 E-08	MGI:1051 23	0007601 // visual perception (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0844) /// 0006468 // protein phosphorylation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000719 InterPro:IPR001245) /// 0006182 // cGMP biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620438) /// 0009190 // cyclic nucleotide biosynthetic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) /// 0050896 // response to stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0716) /// 0035556 // intracellular signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) /// 0006182 // cGMP biosynthetic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000229249) /// 0007168 // receptor guanylyl cyclase signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000937789)
Megf10	14.776583 34	4.02505 E-10	MGI:2685 177	0014816 // satellite cell differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96KG7) /// 0014841 // satellite cell proliferation (MGI:MGI:5319607 PMID:18056409 [IDA]) /// 0043654 // recognition of apoptotic cell (MGI:MGI:4414741 PMID:19915564 [IMP]) /// 0034109 // homotypic cell-cell adhesion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96KG7) /// 0007517 // muscle organ development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0517) /// 0043654 // recognition of apoptotic cell (MGI:MGI:4414741 PMID:19915564 [IDA]) /// 0014816 // satellite cell differentiation (MGI:MGI:5319607 PMID:18056409 [IMP]) /// 0014719 // satellite cell activation (MGI:MGI:5319607 PMID:18056409 [IMP]) /// 0051147 // regulation of muscle cell differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96KG7) /// 0006909 // phagocytosis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0581) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0048641 // regulation of skeletal muscle tissue

				development (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96KG7) /// 0055001 // muscle cell development (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96KG7)
Abca4	14.727725 83	5.7759E -10	MGI:1094 24	0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR026082 InterPro:IPR005951) /// 0045494 // photoreceptor cell maintenance (MGI:MGI:2136674 PMID:11431429 [IMP] MGI:MGI:1857860) /// 0006649 // phospholipid transfer to membrane (MGI:MGI:1340797 PMID:10412977 [IMP] MGI:MGI:1857860) /// 0050896 // response to stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0716) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0007601 // visual perception (MGI:MGI:1340797 PMID:10412977 [IMP] MGI:MGI:1857860)
Mtcl1	14.711328 37	1.11367 E-11	MGI:1915 867	0010506 // regulation of autophagy (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR027881) /// 0090314 // positive regulation of protein targeting to membrane (MGI:MGI:5553212 PMID:23902687 [IDA]) /// 0001578 // microtubule bundle formation (MGI:MGI:5553212 PMID:23902687 [IDA]) /// 2000576 // positive regulation of microtubule motor activity (MGI:MGI:5553212 PMID:23902687 [IDA]) /// 0045197 // establishment or maintenance of epithelial cell apical/basal polarity (MGI:MGI:5553212 PMID:23902687 [IDA])
Nptx2	14.681605 15	2.21413 E-08	MGI:1858 209	0008306 // associative learning (MGI:MGI:3765098 PMID:18057201 [IMP] MGI:MGI:3765981)
Sfrp4	14.663396 55	6.67602 E-11	MGI:8920 10	0090090 // negative regulation of canonical Wnt receptor signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621075) /// 0002092 // positive regulation of receptor internalization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6FHJ7) /// 0008285 // negative regulation of cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6FHJ7) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0035567 // non-canonical Wnt receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000139394) /// 0098779 // 0046329 // negative regulation of JNK cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621075) /// 0010628 // positive regulation of gene expression (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6FHJ7) /// 0090090 // negative regulation of canonical Wnt receptor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6FHJ7) /// 0090263 // positive regulation of canonical Wnt receptor signaling pathway (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:Q6FHJ7) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6FHJ7) /// 0016055 // Wnt receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0879) /// 1902174 /// 0008285 // negative regulation of cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621075) /// 0045606 // positive regulation of epidermal cell differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6FHJ7) /// 0060070 // canonical Wnt receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000139394) /// 0055062 // phosphate ion homeostasis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6FHJ7) /// 0030154 // cell differentiation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0221) /// 0043433 // negative regulation of sequence-specific DNA binding transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6FHJ7) /// 2000119 // negative regulation of sodium-dependent phosphate transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6FHJ7)
Gabrb2	14.625911 81	5.175E- 08	MGI:9562 0	0043524 // negative regulation of neuron apoptotic process (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0071420 // cellular response to histamine (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2650) /// 1901215 // negative regulation of neuron death (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0007605 // sensory perception of sound (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0006810 // transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006202) /// 0051932 // synaptic transmission, GABAergic (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2650) /// 0006821 // chloride transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0869) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006028 InterPro:IPR002289 InterPro:IPR006201 InterPro:IPR006029) /// 1902476 /// 0043523 // regulation of neuron apoptotic process (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0048666 // neuron development (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0060119 // inner ear receptor cell development (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0060384 //

				innervation (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0090102 // cochlea development (MGI:MGI:3664129 PMID:17021187 [IMP]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Ermn	14.623818 89	5.33049 E-11	MGI:1925 017	0008360 // regulation of cell shape (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8TAM6) /// 0031344 // regulation of cell projection organization (MGI:MGI:3612229 PMID:16421295 [IDA]) /// 0007015 // actin filament organization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8TAM6) /// 0008360 // regulation of cell shape (MGI:MGI:3612229 PMID:16421295 [IDA]) /// 0001763 // morphogenesis of a branching structure (MGI:MGI:3612229 PMID:16421295 [IDA]) /// 0007015 // actin filament organization (MGI:MGI:3612229 PMID:16421295 [IDA]) /// 0031344 // regulation of cell projection organization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8TAM6)
Trpm1	14.620953 22	3.10386 E-11	MGI:1330 305	0060402 // calcium ion transport into cytosol (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q7Z4N2) /// 0071482 // cellular response to light stimulus (MGI:MGI:4420740 PMID:19966281 [IMP] MGI:MGI:4421441) /// 0046548 // retinal rod cell development (MGI:MGI:4420740 PMID:19966281 [IMP] MGI:MGI:4421441) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0007165 // signal transduction (MGI:MGI:4420740 PMID:19966281 [IGI] MGI:MGI:1351343) /// 0007601 // visual perception (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q7Z4N2) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0034220 // ion transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR029588) /// 0071482 // cellular response to light stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q7Z4N2) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0050896 // response to stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0716) /// 0051262 // protein tetramerization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR032415) /// 0007216 // G-protein coupled glutamate receptor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q7Z4N2) /// 0071482 // cellular response to light stimulus (MGI:MGI:4849309 PMID:21052544 [IMP]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0071482 // cellular response to light stimulus (MGI:MGI:4398796 PMID:19861548 [IMP])
Faxc	14.596468 61	6.54368 E-15	MGI:1923 382	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Pcsk1n	14.501295 29	7.59237 E-08	MGI:1353 431	0002021 // response to dietary excess (MGI:MGI:3629450 PMID:16631141 [IDA]) /// 0010951 // negative regulation of endopeptidase activity (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR010832) /// 0009409 // response to cold (MGI:MGI:3629450 PMID:16631141 [IDA]) /// 0007218 // neuropeptide signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0527) /// 0016486 // peptide hormone processing (MGI:MGI:1351397 PMID:10632593 [IDA])
Zfp2	14.485570 68	8.3368E -12	MGI:9916 7	0006355 // regulation of transcription, DNA-dependent (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001225609) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804)
Wbscr17	14.481290 2	4.18066 E-11	MGI:2137 594	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Zfp365	14.401452 98	4.415E- 11	MGI:2143 676	0033566 // gamma-tubulin complex localization (MGI:MGI:3625768 PMID:16617106 [ISO] UniProtKB:Q70YC4) /// 0000281 // cytokinesis after mitosis (MGI:MGI:3625768 PMID:16617106 [ISO] UniProtKB:Q70YC4)
Mmp2	14.316017 96	2.48273 E-25	MGI:9700 9	0001525 // angiogenesis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0037) /// 0001666 // response to hypoxia (MGI:MGI:3721729 PMID:17382917 [IDA]) /// 0007162 // negative regulation of cell adhesion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) /// 0006979 // response to oxidative stress (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) /// 0071230 // cellular response to amino acid stimulus (MGI:MGI:4833768 PMID:20548288 [IDA]) /// 0006508 // proteolysis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) /// 0048771 // tissue remodeling (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) ///

				<p>0048705 // skeletal system morphogenesis (MGI:MGI:3710444 PMID:17440987 [IGI] MGI:MGI:88467) // 0060740 // prostate gland epithelium morphogenesis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0016477 // cell migration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0001957 // intramembranous ossification (MGI:MGI:3710444 PMID:17440987 [IGI] MGI:MGI:88467) // 0001541 // ovarian follicle development (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0045089 // positive regulation of innate immune response (MGI:MGI:5435352 PMID:22509276 [IDA]) // 0060325 // face morphogenesis (MGI:MGI:3710444 PMID:17440987 [IGI] MGI:MGI:88467) // 0030574 // collagen catabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0030574 // collagen catabolic process (MGI:MGI:3710444 PMID:17440987 [IMP] MGI:MGI:2386252) // 0001666 // response to hypoxia (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0014012 // peripheral nervous system axon regeneration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0009612 // response to mechanical stimulus (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0001955 // blood vessel maturation (MGI:MGI:3621661 PMID:11747814 [IGI] MGI:MGI:1855698) // 0006508 // proteolysis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P08253) // 0042542 // response to hydrogen peroxide (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0060346 // bone trabecula formation (MGI:MGI:3710444 PMID:17440987 [IGI] MGI:MGI:88467) // 0007566 // embryo implantation (MGI:MGI:3813178 PMID:18556655 [IDA]) // 0043627 // response to estrogen stimulus (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0071392 // cellular response to estradiol stimulus (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0045906 // negative regulation of vasoconstriction (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0042493 // response to drug (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0030335 // positive regulation of cell migration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316) // 0007507 // heart development (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621316)</p>
Nfasc	14.297611 54	3.01725 E-08	MGI:1047 53	<p>0019226 // transmission of nerve impulse (MGI:MGI:3621515 PMID:16337912 [IMP] MGI:MGI:3808598) // 0045162 // clustering of voltage-gated sodium channels (MGI:MGI:4839704 PMID:20188654 [IMP] MGI:MGI:3808598) // 0030913 // paranodal junction assembly (MGI:MGI:4452171 PMID:20371806 [IMP] MGI:MGI:4837620) // 0007422 // peripheral nervous system development (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR026965) // 0002175 // protein localization to paranode region of axon (MGI:MGI:4452171 PMID:20371806 [IMP] MGI:MGI:4837620) // 0030913 // paranodal junction assembly (MGI:MGI:3621515 PMID:16337912 [IMP] MGI:MGI:3808598) // 0042552 // myelination (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR026965) // 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) // 0050808 // synapse organization (MGI:MGI:3510083 PMID:15479642 [IMP]) // 0071205 // protein localization to juxtaparanode region of axon (MGI:MGI:4452171 PMID:20371806 [IMP] MGI:MGI:4837620) // 0007411 // axon guidance (MGI:MGI:3510083 PMID:15479642 [IDA]) // 0072661 // protein targeting to plasma membrane (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620911)</p>
Islr	14.294678 63	1.59718 E-26	MGI:1349 645	
Adcy8	14.287205 04	4.14194 E-09	MGI:1341 110	<p>0007189 // adenylate cyclase-activating G-protein coupled receptor signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2036) // 0007193 // adenylate cyclase-inhibiting G-protein coupled receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001728527) // 0019933 // cAMP-mediated signaling (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2036) // 0007189 // adenylate cyclase-activating G-protein coupled receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001728527) // 0009190 // cyclic nucleotide biosynthetic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) // 0019933 // cAMP-mediated signaling (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001728527) // 0035556 // intracellular signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) // 0006171 // cAMP biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2036) // 0007616 // long-term memory (MGI:MGI:1344240 PMID:10482244 [IGI] MGI:MGI:99677)</p>
Dgki	14.266045 78	1.15673 E-10	MGI:2443 430	<p>0060079 // regulation of excitatory postsynaptic membrane potential (MGI:MGI:4936793 PMID:21119615 [IMP] MGI:MGI:3584141) // 0043087 // regulation of GTPase activity (MGI:MGI:3583869 PMID:15894621 [IMP])</p>

				<p>MGI:MGI:3584141) /// 0046959 // habituation (MGI:MGI:4936793 PMID:21119615 [IMP] MGI:MGI:3584141) /// 1900452 // regulation of long term synaptic depression (MGI:MGI:4936793 PMID:21119615 [IMP] MGI:MGI:3584141) /// 0007269 // neurotransmitter secretion (MGI:MGI:4936793 PMID:21119615 [IMP] MGI:MGI:3584141) /// 0046579 // positive regulation of Ras protein signal transduction (MGI:MGI:3583869 PMID:15894621 [IMP] MGI:MGI:3584141) /// 0051966 // regulation of synaptic transmission, glutamatergic (MGI:MGI:4936793 PMID:21119615 [IMP] MGI:MGI:3584141)</p>
Asic2	14.215367 72	7.79015 E-08	MGI:1100 867	<p>0034220 // ion transmembrane transport (MGI:MGI:3629815 PMID:15470133 [IMP] MGI:MGI:2180111) /// 0003026 // regulation of systemic arterial blood pressure by aortic arch baroreceptor feedback (MGI:MGI:4436814 PMID:20064394 [IMP] MGI:MGI:2180111) /// 0006812 // cation transport (MGI:MGI:2158965 PMID:11854527 [IDA]) /// 0006814 // sodium ion transport (MGI:MGI:1933515 PMID:11306621 [IDA]) /// 0010447 // response to acidity (MGI:MGI:2158965 PMID:11854527 [IDA]) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:3721189 PMID:14960591 [IMP] MGI:MGI:2180111) /// 0009612 // response to mechanical stimulus (MGI:MGI:2180082 PMID:11069180 [IMP] MGI:MGI:2180111) /// 0071468 // cellular response to acidity (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2017) /// 0042391 // regulation of membrane potential (MGI:MGI:4835641 PMID:19590043 [IMP] MGI:MGI:2180111) /// 0010468 // regulation of gene expression (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q16515) /// 0034220 // ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2017) /// 0035418 // protein localization to synapse (MGI:MGI:3851850 PMID:19571134 [IMP] MGI:MGI:2180111) /// 0019229 // regulation of vasoconstriction (MGI:MGI:3794223 PMID:18296560 [IMP] MGI:MGI:2180111) /// 0034220 // ion transmembrane transport (MGI:MGI:4835641 PMID:19590043 [IMP] MGI:MGI:2180111) /// 0050974 // detection of mechanical stimulus involved in sensory perception (MGI:MGI:2180082 PMID:11069180 [IMP] MGI:MGI:2180111) /// 0006814 // sodium ion transport (MGI:MGI:1099545 PMID:9368048 [IDA]) /// 0034220 // ion transmembrane transport (MGI:MGI:3721189 PMID:14960591 [IMP] MGI:MGI:2180111) /// 0030193 // regulation of blood coagulation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q16515) /// 0006812 // cation transport (MGI:MGI:2158965 PMID:11854527 [IMP] MGI:MGI:2180111) /// 0010447 // response to acidity (MGI:MGI:2158965 PMID:11854527 [IMP] MGI:MGI:2180111) /// 0010447 // response to acidity (MGI:MGI:1933515 PMID:11306621 [IDA]) /// 0035725 // sodium ion transmembrane transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2017) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0007605 // sensory perception of sound (MGI:MGI:3530929 PMID:15537887 [IMP] MGI:MGI:2180111) /// 0006814 // sodium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2017) /// 0035690 // cellular response to drug (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2017) /// 0051965 // positive regulation of synapse assembly (MGI:MGI:3851850 PMID:19571134 [IMP] MGI:MGI:2180111) /// 2001259 // positive regulation of cation channel activity (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2017) /// 0034220 // ion transmembrane transport (MGI:MGI:3774872 PMID:18256271 [IDA]) /// 0034220 // ion transmembrane transport (MGI:MGI:3721189 PMID:14960591 [IDA]) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:3042539 PMID:14762118 [IMP] MGI:MGI:3043849) /// 0050915 // sensory perception of sour taste (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q16515) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0007602 // phototransduction (MGI:MGI:3042539 PMID:14762118 [IMP] MGI:MGI:3043849)</p>
Bcat1	14.137165 77	8.53526 E-23	MGI:1048 61	<p>0009081 // branched-chain amino acid metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005786) /// 0009083 // branched-chain amino acid catabolic process (MGI:MGI:3027291 PMID:14755340 [IDA]) /// 0031571 // mitotic G1 DNA damage checkpoint (MGI:MGI:81557 PMID:8692959 [ISA] UniProtKB:P38891) /// 0008152 // metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001544 InterPro:IPR018300) /// 0034644 // cellular response to UV (MGI:MGI:81557 PMID:8692959 [ISA] UniProtKB:P38891) /// 0009082 // branched-chain amino acid biosynthetic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0100) /// 0008652 // cellular amino acid biosynthetic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0028)</p>

Col5a2	14.130174 61	1.59045 E-41	MGI:8845 8	0030199 // collagen fibril organization (MGI:MGI:3047505 PMID:15199158 [IMP]) /// 0043588 // skin development (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05997) /// 0048592 // eye morphogenesis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05997) /// 0001501 // skeletal system development (MGI:MGI:70182 PMID:7704020 [IMP] MGI:MGI:2152946) /// 0030199 // collagen fibril organization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05997) /// 0071230 // cellular response to amino acid stimulus (MGI:MGI:4833768 PMID:20548288 [IDA]) /// 1903225 /// 0043588 // skin development (MGI:MGI:3047505 PMID:15199158 [IMP])
Skida1	14.103961 29	2.61238 E-11	MGI:1919 918	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Luzp2	14.103525 52	3.95395 E-09	MGI:1889 615	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Tub	14.103207 51	2.04123 E-07	MGI:2651 573	0045494 // photoreceptor cell maintenance (MGI:MGI:1352376 PMID:10629044 [IMP] MGI:MGI:1857081) /// 0006910 // phagocytosis, recognition (MGI:MGI:4867371 PMID:20978472 [IDA]) /// 0097500 /// 1903441 /// 0050896 // response to stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0716) /// 0007605 // sensory perception of sound (MGI:MGI:2177887 PMID:11925566 [IMP] MGI:MGI:1861349) /// 0006909 // phagocytosis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0581) /// 0006910 // phagocytosis, recognition (MGI:MGI:4441109 PMID:19837063 [IMP] MGI:MGI:1861349) /// 0060041 // retina development in camera-type eye (MGI:MGI:4849309 PMID:21052544 [IMP]) /// 0007605 // sensory perception of sound (MGI:MGI:4849309 PMID:21052544 [IMP]) /// 1903546 /// 0050766 // positive regulation of phagocytosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P50607)
Nrsn1	14.101005 28	1.34411 E-08	MGI:8946 62	0007399 // nervous system development (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR029698) /// 0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
RP23- 54G8.4	14.093473 39	1.90743 E-07		
Cacna1h	14.092389 94	1.80471 E-13	MGI:1928 842	0006816 // calcium ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68943) /// 0034765 // regulation of ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0851) /// 0070509 // calcium ion import (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68943) /// 0034651 // cortisol biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68943) /// 0034220 // ion transmembrane transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000004140) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0107) /// 0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0032342 // aldosterone biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68943) /// 0006816 // calcium ion transport (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001295293) /// 0006811 // ion transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0070588 // calcium ion transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005445) /// 0034651 // cortisol biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O95180) /// 0086010 // membrane depolarization involved in regulation of action potential (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000004140) /// 2000344 // positive regulation of acrosome reaction (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O95180) /// 0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005821) /// 0045956 // positive regulation of calcium ion-dependent exocytosis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000004815) /// 0032342 // aldosterone biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O95180) /// 0070509 // calcium ion import (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O95180) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0019233 // sensory perception of pain (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:68943) /// 0042391 // regulation of membrane potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O95180)

Kctd8	14.014667 66	1.05434 E-07	MGI:2443 804	0051260 // protein homooligomerization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003131) /// 0008277 // regulation of G-protein coupled receptor protein signaling pathway (MGI:MGI:4462115 PMID:20400944 [IGI] MGI:MGI:1860139)
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Appendix 4. Up-regulated genes in 7 dpi mouse ocular cells compared to 2 dpi mouse ocular cells due to infection by *P. aeruginosa* $\Delta wspF$ mutant.

Appendix (5)

Feature ID	Fold change	P value	Databas e identifier	Annotations - GO biological process
Ngp	- 22.656 24705	9.316 67E- 16	MGI:10 5983	0010466 // negative regulation of peptidase activity (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0646) /// 0006952 // defense response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001894) /// 1901491 // negative regulation of lymphangiogenesis (MGI:MGI:5616309 PMID:21518852 [IDA]) /// 0016525 // negative regulation of angiogenesis (MGI:MGI:5616309 PMID:21518852 [IDA])
II10	- 21.444 989	2.827 87E- 33	MGI:96 537	0006954 // inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0044130 // negative regulation of growth of symbiont in host (MGI:MGI:3774790 PMID:12452830 [IMP] MGI:MGI:1857199) /// 0051091 // positive regulation of sequence-specific DNA binding transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0042832 // defense response to protozoan (MGI:MGI:3828894 PMID:19047410 [IDA]) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:3828894 PMID:19047410 [IDA]) /// 0002904 // positive regulation of B cell apoptotic process (MGI:MGI:892164 PMID:9184696 [ISO] UniProtKB:P22301) /// 0051930 // regulation of sensory perception of pain (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2886) /// 0042742 // defense response to bacterium (MGI:MGI:1861065 PMID:10899905 [IDA]) /// 0030886 // negative regulation of myeloid dendritic cell activation (MGI:MGI:3051177 PMID:15240714 [IMP] MGI:MGI:1857199) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3044839 PMID:15187136 [IDA]) /// 0060670 // branching involved in labyrinthine layer morphogenesis (MGI:MGI:3664708 PMID:12842419 [IMP] MGI:MGI:1857199) /// 0002875 // negative regulation of chronic inflammatory response to antigenic stimulus (MGI:MGI:3774790 PMID:12452830 [IMP] MGI:MGI:1857199) /// 0050715 // positive regulation of cytokine secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0030889 // negative regulation of B cell proliferation (MGI:MGI:892164 PMID:9184696 [ISO] UniProtKB:P22301) /// 0006955 // immune response (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2886) /// 0002740 // negative regulation of cytokine secretion involved in immune response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0032695 // negative regulation of interleukin-12 production (MGI:MGI:3051177 PMID:15240714 [IMP] MGI:MGI:1857199) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:5013871 PMID:21609717 [IDA]) /// 0010468 // regulation of gene expression (MGI:MGI:892164 PMID:9184696 [ISO] UniProtKB:P22301) /// 0032720 // negative regulation of tumor necrosis factor production (MGI:MGI:3774790 PMID:12452830 [IMP] MGI:MGI:1857199) /// 0032800 // receptor biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0035729 // cellular response to hepatocyte growth factor stimulus (MGI:MGI:4849876 PMID:21072211 [IDA]) /// 0032715 // negative regulation of interleukin-6 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0045019 // negative regulation of nitric oxide biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2886) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2886) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2886) /// 0060302 // negative regulation of cytokine activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0045348 // positive regulation of MHC class II biosynthetic process (MGI:MGI:3033882 PMID:11027433 [IDA]) /// 1904057 /// 0001818 // negative regulation of cytokine production (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2886) /// 0002237 // response to molecule of bacterial origin (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0042536 // negative regulation of tumor necrosis factor biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2886) /// 0051045 // negative regulation of membrane protein ectodomain proteolysis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:3790904 PMID:18270204 [IMP]) /// 0050807 // regulation of synapse organization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2886) /// 0032689 // negative regulation of interferon-gamma production (MGI:MGI:3774790 PMID:12452830 [IMP] MGI:MGI:1857199) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0043032 // positive regulation of macrophage activation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2886) /// 0051384 // response to glucocorticoid stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22301) /// 0046427 // positive regulation of JAK-STAT cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000172385)
Gm21370	- 20.514 56951	1.409 67E- 15		

Il23a	- 20.372 98546	5.829 76E- 36	MGI:19 32410	0010535 // positive regulation of activation of JAK2 kinase activity (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000409283) /// 0032725 // positive regulation of granulocyte macrophage colony-stimulating factor production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0001916 // positive regulation of T cell mediated cytotoxicity (MGI:MGI:3027369 PMID:14688363 [IDA]) /// 0042102 // positive regulation of T cell proliferation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000409283) /// 0051607 // defense response to virus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0051) /// 0032740 // positive regulation of interleukin-17 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0051142 // positive regulation of NK T cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR010831) /// 0032760 // positive regulation of tumor necrosis factor production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0045672 // positive regulation of osteoclast differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0042098 // T cell proliferation (MGI:MGI:3722056 PMID:16982811 [IDA]) /// 0042523 // positive regulation of tyrosine phosphorylation of Stat5 protein (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0042510 // regulation of tyrosine phosphorylation of Stat1 protein (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0051135 // positive regulation of NK T cell activation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0032819 // positive regulation of natural killer cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0042102 // positive regulation of T cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0002827 // positive regulation of T-helper 1 type immune response (MGI:MGI:3027369 PMID:14688363 [IDA]) /// 0032693 // negative regulation of interleukin-10 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 2000318 // positive regulation of T-helper 17 type immune response (MGI:MGI:3851279 PMID:19501566 [IDA]) /// 0048771 // tissue remodeling (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0797) /// 0050829 // defense response to Gram-negative bacterium (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0090023 // positive regulation of neutrophil chemotaxis (MGI:MGI:3841502 PMID:19289819 [IDA]) /// 0032729 // positive regulation of interferon-gamma production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0043382 // positive regulation of memory T cell differentiation (MGI:MGI:3027369 PMID:14688363 [IDA]) /// 0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) /// 0002827 // positive regulation of T-helper 1 type immune response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0002230 // positive regulation of defense response to virus by host (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0032735 // positive regulation of interleukin-12 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4355633 PMID:19666510 [IGI] MGI:MGI:96543 MGI:MGI:96542) /// 0042517 // positive regulation of tyrosine phosphorylation of Stat3 protein (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0002230 // positive regulation of defense response to virus by host (MGI:MGI:3027369 PMID:14688363 [IDA]) /// 0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0010535 // positive regulation of activation of JAK2 kinase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 2000330 // positive regulation of T-helper 17 cell lineage commitment (MGI:MGI:3851279 PMID:19501566 [IDA]) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0032733 // positive regulation of interleukin-10 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0042520 // positive regulation of tyrosine phosphorylation of Stat4 protein (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7) /// 0042104 // positive regulation of activated T cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NPF7)
Ankrd22	- 19.700 79825	3.568 95E- 46	MGI:12 77101	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Pax8	- 19.434 97918	8.541 88E- 20	MGI:97 492	0071371 // cellular response to gonadotropin stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q06710) /// 0001823 // mesonephros development (MGI:MGI:2445273 PMID:12435636 [IMP]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620434) /// 0006366 // transcription from RNA polymerase II promoter (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620434) /// 0042981 // regulation of apoptotic process (MGI:MGI:2445273 PMID:12435636 [IMP]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:78758 PMID:8413205 [IDA]) /// 1900212 // negative regulation of mesenchymal cell apoptotic process involved in metanephros development (MGI:MGI:3704067 PMID:17314325 [IMP]) /// 2000611 // positive regulation of thyroid hormone generation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q06710) /// 0001656 // metanephros development (MGI:MGI:2445273 PMID:12435636 [IGI] MGI:MGI:97486) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:892799 PMID:9214635 [ISO] UniProtKB:P51974) /// 1900215 // negative regulation of apoptotic process involved in metanephric collecting duct development

				(MGI:MGI:3704067 PMID:17314325 [IMP]) /// 0030154 // cell differentiation (MGI:MGI:1203285 PMID:9590297 [IMP] MGI:MGI:2156985) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q06710) /// 0072108 // positive regulation of mesenchymal to epithelial transition involved in metanephros morphogenesis (MGI:MGI:2445273 PMID:12435636 [IMP]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:3611949 PMID:16319112 [IGI] UniProtKB:P32114) /// 0048793 // pronephros development (MGI:MGI:2445273 PMID:12435636 [IMP]) /// 2000612 // regulation of thyroid-stimulating hormone secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q06710) /// 0030878 // thyroid gland development (MGI:MGI:1203285 PMID:9590297 [IMP] MGI:MGI:2156985) /// 0072305 // negative regulation of mesenchymal cell apoptotic process involved in metanephric nephron morphogenesis (MGI:MGI:3704067 PMID:17314325 [IMP]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q06710) /// 0030878 // thyroid gland development (MGI:MGI:2156109 PMID:11773436 [IGI] MGI:MGI:98742) /// 0072221 // metanephric distal convoluted tubule development (MGI:MGI:3704067 PMID:17314325 [IMP]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1334982 PMID:10197584 [TAS]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:3693390 PMID:12441357 [IDA]) /// 0072289 // metanephric nephron tubule formation (MGI:MGI:3704067 PMID:17314325 [IMP]) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0042472 // inner ear morphogenesis (MGI:MGI:4822275 PMID:20727173 [IGI] UniProtKB:P32114) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:3704067 PMID:17314325 [IMP]) /// 0030878 // thyroid gland development (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q06710) /// 2000611 // positive regulation of thyroid hormone generation (MGI:MGI:3691903 PMID:12586753 [IMP]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:3691903 PMID:12586753 [IMP]) /// 0090190 // positive regulation of branching involved in ureteric bud morphogenesis (MGI:MGI:3704067 PMID:17314325 [IMP]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:3697544 PMID:17047028 [IDA]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:2445273 PMID:12435636 [IMP]) /// 0001655 // urogenital system development (MGI:MGI:2445273 PMID:12435636 [IGI] UniProtKB:P32114) /// 1900218 // negative regulation of apoptotic process involved in metanephric nephron tubule development (MGI:MGI:3704067 PMID:17314325 [IMP]) /// 0072307 // regulation of metanephric nephron tubule epithelial cell differentiation (MGI:MGI:3704067 PMID:17314325 [IMP]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620434) /// 2000594 // positive regulation of metanephric DCT cell differentiation (MGI:MGI:3704067 PMID:17314325 [IMP]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q06710) /// 0009887 // organ morphogenesis (MGI:MGI:1334982 PMID:10197584 [TAS])
Ifitm6	- 19.364 7654	5.821 16E-21	MGI:26 86976	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Stfa211	- 18.889 50428	7.876 E-32	MGI:35 24944	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Mybph	- 18.841 5885	3.765 05E-16	MGI:18 58196	0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Gm5483	- 18.645 30295	1.546 85E-33		
Tnf	- 18.439 82767	1.297 03E-41	MGI:10 4798	0060559 // positive regulation of calcidiol 1-monoxygenase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0060664 // epithelial cell proliferation involved in salivary gland morphogenesis (MGI:MGI:1931422 PMID:11241200 [IDA]) /// 0002740 // negative regulation of cytokine secretion involved in immune response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0030730 // sequestering of triglyceride (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0002925 // positive regulation of humoral immune response mediated by circulating immunoglobulin (MGI:MGI:3690573 PMID:9834074 [IGI] MGI:MGI:104797) /// 0051384 // response to glucocorticoid stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0071803 // positive regulation of podosome assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0006915 // apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0032741 // positive regulation of interleukin-18 production (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0097527 // 0071222 // cellular response to lipopolysaccharide (MGI:MGI:3828894 PMID:19047410 [IDA]) /// 0048661 // positive regulation of smooth

			<p>muscle cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0030198 // extracellular matrix organization (MGI:MGI:3510270 PMID:15381731 [IDA]) /// 0010629 // negative regulation of gene expression (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0001775 // cell activation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0046325 // negative regulation of glucose import (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0006952 // defense response (MGI:MGI:62592 PMID:8395024 [IMP] MGI:MGI:1861040) /// 0006954 // inflammatory response (MGI:MGI:53235 PMID:8387893 [TAS]) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:3029504 PMID:12431371 [IGI] MGI:MGI:1096330) /// 0000185 // activation of MAPKKK activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0045080 // positive regulation of chemokine biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0009615 // response to virus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0043406 // positive regulation of MAP kinase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0050715 // positive regulation of cytokine secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006053 InterPro:IPR002959 InterPro:IPR006052) /// 0046325 // negative regulation of glucose import (MGI:MGI:2181851 PMID:12068289 [IDA]) /// 0045670 // regulation of osteoclast differentiation (MGI:MGI:2448204 PMID:12490655 [IDA]) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:68569 PMID:8043507 [IDA]) /// 0043507 // positive regulation of JUN kinase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0050796 // regulation of insulin secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0006954 // inflammatory response (MGI:MGI:65999 PMID:8171322 [TAS]) /// 0010033 // response to organic substance (MGI:MGI:3836717 PMID:17475835 [IDA]) /// 0043123 // positive regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0046330 // positive regulation of JNK cascade (MGI:MGI:3607973 PMID:16260493 [IGI] MGI:MGI:1346877) /// 0019722 // calcium-mediated signaling (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0051044 // positive regulation of membrane protein ectodomain proteolysis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0043068 // positive regulation of programmed cell death (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:4420852 PMID:20080598 [IGI] MGI:MGI:1928487) /// 1901224 // positive regulation of NIK/NF-kappaB cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0046330 // positive regulation of JNK cascade (MGI:MGI:3607973 PMID:16260493 [IDA]) /// 0050708 // regulation of protein secretion (MGI:MGI:3848759 PMID:19293336 [IDA]) /// 0045668 // negative regulation of osteoblast differentiation (MGI:MGI:5285024 PMID:21689636 [IDA]) /// 0034138 // toll-like receptor 3 signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0045892 // negative regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0008285 // negative regulation of cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:65999 PMID:8171322 [TAS]) /// 0031642 // negative regulation of myelination (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0006006 // glucose metabolic process (MGI:MGI:2181851 PMID:12068289 [IDA]) /// 0001932 // regulation of protein phosphorylation (MGI:MGI:3045683 PMID:15169905 [IDA]) /// 0045429 // positive regulation of nitric oxide biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3761912 PMID:17670746 [IDA]) /// 0010693 // negative regulation of alkaline phosphatase activity (MGI:MGI:5285024 PMID:21689636 [IDA]) /// 2000334 // positive regulation of blood microparticle formation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0033209 // tumor necrosis factor-mediated signaling pathway (MGI:MGI:63487 PMID:3898078 [IDA]) /// 0051798 // positive regulation of hair follicle development (MGI:MGI:3624581 PMID:16702408 [IMP]) /// 0006919 // activation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:3603971 PMID:16183742 [IDA]) /// 0045416 // positive regulation of interleukin-8 biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0043122 // regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0060693 // regulation of branching involved in salivary gland morphogenesis (MGI:MGI:1931422 PMID:11241200 [IDA]) /// 0007165 // signal transduction (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0071316 // cellular response to nicotine (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0043491 // protein kinase B signaling cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0051091 // positive regulation of sequence-specific DNA binding transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 2000010 // positive regulation of protein localization to cell surface (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0033209 // tumor necrosis factor-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0051222 // positive regulation of protein transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0006952 // defense response (MGI:MGI:894912 PMID:9223320 [IMP] MGI:MGI:1860250) /// 0033138 // positive</p>
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			<p> regulation of peptidyl-serine phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0097191 // extrinsic apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0030866 // cortical actin cytoskeleton organization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 2000377 // regulation of reactive oxygen species metabolic process (MGI:MGI:5315337 PMID:21052097 [IDA]) /// 0007254 // JNK cascade (MGI:MGI:3689241 PMID:17015619 [IGI] MGI:MGI:1341850) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0097190 // apoptotic signaling pathway (MGI:MGI:67096 PMID:8208546 [IDA]) /// 0043123 // positive regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:3039643 PMID:12867038 [IDA]) /// 1903140 /// 0006959 // humoral immune response (MGI:MGI:1306673 PMID:8879212 [IMP] MGI:MGI:2149024) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4412460 PMID:18025219 [IGI] MGI:MGI:107656) /// 0000165 // MAPK cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 1904999 /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:1097308 PMID:9305915 [IDA]) /// 0000187 // activation of MAPK activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0031334 // positive regulation of protein complex assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0051222 // positive regulation of protein transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0032755 // positive regulation of interleukin-6 production (MGI:MGI:2176422 PMID:11894098 [IDA]) /// 0006927 // transformed cell apoptotic process (MGI:MGI:1098089 PMID:9368616 [TAS]) /// 0008630 // intrinsic apoptotic signaling pathway in response to DNA damage (MGI:MGI:3709926 PMID:17242187 [IDA]) /// 0043123 // positive regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:5521568 PMID:22089168 [IDA]) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:4420852 PMID:20080598 [IGI] MGI:MGI:1929004) /// 0031622 // positive regulation of fever generation (MGI:MGI:4413614 PMID:19940926 [IDA]) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0030316 // osteoclast differentiation (MGI:MGI:3525391 PMID:15485831 [IGI] MGI:MGI:1100089 MGI:MGI:99484) /// 0050900 // leukocyte migration (MGI:MGI:3036957 PMID:15034066 [IDA]) /// 0050901 // leukocyte tethering or rolling (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0071230 // cellular response to amino acid stimulus (MGI:MGI:4833768 PMID:20548288 [IDA]) /// 0002037 // negative regulation of L-glutamate transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0010628 // positive regulation of gene expression (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0060557 // positive regulation of vitamin D biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0042742 // defense response to bacterium (MGI:MGI:1861065 PMID:10899905 [IDA]) /// 0043123 // positive regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:3607973 PMID:16260493 [IGI] MGI:MGI:1346877) /// 0006919 // activation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0046330 // positive regulation of JNK cascade (MGI:MGI:4420852 PMID:20080598 [IDA]) /// 0097191 // extrinsic apoptotic signaling pathway (MGI:MGI:5510543 PMID:19498109 [IGI] MGI:MGI:108212) /// 0050995 // negative regulation of lipid catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0002876 // positive regulation of chronic inflammatory response to antigenic stimulus (MGI:MGI:3690573 PMID:9834074 [IGI] MGI:MGI:104797) /// 0090002 // establishment of protein localization to plasma membrane (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:1097308 PMID:9305915 [IDA]) /// 0045860 // positive regulation of protein kinase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0043123 // positive regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0045760 // positive regulation of action potential (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0050806 // positive regulation of synaptic transmission (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0045672 // positive regulation of osteoclast differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 1901671 // positive regulation of superoxide dismutase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0043123 // positive regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:3607973 PMID:16260493 [IDA]) /// 0006927 // transformed cell apoptotic process (MGI:MGI:75691 PMID:7636227 [TAS]) /// 0001934 // positive regulation of protein phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0043242 // negative regulation of protein complex disassembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0097191 // extrinsic apoptotic signaling pathway (MGI:MGI:5521568 PMID:22089168 [IGI] MGI:MGI:104798 MGI:MGI:1261423) /// 0032496 // response to lipopolysaccharide (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0050766 // positive regulation of phagocytosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0032729 // positive regulation of interferon-gamma production (MGI:MGI:3690573 PMID:9834074 [IGI] MGI:MGI:104797) /// 0071407 // cellular response to organic cyclic compound (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0071222 // cellular </p>
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				<p>response to lipopolysaccharide (MGI:MGI:5013875 PMID:21606371 [IDA]) /// 0042127 // regulation of cell proliferation (MGI:MGI:2176657 PMID:11799106 [IDA]) /// 0045840 // positive regulation of mitosis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0006954 // inflammatory response (MGI:MGI:4881588 PMID:21148126 [IGI] MGI:MGI:2687194 MGI:MGI:893592) /// 0042346 // positive regulation of NF-kappaB import into nucleus (MGI:MGI:5285024 PMID:21689636 [IMP]) /// 0044130 // negative regulation of growth of symbiont in host (MGI:MGI:3690573 PMID:9834074 [IGI] MGI:MGI:104797) /// 0060693 // regulation of branching involved in salivary gland morphogenesis (MGI:MGI:1931422 PMID:11241200 [IMP]) /// 0061048 // negative regulation of branching involved in lung morphogenesis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0002439 // chronic inflammatory response to antigenic stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0043525 // positive regulation of neuron apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0043243 // positive regulation of protein complex disassembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:3608448 PMID:12761567 [IDA]) /// 0051897 // positive regulation of protein kinase B signaling cascade (MGI:MGI:4420852 PMID:20080598 [IDA]) /// 0097190 // apoptotic signaling pathway (MGI:MGI:3525895 PMID:15629131 [IDA]) /// 0001819 // positive regulation of cytokine production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0045994 // positive regulation of translational initiation by iron (MGI:MGI:2152007 PMID:11588035 [IDA]) /// 0006954 // inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0045123 // cellular extravasation (MGI:MGI:2658799 PMID:10528208 [IDA]) /// 0032757 // positive regulation of interleukin-8 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0045662 // negative regulation of myoblast differentiation (MGI:MGI:5532227 PMID:23844157 [IMP]) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:4437182 PMID:20060382 [IDA]) /// 0006927 // transformed cell apoptotic process (MGI:MGI:65999 PMID:8171322 [TAS]) /// 0051533 // positive regulation of NFAT protein import into nucleus (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:P01375) /// 0010628 // positive regulation of gene expression (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:5285024 PMID:21689636 [IDA]) /// 0007275 // multicellular organismal development (MGI:MGI:1098089 PMID:9368616 [IMP] MGI:MGI:1860953) /// 0050966 // detection of mechanical stimulus involved in sensory perception of pain (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0031663 // lipopolysaccharide-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0045785 // positive regulation of cell adhesion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0035509 // negative regulation of myosin-light-chain-phosphatase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0051023 // regulation of immunoglobulin secretion (MGI:MGI:2680840 PMID:12958312 [IDA]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3844151 PMID:19404405 [IDA]) /// 0008283 // cell proliferation (MGI:MGI:75691 PMID:7636227 [TAS]) /// 2000343 // positive regulation of chemokine (C-X-C motif) ligand 2 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0032715 // negative regulation of interleukin-6 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0050729 // positive regulation of inflammatory response (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3876) /// 0000060 // protein import into nucleus, translocation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0045071 // negative regulation of viral genome replication (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0050830 // defense response to Gram-positive bacterium (MGI:MGI:3690573 PMID:9834074 [IGI] MGI:MGI:104797) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0032722 // positive regulation of chemokine production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:3575325 PMID:15790681 [ISO] UniProtKB:P01375) /// 2001240 // negative regulation of extrinsic apoptotic signaling pathway in absence of ligand (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0032800 // receptor biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0034116 // positive regulation of heterotypic cell-cell adhesion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0043280 // positive regulation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0009887 // organ morphogenesis (MGI:MGI:1306673 PMID:8879212 [IMP] MGI:MGI:2149024) /// 0042346 // positive regulation of NF-kappaB import into nucleus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:P01375) /// 1903347 /// 0006927 // transformed cell apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01375)</p>
Enthd1	- 18.286	2.054 54E-	MGI:26 86088	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])

	41945	11		
Il1a	- 17.226 59951	6.925 43E- 29	MGI:96 542	0051930 // regulation of sensory perception of pain (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2890) /// 0050714 // positive regulation of protein secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01583) /// 0043123 // positive regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000008680) /// 0045766 // positive regulation of angiogenesis (MGI:MGI:2652930 PMID:12598651 [IMP]) /// 0045086 // positive regulation of interleukin-2 biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01583) /// 0070498 // interleukin-1-mediated signaling pathway (MGI:MGI:5468848 PMID:23395675 [IDA]) /// 0071639 // positive regulation of monocyte chemotactic protein-1 production (MGI:MGI:5468848 PMID:23395675 [IDA]) /// 0034605 // cellular response to heat (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01583) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000008570) /// 0010628 // positive regulation of gene expression (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01583) /// 0046330 // positive regulation of JNK cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000008680) /// 0035234 // germ cell programmed cell death (MGI:MGI:3691999 PMID:11536012 [IGI] MGI:MGI:96543) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4355633 PMID:19666510 [IGI] MGI:MGI:96543 MGI:MGI:1932410) /// 0032956 // regulation of actin cytoskeleton organization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2890) /// 0045840 // positive regulation of mitosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01583) /// 0051781 // positive regulation of cell division (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0497) /// 0008285 // negative regulation of cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01583) /// 0010575 // positive regulation vascular endothelial growth factor production (MGI:MGI:2652930 PMID:12598651 [IMP]) /// 0032874 // positive regulation of stress-activated MAPK cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2890) /// 1904445 // 2000391 // positive regulation of neutrophil extravasation (MGI:MGI:5468848 PMID:23395675 [IDA]) /// 0032755 // positive regulation of interleukin-6 production (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2890) /// 0046688 // response to copper ion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01583) /// 0032308 // positive regulation of prostaglandin secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2890) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4355633 PMID:19666510 [IGI] MGI:MGI:96543 MGI:MGI:1890474) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4355633 PMID:19666510 [IGI] MGI:MGI:107364 MGI:MGI:96543) /// 0010893 // positive regulation of steroid biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2890) /// 1902624 /// 0001660 // fever generation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0666) /// 0043123 // positive regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2890) /// 0050715 // positive regulation of cytokine secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01583) /// 0045086 // positive regulation of interleukin-2 biosynthetic process (MGI:MGI:5468848 PMID:23395675 [IDA]) /// 0031424 // keratinization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2890) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01583) /// 0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003295 InterPro:IPR003294 InterPro:IPR003502) /// 0002248 // connective tissue replacement involved in inflammatory response wound healing (MGI:MGI:3621265 PMID:15784728 [IMP]) /// 0097192 // extrinsic apoptotic signaling pathway in absence of ligand (MGI:MGI:3691999 PMID:11536012 [IMP] MGI:MGI:2157371) /// 0070374 // positive regulation of ERK1 and ERK2 cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2890) /// 0046330 // positive regulation of JNK cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2890) /// 0006954 // inflammatory response (MGI:MGI:5468848 PMID:23395675 [IDA]) /// 0032755 // positive regulation of interleukin-6 production (MGI:MGI:5468848 PMID:23395675 [IDA])
5031414 D18Rik	- 16.965 98242	2.179 02E- 32	MGI:26 85590	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Pnpla1	- 16.760 08492	2.125 58E- 14	MGI:36 17850	0006629 // lipid metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002641) /// 0008152 // metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR016035) /// 0006629 // lipid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0443) /// 0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND]) /// 0016042 // lipid catabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0442)
Ccl4	- 16.258 56014	3.390 99E- 39	MGI:98 261	0043922 // negative regulation by host of viral transcription (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13236) /// 0006935 // chemotaxis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0145) /// 0050850 // positive regulation of calcium-mediated signaling (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13236) /// 0048247 // lymphocyte chemotaxis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0071346 //

				<p>cellular response to interferon-gamma (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0009636 // response to toxic substance (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13236) /// 0006954 // inflammatory response (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620441) /// 0030593 // neutrophil chemotaxis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000827 InterPro:IPR001811) /// 0030595 // leukocyte chemotaxis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620441) /// 0032760 // positive regulation of tumor necrosis factor production (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620441) /// 0002548 // monocyte chemotaxis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0043547 // positive regulation of GTPase activity (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0051928 // positive regulation of calcium ion transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13236) /// 0071347 // cellular response to interleukin-1 (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0006954 // inflammatory response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0071356 // cellular response to tumor necrosis factor (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0070098 // chemokine-mediated signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0050729 // positive regulation of inflammatory response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001381552) /// 0070374 // positive regulation of ERK1 and ERK2 cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0043117 // positive regulation of vascular permeability (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620441) /// 0035690 // cellular response to drug (MGI:MGI:5619708 PMID:24486487 [IDA]) /// 2000503 // positive regulation of natural killer cell chemotaxis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13236)</p>
Ccl3	- 16.174 14906	1.874 03E- 34	MGI:98 260	<p>0045672 // positive regulation of osteoclast differentiation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3647) /// 0006935 // chemotaxis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0145) /// 0007204 // elevation of cytosolic calcium ion concentration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3647) /// 0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000827 InterPro:IPR001811) /// 0002548 // monocyte chemotaxis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0043525 // positive regulation of neuron apoptotic process (MGI:MGI:3044466 PMID:15155903 [IGI] UniProtKB:P20060) /// 0071347 // cellular response to interleukin-1 (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0048246 // macrophage chemotaxis (MGI:MGI:5301204 PMID:21784977 [IGI] UniProtKB:P22893) /// 0030593 // neutrophil chemotaxis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3647) /// 0050718 // positive regulation of interleukin-1 beta secretion (MGI:MGI:5301204 PMID:21784977 [IGI] UniProtKB:P22893) /// 0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) /// 0048247 // lymphocyte chemotaxis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0071346 // cellular response to interferon-gamma (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0032760 // positive regulation of tumor necrosis factor production (MGI:MGI:5301204 PMID:21784977 [IGI] UniProtKB:P22893) /// 0030593 // neutrophil chemotaxis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0050729 // positive regulation of inflammatory response (MGI:MGI:5301204 PMID:21784977 [IGI] UniProtKB:P22893) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3044466 PMID:15155903 [IMP]) /// 0043547 // positive regulation of GTPase activity (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0008360 // regulation of cell shape (MGI:MGI:3044466 PMID:15155903 [IDA]) /// 0030595 // leukocyte chemotaxis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3647) /// 0043615 // astrocyte cell migration (MGI:MGI:3044466 PMID:15155903 [IDA]) /// 0071356 // cellular response to tumor necrosis factor (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0070098 // chemokine-mediated signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709) /// 0070374 // positive regulation of ERK1 and ERK2 cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000245709)</p>
Il1f5	- 15.831 98681	3.802 9E- 12	MGI:18 59325	<p>0032715 // negative regulation of interleukin-6 production (MGI:MGI:5300146 PMID:21860022 [IGI] MGI:MGI:1859324 MGI:MGI:1916927 MGI:MGI:2449929) /// 1902714 /// 0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0019732 // antifungal humoral response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UBH0) /// 0001960 // negative regulation of cytokine-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UBH0) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000008570) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0032700 // negative regulation of interleukin-17 production (MGI:MGI:4834177 GO_REF:0000096 [ISO])</p>

				UniProtKB:Q9UBH0)
Fam71f1	- 15.593 56837	1.332 24E- 08	MGI:30 32524	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Mrgpra2a	- 15.587 26983	5.730 32E- 25	MGI:38 21888	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Rhov	- 14.907 99696	9.547 3E- 34	MGI:24 44227	0007165 // signal transduction (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:628824) // 0007264 // small GTPase mediated signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001806 InterPro:IPR003578)
Spr1b	- 14.762 716	7.248 61E- 08	MGI:10 6659	0031424 // keratinization (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0417) // 0030216 // keratinocyte differentiation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001908662) // 0008360 // regulation of cell shape (MGI:MGI:1327022 PMID:9931436 [TAS]) // 0018149 // peptide cross-linking (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001908662)
Itgb2l	- 14.505 6501	1.877 75E- 10	MGI:12 77979	0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) // 0007229 // integrin-mediated signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0401)
Irak3	- 14.465 01097	5.833 07E- 41	MGI:19 21164	0006915 // apoptotic process (MGI:MGI:2665373 PMID:12819136 [RCA]) // 0032720 // negative regulation of tumor necrosis factor production (MGI:MGI:2183694 PMID:12150927 [IMP]) // 0034122 // negative regulation of toll-like receptor signaling pathway (MGI:MGI:2183694 PMID:12150927 [IMP]) // 0032088 // negative regulation of NF-kappaB transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0043407 // negative regulation of MAP kinase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:2181508 PMID:12054681 [IDA]) // 0006468 // protein phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0006468 // protein phosphorylation (MGI:MGI:2181508 PMID:12054681 [IDA]) // 0009615 // response to virus (MGI:MGI:2183694 PMID:12150927 [IC] GO:0043330) // 0016310 // phosphorylation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0418) // 0042981 // regulation of apoptotic process (MGI:MGI:2665373 PMID:12819136 [RCA]) // 0032695 // negative regulation of interleukin-12 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0019221 // cytokine-mediated signaling pathway (MGI:MGI:2181508 PMID:12054681 [IDA]) // 0042177 // negative regulation of protein catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000488) // 0032496 // response to lipopolysaccharide (MGI:MGI:2183694 PMID:12150927 [IMP]) // 0001960 // negative regulation of cytokine-mediated signaling pathway (MGI:MGI:2183694 PMID:12150927 [IC] GO:0032715) // 0046777 // protein autophosphorylation (MGI:MGI:2181508 PMID:12054681 [IDA]) // 0032715 // negative regulation of interleukin-6 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0032720 // negative regulation of tumor necrosis factor production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0010936 // negative regulation of macrophage cytokine production (MGI:MGI:2183694 PMID:12150927 [IMP]) // 0032494 // response to peptidoglycan (MGI:MGI:2183694 PMID:12150927 [IMP]) // 0032715 // negative regulation of interleukin-6 production (MGI:MGI:2183694 PMID:12150927 [IMP]) // 0043330 // response to exogenous dsRNA (MGI:MGI:2183694 PMID:12150927 [IMP]) // 0032695 // negative regulation of interleukin-12 production (MGI:MGI:2183694 PMID:12150927 [IMP]) // 0043244 // regulation of protein complex disassembly (MGI:MGI:2181508 PMID:12054681 [IDA]) // 0043242 // negative regulation of protein complex disassembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0070555 // response to interleukin-1 (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0070498 // interleukin-1-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y616) // 0045824 // negative regulation of innate immune response (MGI:MGI:2183694 PMID:12150927 [IMP]) // 0042177 // negative regulation of protein catabolic process (MGI:MGI:3843426 PMID:17379480 [IMP]) // 0010933 // positive regulation of macrophage tolerance induction (MGI:MGI:2183694 PMID:12150927 [IMP]) // 0070498 // interleukin-1-mediated signaling pathway (MGI:MGI:2181508 PMID:12054681 [IDA]) // 0043407 // negative regulation of MAP kinase activity (MGI:MGI:3843426 PMID:17379480 [IMP])
A530032 D15Rik	- 14.324	3.001 14E-	MGI:30 37746	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])

	48742	20		
E330009J 07Rik	- 14.189 8278	2.130 29E- 37	MGI:24 44256	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Siglece	- 13.972 75113	2.354 99E- 49	MGI:19 32475	0060101 // negative regulation of phagocytosis, engulfment (MGI:MGI:5529741 PMID:24227736 [IDA]) /// 0060101 // negative regulation of phagocytosis, engulfment (MGI:MGI:5529741 PMID:24227736 [IMP]) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:5529741 PMID:24227736 [IMP]) /// 0007155 // cell adhesion (MGI:MGI:1930828 PMID:11171044 [IDA])
Pfkfb3	- 13.777 37092	1.827 44E- 34	MGI:21 81202	0046835 // carbohydrate phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q16875) /// 0006003 // fructose 2,6-bisphosphate metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619776)
Hsd11b1	- 13.477 2914	3.865 68E- 26	MGI:10 3562	0043456 // regulation of pentose-phosphate shunt (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2834) /// 0008202 // steroid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0753) /// 0006629 // lipid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0443) /// 0030324 // lung development (MGI:MGI:2446008 PMID:12439781 [IMP] MGI:MGI:2385796) /// 0006713 // glucocorticoid catabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2834) /// 0006704 // glucocorticoid biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2834) /// 0055114 // oxidation-reduction process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0560)
Mrgpra2b	- 13.207 82865	7.024 94E- 25	MGI:30 33098	
Chil5	- 13.196 48921	6.151 24E- 09	MGI:26 76649	0006032 // chitin catabolic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000126434)
Gas7	- 13.110 67054	7.235 2E- 33	MGI:12 02388	0030182 // neuron differentiation (MGI:MGI:3698406 PMID:15725398 [IDA]) /// 0007399 // nervous system development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0524) /// 0030041 // actin filament polymerization (MGI:MGI:2159085 PMID:11795944 [IDA]) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0008360 // regulation of cell shape (MGI:MGI:2159085 PMID:11795944 [IDA]) /// 0051017 // actin filament bundle assembly (MGI:MGI:2159085 PMID:11795944 [IDA]) /// 0048812 // neuron projection morphogenesis (MGI:MGI:1289379 PMID:9736752 [IMP]) /// 0030154 // cell differentiation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0221)
Csf3	- 13.025 0384	9.682 93E- 56	MGI:13 39751	0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR030474) /// 0032092 // positive regulation of protein binding (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09919) /// 0033138 // positive regulation of peptidyl-serine phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09919) /// 2000251 // positive regulation of actin cytoskeleton reorganization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09919) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09919) /// 0014068 // positive regulation of phosphatidylinositol 3-kinase cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09919) /// 0030838 // positive regulation of actin filament polymerization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09919) /// 0051897 // positive regulation of protein kinase B signaling cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09919) /// 0042993 // positive regulation of transcription factor import into nucleus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09919) /// 0071345 // cellular response to cytokine stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09919) /// 1901215 // negative regulation of neuron death (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2426) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2426) /// 0050731 // positive regulation of peptidyl-tyrosine phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09919) /// 0030851 // granulocyte differentiation (MGI:MGI:3688357 PMID:15664994 [NAS]) /// 0045639 // positive regulation of myeloid cell differentiation (MGI:MGI:5529751 PMID:24216483 [IGI] MGI:MGI:1345151) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000053735)
9130230 L23Rik	- 12.896 17579	2.844 32E- 33	MGI:30 41166	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])

Tnfaip3	- 12.796 27155	6.049 86E- 27	MGI:11 96377	<p>0009611 // response to wounding (MGI:MGI:4943825 PMID:20430393 [NAS]) /// 0070429 // negative regulation of nucleotide-binding oligomerization domain containing 1 signaling pathway (MGI:MGI:3777503 PMID:18342009 [IMP]) /// 0032715 // negative regulation of interleukin-6 production (MGI:MGI:3763997 PMID:18006655 [IMP]) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:4946158 PMID:21088135 [IMP]) /// 0035871 // protein K11-linked deubiquitination (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0071108 // protein K48-linked deubiquitination (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000332227) /// 0034115 // negative regulation of heterotypic cell-cell adhesion (MGI:MGI:4943658 PMID:19252225 [NAS]) /// 0002237 // response to molecule of bacterial origin (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0072666 // establishment of protein localization to vacuole (MGI:MGI:3839729 PMID:18952128 [IDA]) /// 0034140 // negative regulation of toll-like receptor 3 signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0002315 // marginal zone B cell differentiation (MGI:MGI:4946158 PMID:21088135 [NAS]) /// 0032703 // negative regulation of interleukin-2 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0008152 // metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0511) /// 0048662 // negative regulation of smooth muscle cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0006508 // proteolysis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0645) /// 0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) /// 2000349 // negative regulation of CD40 signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0032715 // negative regulation of interleukin-6 production (MGI:MGI:4946158 PMID:21088135 [IMP]) /// 0070936 // protein K48-linked ubiquitination (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0034148 // negative regulation of toll-like receptor 5 signaling pathway (MGI:MGI:4943853 PMID:19912257 [IDA]) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:5490396 PMID:23609450 [IDA]) /// 0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0032691 // negative regulation of interleukin-1 beta production (MGI:MGI:3777503 PMID:18342009 [IMP]) /// 0031397 // negative regulation of protein ubiquitination (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0071947 // protein deubiquitination involved in ubiquitin-dependent protein catabolic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001001090) /// 0010507 // negative regulation of autophagy (MGI:MGI:4999706 PMID:20501938 [NAS]) /// 1903364 /// 0043124 // negative regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:3777503 PMID:18342009 [IMP]) /// 0002637 // regulation of immunoglobulin production (MGI:MGI:4946158 PMID:21088135 [IC] GO:0001922) /// 0043124 // negative regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0043124 // negative regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4946158 PMID:21088135 [IMP]) /// 0032495 // response to muramyl dipeptide (MGI:MGI:3777503 PMID:18342009 [IMP]) /// 0034115 // negative regulation of heterotypic cell-cell adhesion (MGI:MGI:3763997 PMID:18006655 [NAS]) /// 0002677 // negative regulation of chronic inflammatory response (MGI:MGI:3763997 PMID:18006655 [IMP]) /// 0070536 // protein K63-linked deubiquitination (MGI:MGI:5562489 PMID:24012418 [IDA]) /// 0032088 // negative regulation of NF-kappaB transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0070536 // protein K63-linked deubiquitination (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 2000352 // negative regulation of endothelial cell apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0035871 // protein K11-linked deubiquitination (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000332227) /// 0045088 // regulation of innate immune response (MGI:MGI:4946158 PMID:21088135 [IC] GO:0001922) /// 0070301 // cellular response to hydrogen peroxide (MGI:MGI:5490396 PMID:23609450 [IMP]) /// 0050869 // negative regulation of B cell activation (MGI:MGI:4946158 PMID:21088135 [IDA]) /// 0071108 // protein K48-linked deubiquitination (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0072573 // tolerance induction to lipopolysaccharide (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 1902042 /// 0002632 // negative regulation of granuloma formation (MGI:MGI:3763997 PMID:18006655 [NAS]) /// 0045732 // positive regulation of protein catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P21580) /// 0032691 // negative regulation of interleukin-1 beta production (MGI:MGI:3763997 PMID:18006655 [IMP]) /// 0060548 // negative regulation of cell death (MGI:MGI:3055167 PMID:11009421 [IMP]) /// 0001922 // B-1 B cell homeostasis (MGI:MGI:4946158 PMID:21088135 [IMP]) /// 0002237 // response to molecule of bacterial origin (MGI:MGI:4943853 PMID:19912257 [IDA]) /// 0016579 // protein deubiquitination (MGI:MGI:3777503 PMID:18342009 [IDA]) /// 0032715 // negative regulation of interleukin-6 production (MGI:MGI:3777503 PMID:18342009 [IMP]) /// 0045736 // negative regulation of cyclin-dependent protein serine/threonine kinase activity (MGI:MGI:4943408 PMID:15962316 [IDA]) /// 0070433 // negative regulation of nucleotide-binding oligomerization domain containing 2 signaling pathway (MGI:MGI:3777503 PMID:18342009 [IDA]) /// 0045824 // negative regulation of innate immune response (MGI:MGI:5490396 PMID:23609450 [IMP]) /// 0002634 // regulation of germinal center formation (MGI:MGI:4946158 PMID:21088135 [IMP]) /// 0032720 // negative regulation of tumor necrosis factor production (MGI:MGI:4946158 PMID:21088135 [IMP]) ///</p>
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				2000347 // positive regulation of hepatocyte proliferation (MGI:MGI:4943408 PMID:15962316 [IDA])
Ebi3	- 12.577 49722	4.280 31E- 28	MGI:13 54171	0042098 // T cell proliferation (MGI:MGI:2181922 PMID:12121660 [IDA]) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q14213)
Gucy2g	- 12.497 77568	3.624 14E- 10	MGI:10 6025	0006468 // protein phosphorylation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000719 InterPro:IPR001245) /// 0007165 // signal transduction (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000228924) /// 0009190 // cyclic nucleotide biosynthetic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) /// 0035556 // intracellular signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001054 InterPro:IPR018297) /// 0006182 // cGMP biosynthetic process (MGI:MGI:1194478 PMID:9422765 [ISS]) /// 0006182 // cGMP biosynthetic process (MGI:MGI:3037474 PMID:14713286 [IDA])
Gm42800	- 12.449 84633	2.849 41E- 07		
Olfm4	- 12.295 44049	5.119 81E- 21	MGI:26 85142	0051260 // protein homooligomerization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6UX06) /// 0043124 // negative regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4457946 PMID:20534456 [IDA]) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0050777 // negative regulation of immune response (MGI:MGI:4457946 PMID:20534456 [IMP] MGI:MGI:4461923) /// 1900026 // positive regulation of substrate adhesion-dependent cell spreading (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6UX06)
2010005 H15Rik	- 12.272 42281	4.173 46E- 19	MGI:19 24020	
F3	- 12.146 99408	1.118 62E- 33	MGI:88 381	0007596 // blood coagulation (MGI:MGI:2149494 PMID:11511099 [TAS]) /// 0014911 // positive regulation of smooth muscle cell migration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2587) /// 0045766 // positive regulation of angiogenesis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13726) /// 0007596 // blood coagulation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13726) /// 0002541 // activation of plasma proteins involved in acute inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13726) /// 0006919 // activation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13726) /// 0007599 // hemostasis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0356) /// 0010641 // positive regulation of platelet-derived growth factor receptor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13726) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000466212) /// 0051897 // positive regulation of protein kinase B signaling cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13726) /// 0001938 // positive regulation of endothelial cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P13726)
F10	- 12.126 77689	6.575 22E- 29	MGI:10 3107	0051897 // positive regulation of protein kinase B signaling cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P00742) /// 0007599 // hemostasis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0356) /// 0006508 // proteolysis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001314 InterPro:IPR001254 InterPro:IPR018114) /// 0007596 // blood coagulation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61850) /// 0006508 // proteolysis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0645)
Stfa3	- 12.037 88537	1.880 57E- 23	MGI:10 6196	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Rab11fip 1	- 12.035 65564	5.833 07E- 41	MGI:19 23017	0070164 // negative regulation of adiponectin secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6WKZ4) /// 0045055 // regulated secretory pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000405433) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0015031 // protein transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0653)
Gm7897	- 12.001 22447	3.741 7E- 13	MGI:36 48011	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Orl1	- 11.703	2.034 51E-	MGI:12	0007159 // leukocyte cell-cell adhesion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620515) /// 0006954 // inflammatory response (MGI:MGI:4417868 GO_REF:0000096

	74875	34	61434	[ISO] RGD:620515) /// 0008219 // cell death (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620515) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0007155 // cell adhesion (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0130) /// 0042157 // lipoprotein metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620515)
Gm26809	- 11.677 62565	9.443 75E- 24		
Pik3ap1	- 11.586 51476	1.380 67E- 28	MGI:19 33177	0034122 // negative regulation of toll-like receptor signaling pathway (MGI:MGI:5487531 PMID:20728433 [IMP]) /// 0034162 // toll-like receptor 9 signaling pathway (MGI:MGI:5305503 PMID:22187460 [IMP]) /// 0014068 // positive regulation of phosphatidylinositol 3-kinase cascade (MGI:MGI:5305503 PMID:22187460 [IMP]) /// 0034154 // toll-like receptor 7 signaling pathway (MGI:MGI:5305504 PMID:22187458 [IMP]) /// 0014068 // positive regulation of phosphatidylinositol 3-kinase cascade (MGI:MGI:5305504 PMID:22187458 [IMP]) /// 0034142 // toll-like receptor 4 signaling pathway (MGI:MGI:5305504 PMID:22187458 [IMP]) /// 0034142 // toll-like receptor 4 signaling pathway (MGI:MGI:5305503 PMID:22187460 [IMP]) /// 0034123 // positive regulation of toll-like receptor signaling pathway (MGI:MGI:5487531 PMID:20728433 [IMP]) /// 0043122 // regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:5305504 PMID:22187458 [IMP]) /// 0043408 // regulation of MAPK cascade (MGI:MGI:5305504 PMID:22187458 [IMP]) /// 0034134 // toll-like receptor 2 signaling pathway (MGI:MGI:5305503 PMID:22187460 [IMP]) /// 0034162 // toll-like receptor 9 signaling pathway (MGI:MGI:5305504 PMID:22187458 [IMP]) /// 0050727 // regulation of inflammatory response (MGI:MGI:5305503 PMID:22187460 [IMP])
Dgat2	- 11.487 89799	6.048 27E- 39	MGI:19 15050	0055089 // fatty acid homeostasis (MGI:MGI:3778742 PMID:18252207 [IGI] UniProtKB:Q9Z2A7) /// 0046339 // diacylglycerol metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620329) /// 0071400 // cellular response to oleic acid (MGI:MGI:5293272 PMID:21680734 [IMP]) /// 0046339 // diacylglycerol metabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96PD7) /// 0060613 // fat pad development (MGI:MGI:3778742 PMID:18252207 [IMP]) /// 0006629 // lipid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0443) /// 0050746 // regulation of lipoprotein metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620329) /// 0035336 // long-chain fatty-acyl-CoA metabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96PD7) /// 0019432 // triglyceride biosynthetic process (MGI:MGI:3036977 PMID:14668353 [IMP] MGI:MGI:3037903) /// 0045722 // positive regulation of gluconeogenesis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620329) /// 0019432 // triglyceride biosynthetic process (MGI:MGI:2151970 PMID:11481335 [IDA]) /// 0035356 // cellular triglyceride homeostasis (MGI:MGI:3036977 PMID:14668353 [IMP]) /// 0035336 // long-chain fatty-acyl-CoA metabolic process (MGI:MGI:2151970 PMID:11481335 [IDA]) /// 0019432 // triglyceride biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96PD7) /// 0046339 // diacylglycerol metabolic process (MGI:MGI:2151970 PMID:11481335 [IDA]) /// 0090181 // regulation of cholesterol metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620329) /// 0019915 // lipid storage (MGI:MGI:5293272 PMID:21680734 [IMP]) /// 0042632 // cholesterol homeostasis (MGI:MGI:3778742 PMID:18252207 [IMP]) /// 0046322 // negative regulation of fatty acid oxidation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620329) /// 0019915 // lipid storage (MGI:MGI:5306738 PMID:21317108 [IGI] UniProtKB:Q9DCV3) /// 0019432 // triglyceride biosynthetic process (MGI:MGI:2181469 PMID:12077311 [IDA]) /// 0010867 // positive regulation of triglyceride biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620329) /// 0034383 // low-density lipoprotein particle clearance (MGI:MGI:3784112 PMID:18175806 [IMP]) /// 0006071 // glycerol metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0319) /// 0097006 // regulation of plasma lipoprotein particle levels (MGI:MGI:3778742 PMID:18252207 [IMP])
Cxcl2	- 11.364 15604	2.154 5E- 21	MGI:13 40094	0090023 // positive regulation of neutrophil chemotaxis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001303132) /// 0030593 // neutrophil chemotaxis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70069) /// 0070997 // neuron death (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70069) /// 0006935 // chemotaxis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0145) /// 0007204 // elevation of cytosolic calcium ion concentration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70069) /// 0030595 // leukocyte chemotaxis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70069) /// 0032496 // response to lipopolysaccharide (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000021269) /// 0006954 // inflammatory response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000021269) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000021269) /// 0006955 // immune response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000021269) /// 0002237 // response to molecule of bacterial origin (MGI:MGI:4943853 PMID:19912257 [IDA]) /// 0042127 // regulation of cell proliferation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000021269) /// 0070098 // chemokine-mediated signaling pathway

				(MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000021269)
Hcar2	- 11.353 9916	1.958 07E- 27	MGI:19 33383	0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0033031 // positive regulation of neutrophil apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8TDS4) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:727952) /// 0050995 // negative regulation of lipid catabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:727952) /// 0070165 // positive regulation of adiponectin secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:727952) /// 0001781 // neutrophil apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8TDS4) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807)
Wfdc17	- 11.147 36127	5.635 17E- 21	MGI:36 49773	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
I830127L 07Rik	- 11.125 54131	2.165 01E- 10		
Il1f6	- 10.974 18791	6.186 88E- 24	MGI:18 59324	0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0001819 // positive regulation of cytokine production (MGI:MGI:5300146 PMID:21860022 [IDA]) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000008570) /// 0032755 // positive regulation of interleukin-6 production (MGI:MGI:5300146 PMID:21860022 [IGI] MGI:MGI:1913107) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0006954 // inflammatory response (MGI:MGI:1355196 PMID:10744718 [TAS]) /// 0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR027163)
Lipg	- 10.897 63552	3.031 61E- 21	MGI:13 41803	0010983 // positive regulation of high-density lipoprotein particle clearance (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5X9) /// 0032376 // positive regulation of cholesterol transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5X9) /// 0055091 // phospholipid homeostasis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5X9) /// 0043691 // reverse cholesterol transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5X9) /// 0034375 // high-density lipoprotein particle remodeling (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5X9) /// 0006629 // lipid metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR016272 InterPro:IPR002330) /// 0008283 // cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1310740) /// 0006629 // lipid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0443) /// 0016042 // lipid catabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0442) /// 0042632 // cholesterol homeostasis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5X9) /// 0050746 // regulation of lipoprotein metabolic process (MGI:MGI:3770473 PMID:17681148 [IMP] MGI:MGI:2450672)
Gm18342	- 10.828 27172	4.624 5E- 10		
Psd4	- 10.648 40964	3.538 12E- 46	MGI:26 74093	0032012 // regulation of ARF protein signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000904)
1700047 M11Rik	- 10.608 8313	1.933 47E- 17		
Ero1l	- 10.572 57547	4.291 78E- 31	MGI:13 54385	0006457 // protein folding (MGI:MGI:1353675 PMID:10671517 [ISO] EMBL:AF081886) /// 0051085 // chaperone mediated protein folding requiring cofactor (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96HE7) /// 0030968 // endoplasmic reticulum unfolded protein response (MGI:MGI:3525819 PMID:15601821 [IDA]) /// 0070059 // intrinsic apoptotic signaling pathway in response to endoplasmic reticulum stress (MGI:MGI:4366390 PMID:19752026 [IMP]) /// 0030198 // extracellular matrix organization (MGI:MGI:5461404 PMID:22981861 [IGI] MGI:MGI:1914725 MGI:MGI:1859815) /// 0045454 // cell redox homeostasis (MGI:MGI:5489003 PMID:23589496 [IGI] MGI:MGI:1914725 MGI:MGI:1859815) /// 0050873 // brown fat cell differentiation (MGI:MGI:3801349 PMID:18492766 [IDA]) /// 0051209 // release of sequestered calcium ion into cytosol (MGI:MGI:4366390 PMID:19752026 [IMP]) /// 0034976 // response to endoplasmic reticulum stress (MGI:MGI:4366390 PMID:19752026 [IDA]) /// 0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0022417 // protein maturation by protein folding (MGI:MGI:5461404 PMID:22981861 [IGI] MGI:MGI:1914725 MGI:MGI:1859815) /// 0055114 // oxidation-reduction process

				(MGI:MGI:5620560 PMID:25452428 [IDA]) /// 0019471 // 4-hydroxyproline metabolic process (MGI:MGI:5461404 PMID:22981861 [IGI] MGI:MGI:1914725 MGI:MGI:1859815) /// 0006457 // protein folding (MGI:MGI:3525819 PMID:15601821 [IDA]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Stfa1	- 10.556 43712	3.710 78E- 16	MGI:10 6198	0010951 // negative regulation of endopeptidase activity (MGI:MGI:3653980 PMID:16831429 [IDA])
Pram1	- 10.524 84364	1.916 27E- 11	MGI:35 76625	0043313 // regulation of neutrophil degranulation (MGI:MGI:3525750 PMID:15572693 [IMP] MGI:MGI:3579812) /// 0007229 // integrin-mediated signaling pathway (MGI:MGI:3525750 PMID:15572693 [IMP] MGI:MGI:3579812)
S100a8	- 10.474 54063	2.638 93E- 16	MGI:88 244	0018119 // peptidyl-cysteine S-nitrosylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05109) /// 0002523 // leukocyte migration involved in inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05109) /// 0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) /// 0030593 // neutrophil chemotaxis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05109) /// 0006935 // chemotaxis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0145) /// 0006919 // activation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05109) /// 0050729 // positive regulation of inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05109) /// 0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0050727 // regulation of inflammatory response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028474) /// 0006914 // autophagy (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05109) /// 0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0070488 // neutrophil aggregation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05109) /// 0002793 // positive regulation of peptide secretion (MGI:MGI:3835701 PMID:18820689 [IDA]) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0045087 // innate immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028474) /// 2001244 // positive regulation of intrinsic apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P05109) /// 0002793 // positive regulation of peptide secretion (MGI:MGI:3835701 PMID:18820689 [IMP]) /// 0014002 // astrocyte development (MGI:MGI:5440388 PMID:22577135 [IGI] MGI:MGI:1338947)
Gpr84	- 10.210 24703	1.132 29E- 30	MGI:19 34129	0007218 // neuropeptide signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000660491) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000276) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297) /// 0007200 // phospholipase C-activating G-protein coupled receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000660491)
Fas	- 10.209 9337	6.621 47E- 32	MGI:95 484	0071455 // cellular response to hyperoxia (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P25445) /// 0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR008063) /// 0043029 // T cell homeostasis (MGI:MGI:79355 PMID:8640868 [IMP] MGI:MGI:1856384) /// 0051260 // protein homoooligomerization (MGI:MGI:77677 PMID:8524870 [IDA]) /// 0070230 // positive regulation of lymphocyte apoptotic process (MGI:MGI:3576402 PMID:15632112 [IDA]) /// 0051384 // response to glucocorticoid stimulus (MGI:MGI:79355 PMID:8640868 [IMP] MGI:MGI:1856334) /// 0097284 // hepatocyte apoptotic process (MGI:MGI:5566519 PMID:20436477 [IGI] MGI:MGI:1929260 MGI:MGI:108093) /// 0006925 // inflammatory cell apoptotic process (MGI:MGI:2687085 PMID:12801066 [IMP]) /// 0097527 /// 0006915 // apoptotic process (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:P25445) /// 0043280 // positive regulation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619831) /// 0051402 // neuron apoptotic process (MGI:MGI:4829576 PMID:20530871 [IMP] MGI:MGI:1856334) /// 0006927 // transformed cell apoptotic process (MGI:MGI:2687085 PMID:12801066 [IDA]) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:76989 PMID:7595210 [IDA]) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:3819026 PMID:18363966 [IDA]) /// 0042127 // regulation of cell proliferation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000753849) /// 0097191 // extrinsic apoptotic signaling pathway (MGI:MGI:2183141 PMID:12011074 [IMP]) /// 0097191 // extrinsic apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P25445) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:5009197 PMID:10950869 [IDA]) /// 2001238 // positive regulation of extrinsic apoptotic signaling pathway (MGI:MGI:3576402 PMID:15632112 [IDA]) /// 0032464 // positive regulation of protein homoooligomerization (MGI:MGI:5009197 PMID:10950869 [IDA]) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:3029504 PMID:12431371 [IGI] MGI:MGI:1096330) /// 0045060 // negative thymic T cell selection (MGI:MGI:1340173 PMID:10429671 [IMP] MGI:MGI:1856334) /// 0097190 // apoptotic signaling pathway (MGI:MGI:80946 PMID:8666928 [IDA]) /// 0097049 // motor

				<p>neuron apoptotic process (MGI:MGI:2675560 PMID:13679421 [IMP] MGI:MGI:1861923) /// 0009636 // response to toxic substance (MGI:MGI:78883 PMID:8557033 [IMP] MGI:MGI:1856334) /// 0097049 // motor neuron apoptotic process (MGI:MGI:2675560 PMID:13679421 [IMP] MGI:MGI:1856334) /// 0097191 // extrinsic apoptotic signaling pathway (MGI:MGI:3818355 PMID:17980593 [IDA]) /// 0006924 // activation-induced cell death of T cells (MGI:MGI:73864 PMID:7602121 [IMP] MGI:MGI:1856334 MGI:MGI:1856384) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:3029504 PMID:12431371 [IMP]) /// 0032496 // response to lipopolysaccharide (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000753849) /// 0045637 // regulation of myeloid cell differentiation (MGI:MGI:1275871 PMID:9697835 [IMP] MGI:MGI:1856334) /// 0006924 // activation-induced cell death of T cells (MGI:MGI:79355 PMID:8640868 [IMP] MGI:MGI:1856334) /// 0010468 // regulation of gene expression (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619831) /// 0019724 // B cell mediated immunity (MGI:MGI:3773559 PMID:18199416 [IMP]) /// 0031104 // dendrite regeneration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619831) /// 0006915 // apoptotic process (MGI:MGI:81811 PMID:8700551 [IMP] MGI:MGI:1856334) /// 0002377 // immunoglobulin production (MGI:MGI:3773559 PMID:18199416 [IMP] MGI:MGI:1856334) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:77677 PMID:8524870 [IMP]) /// 0051384 // response to glucocorticoid stimulus (MGI:MGI:73864 PMID:7602121 [IMP] MGI:MGI:1856334 MGI:MGI:1856384) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619831) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:2687085 PMID:12801066 [IDA]) /// 0043410 // positive regulation of MAPK cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001499622) /// 0090200 // positive regulation of release of cytochrome c from mitochondria (MGI:MGI:5009197 PMID:10950869 [IC] GO:0032464) /// 0010942 // positive regulation of cell death (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619831) /// 0097192 // extrinsic apoptotic signaling pathway in absence of ligand (MGI:MGI:2675560 PMID:13679421 [IMP] MGI:MGI:1856334) /// 0048536 // spleen development (MGI:MGI:3773559 PMID:18199416 [IMP] MGI:MGI:1856334) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P25445) /// 0097192 // extrinsic apoptotic signaling pathway in absence of ligand (MGI:MGI:2675560 PMID:13679421 [IMP] MGI:MGI:1861923) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:3687663 PMID:10588860 [IDA]) /// 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000488 InterPro:IPR008063) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:1340173 PMID:10429671 [IMP] MGI:MGI:1856334) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:2687085 PMID:12801066 [IMP]) /// 0097190 // apoptotic signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619831) /// 0045619 // regulation of lymphocyte differentiation (MGI:MGI:55958 PMID:6610701 [IMP] MGI:MGI:1856334) /// 0006925 // inflammatory cell apoptotic process (MGI:MGI:2687085 PMID:12801066 [IDA]) /// 0042981 // regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619831) /// 0003014 // renal system process (MGI:MGI:79355 PMID:8640868 [IMP] MGI:MGI:1856334) /// 0006954 // inflammatory response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000753849) /// 0007420 // brain development (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001895566) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:77677 PMID:8524870 [IDA]) /// 0008625 // extrinsic apoptotic signaling pathway via death domain receptors (MGI:MGI:3038547 PMID:15039234 [IDA]) /// 0033209 // tumor necrosis factor-mediated signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619831) /// 0006924 // activation-induced cell death of T cells (MGI:MGI:2670301 PMID:12702495 [IDA]) /// 0010467 // gene expression (MGI:MGI:73864 PMID:7602121 [IMP] MGI:MGI:1856334 MGI:MGI:1856384) /// 2001241 // positive regulation of extrinsic apoptotic signaling pathway in absence of ligand (MGI:MGI:3038547 PMID:15039234 [IMP] MGI:MGI:1856334) /// 0043281 // regulation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001895566) /// 0071285 // cellular response to lithium ion (MGI:MGI:4829576 PMID:20530871 [IMP] MGI:MGI:1856334) /// 0050869 // negative regulation of B cell activation (MGI:MGI:55958 PMID:6610701 [IMP] MGI:MGI:1856334) /// 0042127 // regulation of cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:619831) /// 0097190 // apoptotic signaling pathway (MGI:MGI:65483 PMID:7511063 [IDA])</p>
Nr4a1	- 10.207 00826	1.162 23E- 26	MGI:13 52454	<p>0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:87364 PMID:9155013 [IDA]) /// 0061469 // regulation of type B pancreatic cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620029) /// 0006915 // apoptotic process (MGI:MGI:3721333 PMID:17434920 [IMP] MGI:MGI:2182325) /// 0035767 // endothelial cell chemotaxis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22736) /// 0043154 // negative regulation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:2667579 PMID:12815108 [IDA]) /// 0043401 // steroid hormone mediated signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000536) /// 0071310 // cellular response to organic substance (MGI:MGI:4947150 PMID:21357543 [IDA]) /// 0045944 // positive regulation of transcription</p>

				<p>from RNA polymerase II promoter (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620029) /// 0010035 // response to inorganic substance (MGI:MGI:80763 PMID:1491694 [ISA] RefSeq:NP_077364) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3579756 PMID:15701640 [IGI] MGI:MGI:97874 MGI:MGI:1339708) /// 0035924 // cellular response to vascular endothelial growth factor stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22736) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:2683352 PMID:14657025 [IDA]) /// 0002042 // cell migration involved in sprouting angiogenesis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22736) /// 0044344 // cellular response to fibroblast growth factor stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22736) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:2683352 PMID:14657025 [IDA]) /// 0045444 // fat cell differentiation (MGI:MGI:5645207 PMID:18945812 [IDA]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3047463 PMID:15155786 [IGI] MGI:MGI:1276523 MGI:MGI:1352460) /// 0035914 // skeletal muscle cell differentiation (MGI:MGI:5300631 PMID:22147266 [IMP]) /// 0001938 // positive regulation of endothelial cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P22736) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0045786 // negative regulation of cell cycle (MGI:MGI:5645207 PMID:18945812 [IDA]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:P22736) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3047463 PMID:15155786 [IDA]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003071 InterPro:IPR003070 InterPro:IPR000536 InterPro:IPR001723 InterPro:IPR001628 InterPro:IPR013088) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:84485 PMID:8961274 [IDA]) /// 0071376 // cellular response to corticotropin-releasing hormone stimulus (MGI:MGI:5645213 PMID:10523643 [IDA]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:84485 PMID:8961274 [IDA])</p>
Tnfr1	- 10.202 20353	8.591 66E- 38	MGI:19 26194	<p>0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) /// 0085032 // modulation by symbiont of host I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q15025) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:5305352 PMID:22011580 [IMP]) /// 0043124 // negative regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:5319605 PMID:18212736 [IDA]) /// 0006508 // proteolysis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q15025) /// 0050729 // positive regulation of inflammatory response (MGI:MGI:5305352 PMID:22011580 [IMP]) /// 0043124 // negative regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q15025) /// 0002755 // MyD88-dependent toll-like receptor signaling pathway (MGI:MGI:5305352 PMID:22011580 [IDA]) /// 0009101 // glycoprotein biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q15025) /// 0007159 // leukocyte cell-cell adhesion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q15025) /// 0070373 // negative regulation of ERK1 and ERK2 cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q15025)</p>
Nlrp3	- 10.171 37978	6.984 15E- 22	MGI:26 53833	<p>0002830 // positive regulation of type 2 immune response (MGI:MGI:5689221 PMID:26098997 [IMP]) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96P20) /// 0032611 // interleukin-1 beta production (MGI:MGI:5446983 PMID:22753929 [IMP] MGI:MGI:5465108) /// 0006919 // activation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:3697006 PMID:17008311 [IMP] MGI:MGI:3686871) /// 0050701 // interleukin-1 secretion (MGI:MGI:3697006 PMID:17008311 [IMP] MGI:MGI:3686871) /// 0006954 // inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96P20) /// 0032621 // interleukin-18 production (MGI:MGI:3697006 PMID:17008311 [IMP] MGI:MGI:3686871) /// 0043280 // positive regulation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96P20) /// 0042347 // negative regulation of NF-kappaB import into nucleus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96P20) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:5689221 PMID:26098997 [IDA]) /// 0050727 // regulation of inflammatory response (MGI:MGI:5311078 PMID:22297845 [IMP] MGI:MGI:3686871) /// 0045630 // positive regulation of T-helper 2 cell differentiation (MGI:MGI:5689221 PMID:26098997 [IMP]) /// 0032753 // positive regulation of interleukin-4 production (MGI:MGI:5689221 PMID:26098997 [IDA]) /// 0051607 // defense response to virus (MGI:MGI:3697006 PMID:17008311 [IMP] MGI:MGI:3686871) /// 0050718 // positive regulation of interleukin-1 beta secretion (MGI:MGI:5547461 PMID:23997220 [IGI] MGI:MGI:2686159) /// 0032088 // negative regulation of NF-kappaB transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96P20) /// 0002674 // negative regulation of acute inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96P20) /// 0006351 // transcription, DNA-dependent</p>

				(MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0050718 // positive regulation of interleukin-1 beta secretion (MGI:MGI:5468674 PMID:22002608 [IGI] MGI:MGI:1931465 MGI:MGI:107700) /// 2000321 // positive regulation of T-helper 17 cell differentiation (MGI:MGI:5689221 PMID:26098997 [IMP]) /// 0032754 // positive regulation of interleukin-5 production (MGI:MGI:5689221 PMID:26098997 [IMP]) /// 0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 2000553 // positive regulation of T-helper 2 cell cytokine production (MGI:MGI:5689221 PMID:26098997 [IMP]) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96P20) /// 0044546 // NLRP3 inflammasome complex assembly (MGI:MGI:5446983 PMID:22753929 [IMP] MGI:MGI:5465108) /// 0032736 // positive regulation of interleukin-13 production (MGI:MGI:5689221 PMID:26098997 [IMP]) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96P20) /// 0050713 // negative regulation of interleukin-1 beta secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96P20) /// 0050718 // positive regulation of interleukin-1 beta secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96P20)
Fam169b	- 10.138 29772	4.088 15E- 20	MGI:36 44026	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Tmem38 b	- 10.083 52291	4.212 4E- 41	MGI:10 98718	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0006813 // potassium ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0633) /// 0015672 // monovalent inorganic cation transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR007866) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0071805 // potassium ion transmembrane transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0631)
Nos2	- 10.077 90912	2.277 52E- 25	MGI:97 361	0055114 // oxidation-reduction process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003097 InterPro:IPR017927 InterPro:IPR001094 InterPro:IPR001709 InterPro:IPR023173 InterPro:IPR004030 InterPro:IPR001433 InterPro:IPR017938) /// 0045776 // negative regulation of blood pressure (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000453988) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:3821815 PMID:18791161 [IDA]) /// 0010629 // negative regulation of gene expression (MGI:MGI:5319619 PMID:12085352 [IGI] UniProtKB:P35228) /// 0071407 // cellular response to organic cyclic compound (MGI:MGI:3850788 PMID:19414010 [ISO] UniProtKB:Q06518) /// 0018119 // peptidyl-cysteine S-nitrosylation (MGI:MGI:4887336 PMID:16373578 [IDA]) /// 0007263 // nitric oxide mediated signal transduction (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001066032) /// 0072604 // interleukin-6 secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35228) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:4412460 PMID:18025219 [IDA]) /// 0072606 // interleukin-8 secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35228) /// 0001542 // ovulation from ovarian follicle (MGI:MGI:2157249 PMID:11779605 [IMP] MGI:MGI:2158791) /// 0006809 // nitric oxide biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35228) /// 0006527 // arginine catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35228) /// 0042127 // regulation of cell proliferation (MGI:MGI:2154629 PMID:11731407 [IGI] MGI:MGI:88039) /// 0051712 // positive regulation of killing of cells of other organism (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35228) /// 0006954 // inflammatory response (MGI:MGI:3687888 PMID:12855682 [TAS]) /// 0071346 // cellular response to interferon-gamma (MGI:MGI:4412460 PMID:18025219 [IDA]) /// 0006809 // nitric oxide biosynthetic process (MGI:MGI:3807769 PMID:9271491 [IDA]) /// 0035690 // cellular response to drug (MGI:MGI:5619708 PMID:24486487 [IDA]) /// 0050796 // regulation of insulin secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35228) /// 0055114 // oxidation-reduction process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0560) /// 0042742 // defense response to bacterium (MGI:MGI:2673089 PMID:12933833 [IMP] MGI:MGI:1857228) /// 0042127 // regulation of cell proliferation (MGI:MGI:2151649 PMID:11606502 [IGI] MGI:MGI:88039) /// 0006801 // superoxide metabolic process (MGI:MGI:2673089 PMID:12933833 [IMP] MGI:MGI:1857228) /// 0001666 // response to hypoxia (MGI:MGI:2674212 PMID:12960352 [IDA]) /// 0031284 // positive regulation of guanylate cyclase activity (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001066032) /// 0032310 // prostaglandin secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35228) /// 0010629 // negative regulation of gene expression (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35228) /// 0042177 // negative regulation of protein catabolic process (MGI:MGI:4943392 PMID:18003616 [IDA]) /// 0042742 // defense response to bacterium (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35228) /// 0006809 // nitric oxide biosynthetic process (MGI:MGI:3807772 PMID:1383204 [IDA]) /// 0032496 // response to lipopolysaccharide (MGI:MGI:5308514 PMID:22073225 [IDA]) /// 0045909 // positive regulation of vasodilation (MGI:MGI:4459044 GO_REF:0000033 [IBA])

				PANTHER:PTN000453988) /// 0071345 // cellular response to cytokine stimulus (MGI:MGI:3850788 PMID:19414010 [ISO] UniProtKB:Q06518) /// 0006527 // arginine catabolic process (MGI:MGI:3807772 PMID:1383204 [IDA]) /// 1900015 // regulation of cytokine production involved in inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35228)
Saa1	- 10.030 4939	8.361 63E- 14	MGI:98 221	0006953 // acute-phase response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000096) /// 0008203 // cholesterol metabolic process (MGI:MGI:1096057 PMID:9300780 [IDA]) /// 0060326 // cell chemotaxis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000603423) /// 0006953 // acute-phase response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0011)
Ncf1	- 10.025 28109	6.469 22E- 21	MGI:97 283	0002679 // respiratory burst involved in defense response (MGI:MGI:2182072 PMID:10714686 [IMP] MGI:MGI:3576788) /// 0006691 // leukotriene metabolic process (MGI:MGI:2176389 PMID:11867678 [IMP] MGI:MGI:1934143) /// 0009617 // response to bacterium (MGI:MGI:1353689 PMID:10678931 [IMP] MGI:MGI:1934143) /// 0050665 // hydrogen peroxide biosynthetic process (MGI:MGI:3050718 PMID:15258578 [IMP] MGI:MGI:1934143) /// 0001878 // response to yeast (MGI:MGI:2182072 PMID:10714686 [IMP] MGI:MGI:3576788) /// 0008283 // cell proliferation (MGI:MGI:1889180 PMID:10987289 [IMP] MGI:MGI:1934143) /// 0050832 // defense response to fungus (MGI:MGI:2182072 PMID:10714686 [IMP] MGI:MGI:3576788) /// 0070946 // neutrophil mediated killing of gram-positive bacterium (MGI:MGI:4353632 PMID:11907569 [IMP] MGI:MGI:3576788) /// 0042554 // superoxide anion generation (MGI:MGI:1354608 PMID:10725280 [IMP] MGI:MGI:1934143) /// 0045730 // respiratory burst (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61307) /// 0006742 // NADP catabolic process (MGI:MGI:1351390 PMID:10647999 [ISA] EMBL:AF079302) /// 0006612 // protein targeting to membrane (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P14598) /// 0006954 // inflammatory response (MGI:MGI:2176389 PMID:11867678 [IMP] MGI:MGI:1934143) /// 0042742 // defense response to bacterium (MGI:MGI:3718167 PMID:17526748 [IMP] MGI:MGI:2661962) /// 0070947 // neutrophil mediated killing of fungus (MGI:MGI:4353632 PMID:11907569 [IMP] MGI:MGI:3576788) /// 0001878 // response to yeast (MGI:MGI:4353632 PMID:11907569 [IMP] MGI:MGI:3576788) /// 0045986 // negative regulation of smooth muscle contraction (MGI:MGI:3771783 PMID:17993584 [IMP] MGI:MGI:1934143) /// 0042554 // superoxide anion generation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P14598) /// 0055114 // oxidation-reduction process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61307) /// 0001909 // leukocyte mediated cytotoxicity (MGI:MGI:3718167 PMID:17526748 [IMP] MGI:MGI:2661962) /// 0050830 // defense response to Gram-positive bacterium (MGI:MGI:4353632 PMID:11907569 [IMP] MGI:MGI:3576788) /// 0006915 // apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61307) /// 0006968 // cellular defense response (MGI:MGI:75890 PMID:7650482 [IMP] MGI:MGI:1934143) /// 0045730 // respiratory burst (MGI:MGI:3613402 PMID:15626477 [IMP] MGI:MGI:3576788) /// 0042554 // superoxide anion generation (MGI:MGI:1930845 PMID:11156938 [IMP] MGI:MGI:1934143) /// 0042742 // defense response to bacterium (MGI:MGI:86599 PMID:9116268 [IMP] MGI:MGI:1934143) /// 0050832 // defense response to fungus (MGI:MGI:3588470 PMID:16041040 [IMP] MGI:MGI:1934143) /// 0055114 // oxidation-reduction process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P14598)
Ereg	- 9.9933 1897	1.199 79E- 41	MGI:10 7508	0045740 // positive regulation of DNA replication (MGI:MGI:3687425 PMID:7706296 [IDA]) /// 0045741 // positive regulation of epidermal growth factor-activated receptor activity (MGI:MGI:3687677 PMID:9990076 [ISS] UniProtKB:Q9Z0L5) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0001525 // angiogenesis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0037) /// 0008285 // negative regulation of cell proliferation (MGI:MGI:3687425 PMID:7706296 [IDA]) /// 0045840 // positive regulation of mitosis (MGI:MGI:3687677 PMID:9990076 [ISS] UniProtKB:Q9Z0L5) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0048661 // positive regulation of smooth muscle cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0045740 // positive regulation of DNA replication (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0045740 // positive regulation of DNA replication (MGI:MGI:1333540 PMID:9337852 [IDA]) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:3690185 PMID:9419975 [ISS] UniProtKB:O14944) /// 0045860 // positive regulation of protein kinase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0045892 // negative regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0042327 // positive regulation of phosphorylation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0001550 // ovarian cumulus expansion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0045741 // positive regulation of epidermal growth factor-activated receptor activity (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0051781 // positive regulation of cell division (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0497) /// 0009299 // mRNA transcription (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0042327 // positive regulation of phosphorylation

				(MGI:MGI:3690185 PMID:9419975 [ISS] UniProtKB:O14944) /// 0048146 // positive regulation of fibroblast proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0045840 // positive regulation of mitosis (MGI:MGI:3687425 PMID:7706296 [IDA]) /// 0048160 // primary follicle stage (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0009653 // anatomical structure morphogenesis (MGI:MGI:1333540 PMID:9337852 [TAS]) /// 0043616 // keratinocyte proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0007173 // epidermal growth factor receptor signaling pathway (MGI:MGI:3687425 PMID:7706296 [IDA]) /// 0001819 // positive regulation of cytokine production (MGI:MGI:3604223 PMID:16182244 [IMP]) /// 0009887 // organ morphogenesis (MGI:MGI:1333540 PMID:9337852 [TAS]) /// 0030728 // ovulation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0042327 // positive regulation of phosphorylation (MGI:MGI:3687677 PMID:9990076 [ISS] UniProtKB:Q9Z0L5) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:3687425 PMID:7706296 [IDA]) /// 0051151 // negative regulation of smooth muscle cell differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0042327 // positive regulation of phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0042108 // positive regulation of cytokine biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0007143 // female meiosis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0045840 // positive regulation of mitosis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0007267 // cell-cell signaling (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0045089 // positive regulation of innate immune response (MGI:MGI:3604223 PMID:16182244 [IMP]) /// 0045410 // positive regulation of interleukin-6 biosynthetic process (MGI:MGI:3604223 PMID:16182244 [IMP]) /// 0042700 // luteinizing hormone signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0045740 // positive regulation of DNA replication (MGI:MGI:3687677 PMID:9990076 [ISS] UniProtKB:Q9Z0L5) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14944) /// 0001556 // oocyte maturation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0030154 // cell differentiation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0221) /// 0045740 // positive regulation of DNA replication (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620299) /// 0048661 // positive regulation of smooth muscle cell proliferation (MGI:MGI:3687677 PMID:9990076 [ISS] UniProtKB:Q9Z0L5)
Ifnlr1	- 9.8091 64634	4.810 94E- 58	MGI:24 29859	0051607 // defense response to virus (MGI:MGI:5009066 PMID:21518880 [IMP]) /// 0002385 // mucosal immune response (MGI:MGI:5009066 PMID:21518880 [IMP]) /// 0050691 // regulation of defense response to virus by host (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8IU57) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000466212) /// 0051607 // defense response to virus (MGI:MGI:3774908 PMID:18250457 [IGI] MGI:MGI:2156367 MGI:MGI:1932389)
Rpl3l	- 9.7431 63422	9.740 17E- 09	MGI:19 13461	0006412 // translation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000146039) /// 0000027 // ribosomal large subunit assembly (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000146039)
Gm14963	- 9.6821 88767	5.617 8E- 17	MGI:37 05162	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Abca12	- 9.6366 00985	1.054 56E- 05	MGI:26 76312	0061436 // establishment of skin barrier (MGI:MGI:3807143 PMID:18632686 [IMP] MGI:MGI:3809668) /// 0043129 // surfactant homeostasis (MGI:MGI:3829841 PMID:18957418 [IMP] MGI:MGI:3528440) /// 0031424 // keratinization (MGI:MGI:3829841 PMID:18957418 [IMP] MGI:MGI:3528440) /// 0043129 // surfactant homeostasis (MGI:MGI:3807143 PMID:18632686 [IMP] MGI:MGI:3809668) /// 0010875 // positive regulation of cholesterol efflux (MGI:MGI:5510615 PMID:23931754 [IGI] MGI:MGI:1352463) /// 0010875 // positive regulation of cholesterol efflux (MGI:MGI:5510615 PMID:23931754 [IMP] MGI:MGI:4461044) /// 0032940 // secretion by cell (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q86UK0) /// 0055088 // lipid homeostasis (MGI:MGI:4460077 PMID:18802465 [IMP] MGI:MGI:4461044) /// 0030216 // keratinocyte differentiation (MGI:MGI:4460077 PMID:18802465 [IMP] MGI:MGI:4461044) /// 0033700 // phospholipid efflux (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000442579) /// 2000010 // positive regulation of protein localization to cell surface (MGI:MGI:5510615 PMID:23931754 [IMP]) /// 0048286 // lung alveolus development (MGI:MGI:3829841 PMID:18957418 [IMP] MGI:MGI:3528440) /// 0061436 // establishment of skin barrier (MGI:MGI:4460077 PMID:18802465 [IMP] MGI:MGI:4461044) /// 0033700 // phospholipid efflux (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q86UK0) /// 0031424 // keratinization (MGI:MGI:3807143 PMID:18632686 [IMP] MGI:MGI:3809668) /// 0006869 // lipid transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q86UK0) /// 0061436 // establishment of skin barrier (MGI:MGI:3829841 PMID:18957418 [IMP] MGI:MGI:3528440) /// 0048286 // lung alveolus development (MGI:MGI:3807143 PMID:18632686 [IMP] MGI:MGI:3809668) /// 0035627 // ceramide transport (MGI:MGI:3829841 PMID:18957418 [IMP] MGI:MGI:3528440) /// 0031424 //

				keratinization (MGI:MGI:4460077 PMID:18802465 [IMP] MGI:MGI:4461044) /// 0072659 // protein localization to plasma membrane (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q86UK0) /// 0010875 // positive regulation of cholesterol efflux (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q86UK0) /// 0045055 // regulated secretory pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q86UK0)
Gadd45a	- 9.5819 77831	2.519 72E- 25	MGI:10 7799	0006950 // response to stress (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR024824) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P24522) /// 0006469 // negative regulation of protein kinase activity (MGI:MGI:2384369 PMID:12124778 [IDA]) /// 0042770 // signal transduction in response to DNA damage (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P24522) /// 1900745 // positive regulation of p38MAPK cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P24522) /// 0000185 // activation of MAPKKK activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P24522) /// 0007049 // cell cycle (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0131) /// 0006974 // response to DNA damage stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0227) /// 0051726 // regulation of cell cycle (MGI:MGI:2384369 PMID:12124778 [IDA]) /// 0007050 // cell cycle arrest (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0338) /// 0071479 // cellular response to ionizing radiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P24522) /// 2000379 // positive regulation of reactive oxygen species metabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P24522) /// 0007098 // centrosome cycle (MGI:MGI:3050174 PMID:15123655 [IGI] MGI:MGI:104537) /// 0071850 // mitotic cell cycle arrest (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P24522) /// 0046330 // positive regulation of JNK cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P24522)
2010109I 03Rik	- 9.5785 5961	1.950 64E- 09	MGI:19 14288	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Ccdc88b	- 9.5643 23865	3.821 92E- 33	MGI:19 25567	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Kdm6b	- 9.5591 1042	3.184 3E- 33	MGI:24 48492	0045446 // endothelial cell differentiation (MGI:MGI:5574281 PMID:23856522 [IMP]) /// 0048333 // mesodermal cell differentiation (MGI:MGI:5574281 PMID:23856522 [IMP]) /// 0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) /// 0055007 // cardiac muscle cell differentiation (MGI:MGI:5574281 PMID:23856522 [IMP]) /// 0016568 // chromatin modification (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0156) /// 0045165 // cell fate commitment (MGI:MGI:3809360 PMID:18716661 [IMP]) /// 0016577 // histone demethylation (MGI:MGI:3764743 PMID:17928865 [IMP]) /// 0071557 // histone H3-K27 demethylation (MGI:MGI:5574281 PMID:23856522 [IDA]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:5574281 PMID:23856522 [IMP]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3764743 PMID:17928865 [IDA]) /// 0021766 // hippocampus development (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1307629) /// 0071557 // histone H3-K27 demethylation (MGI:MGI:3809360 PMID:18716661 [IMP]) /// 0010468 // regulation of gene expression (MGI:MGI:3809360 PMID:18716661 [IMP]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3764743 PMID:17928865 [IMP]) /// 0070301 // cellular response to hydrogen peroxide (MGI:MGI:5496352 PMID:20808772 [IDA]) /// 0055114 // oxidation-reduction process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0560)
Il1m	- 9.5352 71344	1.868 02E- 29	MGI:96 547	0019233 // sensory perception of pain (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621159) /// 0030073 // insulin secretion (MGI:MGI:2675567 PMID:12975454 [IMP] MGI:MGI:2157397) /// 0006629 // lipid metabolic process (MGI:MGI:2675567 PMID:12975454 [IMP] MGI:MGI:2157397) /// 0045837 // negative regulation of membrane potential (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621159) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000008570) /// 0043507 // positive regulation of JUN kinase activity (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621159) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621159) /// 0051384 // response to glucocorticoid stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P18510) /// 0001960 // negative regulation of cytokine-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P18510) /// 0007613 // memory (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621159) /// 0014050 // negative regulation of glutamate secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621159) /// 2000660 // negative regulation of interleukin-1-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P18510) /// 0001660 // fever generation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621159) /// 0034115 // negative regulation of heterotypic cell-cell adhesion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P18510) /// 0030336 // negative regulation of cell migration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621159) /// 0006953 // acute-phase

				response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P18510)
Traf1	- 9.5247 18275	1.014 34E- 31	MGI:10 1836	0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0042981 // regulation of apoptotic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR012227 InterPro:IPR027136) /// 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13077) /// 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR012227 InterPro:IPR027136) /// 2001236 // regulation of extrinsic apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q13077)
Gm16754	- 9.5118 59354	1.290 14E- 11		
Hilpda	- 9.4723 82079	5.545 27E- 26	MGI:19 16823	0098792 /// 0010884 // positive regulation of lipid storage (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5L2) /// 0002230 // positive regulation of defense response to virus by host (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5L2) /// 0035425 // autocrine signaling (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5L2) /// 0001819 // positive regulation of cytokine production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5L2) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y5L2) /// 0035425 // autocrine signaling (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000424026)
Vasp	- 9.4437 6139	3.513 81E- 37	MGI:10 9268	0007411 // axon guidance (MGI:MGI:3054149 PMID:15371503 [IGI] MGI:MGI:108360) /// 0051289 // protein homotetramerization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR017354) /// 0008154 // actin polymerization or depolymerization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR017354) /// 0030838 // positive regulation of actin filament polymerization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P50552) /// 0030036 // actin cytoskeleton organization (MGI:MGI:3054149 PMID:15371503 [IGI] MGI:MGI:108360) /// 0001843 // neural tube closure (MGI:MGI:3054149 PMID:15371503 [IGI] MGI:MGI:108360)
Irak2	- 9.4278 75508	7.645 78E- 33	MGI:24 29603	0070498 // interleukin-1-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O43187) /// 0001959 // regulation of cytokine-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O43187) /// 0043433 // negative regulation of sequence-specific DNA binding transcription factor activity (MGI:MGI:3046371 PMID:15082713 [IDA]) /// 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O43187) /// 0070498 // interleukin-1-mediated signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001563216) /// 0006468 // protein phosphorylation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000719) /// 0046777 // protein autophosphorylation (MGI:MGI:2388552 PMID:12220507 [IDA]) /// 0070555 // response to interleukin-1 (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O43187) /// 0031663 // lipopolysaccharide-mediated signaling pathway (MGI:MGI:3046371 PMID:15082713 [IDA]) /// 0042981 // regulation of apoptotic process (MGI:MGI:2665373 PMID:12819136 [RCA]) /// 0007250 // activation of NF-kappaB-inducing kinase activity (MGI:MGI:2388552 PMID:12220507 [IDA]) /// 0032088 // negative regulation of NF-kappaB transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O43187) /// 0002224 // toll-like receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001563216) /// 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000488) /// 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:3046371 PMID:15082713 [IDA])
Proz	- 9.3909 55238	1.299 67E- 18	MGI:18 60488	0007596 // blood coagulation (MGI:MGI:1859486 PMID:10829076 [IMP] MGI:MGI:1931524) /// 0007599 // hemostasis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0356) /// 0006508 // proteolysis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001254) /// 0007596 // blood coagulation (MGI:MGI:1859486 PMID:10829076 [IDA])
Stambp1	- 9.3651 52644	4.622 12E- 41	MGI:19 23880	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND]) /// 0006508 // proteolysis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0645)
Echdc3	- 9.3169 19777	8.482 66E- 15	MGI:19 15106	0008152 // metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001753) /// 0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Ccr12	- 9.2491 94366	3.799 08E- 19	MGI:19 20904	0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000355 InterPro:IPR000276) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0006954 // inflammatory response (MGI:MGI:3811950 PMID:18794339

				[IDA]) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297) /// 0006935 // chemotaxis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000355)
Bcl2l1	- 9.2460 70995	1.611 42E- 35	MGI:88 139	0007093 // mitotic cell cycle checkpoint (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q07817) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:1860555 PMID:10894153 [IMP] MGI:MGI:2176699) /// 0001541 // ovarian follicle development (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2200) /// 0071312 // cellular response to alkaloid (MGI:MGI:3057092 PMID:15231831 [IDA]) /// 0046902 // regulation of mitochondrial membrane permeability (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q07817) /// 0090201 // negative regulation of release of cytochrome c from mitochondria (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q07817) /// 0097284 // hepatocyte apoptotic process (MGI:MGI:1351384 PMID:10618441 [IMP] MGI:MGI:2158303) /// 0008283 // cell proliferation (MGI:MGI:892190 PMID:9176392 [IDA]) /// 1900118 // negative regulation of execution phase of apoptosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q07817) /// 0008630 // intrinsic apoptotic signaling pathway in response to DNA damage (MGI:MGI:2677658 PMID:14517295 [IMP] MGI:MGI:2158303) /// 0042981 // regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2200) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:81233 PMID:8798158 [IDA]) /// 0043524 // negative regulation of neuron apoptotic process (MGI:MGI:79659 PMID:8625820 [IDA]) /// 0007283 // spermatogenesis (MGI:MGI:1860555 PMID:10894153 [IGI] MGI:MGI:99702) /// 0043524 // negative regulation of neuron apoptotic process (MGI:MGI:1929535 PMID:11150333 [IMP] MGI:MGI:2158303) /// 0002931 // response to ischemia (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2200) /// 0001541 // ovarian follicle development (MGI:MGI:1860555 PMID:10894153 [IGI] MGI:MGI:99702) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:75819 PMID:7650367 [ISO] UniProtKB:Q07817) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:1326944 PMID:9867803 [IDA]) /// 0071839 // apoptotic process in bone marrow (MGI:MGI:1351384 PMID:10618441 [IMP] MGI:MGI:2158303) /// 0071230 // cellular response to amino acid stimulus (MGI:MGI:3057092 PMID:15231831 [IMP] MGI:MGI:2675966) /// 0007281 // germ cell development (MGI:MGI:1860555 PMID:10894153 [IMP] MGI:MGI:2176699) /// 0043524 // negative regulation of neuron apoptotic process (MGI:MGI:1929535 PMID:11150333 [IGI] MGI:MGI:1277950) /// 0034097 // response to cytokine stimulus (MGI:MGI:892164 PMID:9184696 [ISO] UniProtKB:Q07817) /// 0043154 // negative regulation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2200) /// 0060154 // cellular process regulating host cell cycle in response to virus (MGI:MGI:3057092 PMID:15231831 [IMP] MGI:MGI:2675966) /// 0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0051402 // neuron apoptotic process (MGI:MGI:1351384 PMID:10618441 [IGI] MGI:MGI:107739) /// 1902230 /// 0043066 // negative regulation of apoptotic process (MGI:MGI:3700106 PMID:17267035 [IDA]) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:81233 PMID:8798158 [IDA]) /// 0043524 // negative regulation of neuron apoptotic process (MGI:MGI:3057092 PMID:15231831 [IDA]) /// 0009314 // response to radiation (MGI:MGI:2677658 PMID:14517295 [IMP] MGI:MGI:2158303) /// 0090005 // negative regulation of establishment of protein localization to plasma membrane (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q07817) /// 0019050 // suppression by virus of host apoptotic process (MGI:MGI:3057092 PMID:15231831 [ISO] UniProtKB:Q07817) /// 0001541 // ovarian follicle development (MGI:MGI:1860555 PMID:10894153 [IMP] MGI:MGI:2176699) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:3700106 PMID:17267035 [IDA]) /// 0051402 // neuron apoptotic process (MGI:MGI:1351384 PMID:10618441 [IMP] MGI:MGI:2158303) /// 0040007 // growth (MGI:MGI:1860555 PMID:10894153 [IMP] MGI:MGI:2176699) /// 2001243 // negative regulation of intrinsic apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q07817) /// 2000811 // negative regulation of anoikis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q07817) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:2677658 PMID:14517295 [IMP]) /// 0046898 // response to cycloheximide (MGI:MGI:892190 PMID:9176392 [IDA]) /// 0071480 // cellular response to gamma radiation (MGI:MGI:3057092 PMID:15231831 [IMP]) /// 0007281 // germ cell development (MGI:MGI:1860555 PMID:10894153 [IGI] MGI:MGI:99702) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:69011 PMID:7607090 [IDA]) /// 0001701 // in utero embryonic development (MGI:MGI:1351384 PMID:10618441 [IMP] MGI:MGI:2158303) /// 0070584 // mitochondrion morphogenesis (MGI:MGI:5432058 PMID:20671748 [IGI] MGI:MGI:99702) /// 0009566 // fertilization (MGI:MGI:1860555 PMID:10894153 [IGI] MGI:MGI:99702) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:2158953 PMID:11717309 [IDA]) /// 0000910 // cytokinesis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q07817) /// 0001836 // release of cytochrome c from mitochondria (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q07817) /// 0043524 // negative regulation of neuron apoptotic process (MGI:MGI:72933 PMID:7753802 [IDA]) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2200) /// 0097192 // extrinsic apoptotic signaling pathway in absence of ligand (MGI:MGI:2183839 PMID:12115603 [IMP]) /// 0009615 // response to virus (MGI:MGI:3057092 PMID:15231831 [IDA]) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO])

				UniProtKB:Q07817) /// 2001243 // negative regulation of intrinsic apoptotic signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000135647) /// 0008584 // male gonad development (MGI:MGI:1860555 PMID:10894153 [IMP] MGI:MGI:2176699) /// 0001836 // release of cytochrome c from mitochondria (MGI:MGI:3688960 PMID:17052454 [IGI] MGI:MGI:99702) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:82784 PMID:8798452 [IGI] MGI:MGI:99702) /// 0043524 // negative regulation of neuron apoptotic process (MGI:MGI:86927 PMID:9096145 [IGI] MGI:MGI:99702) /// 0051881 // regulation of mitochondrial membrane potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q07817)
Il1f9	- 9.2405 9625	3.728 78E- 32	MGI:24 49929	1901740 // negative regulation of myoblast fusion (MGI:MGI:5532227 PMID:23844157 [IMP]) /// 0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) /// 0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0001819 // positive regulation of cytokine production (MGI:MGI:5300146 PMID:21860022 [IDA]) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000008570) /// 0032755 // positive regulation of interleukin-6 production (MGI:MGI:5300146 PMID:21860022 [IGI] MGI:MGI:1913107) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0045662 // negative regulation of myoblast differentiation (MGI:MGI:5532227 PMID:23844157 [IMP])
Prdx6b	- 9.2405 60723	5.043 71E- 07	MGI:13 36888	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Nfkbib	- 9.2401 73069	1.013 83E- 29	MGI:10 4752	0007253 // cytoplasmic sequestering of NF-kappaB (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621887) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:4437182 PMID:20060382 [IDA]) /// 0007165 // signal transduction (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621887)
Hck	- 9.2262 94035	2.822 93E- 30	MGI:96 052	0050764 // regulation of phagocytosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P08631) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000700963) /// 0046777 // protein autophosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P08631) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P08631) /// 0006887 // exocytosis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0268) /// 0030154 // cell differentiation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000700357) /// 0016310 // phosphorylation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0418) /// 0051090 // regulation of sequence-specific DNA binding transcription factor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P08631) /// 0018108 // peptidyl-tyrosine phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P08631) /// 0006909 // phagocytosis (MGI:MGI:65050 PMID:8125254 [IMP] MGI:MGI:2384049) /// 0071801 // regulation of podosome assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P08631) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P08631) /// 0007169 // transmembrane receptor protein tyrosine kinase signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000700357) /// 0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) /// 0050764 // regulation of phagocytosis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000700963) /// 2000251 // positive regulation of actin cytoskeleton reorganization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P08631) /// 0006468 // protein phosphorylation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000719 InterPro:IPR001245 InterPro:IPR008266 InterPro:IPR020635) /// 0008360 // regulation of cell shape (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P08631) /// 0045087 // innate immune response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000700357) /// 0007010 // cytoskeleton organization (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000700963) /// 0050830 // defense response to Gram-positive bacterium (MGI:MGI:65050 PMID:8125254 [IGI] MGI:MGI:95527) /// 0038083 // peptidyl-tyrosine autophosphorylation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000700357) /// 0042127 // regulation of cell proliferation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000700357) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0071801 // regulation of podosome assembly (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000700963)
Dusp16	- 9.2222 25108	2.266 3E- 30	MGI:19 17936	0043409 // negative regulation of MAPK cascade (MGI:MGI:2151972 PMID:11489891 [IDA]) /// 0000188 // inactivation of MAPK activity (MGI:MGI:2151972 PMID:11489891 [IDA])
RP23- 191I16.4	- 9.1389	4.768 36E-		

	69917	08		
F630028 O10Rik	- 9.1362 96899	2.961 97E- 25		
Gm11714	- 9.1249 41487	1.117 54E- 08	MGI:36 49214	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Fpr1	- 9.0773 60425	3.391 86E- 23	MGI:10 7443	0007200 // phospholipase C-activating G-protein coupled receptor signaling pathway (MGI:MGI:5467169 PMID:22859307 [IDA]) /// 0006935 // chemotaxis (MGI:MGI:2447219 PMID:12470609 [TAS]) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2447219 PMID:12470609 [IDA]) /// 0007200 // phospholipase C-activating G-protein coupled receptor signaling pathway (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:P21462) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807)
Dgkg	- 8.9327 4119	4.173 46E- 19	MGI:10 5060	0007205 // protein kinase C-activating G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000756) /// 0035556 // intracellular signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002219) /// 0016310 // phosphorylation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0418)
Upp1	- 8.8750 03486	7.416 77E- 41	MGI:10 97668	0009116 // nucleoside metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000845) /// 0006220 // pyrimidine nucleotide metabolic process (MGI:MGI:3584214 PMID:15772079 [IMP] MGI:MGI:3586525) /// 0009166 // nucleotide catabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR010059) /// 0046108 // uridine metabolic process (MGI:MGI:3584214 PMID:15772079 [IMP] MGI:MGI:3586525) /// 0006218 // uridine catabolic process (MGI:MGI:5476603 PMID:23355744 [IDA])
Gramd1a	- 8.8549 22959	9.841 05E- 29	MGI:10 5490	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Adgb	- 8.8000 34621	5.709 5E- 21	MGI:36 05549	0006508 // proteolysis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000021568)
Cd80	- 8.7770 96549	8.483 85E- 34	MGI:10 1775	0050731 // positive regulation of peptidyl-tyrosine phosphorylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P33681) /// 0046641 // positive regulation of alpha-beta T cell proliferation (MGI:MGI:3757624 PMID:1385153 [IDA]) /// 0031295 // T cell costimulation (MGI:MGI:3521631 PMID:15568026 [IDA]) /// 0042102 // positive regulation of T cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2314) /// 0042102 // positive regulation of T cell proliferation (MGI:MGI:5544872 PMID:23793062 [IGI] MGI:MGI:101773) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:3828894 PMID:19047410 [IDA]) /// 0031295 // T cell costimulation (MGI:MGI:3757624 PMID:1385153 [IDA])
Noct	- 8.7489 65714	2.270 77E- 33	MGI:10 9382	0045995 // regulation of embryonic development (MGI:MGI:5494762 PMID:23449310 [IMP]) /// 0045600 // positive regulation of fat cell differentiation (MGI:MGI:4457955 PMID:20498072 [IMP]) /// 0010629 // negative regulation of gene expression (MGI:MGI:4837993 PMID:20685873 [IMP]) /// 0042752 // regulation of circadian rhythm (MGI:MGI:5308514 PMID:22073225 [IMP]) /// 0006397 // mRNA processing (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0507) /// 0009991 // response to extracellular stimulus (MGI:MGI:5567912 PMID:17400819 [IDA]) /// 0033962 // cytoplasmic mRNA processing body assembly (MGI:MGI:3807625 PMID:18625844 [IGI] MGI:MGI:1298230) /// 0000290 // deadenylation-dependent decapping of nuclear-transcribed mRNA (MGI:MGI:3807625 PMID:18625844 [IGI] MGI:MGI:1298230) /// 0032496 // response to lipopolysaccharide (MGI:MGI:5308514 PMID:22073225 [IDA]) /// 0048255 // mRNA stabilization (MGI:MGI:5308514 PMID:22073225 [IMP]) /// 0032922 // circadian regulation of gene expression (MGI:MGI:4837993 PMID:20685873 [IMP]) /// 0048511 // rhythmic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0090) /// 0045668 // negative regulation of osteoblast differentiation (MGI:MGI:4457955 PMID:20498072 [IMP])
Atp10d	- 8.7474 26961	2.553 85E- 32		
Hrh2	- 8.7446 05866	1.194 37E- 36	MGI:10 8482	0007613 // memory (MGI:MGI:3703474 PMID:17145090 [IMP] MGI:MGI:2182949) /// 0048565 // digestive tract development (MGI:MGI:3606849 PMID:15476751 [IMP] MGI:MGI:3607154) /// 0048565 // digestive tract development (MGI:MGI:1860000 PMID:10862789 [IMP] MGI:MGI:2182949) /// 0001697 // histamine-

				<p>induced gastric acid secretion (MGI:MGI:1860000 PMID:10862789 [IMP] MGI:MGI:2182949) /// 0001697 // histamine-induced gastric acid secretion (MGI:MGI:3606849 PMID:15476751 [IMP] MGI:MGI:3607154) /// 1900139 // negative regulation of arachidonic acid secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2831) /// 0048732 // gland development (MGI:MGI:3606849 PMID:15476751 [IMP] MGI:MGI:3607154) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000276 InterPro:IPR000503) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297) /// 0006955 // immune response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000664982) /// 0001696 // gastric acid secretion (MGI:MGI:3606849 PMID:15476751 [IGI] MGI:MGI:99479) /// 0003382 // epithelial cell morphogenesis (MGI:MGI:1860000 PMID:10862789 [IMP] MGI:MGI:2182949) /// 0008542 // visual learning (MGI:MGI:3703474 PMID:17145090 [IMP] MGI:MGI:2182949) /// 0045907 // positive regulation of vasoconstriction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000503) /// 0048167 // regulation of synaptic plasticity (MGI:MGI:3703474 PMID:17145090 [IMP] MGI:MGI:2182949) /// 0001698 // gastrin-induced gastric acid secretion (MGI:MGI:3606849 PMID:15476751 [IMP] MGI:MGI:3607154) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0001698 // gastrin-induced gastric acid secretion (MGI:MGI:1860000 PMID:10862789 [IMP] MGI:MGI:2182949) /// 1901998 // toxin transport (MGI:MGI:5492256 PMID:23716698 [IMP])</p>
Impa2	- 8.7251 07886	1.493 9E- 29	MGI:21 49728	<p>0046855 // inositol phosphate dephosphorylation (MGI:MGI:3698657 PMID:17068342 [ISO] UniProtKB:O14732) /// 0006020 // inositol metabolic process (MGI:MGI:2148328 PMID:11418250 [TAS]) /// 0046855 // inositol phosphate dephosphorylation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000465134) /// 0007165 // signal transduction (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000465134) /// 0046854 // phosphatidylinositol phosphorylation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR020552 InterPro:IPR000760 InterPro:IPR020550)</p>
Spr2f	- 8.6942 90298	2.600 83E- 28	MGI:13 30349	<p>0008544 // epidermis development (MGI:MGI:3687436 PMID:8325635 [NAS]) /// 0030216 // keratinocyte differentiation (MGI:MGI:3687436 PMID:8325635 [NAS]) /// 0031424 // keratinization (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0417) /// 0030216 // keratinocyte differentiation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001908662) /// 0032355 // response to estradiol stimulus (MGI:MGI:3690150 PMID:15232223 [IDA]) /// 0018149 // peptide cross-linking (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001908662)</p>
P2ry2	- 8.6410 78209	4.347 64E- 39	MGI:10 5107	<p>0030279 // negative regulation of ossification (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:62088) /// 0060406 // positive regulation of penile erection (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:62088) /// 0070257 // positive regulation of mucus secretion (MGI:MGI:3833522 PMID:17728398 [IMP] MGI:MGI:3613160) /// 0007204 // elevation of cytosolic calcium ion concentration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:62088) /// 0032722 // positive regulation of chemokine production (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:62088) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000276) /// 0019233 // sensory perception of pain (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:62088) /// 0007200 // phospholipase C-activating G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000356) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297) /// 0042312 // regulation of vasodilation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:62088) /// 0014911 // positive regulation of smooth muscle cell migration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:62088) /// 0032308 // positive regulation of prostaglandin secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:62088) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0010976 // positive regulation of neuron projection development (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:62088)</p>
Il12a	- 8.6310 777	3.096 75E- 18	MGI:96 539	<p>0048662 // negative regulation of smooth muscle cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) /// 0042520 // positive regulation of tyrosine phosphorylation of Stat4 protein (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) /// 0045582 // positive regulation of T cell differentiation (MGI:MGI:5461742 PMID:22968459 [IGI] MGI:MGI:1916927) /// 0032729 // positive regulation of interferon-gamma production (MGI:MGI:3653161 PMID:9348310 [IGI] MGI:MGI:96540) /// 0032729 // positive regulation of interferon-gamma production (MGI:MGI:5013687 PMID:21444916 [IDA]) /// 0034393 // positive regulation of smooth muscle cell apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) /// 0001916 // positive regulation of T cell mediated cytotoxicity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) /// 0032729 // positive regulation of interferon-gamma production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) /// 0042832 // defense response to protozoan (MGI:MGI:3653161 PMID:9348310 [IGI] MGI:MGI:96540) /// 0051135 // positive regulation of NK T cell activation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) ///</p>

				0042102 // positive regulation of T cell proliferation (MGI:MGI:1926579 PMID:11057672 [IDA]) // 0042832 // defense response to protozoan (MGI:MGI:3828894 PMID:19047410 [IDA]) // 0042832 // defense response to protozoan (MGI:MGI:3820354 PMID:19050265 [IDA]) // 0071222 // cellular response to lipopolysaccharide (MGI:MGI:3828894 PMID:19047410 [IDA]) // 0045785 // positive regulation of cell adhesion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0016477 // cell migration (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0045954 // positive regulation of natural killer cell mediated cytotoxicity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0097191 // extrinsic apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0006955 // immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR004281) // 0032700 // negative regulation of interleukin-17 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 2000510 // positive regulation of dendritic cell chemotaxis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0002860 // positive regulation of natural killer cell mediated cytotoxicity directed against tumor cell target (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0032496 // response to lipopolysaccharide (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0098586 // 0007050 // cell cycle arrest (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0050671 // positive regulation of lymphocyte proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0032946 // positive regulation of mononuclear cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0010224 // response to UV-B (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459) // 0032816 // positive regulation of natural killer cell activation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P29459)
Cd69	- 8.6211 892	8.264 51E- 16	MGI:88 343	
Nfkbiz	- 8.5822 76574	1.015 14E- 23	MGI:19 31595	0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) // 0006954 // inflammatory response (MGI:MGI:1927684 PMID:11086164 [IDA]) // 0006357 // regulation of transcription from RNA polymerase II promoter (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001538048) // 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804)
Slfn2	- 8.5632 74636	3.478 31E- 24	MGI:13 13258	0008285 // negative regulation of cell proliferation (MGI:MGI:1315083 PMID:9846487 [IDA])
Gm14636	- 8.5268 10545	1.322 62E- 32	MGI:36 41976	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Tgif1	- 8.5154 74697	1.500 01E- 35	MGI:11 94497	0048146 // positive regulation of fibroblast proliferation (MGI:MGI:3629366 PMID:16705179 [IMP] MGI:MGI:3652354) // 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:3615867 PMID:16428452 [IGI] MGI:MGI:98214) // 0038092 // nodal signaling pathway (MGI:MGI:4430444 PMID:20040491 [IGI] MGI:MGI:1915299) // 0048387 // negative regulation of retinoic acid receptor signaling pathway (MGI:MGI:3615867 PMID:16428452 [IMP] MGI:MGI:3617788) // 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) // 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR008422) // 0008285 // negative regulation of cell proliferation (MGI:MGI:3697552 PMID:17082251 [IMP] MGI:MGI:3698004) // 0001843 // neural tube closure (MGI:MGI:3697552 PMID:17082251 [IMP] MGI:MGI:3698004) // 0045666 // positive regulation of neuron differentiation (MGI:MGI:3826282 PMID:18973577 [IDA]) // 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) // 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q15583) // 0007368 // determination of left/right symmetry (MGI:MGI:3629366 PMID:16705179 [IMP] MGI:MGI:3652354) // 0010470 // regulation of gastrulation (MGI:MGI:4430444 PMID:20040491 [IGI] MGI:MGI:1915299 MGI:MGI:97359) // 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:2154458 GO_REF:0000008 [ISO] EMBL:AF179900) // 0009953 // dorsal/ventral pattern formation (MGI:MGI:3697552 PMID:17082251 [IMP] MGI:MGI:3698004) // 0060041 // retina development in camera-type eye (MGI:MGI:3826282 PMID:18973577 [IDA]) // 0010629 // negative regulation of gene expression (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1310517)
Nfkbia	- 8.4741 47998	7.322 59E- 21	MGI:10 4741	0032496 // response to lipopolysaccharide (MGI:MGI:2670551 PMID:12872135 [IDA]) // 0034142 // toll-like receptor 4 signaling pathway (MGI:MGI:3775161 PMID:18261938 [IDA]) // 0031663 // lipopolysaccharide-mediated signaling pathway (MGI:MGI:3775161 PMID:18261938 [IDA]) // 0032495 // response to muramyl dipeptide (MGI:MGI:3528786 PMID:15692051 [IDA]) // 0045746 // negative regulation of Notch

				<p>signaling pathway (MGI:MGI:3576806 PMID:15845452 [IMP] MGI:MGI:3577709,MGI:MGI:2176180) /// 0010468 // regulation of gene expression (MGI:MGI:5139961 PMID:21737317 [IMP]) /// 0007253 // cytoplasmic sequestering of NF-kappaB (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3171) /// 0042994 // cytoplasmic sequestering of transcription factor (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P25963) /// 0071345 // cellular response to cytokine stimulus (MGI:MGI:3850788 PMID:19414010 [ISO] UniProtKB:Q63746) /// 0035994 // response to muscle stretch (MGI:MGI:4822295 PMID:20442316 [IDA]) /// 0010745 // negative regulation of macrophage derived foam cell differentiation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P25963) /// 0032270 // positive regulation of cellular protein metabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P25963) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:3805145 PMID:18505784 [IMP]) /// 0031663 // lipopolysaccharide-mediated signaling pathway (MGI:MGI:2670551 PMID:12872135 [IDA]) /// 0070427 // nucleotide-binding oligomerization domain containing 1 signaling pathway (MGI:MGI:3775161 PMID:18261938 [IDA]) /// 0071407 // cellular response to organic cyclic compound (MGI:MGI:3850788 PMID:19414010 [ISO] UniProtKB:Q63746) /// 0010888 // negative regulation of lipid storage (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P25963) /// 0043330 // response to exogenous dsRNA (MGI:MGI:2670551 PMID:12872135 [IDA]) /// 0000060 // protein import into nucleus, translocation (MGI:MGI:2176657 PMID:11799106 [IDA]) /// 0070431 // nucleotide-binding oligomerization domain containing 2 signaling pathway (MGI:MGI:3775161 PMID:18261938 [IDA]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P25963) /// 0032088 // negative regulation of NF-kappaB transcription factor activity (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:P25963) /// 0045638 // negative regulation of myeloid cell differentiation (MGI:MGI:3576806 PMID:15845452 [IMP] MGI:MGI:3577709,MGI:MGI:2176180) /// 0007253 // cytoplasmic sequestering of NF-kappaB (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P25963) /// 0042127 // regulation of cell proliferation (MGI:MGI:2176657 PMID:11799106 [IDA]) /// 0010875 // positive regulation of cholesterol efflux (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P25963) /// 0071216 // cellular response to biotic stimulus (MGI:MGI:5500156 PMID:23262141 [IDA])</p>
Npepps	- 8.4740 07886	9.444 81E- 48	MGI:11 01358	<p>0071456 // cellular response to hypoxia (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P55786) /// 0043171 // peptide catabolic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000164249) /// 1903955 /// 0006508 // proteolysis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000164249)</p>
Qsox1	- 8.4636 70168	3.778 36E- 38	MGI:13 30818	<p>0016242 // negative regulation of macroautophagy (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O00391) /// 0045454 // cell redox homeostasis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR013766) /// 0006457 // protein folding (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000528008) /// 0006457 // protein folding (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O00391) /// 0055114 // oxidation-reduction process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR017905) /// 0055114 // oxidation-reduction process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0560)</p>
Irg1	- 8.4256 67203	2.224 35E- 17		
Mocos	- 8.3756 42858	5.083 33E- 40	MGI:19 15841	<p>0043545 // molybdopterin cofactor metabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96EN8) /// 0006777 // Mo-molybdopterin cofactor biosynthetic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028886) /// 0006777 // Mo-molybdopterin cofactor biosynthetic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0501)</p>
Fnd3c2	- 8.3745 35351	6.834 11E- 07	MGI:26 85621	<p>0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])</p>
Mreg	- 8.3598 54961	6.336 29E- 35	MGI:21 51839	<p>0030318 // melanocyte differentiation (MGI:MGI:77000 PMID:2379821 [IMP] MGI:MGI:1856847) /// 0030318 // melanocyte differentiation (MGI:MGI:68866 PMID:7828830 [IMP] MGI:MGI:1856847) /// 0042640 // anagen (MGI:MGI:3513741 PMID:15550542 [IMP] MGI:MGI:1856847) /// 0043473 // pigmentation (MGI:MGI:77000 PMID:2379821 [IMP] MGI:MGI:1856847) /// 0043473 // pigmentation (MGI:MGI:68399 PMID:3141922 [IMP] MGI:MGI:1856847) /// 0043473 // pigmentation (MGI:MGI:68866 PMID:7828830 [IMP] MGI:MGI:1856847) /// 0048066 // developmental pigmentation (MGI:MGI:3513741 PMID:15550542 [IMP] MGI:MGI:1856847) /// 0032402 // melanosome transport (MGI:MGI:5492030 PMID:22275436 [IDA])</p>
Rel	- 8.3592	9.490 32E-	MGI:97 897	<p>0006366 // transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q04864) /// 0045087 // innate immune response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216)</p>

	34293	35		<p>/// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0001816 // cytokine production (MGI:MGI:3050756 PMID:15220916 [IMP]) /// 0038061 // NIK/NF-kappaB cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0007249 // I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1311231) /// 0007249 // I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0034097 // response to cytokine stimulus (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000451 InterPro:IPR008967 InterPro:IPR011539) /// 0033554 // cellular response to stress (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0006954 // inflammatory response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 1901215 // negative regulation of neuron death (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1311231) /// 0045084 // positive regulation of interleukin-12 biosynthetic process (MGI:MGI:2679145 PMID:14568984 [IMP]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0010629 // negative regulation of gene expression (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q04864) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q04864) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:2679145 PMID:14568984 [IDA]) /// 0032688 // negative regulation of interferon-beta production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q04864)</p>
Padi4	- 8.3424 85396	1.234 75E- 21	MGI:13 38898	<p>0018101 // peptidyl-citrulline biosynthetic process from peptidyl-arginine (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UM07) /// 0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0006338 // chromatin remodeling (MGI:MGI:5545819 PMID:24463520 [IMP]) /// 0018101 // peptidyl-citrulline biosynthetic process from peptidyl-arginine (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3290) /// 0019827 // stem cell maintenance (MGI:MGI:5545819 PMID:24463520 [IMP]) /// 0036413 // 0016568 // chromatin modification (MGI:MGI:5545819 PMID:24463520 [IMP]) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0006334 // nucleosome assembly (MGI:MGI:5545819 PMID:24463520 [IMP]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0036414</p>
Hc	- 8.3317 08742	2.222 77E- 13	MGI:96 031	<p>0001701 // in utero embryonic development (MGI:MGI:3833206 PMID:18947875 [IGI] MGI:MGI:88513) /// 0090197 // positive regulation of chemokine secretion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01031) /// 0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) /// 0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0010575 // positive regulation vascular endothelial growth factor production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01031) /// 0019835 // cytolysis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0204) /// 0045766 // positive regulation of angiogenesis (MGI:MGI:3617287 PMID:16452172 [IMP]) /// 0006958 // complement activation, classical pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0180) /// 0006957 // complement activation, alternative pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0179) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0098779 /// 0010760 // negative regulation of macrophage chemotaxis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P01031)</p>
Tnfrsf23	- 8.3234 89075	2.173 11E- 35	MGI:19 30269	1902042
Trim72	- 8.3204 78438	7.687 63E- 12	MGI:36 12190	<p>0006887 // exocytosis (MGI:MGI:3839715 PMID:19029292 [TAS]) /// 0043569 // negative regulation of insulin-like growth factor receptor signaling pathway (MGI:MGI:5602876 PMID:23965929 [IGI] MGI:MGI:96432) /// 0043161 // proteasomal ubiquitin-dependent protein catabolic process (MGI:MGI:5602876 PMID:23965929 [IMP]) /// 0046627 // negative regulation of insulin receptor signaling pathway (MGI:MGI:5602876 PMID:23965929 [IDA]) /// 0001778 // plasma membrane repair (MGI:MGI:3839036 PMID:19043407 [IMP]) /// 0016567 // protein ubiquitination (MGI:MGI:5602876 PMID:23965929 [IMP]) /// 0003012 // muscle system process (MGI:MGI:3839036 PMID:19043407 [IMP]) /// 0010832 // negative regulation of myotube differentiation (MGI:MGI:5602876 PMID:23965929 [IDA]) /// 0051260 // protein homooligomerization (MGI:MGI:3839036 PMID:19043407 [IPI] UniProtKB:Q1XH17) /// 0006900 // membrane budding (MGI:MGI:3839715 PMID:19029292 [TAS]) /// 0007517 // muscle organ development (MGI:MGI:3839036 PMID:19043407 [IMP]) /// 0001778 // plasma</p>

				membrane repair (MGI:MGI:3851308 PMID:19380584 [IMP]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Best1	- 8.2666 48804	8.093 18E- 21	MGI:13 46332	0006811 // ion transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0406) /// 0051924 // regulation of calcium ion transport (MGI:MGI:3795256 PMID:16636205 [IMP] MGI:MGI:3795281) /// 0030321 // transepithelial chloride transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O76090) /// 1902476 /// 0006821 // chloride transport (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:O76090) /// 0007601 // visual perception (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR033041) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0050908 // detection of light stimulus involved in visual perception (MGI:MGI:3795256 PMID:16636205 [IMP] MGI:MGI:3795281)
S100a9	- 8.2278 66144	2.154 13E- 17	MGI:13 38947	0006954 // inflammatory response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0395) /// 0006919 // activation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P06702) /// 0006935 // chemotaxis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0145) /// 0018119 // peptidyl-cysteine S-nitrosylation (MGI:MGI:5621255 PMID:25417112 [IMP]) /// 0031532 // actin cytoskeleton reorganization (MGI:MGI:2449751 PMID:12529407 [IMP] MGI:MGI:2450165) /// 2001244 // positive regulation of intrinsic apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P06702) /// 0070488 // neutrophil aggregation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P06702) /// 0030194 // positive regulation of blood coagulation (MGI:MGI:5582990 PMID:24691441 [IMP]) /// 0006417 // regulation of translation (MGI:MGI:5621255 PMID:25417112 [IMP]) /// 0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0050727 // regulation of inflammatory response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028475) /// 0030593 // neutrophil chemotaxis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P06702) /// 0002523 // leukocyte migration involved in inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P06702) /// 0002793 // positive regulation of peptide secretion (MGI:MGI:3835701 PMID:18820689 [IDA]) /// 0045087 // innate immune response (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR028475) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0030595 // leukocyte chemotaxis (MGI:MGI:2449751 PMID:12529407 [IMP] MGI:MGI:2450165) /// 0045113 // regulation of integrin biosynthetic process (MGI:MGI:2449751 PMID:12529407 [IMP] MGI:MGI:2450165) /// 0050729 // positive regulation of inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P06702) /// 0002793 // positive regulation of peptide secretion (MGI:MGI:3835701 PMID:18820689 [IMP]) /// 0006914 // autophagy (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P06702) /// 0014002 // astrocyte development (MGI:MGI:5440388 PMID:22577135 [IGI] MGI:MGI:88244) /// 0035606 // peptidyl-cysteine S-trans-nitrosylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P06702)
Ceacam16	- 8.2225 87505	1.356 6E- 08	MGI:26 85615	0007605 // sensory perception of sound (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:Q2WEN9)
Smox	- 8.2101 39995	2.690 73E- 24	MGI:24 45356	0046208 // spermine catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NWM0) /// 0006598 // polyamine catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NWM0) /// 0046208 // spermine catabolic process (MGI:MGI:2429361 PMID:12141946 [IDA]) /// 0055114 // oxidation-reduction process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9NWM0) /// 0046208 // spermine catabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1306049)
Tnfrsf1b	- 8.0925 57984	7.472 83E- 29	MGI:13 14883	0050728 // negative regulation of inflammatory response (MGI:MGI:2152007 PMID:11588035 [IMP] MGI:MGI:1857262) /// 0006954 // inflammatory response (MGI:MGI:1194456 PMID:9551933 [IMP] MGI:MGI:1860087) /// 0008630 // intrinsic apoptotic signaling pathway in response to DNA damage (MGI:MGI:3709926 PMID:17242187 [IMP]) /// 0043410 // positive regulation of MAPK cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001499622) /// 0050779 // RNA destabilization (MGI:MGI:2152007 PMID:11588035 [IMP] MGI:MGI:1857262) /// 0032496 // response to lipopolysaccharide (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000753849) /// 0042981 // regulation of apoptotic process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000753849) /// 0097191 // extrinsic apoptotic signaling pathway (MGI:MGI:69721 PMID:7990930 [IMP] MGI:MGI:1857262) /// 0007275 // multicellular organismal development (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000753849) /// 0007166 // cell surface receptor signaling pathway (MGI:MGI:1194456 PMID:9551933 [IMP] MGI:MGI:1860087) /// 0006955 // immune response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000753849) /// 0008283 // cell proliferation (MGI:MGI:69721 PMID:7990930 [TAS]) /// 0042127 // regulation of cell proliferation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000753849) /// 0006955 //

				immune response (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:621238) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P20333) /// 0051044 // positive regulation of membrane protein ectodomain proteolysis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P20333)
TxInb	- 8.0861 52455	1.721 86E- 12	MGI:26 71945	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
BC02877 7	- 8.0757 81853	5.986 5E- 06		
Sp140	- 8.0666 45252	7.537 12E- 18	MGI:37 02467	
Mefv	- 8.0591 81536	8.478 99E- 22	MGI:18 59396	2001056 // positive regulation of cysteine-type endopeptidase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15553) /// 0045087 // innate immune response (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0399) /// 0010508 // positive regulation of autophagy (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15553) /// 0032691 // negative regulation of interleukin-1 beta production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15553) /// 1900226 // negative regulation of NLRP3 inflammasome complex assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15553) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15553) /// 1900016 // negative regulation of cytokine production involved in inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15553) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0071641 // negative regulation of macrophage inflammatory protein 1 alpha production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15553) /// 0034341 // response to interferon-gamma (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15553) /// 0006954 // inflammatory response (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15553) /// 0032695 // negative regulation of interleukin-12 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15553)
Adora2b	- 8.0581 83948	8.416 69E- 33	MGI:99 403	0045765 // regulation of angiogenesis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2050) /// 0007189 // adenylate cyclase-activating G-protein coupled receptor signaling pathway (MGI:MGI:3664521 PMID:16841096 [IMP]) /// 0007189 // adenylate cyclase-activating G-protein coupled receptor signaling pathway (MGI:MGI:3794903 PMID:18340377 [IMP] MGI:MGI:3773754) /// 0045909 // positive regulation of vasodilation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2050) /// 0031284 // positive regulation of guanylate cyclase activity (MGI:MGI:3794903 PMID:18340377 [IMP] MGI:MGI:3773754) /// 0032966 // negative regulation of collagen biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2050) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001435 InterPro:IPR000276) /// 0030819 // positive regulation of cAMP biosynthetic process (MGI:MGI:3794903 PMID:18340377 [IMP] MGI:MGI:3773754) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2050) /// 0010893 // positive regulation of steroid biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2050) /// 0033605 // positive regulation of catecholamine secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2050) /// 0008285 // negative regulation of cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2050) /// 0032755 // positive regulation of interleukin-6 production (MGI:MGI:3806198 PMID:18559975 [IMP] MGI:MGI:3773754) /// 0032722 // positive regulation of chemokine production (MGI:MGI:3806198 PMID:18559975 [IMP] MGI:MGI:3773754) /// 0001973 // adenosine receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001634) /// 0043306 // positive regulation of mast cell degranulation (MGI:MGI:3776334 PMID:11454903 [IMP]) /// 0060087 // relaxation of vascular smooth muscle (MGI:MGI:3794903 PMID:18340377 [IMP] MGI:MGI:3773754) /// 0002882 // positive regulation of chronic inflammatory response to non-antigenic stimulus (MGI:MGI:3664521 PMID:16841096 [IMP]) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297) /// 0010701 // positive regulation of norepinephrine secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2050) /// 0030819 // positive regulation of cAMP biosynthetic process (MGI:MGI:3664521 PMID:16841096 [IMP]) /// 0031668 // cellular response to extracellular stimulus (MGI:MGI:65736 PMID:8157966 [IDA]) /// 0030828 // positive regulation of cGMP biosynthetic process (MGI:MGI:3794903 PMID:18340377 [IMP] MGI:MGI:3773754) /// 0030819 // positive regulation of cAMP biosynthetic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:2050) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0010575 // positive regulation vascular endothelial growth factor production (MGI:MGI:3806198 PMID:18559975 [IMP] MGI:MGI:3773754)

2810474 O19Rik	- 8.0435 64485	2.805 94E- 32	MGI:19 14496	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Zfp36	- 8.0227 06179	3.381 E-21	MGI:99 180	0000288 // nuclear-transcribed mRNA catabolic process, deadenylation-dependent decay (MGI:MGI:3589099 PMID:15814898 [IDA]) /// 0000288 // nuclear-transcribed mRNA catabolic process, deadenylation-dependent decay (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P26651) /// 0006402 // mRNA catabolic process (MGI:MGI:2176348 PMID:11782475 [ISO] UniProtKB:P26651) /// 0006402 // mRNA catabolic process (MGI:MGI:1859531 PMID:10751406 [ISO] UniProtKB:P26651) /// 0032680 // regulation of tumor necrosis factor production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P26651) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:2152007 PMID:11588035 [IMP] MGI:MGI:2652418) /// 1900153 // positive regulation of nuclear-transcribed mRNA catabolic process, deadenylation-dependent decay (MGI:MGI:5487524 PMID:21278420 [IDA]) /// 0042594 // response to starvation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P26651) /// 0043488 // regulation of mRNA stability (MGI:MGI:3511379 PMID:15467755 [IDA]) /// 0070935 // 3'-UTR-mediated mRNA stabilization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P26651) /// 0006402 // mRNA catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P26651) /// 0045638 // negative regulation of myeloid cell differentiation (MGI:MGI:2152007 PMID:11588035 [IMP] MGI:MGI:2652418) /// 0035278 // negative regulation of translation involved in gene silencing by miRNA (MGI:MGI:5487524 PMID:21278420 [IDA]) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:5301204 PMID:21784977 [IMP]) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:81466 PMID:8630730 [IMP] MGI:MGI:2652418) /// 0060213 // positive regulation of nuclear-transcribed mRNA poly(A) tail shortening (MGI:MGI:5487524 PMID:21278420 [IDA]) /// 0000289 // nuclear-transcribed mRNA poly(A) tail shortening (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P26651) /// 0050779 // RNA destabilization (MGI:MGI:2152007 PMID:11588035 [IMP] MGI:MGI:2652418) /// 0000289 // nuclear-transcribed mRNA poly(A) tail shortening (MGI:MGI:3589099 PMID:15814898 [IDA]) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P26651) /// 0060213 // positive regulation of nuclear-transcribed mRNA poly(A) tail shortening (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P26651) /// 0035556 // intracellular signal transduction (MGI:MGI:73465 PMID:7768935 [IDA]) /// 0006357 // regulation of transcription from RNA polymerase II promoter (MGI:MGI:4457825 PMID:20410487 [IGI] MGI:MGI:3783378) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:5301204 PMID:21784977 [IMP])
Sgms2	- 8.0129 34255	1.587 45E- 23	MGI:19 21692	0006665 // sphingolipid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0746) /// 0006686 // sphingomyelin biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q8NHU3) /// 0006629 // lipid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0443) /// 0006686 // sphingomyelin biosynthetic process (MGI:MGI:3613454 PMID:14685263 [ISS] UniProtKB:Q8NHU3) /// 0016310 // phosphorylation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0418)
Pnrc1	- 8.0119 41285	4.777 04E- 29	MGI:19 17838	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Slc25a18	- 8.0052 59188	1.048 69E- 15	MGI:19 19053	0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002067) /// 0006412 // translation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000211803) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Cdc42ep 2	- 7.9701 4777	8.879 78E- 22	MGI:19 29744	0008360 // regulation of cell shape (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14613) /// 0030036 // actin cytoskeleton organization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14613) /// 0008360 // regulation of cell shape (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001034302) /// 0031274 // positive regulation of pseudopodium assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14613) /// 0043547 // positive regulation of GTPase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14613) /// 0007266 // Rho protein signal transduction (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001034302) /// 0030838 // positive regulation of actin filament polymerization (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001034302) /// 0030838 // positive regulation of actin filament polymerization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14613) /// 0031274 // positive regulation of pseudopodium assembly (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001034302)
Mmp8	- 7.9329	1.996 93E-	MGI:12	0030574 // collagen catabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0177) /// 0006508 // proteolysis (MGI:MGI:4834177 GO_REF:0000096

	27609	13	02395	[ISO] UniProtKB:P22894) /// 0006508 // proteolysis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:631408)
Gadd45b	- 7.9306 32318	2.540 41E- 18	MGI:10 7776	0006950 // response to stress (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR024824) /// 0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 1900745 // positive regulation of p38MAPK cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O75293) /// 0000185 // activation of MAPKKK activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O75293) /// 0000186 // activation of MAPKK activity (MGI:MGI:2387532 PMID:12213961 [IDA]) /// 0006469 // negative regulation of protein kinase activity (MGI:MGI:2384369 PMID:12124778 [IDA]) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O75293) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0046330 // positive regulation of JNK cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O75293) /// 0030154 // cell differentiation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0221) /// 0051726 // regulation of cell cycle (MGI:MGI:2384369 PMID:12124778 [IDA])
Apbb1ip	- 7.9075 26322	6.517 22E- 34	MGI:18 61354	0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000159) /// 0002291 // T cell activation via T cell receptor contact with antigen bound to MHC molecule on antigen presenting cell (MGI:MGI:3714085 PMID:17403904 [IDA]) /// 0045785 // positive regulation of cell adhesion (MGI:MGI:3714085 PMID:17403904 [IDA])
Batf	- 7.8983 43893	2.669 7E- 16	MGI:18 59147	0072539 // T-helper 17 cell differentiation (MGI:MGI:4456325 PMID:20421391 [IMP]) /// 0001816 // cytokine production (MGI:MGI:3851267 PMID:19578362 [IMP]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:5448096 PMID:22983707 [IMP]) /// 0030154 // cell differentiation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR029820) /// 0030330 // DNA damage response, signal transduction by p53 class mediator (MGI:MGI:5448499 PMID:22385964 [IMP]) /// 0045064 // T-helper 2 cell differentiation (MGI:MGI:4456325 PMID:20421391 [IMP]) /// 0060218 // hematopoietic stem cell differentiation (MGI:MGI:5448499 PMID:22385964 [IMP]) /// 0045190 // isotype switching (MGI:MGI:5004732 PMID:21572431 [IMP]) /// 0006974 // response to DNA damage stimulus (MGI:MGI:5448499 PMID:22385964 [IMP]) /// 0006357 // regulation of transcription from RNA polymerase II promoter (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000837 InterPro:IPR029820) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0045064 // T-helper 2 cell differentiation (MGI:MGI:5004732 PMID:21572431 [IMP]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR004827) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0045190 // isotype switching (MGI:MGI:4456325 PMID:20421391 [IMP]) /// 0072539 // T-helper 17 cell differentiation (MGI:MGI:5004732 PMID:21572431 [IMP]) /// 0042832 // defense response to protozoan (MGI:MGI:5441724 PMID:22992524 [IMP]) /// 0002320 // lymphoid progenitor cell differentiation (MGI:MGI:5448499 PMID:22385964 [IMP]) /// 0043011 // myeloid dendritic cell differentiation (MGI:MGI:5441724 PMID:22992524 [IMP]) /// 0072540 // T-helper 17 cell lineage commitment (MGI:MGI:3851267 PMID:19578362 [IMP]) /// 0030154 // cell differentiation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0221) /// 0072540 // T-helper 17 cell lineage commitment (MGI:MGI:5448096 PMID:22983707 [IMP])
Mfsd7a	- 7.8904 62597	2.494 33E- 18	MGI:24 42629	0055085 // transmembrane transport (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR011701) /// 0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813)
Wee2	- 7.8870 0755	1.444 25E- 06	MGI:30 27899	0006468 // protein phosphorylation (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000719 InterPro:IPR008271) /// 0007143 // female meiosis (MGI:MGI:3604224 PMID:16169490 [IMP]) /// 1900194 // negative regulation of oocyte maturation (MGI:MGI:4948986 PMID:21454751 [IMP]) /// 0007067 // mitosis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR017164) /// 0035038 // female pronucleus assembly (MGI:MGI:4948986 PMID:21454751 [IMP]) /// 0051321 // meiotic cell cycle (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0469) /// 0045736 // negative regulation of cyclin-dependent protein serine/threonine kinase activity (MGI:MGI:4948986 PMID:21454751 [IMP]) /// 0060631 // regulation of meiosis I (MGI:MGI:3604224 PMID:16169490 [IMP]) /// 1900194 // negative regulation of oocyte maturation (MGI:MGI:3604224 PMID:16169490 [IMP]) /// 0016310 // phosphorylation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0418)
Gpr141	- 7.8847 07192	4.571 02E- 39	MGI:26 72983	0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000276) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND]) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA])

				UniProtKB-KW:KW-0297)
Chka	- 7.8826 21987	2.637 02E- 55	MGI:10 7760	0006646 // phosphatidylethanolamine biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35790) /// 0006656 // phosphatidylcholine biosynthetic process (MGI:MGI:3623691 PMID:16371353 [IDA]) /// 0008654 // phospholipid biosynthetic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0594) /// 0006629 // lipid metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0443) /// 0006580 // ethanolamine metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61944) /// 0006656 // phosphatidylcholine biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P35790) /// 0016310 // phosphorylation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0418) /// 0019695 // choline metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61944)
Spata13	- 7.8703 81331	5.580 69E- 25	MGI:10 4838	0030032 // lamellipodium assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96N96) /// 0035556 // intracellular signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001331) /// 0046847 // filopodium assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96N96) /// 0043547 // positive regulation of GTPase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96N96) /// 0016477 // cell migration (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96N96) /// 0035023 // regulation of Rho protein signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000219) /// 0030334 // regulation of cell migration (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96N96)
Crtc2	- 7.8660 93591	5.264 43E- 28	MGI:19 21593	0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:5529403 PMID:24051374 [IGI] MGI:MGI:1343094 MGI:MGI:2155884 MGI:MGI:1343101) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:5572980 PMID:24674967 [IDA]) /// 0043970 // histone H3-K9 acetylation (MGI:MGI:5529403 PMID:24051374 [IGI] MGI:MGI:1343094) /// 0006094 // gluconeogenesis (MGI:MGI:3606826 PMID:16148943 [IDA]) /// 0032793 // positive regulation of CREB transcription factor activity (MGI:MGI:3606826 PMID:16148943 [IDA]) /// 0042593 // glucose homeostasis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1308903) /// 0042593 // glucose homeostasis (MGI:MGI:3611510 PMID:16308421 [IMP]) /// 0051289 // protein homotetramerization (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR024783) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 1901998 // toxin transport (MGI:MGI:5492256 PMID:23716698 [IMP])
AI839979	- 7.8576 60546	2.078 92E- 23		
Rac2	- 7.8495 7426	1.308 25E- 28	MGI:97 846	0010592 // positive regulation of lamellipodium assembly (MGI:MGI:4355276 PMID:19625648 [IMP]) /// 0060263 // regulation of respiratory burst (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P15153) /// 0071593 // lymphocyte aggregation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P15153) /// 0090023 // positive regulation of neutrophil chemotaxis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P15153) /// 0006935 // chemotaxis (MGI:MGI:2386148 PMID:12176888 [IDA]) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:2149663 PMID:11435472 [IGI] MGI:MGI:97306) /// 0007264 // small GTPase mediated signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001806 InterPro:IPR003578) /// 0010810 // regulation of cell-substrate adhesion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P15153) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:4939305 PMID:21178006 [IGI] MGI:MGI:98923 MGI:MGI:3040696) /// 0007015 // actin filament organization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P15153) /// 0008284 // positive regulation of cell proliferation (MGI:MGI:2149663 PMID:11435472 [IMP] MGI:MGI:1857701) /// 0045453 // bone resorption (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1307568) /// 0030036 // actin cytoskeleton organization (MGI:MGI:2386148 PMID:12176888 [IDA]) /// 0060753 // regulation of mast cell chemotaxis (MGI:MGI:3655336 PMID:10843388 [IMP]) /// 0090023 // positive regulation of neutrophil chemotaxis (MGI:MGI:4355276 PMID:19625648 [IMP]) /// 0042129 // regulation of T cell proliferation (MGI:MGI:3702218 PMID:11581314 [IMP]) /// 0030036 // actin cytoskeleton organization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:1307568) /// 1903955 /// 0043304 // regulation of mast cell degranulation (MGI:MGI:3655336 PMID:10843388 [IMP]) /// 1902622 /// 0010592 // positive regulation of lamellipodium assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P15153) /// 0030031 // cell projection assembly (MGI:MGI:2386148 PMID:12176888 [IDA])
Gm27167	- 7.8141 65442	2.682 67E- 05		

Lrrfip2	- 7.7945 59864	9.202 8E- 29	MGI:19 18518	0002756 // MyD88-independent toll-like receptor signaling pathway (MGI:MGI:3836337 PMID:19265123 [IDA]) // 0016055 // Wnt receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0879) // 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:3836337 PMID:19265123 [IGI] MGI:MGI:96824) // 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:3836337 PMID:19265123 [IDA]) // 1904469 // 0035660 // MyD88-dependent toll-like receptor 4 signaling pathway (MGI:MGI:3836337 PMID:19265123 [IDA]) // 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:3836337 PMID:19265123 [IMP]) // 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:3836337 PMID:19265123 [IGI] MGI:MGI:108005)
Lin28a	- 7.7743 1178	9.514 23E- 13	MGI:18 90546	0010586 // miRNA metabolic process (MGI:MGI:4441085 PMID:20179095 [IDA]) // 1901724 // positive regulation of cell proliferation involved in kidney development (MGI:MGI:5574232 PMID:24732380 [IMP]) // 0019827 // stem cell maintenance (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H9Z2) // 0031123 // RNA 3'-end processing (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H9Z2) // 0048863 // stem cell differentiation (MGI:MGI:4359358 PMID:18604195 [IMP]) // 0031054 // pre-miRNA processing (MGI:MGI:4359358 PMID:18604195 [IDA]) // 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR002059) // 0048863 // stem cell differentiation (MGI:MGI:4359360 PMID:18292307 [IMP]) // 0045666 // positive regulation of neuron differentiation (MGI:MGI:4441085 PMID:20179095 [IDA]) // 0045727 // positive regulation of translation (MGI:MGI:3709663 PMID:17473174 [IDA]) // 0007281 // germ cell development (MGI:MGI:4354491 PMID:19578360 [IMP]) // 0031047 // gene silencing by RNA (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0943) // 0007281 // germ cell development (MGI:MGI:4354491 PMID:19578360 [IGI] MGI:MGI:99655) // 0060964 // regulation of gene silencing by miRNA (MGI:MGI:4438512 PMID:19898466 [IGI] MGI:MGI:2685973) // 0031054 // pre-miRNA processing (MGI:MGI:4359360 PMID:18292307 [IMP]) // 0045686 // negative regulation of glial cell differentiation (MGI:MGI:4441085 PMID:20179095 [IDA]) // 0010587 // miRNA catabolic process (MGI:MGI:4359358 PMID:18604195 [IMP]) // 0010587 // miRNA catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H9Z2) // 0031054 // pre-miRNA processing (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H9Z2) // 0010587 // miRNA catabolic process (MGI:MGI:4359360 PMID:18292307 [IMP]) // 0031054 // pre-miRNA processing (MGI:MGI:4359358 PMID:18604195 [IMP])
Epgn	- 7.7679 25877	3.902 66E- 12	MGI:19 19170	0045741 // positive regulation of epidermal growth factor-activated receptor activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6UW88) // 0008284 // positive regulation of cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6UW88) // 0045840 // positive regulation of mitosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6UW88) // 0050679 // positive regulation of epithelial cell proliferation (MGI:MGI:1934957 PMID:11278323 [IDA]) // 0045741 // positive regulation of epidermal growth factor-activated receptor activity (MGI:MGI:1934957 PMID:11278323 [IDA]) // 0045840 // positive regulation of mitosis (MGI:MGI:1934957 PMID:11278323 [IDA]) // 0000165 // MAPK cascade (MGI:MGI:1934957 PMID:11278323 [IDA]) // 0001525 // angiogenesis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6UW88) // 0043406 // positive regulation of MAP kinase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q6UW88) // 0000187 // activation of MAPK activity (MGI:MGI:1934957 PMID:11278323 [IDA])
1110002J 07Rik	- 7.7663 87936	3.971 61E- 09	MGI:19 15738	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Olfir433	- 7.7622 631	1.398 72E- 05	MGI:30 30267	0050907 // detection of chemical stimulus involved in sensory perception (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001239295) // 0007608 // sensory perception of smell (MGI:MGI:3029684 PMID:14611657 [ISA] RefSeq:NP_039229) // 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:3029684 PMID:14611657 [ISA] RefSeq:NP_039229) // 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001239295)
Egln3	- 7.7432 47821	8.369 42E- 26	MGI:19 32288	0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) // 0018126 // protein hydroxylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H6Z9) // 0018401 // peptidyl-proline hydroxylation to 4-hydroxy-L-proline (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9H6Z9) // 0001666 // response to hypoxia (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:71019) // 0042127 // regulation of cell proliferation (MGI:MGI:3794960 PMID:18332118 [IMP]) // 0043523 // regulation of neuron apoptotic process (MGI:MGI:3794960 PMID:18332118 [IMP]) // 0019511 // peptidyl-proline hydroxylation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:71019) // 0042127 // regulation of cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:71019) // 0006974 // response to DNA damage stimulus (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0227) // 0055114 // oxidation-reduction process (MGI:MGI:1354194 GO_REF:0000004 [IEA])

				UniProtKB-KW:KW-0560) /// 0055114 // oxidation-reduction process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005123 InterPro:IPR006620)
AstI	- 7.7417 045	5.732 76E- 06	MGI:30 46414	0006508 // proteolysis (MGI:MGI:3046020 PMID:15087446 [ISA] UniProtKB:Q6HA08)
Cflar	- 7.7155 42149	3.519 55E- 32	MGI:13 36166	0007519 // skeletal muscle tissue development (MGI:MGI:5707584 PMID:21364645 [IMP]) /// 0060546 // negative regulation of necroptosis (MGI:MGI:5486419 PMID:22675671 [IGI] MGI:MGI:2154952) /// 0043085 // positive regulation of catalytic activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15519) /// 0014866 // skeletal myofibril assembly (MGI:MGI:5707584 PMID:21364645 [IMP]) /// 0097194 // execution phase of apoptosis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000825206) /// 0043154 // negative regulation of cysteine-type endopeptidase activity involved in apoptotic process (MGI:MGI:3612311 PMID:16263940 [IMP]) /// 0060546 // negative regulation of necroptosis (MGI:MGI:5521568 PMID:22089168 [IGI] MGI:MGI:104798) /// 0014842 // regulation of satellite cell proliferation (MGI:MGI:5707584 PMID:21364645 [IMP]) /// 2001237 // negative regulation of extrinsic apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15519) /// 0014732 // skeletal muscle atrophy (MGI:MGI:5707584 PMID:21364645 [IMP]) /// 0051092 // positive regulation of NF-kappaB transcription factor activity (MGI:MGI:5707584 PMID:21364645 [IMP]) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:3612311 PMID:16263940 [IMP]) /// 1901740 // negative regulation of myoblast fusion (MGI:MGI:5707584 PMID:21364645 [IMP]) /// 1902042 /// 0043403 // skeletal muscle tissue regeneration (MGI:MGI:5707584 PMID:21364645 [IMP]) /// 0006508 // proteolysis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001309) /// 0060546 // negative regulation of necroptosis (MGI:MGI:4947443 PMID:21368763 [IGI] MGI:MGI:2154952 MGI:MGI:1261423 MGI:MGI:104798) /// 2001237 // negative regulation of extrinsic apoptotic signaling pathway (MGI:MGI:5486419 PMID:22675671 [IGI] MGI:MGI:2154952 MGI:MGI:109324) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620847) /// 0060544 // regulation of necroptosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15519) /// 0006915 // apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15519) /// 0042981 // regulation of apoptotic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001875)
Furin	- 7.7074 9514	8.953 01E- 32	MGI:97 513	0016485 // protein processing (MGI:MGI:3526749 PMID:15606899 [ISO] UniProtKB:P09958) /// 0016485 // protein processing (MGI:MGI:4829577 PMID:20530870 [IDA]) /// 0016485 // protein processing (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3274) /// 0009966 // regulation of signal transduction (MGI:MGI:3763867 PMID:17936261 [IDA]) /// 0008283 // cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0032911 // negative regulation of transforming growth factor beta1 production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0032940 // secretion by cell (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0045714 // regulation of low-density lipoprotein particle receptor biosynthetic process (MGI:MGI:4941098 PMID:21147780 [IMP] MGI:MGI:3700008) /// 0030335 // positive regulation of cell migration (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3274) /// 0032902 // nerve growth factor production (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0030511 // positive regulation of transforming growth factor beta receptor signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3274) /// 0016485 // protein processing (MGI:MGI:5527206 PMID:23918928 [IMP] MGI:MGI:3700008) /// 0052548 // regulation of endopeptidase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0006465 // signal peptide processing (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0016485 // protein processing (MGI:MGI:4941098 PMID:21147780 [IMP] MGI:MGI:3700008) /// 0016485 // protein processing (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0032804 // negative regulation of low-density lipoprotein particle receptor catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0010951 // negative regulation of endopeptidase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0043043 // peptide biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0006508 // proteolysis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0645) /// 0006508 // proteolysis (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000209 InterPro:IPR002884) /// 0016486 // peptide hormone processing (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958) /// 0042176 // regulation of protein catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P09958)
Gm17056	- 7.7069 14175	8.685 73E- 31		
Sesn2	- 7.7067	7.629 9E-	MGI:26 51874	0001932 // regulation of protein phosphorylation (MGI:MGI:5444071 PMID:22958918 [IMP] MGI:MGI:3587950) /// 0032868 // response to insulin stimulus (MGI:MGI:5444071 PMID:22958918 [IMP] MGI:MGI:3587950) /// 0090526 // regulation of gluconeogenesis involved in cellular glucose homeostasis (MGI:MGI:5444071 PMID:22958918

	44005	28		<p>[IMP] MGI:MGI:3587950) /// 1901031 // regulation of response to reactive oxygen species (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR006730) /// 2000479 // regulation of cAMP-dependent protein kinase activity (MGI:MGI:5444071 PMID:22958918 [IMP] MGI:MGI:3587950) /// 0070328 // triglyceride homeostasis (MGI:MGI:5444071 PMID:22958918 [IMP] MGI:MGI:3587950) /// 0009749 // response to glucose stimulus (MGI:MGI:5444071 PMID:22958918 [IGI] MGI:MGI:104663 MGI:MGI:1922997) /// 0042593 // glucose homeostasis (MGI:MGI:5444071 PMID:22958918 [IGI] MGI:MGI:104663) /// 0007005 // mitochondrion organization (MGI:MGI:5444071 PMID:22958918 [IMP] MGI:MGI:3587950) /// 0006635 // fatty acid beta-oxidation (MGI:MGI:5444071 PMID:22958918 [IGI] MGI:MGI:104663) /// 0009749 // response to glucose stimulus (MGI:MGI:5444071 PMID:22958918 [IMP] MGI:MGI:3587950) /// 0032868 // response to insulin stimulus (MGI:MGI:5444071 PMID:22958918 [IGI] MGI:MGI:104663 MGI:MGI:1922997) /// 0006914 // autophagy (MGI:MGI:5444071 PMID:22958918 [IMP] MGI:MGI:3587950) /// 0046323 // glucose import (MGI:MGI:5444071 PMID:22958918 [IMP] MGI:MGI:3587950) /// 0043491 // protein kinase B signaling cascade (MGI:MGI:5444071 PMID:22958918 [IMP] MGI:MGI:3587950) /// 0032042 // mitochondrial DNA metabolic process (MGI:MGI:5444071 PMID:22958918 [IMP] MGI:MGI:3587950)</p>
Txndc2	- 7.7037 55881	3.864 19E- 07	MGI:23 89312	<p>0007283 // spermatogenesis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0744) /// 0006662 // glycerol ether metabolic process (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR005746) /// 0055114 // oxidation-reduction process (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000047070) /// 0007275 // multicellular organismal development (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0217) /// 0034614 // cellular response to reactive oxygen species (MGI:MGI:5544180 PMID:23707457 [IGI] MGI:MGI:1920662) /// 0030317 // sperm motility (MGI:MGI:5544180 PMID:23707457 [IGI] MGI:MGI:1920662) /// 0045454 // cell redox homeostasis (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000047070) /// 0030154 // cell differentiation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0221) /// 0000103 // sulfate assimilation (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000047070) /// 0098869</p>
Arhgef3	- 7.7026 67464	1.680 35E- 36	MGI:19 18954	<p>0035556 // intracellular signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001331) /// 0035023 // regulation of Rho protein signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000219)</p>
Nr4a3	- 7.6848 63346	4.213 55E- 17	MGI:13 52457	<p>0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61882) /// 0001707 // mesoderm formation (MGI:MGI:3042044 PMID:13129926 [IMP] MGI:MGI:3043761) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:5295515 PMID:21868379 [IDA]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4838750 PMID:19153266 [IDA]) /// 0050885 // neuromuscular process controlling balance (MGI:MGI:2157256 PMID:11784868 [IMP] MGI:MGI:3037444) /// 0048661 // positive regulation of smooth muscle cell proliferation (MGI:MGI:5297326 PMID:16945922 [IMP]) /// 0010613 // positive regulation of cardiac muscle hypertrophy (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61882) /// 0043401 // steroid hormone mediated signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000536) /// 0042542 // response to hydrogen peroxide (MGI:MGI:4462723 PMID:20566846 [IMP]) /// 0030534 // adult behavior (MGI:MGI:2157256 PMID:11784868 [IMP] MGI:MGI:3037444) /// 0045444 // fat cell differentiation (MGI:MGI:5645207 PMID:18945812 [IDA]) /// 1900625 // positive regulation of monocyte aggregation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92570) /// 0009444 // pyruvate oxidation (MGI:MGI:5645208 PMID:18325999 [IMP]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0038097 // positive regulation of mast cell activation by Fc-epsilon receptor signaling pathway (MGI:MGI:5586645 PMID:24586680 [IMP]) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:5543879 PMID:23897430 [IDA]) /// 0044320 // cellular response to leptin stimulus (MGI:MGI:4353981 PMID:19523439 [IDA]) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR003072 InterPro:IPR003070 InterPro:IPR000536 InterPro:IPR001723 InterPro:IPR001628 InterPro:IPR013088) /// 1903204 /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:5645210 PMID:12709428 [IDA]) /// 0043524 // negative regulation of neuron apoptotic process (MGI:MGI:4462723 PMID:20566846 [IMP]) /// 1903208 /// 0043303 // mast cell degranulation (MGI:MGI:5586645 PMID:24586680 [IMP]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:84485 PMID:8961274 [IDA]) /// 0046321 // positive regulation of fatty acid oxidation (MGI:MGI:5645208 PMID:18325999 [IMP]) /// 0097009 // energy homeostasis (MGI:MGI:5543879 PMID:23897430 [IMP]) /// 0042472 // inner ear morphogenesis (MGI:MGI:2157256 PMID:11784868 [IMP] MGI:MGI:3037444) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:87364 PMID:9155013 [IDA]) /// 0061469 // regulation of type B pancreatic cell proliferation (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61882) /// 0021766 // hippocampus development (MGI:MGI:3056852 PMID:15456880 [IMP] MGI:MGI:3037444) /// 0043066 // negative regulation of apoptotic process (MGI:MGI:4838750 PMID:19153266 [IMP])</p>

				<p>MGI:MGI:3037444) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3047463 PMID:15155786 [IGI] MGI:MGI:1352460) /// 0035726 // common myeloid progenitor cell proliferation (MGI:MGI:5609505 PMID:24806827 [IMP]) /// 0045787 // positive regulation of cell cycle (MGI:MGI:4838750 PMID:19153266 [IMP] MGI:MGI:3037444) /// 1900625 // positive regulation of monocyte aggregation (MGI:MGI:5142195 PMID:20558821 [IMP]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92570) /// 0048752 // semicircular canal morphogenesis (MGI:MGI:2157256 PMID:11784868 [IMP] MGI:MGI:3037444) /// 2000253 // positive regulation of feeding behavior (MGI:MGI:4353981 PMID:19523439 [IMP]) /// 2000505 // regulation of energy homeostasis (MGI:MGI:4353981 PMID:19523439 [IMP]) /// 0007369 // gastrulation (MGI:MGI:3042044 PMID:13129926 [IMP]) /// 0032765 // positive regulation of mast cell cytokine production (MGI:MGI:5586645 PMID:24586680 [IMP]) /// 0060005 // vestibular reflex (MGI:MGI:2157256 PMID:11784868 [IMP] MGI:MGI:3037444) /// 0010828 // positive regulation of glucose transport (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92570) /// 0071870 // cellular response to catecholamine stimulus (MGI:MGI:5645208 PMID:18325999 [IDA]) /// 0048660 // regulation of smooth muscle cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q92570) /// 0045333 // cellular respiration (MGI:MGI:5645208 PMID:18325999 [IMP]) /// 2000108 // positive regulation of leukocyte apoptotic process (MGI:MGI:3839522 PMID:19164597 [IMP]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0043524 // negative regulation of neuron apoptotic process (MGI:MGI:3056852 PMID:15456880 [IMP] MGI:MGI:3037444) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3047463 PMID:15155786 [IDA]) /// 0007411 // axon guidance (MGI:MGI:3056852 PMID:15456880 [IMP] MGI:MGI:3037444) /// 0006366 // transcription from RNA polymerase II promoter (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61882) /// 0071376 // cellular response to corticotropin-releasing hormone stimulus (MGI:MGI:5645213 PMID:10523643 [IDA]) /// 0050679 // positive regulation of epithelial cell proliferation (MGI:MGI:2157256 PMID:11784868 [IMP])</p>
BC117090	- 7.6766 60033	3.719 47E-05	MGI:36 96881	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Slc9a3r1	- 7.6620 86889	2.582 56E-40	MGI:13 49482	<p>0014067 // negative regulation of phosphatidylinositol 3-kinase cascade (MGI:MGI:3617099 PMID:16456542 [IMP]) /// 0044062 // regulation of excretion (MGI:MGI:3687116 PMID:12952857 [IMP] MGI:MGI:2386785) /// 0019933 // cAMP-mediated signaling (MGI:MGI:1345802 PMID:10500246 [ISA] EMBL:U19815) /// 0030336 // negative regulation of cell migration (MGI:MGI:3617099 PMID:16456542 [IGI] MGI:MGI:97528) /// 0044062 // regulation of excretion (MGI:MGI:3692157 PMID:16249272 [IMP] MGI:MGI:2386785) /// 0051898 // negative regulation of protein kinase B signaling cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0060158 // phospholipase C-activating dopamine receptor signaling pathway (MGI:MGI:4819345 PMID:20200151 [IMP] MGI:MGI:2386785) /// 2000146 // negative regulation of cell motility (MGI:MGI:3617099 PMID:16456542 [IMP]) /// 0034635 // glutathione transport (MGI:MGI:4834112 PMID:20404332 [IMP]) /// 0070293 // renal absorption (MGI:MGI:3703405 PMID:16987995 [IMP]) /// 0008285 // negative regulation of cell proliferation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0008360 // regulation of cell shape (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0045930 // negative regulation of mitotic cell cycle (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0022612 // gland morphogenesis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0035414 // negative regulation of catenin import into nucleus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0016055 // Wnt receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0879) /// 2001244 // positive regulation of intrinsic apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0030033 // microvillus assembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0010766 // negative regulation of sodium ion transport (MGI:MGI:3702223 PMID:12586353 [IMP] MGI:MGI:2386785) /// 0045198 // establishment of epithelial cell apical/basal polarity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0097291 // renal phosphate ion absorption (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0019933 // cAMP-mediated signaling (MGI:MGI:3702223 PMID:12586353 [IMP] MGI:MGI:2386785) /// 0034613 // cellular protein localization (MGI:MGI:3687116 PMID:12952857 [IMP] MGI:MGI:2386785) /// 0045859 // regulation of protein kinase activity (MGI:MGI:4943390 PMID:18190691 [IMP]) /// 0030643 // cellular phosphate ion homeostasis (MGI:MGI:2385526 PMID:12169661 [IMP] MGI:MGI:2386785) /// 0070293 // renal absorption (MGI:MGI:2385526 PMID:12169661 [IMP]) /// 0010642 // negative regulation of platelet-derived growth factor receptor signaling pathway (MGI:MGI:4943390 PMID:18190691 [IMP]) /// 0007605 // sensory perception of sound (MGI:MGI:5578076 PMID:24920589 [IMP] MGI:MGI:3526430) /// 0008361 // regulation of cell size (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0032416 // negative regulation of sodium:hydrogen antiporter activity (MGI:MGI:3702223 PMID:12586353 [IMP] MGI:MGI:2386785) /// 0030036 // actin</p>

				<p>cytoskeleton organization (MGI:MGI:3525780 PMID:15591354 [IMP] MGI:MGI:3526430) /// 0070373 // negative regulation of ERK1 and ERK2 cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0051898 // negative regulation of protein kinase B signaling cascade (MGI:MGI:4943390 PMID:18190691 [IMP]) /// 0090002 // establishment of protein localization to plasma membrane (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0014067 // negative regulation of phosphatidylinositol 3-kinase cascade (MGI:MGI:3617099 PMID:16456542 [IGI] MGI:MGI:97528) /// 0007191 // adenylate cyclase-activating dopamine receptor signaling pathway (MGI:MGI:4819345 PMID:20200151 [IMP] MGI:MGI:2386785) /// 0051683 // establishment of Golgi localization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0003096 // renal sodium ion transport (MGI:MGI:3702223 PMID:12586353 [IMP] MGI:MGI:2386785) /// 0040023 // establishment of nucleus localization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14745) /// 0060088 // auditory receptor cell stereocilium organization (MGI:MGI:5578076 PMID:24920589 [IMP] MGI:MGI:3526430) /// 0032782 // bile acid secretion (MGI:MGI:4834112 PMID:20404332 [IMP])</p>
Tacr2	- 7.6470 96996	9.353 02E- 05	MGI:98 477	<p>0007166 // cell surface receptor signaling pathway (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001544342) /// 0070459 // prolactin secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3812) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000276 InterPro:IPR001681 InterPro:IPR000913) /// 0070474 // positive regulation of uterine smooth muscle contraction (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3812) /// 0070472 // regulation of uterine smooth muscle contraction (MGI:MGI:5619483 PMID:15647454 [IDA]) /// 0014057 // positive regulation of acetylcholine secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3812) /// 0007186 // G-protein coupled receptor signaling pathway (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0297) /// 0033685 // negative regulation of luteinizing hormone secretion (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3812) /// 0035106 // operant conditioning (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3812) /// 0045987 // positive regulation of smooth muscle contraction (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000662758) /// 0014827 // intestine smooth muscle contraction (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3812) /// 0043270 // positive regulation of ion transport (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3812) /// 0007217 // tachykinin receptor signaling pathway (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3812) /// 0007165 // signal transduction (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0807) /// 0007268 // synaptic transmission (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000662758) /// 0043117 // positive regulation of vascular permeability (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:3812)</p>
3110043 O2IRik	- 7.6470 02522	1.198 71E- 21	MGI:19 20455	<p>0006897 // endocytosis (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96LT7) /// 0006914 // autophagy (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q96LT7)</p>
Nfkb2	- 7.6420 82877	1.672 6E- 35	MGI:10 99800	<p>0045087 // innate immune response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0038061 // NIK/NF-kappaB cascade (MGI:MGI:5486592 PMID:23583643 [IDA]) /// 0030198 // extracellular matrix organization (MGI:MGI:3655550 PMID:10586052 [IMP] MGI:MGI:2179705) /// 0006357 // regulation of transcription from RNA polymerase II promoter (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR030497) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q00653) /// 0006366 // transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q00653) /// 0007249 // I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0048536 // spleen development (MGI:MGI:3655550 PMID:10586052 [IMP] MGI:MGI:2179705) /// 0034097 // response to cytokine stimulus (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0033554 // cellular response to stress (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0006954 // inflammatory response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0002467 // germinal center formation (MGI:MGI:3655550 PMID:10586052 [IMP] MGI:MGI:2179705) /// 0048511 // rhythmic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0090) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q00653) /// 0048535 // lymph node development (MGI:MGI:1353335 PMID:10687308 [TAS]) /// 0002268 // follicular dendritic cell differentiation (MGI:MGI:3655550 PMID:10586052 [IMP] MGI:MGI:2179705) /// 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000488)</p>

Rabgef1	- 7.6414 25853	8.237 25E- 22	MGI:19 29459	0043305 // negative regulation of mast cell degranulation (MGI:MGI:3050742 PMID:15235600 [IMP] MGI:MGI:3051384) /// 0060368 // regulation of Fc receptor mediated stimulatory signaling pathway (MGI:MGI:3834538 PMID:17341663 [IDA]) /// 0001933 // negative regulation of protein phosphorylation (MGI:MGI:3620385 PMID:16533754 [IMP] MGI:MGI:3051384) /// 1900235 // negative regulation of Kit signaling pathway (MGI:MGI:3620385 PMID:16533754 [IMP] MGI:MGI:3051384) /// 0006897 // endocytosis (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0254) /// 1900165 // negative regulation of interleukin-6 secretion (MGI:MGI:3620385 PMID:16533754 [IMP] MGI:MGI:3051384) /// 0006612 // protein targeting to membrane (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UJ41) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:3050742 PMID:15235600 [IMP] MGI:MGI:3051384) /// 0002686 // negative regulation of leukocyte migration (MGI:MGI:3620385 PMID:16533754 [IMP] MGI:MGI:3051384) /// 0048261 // negative regulation of receptor-mediated endocytosis (MGI:MGI:3620385 PMID:16533754 [IMP] MGI:MGI:3051384) /// 0033004 // negative regulation of mast cell activation (MGI:MGI:3050742 PMID:15235600 [IMP] MGI:MGI:3051384) /// 0060368 // regulation of Fc receptor mediated stimulatory signaling pathway (MGI:MGI:3050742 PMID:15235600 [IMP]) /// 0046580 // negative regulation of Ras protein signal transduction (MGI:MGI:3050742 PMID:15235600 [IMP]) /// 0006810 // transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0813) /// 0015031 // protein transport (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0653) /// 0043547 // positive regulation of GTPase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9UJ41)
Gm13431	- 7.6338 96472	3.824 49E- 05		
Mgam	- 7.6285 59643	3.785 42E- 16	MGI:12 03495	
Gm19705	- 7.6278 8921	1.395 26E- 12		
Sh2b2	- 7.5838 88163	2.548 9E- 22	MGI:13 45171	0050851 // antigen receptor-mediated signaling pathway (MGI:MGI:1859033 PMID:10872802 [IDA]) /// 0030036 // actin cytoskeleton organization (MGI:MGI:3033759 PMID:14993264 [IMP] MGI:MGI:2680256) /// 0050776 // regulation of immune response (MGI:MGI:3033759 PMID:14993264 [IMP] MGI:MGI:2680256) /// 0046325 // negative regulation of glucose import (MGI:MGI:2679365 PMID:14578283 [ISA] MGI:MGI:2680256) /// 0050873 // brown fat cell differentiation (MGI:MGI:3801349 PMID:18492766 [IDA]) /// 0030036 // actin cytoskeleton organization (MGI:MGI:3590011 PMID:15946664 [IPI] UniProtKB:Q3TJD7) /// 0007399 // nervous system development (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69284) /// 0035556 // intracellular signal transduction (MGI:MGI:1859033 PMID:10872802 [IDA]) /// 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR030523 InterPro:IPR030520) /// 0008286 // insulin receptor signaling pathway (MGI:MGI:1334765 PMID:10196204 [IDA]) /// 0019222 // regulation of metabolic process (MGI:MGI:2679365 PMID:14578283 [IMP] MGI:MGI:2680256) /// 0046425 // regulation of JAK-STAT cascade (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14492) /// 0035556 // intracellular signal transduction (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14492) /// 0009967 // positive regulation of signal transduction (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O14492) /// 0019221 // cytokine-mediated signaling pathway (MGI:MGI:1859033 PMID:10872802 [IDA]) /// 0042593 // glucose homeostasis (MGI:MGI:2679365 PMID:14578283 [ISA] MGI:MGI:2680256) /// 0046578 // regulation of Ras protein signal transduction (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:69284) /// 0001922 // B-1 B cell homeostasis (MGI:MGI:3033759 PMID:14993264 [IMP] MGI:MGI:2680256)
6530402 F18Rik	- 7.5837 23795	4.628 91E- 11		
Dennd3	- 7.5783 711	1.277 64E- 27	MGI:21 46009	0044257 // cellular protein catabolic process (MGI:MGI:5448516 PMID:21718402 [IMP]) /// 0008333 // endosome to lysosome transport (MGI:MGI:5448516 PMID:21718402 [IGI]) /// 0043547 // positive regulation of GTPase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:A2RUS2)
Kdm3a	- 7.5758 31197	2.585 6E- 32	MGI:98 847	0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y4C1) /// 0046293 // formaldehyde biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y4C1) /// 2000736 // regulation of stem cell differentiation (MGI:MGI:3759699 PMID:17938240 [IMP]) /// 0016568 // chromatin modification

				(MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0156) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3822125 PMID:17991879 [IDA]) /// 0033169 // histone H3-K9 demethylation (MGI:MGI:3759699 PMID:17938240 [IMP]) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0007290 // spermatid nucleus elongation (MGI:MGI:3763001 PMID:17943087 [IMP] MGI:MGI:3764891) /// 0010468 // regulation of gene expression (MGI:MGI:3759699 PMID:17938240 [IMP]) /// 0030521 // androgen receptor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y4C1) /// 2000036 // regulation of stem cell maintenance (MGI:MGI:3759699 PMID:17938240 [IGI] MGI:MGI:1097166) /// 0033169 // histone H3-K9 demethylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y4C1) /// 0010628 // positive regulation of gene expression (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:708351) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0009755 // hormone-mediated signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q9Y4C1) /// 0036123 // histone H3-K9 dimethylation (MGI:MGI:3822125 PMID:17991879 [IDA]) /// 0007283 // spermatogenesis (MGI:MGI:3763001 PMID:17943087 [IMP] MGI:MGI:3764891) /// 0036123 // histone H3-K9 dimethylation (MGI:MGI:3822125 PMID:17991879 [IMP]) /// 0030154 // cell differentiation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0221) /// 0051573 // negative regulation of histone H3-K9 methylation (MGI:MGI:3763001 PMID:17943087 [IMP] MGI:MGI:3764891) /// 0055114 // oxidation-reduction process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0560)
Pfkfb	- 7.5685 11499	9.734 91E- 30	MGI:18 91833	0006002 // fructose 6-phosphate metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61893) /// 0006096 // glycolysis (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61893) /// 0008152 // metabolic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0021) /// 0051289 // protein homotetramerization (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61893) /// 0098779 /// 0030388 // fructose 1,6-bisphosphate metabolic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:61893) /// 0061615 /// 0016310 // phosphorylation (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0418)
Gm7582	- 7.5560 31848	3.651 24E- 06		
Gm6377	- 7.5297 72383	9.378 7E- 14	MGI:36 47255	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Bnip3	- 7.5293 05074	1.594 51E- 25	MGI:10 9326	0043066 // negative regulation of apoptotic process (MGI:MGI:3796473 PMID:18281291 [IGI] UniProtKB:Q61221) /// 1903715 /// 0008626 // granzyme-mediated apoptotic signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0001666 // response to hypoxia (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620800) /// 0043653 // mitochondrial fragmentation involved in apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0060548 // negative regulation of cell death (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:Q12983) /// 0050873 // brown fat cell differentiation (MGI:MGI:3801349 PMID:18492766 [IDA]) /// 0097345 // mitochondrial outer membrane permeabilization (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0051402 // neuron apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620800) /// 0051607 // defense response to virus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0016239 // positive regulation of macroautophagy (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:Q12983) /// 0071456 // cellular response to hypoxia (MGI:MGI:3796473 PMID:18281291 [IC] GO:2000378) /// 0048102 // autophagic cell death (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620800) /// 0072593 // reactive oxygen species metabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0045837 // negative regulation of membrane potential (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 1990144 /// 0006915 // apoptotic process (MGI:MGI:84904 PMID:7954800 [ISO] UniProtKB:Q12983) /// 0070301 // cellular response to hydrogen peroxide (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620800) /// 0043068 // positive regulation of programmed cell death (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000796011) /// 0046902 // regulation of mitochondrial membrane permeability (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0097193 // intrinsic apoptotic signaling pathway (MGI:MGI:3696331 PMID:16954213 [IGI] MGI:MGI:96224) /// 0090141 // positive regulation of mitochondrial fission (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0043068 // positive regulation of programmed cell death (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0010637 // negative regulation of mitochondrial fusion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0035694 // mitochondrial protein catabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0010821 // regulation of mitochondrion organization (MGI:MGI:3796473 PMID:18281291 [IMP]) /// 0097345 // mitochondrial outer membrane permeabilization (MGI:MGI:4459044 GO_REF:0000033 [IBA]

				<p>PANTHER:PTN001032684) /// 0071456 // cellular response to hypoxia (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:Q12983) /// 0043243 // positive regulation of protein complex disassembly (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0090200 // positive regulation of release of cytochrome c from mitochondria (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 2000378 // negative regulation of reactive oxygen species metabolic process (MGI:MGI:3796473 PMID:18281291 [IGI] UniProtKB:Q61221) /// 0010666 // positive regulation of cardiac muscle cell apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620800) /// 0008219 // cell death (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:620800) /// 0071279 // cellular response to cobalt ion (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:Q12983) /// 0097193 // intrinsic apoptotic signaling pathway (MGI:MGI:3696331 PMID:16954213 [IMP]) /// 1901998 // toxin transport (MGI:MGI:5492256 PMID:23716698 [IMP])</p>
Tiparp	- 7.5182 48106	2.576 12E- 20	MGI:21 59210	<p>0048008 // platelet-derived growth factor receptor signaling pathway (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866) /// 0060325 // face morphogenesis (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866) /// 0048705 // skeletal system morphogenesis (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866) /// 0060021 // palate development (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866) /// 0008585 // female gonad development (MGI:MGI:3820330 PMID:19056881 [IMP] MGI:MGI:3526866) /// 0048745 // smooth muscle tissue development (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866) /// 0044236 // multicellular organismal metabolic process (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866) /// 0008209 // androgen metabolic process (MGI:MGI:3820330 PMID:19056881 [IMP] MGI:MGI:3526866) /// 0006471 // protein ADP-ribosylation (MGI:MGI:2154582 PMID:11716501 [IDA]) /// 0009791 // post-embryonic development (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866) /// 0006807 // nitrogen compound metabolic process (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866) /// 0008210 // estrogen metabolic process (MGI:MGI:3820330 PMID:19056881 [IMP] MGI:MGI:3526866) /// 0045732 // positive regulation of protein catabolic process (MGI:MGI:5507898 PMID:23275542 [ISO] UniProtKB:Q7Z3E1) /// 0001570 // vasculogenesis (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866) /// 0071407 // cellular response to organic cyclic compound (MGI:MGI:5507898 PMID:23275542 [ISO] UniProtKB:Q7Z3E1) /// 0010629 // negative regulation of gene expression (MGI:MGI:5507898 PMID:23275542 [ISO] UniProtKB:Q7Z3E1) /// 0030097 // hemopoiesis (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866) /// 0001822 // kidney development (MGI:MGI:3696608 PMID:17143286 [IMP] MGI:MGI:3526866)</p>
Perl	- 7.5112 28262	3.602 61E- 31	MGI:10 98283	<p>0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:5568183 PMID:24610784 [IMP]) /// 1900744 // regulation of p38MAPK cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:727863) /// 0002028 // regulation of sodium ion transport (MGI:MGI:5568183 PMID:24610784 [IMP]) /// 0007623 // circadian rhythm (MGI:MGI:2179885 PMID:12024206 [TAS]) /// 0045892 // negative regulation of transcription, DNA-dependent (MGI:MGI:1316573 PMID:9856465 [IDA]) /// 0046329 // negative regulation of JNK cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:727863) /// 0043124 // negative regulation of I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:727863) /// 0007623 // circadian rhythm (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:727863) /// 0042634 // regulation of hair cycle (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15534) /// 2000323 // negative regulation of glucocorticoid receptor signaling pathway (MGI:MGI:5567887 PMID:24378737 [IMP]) /// 0032922 // circadian regulation of gene expression (MGI:MGI:3578039 PMID:15888647 [IMP]) /// 0048511 // rhythmic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0090) /// 0070932 // histone H3 deacetylation (MGI:MGI:5014424 PMID:21680841 [IMP]) /// 1900015 // regulation of cytokine production involved in inflammatory response (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:727863) /// 0032922 // circadian regulation of gene expression (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15534) /// 0043967 // histone H4 acetylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15534) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:2388855 PMID:12397359 [IDA]) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:1327772 PMID:9989497 [IDA]) /// 0032922 // circadian regulation of gene expression (MGI:MGI:4429726 PMID:20159955 [IDA]) /// 0045892 // negative regulation of transcription, DNA-dependent (MGI:MGI:3794495 PMID:18316400 [IDA]) /// 0097167 // circadian regulation of translation (MGI:MGI:1935010 PMID:11395012 [IMP]) /// 0051591 // response to cAMP (MGI:MGI:5494765 PMID:23443664 [IDA]) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:5297789 PMID:15147242 [IDA]) /// 0042752 // regulation of circadian rhythm (MGI:MGI:1935010 PMID:11395012 [IMP]) /// 0043966 // histone H3 acetylation (MGI:MGI:5559671 PMID:14645221 [IDA]) /// 0043966 // histone H3 acetylation (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:O15534) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0006355 // regulation of transcription, DNA-dependent</p>

				(MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0010608 // posttranscriptional regulation of gene expression (MGI:MGI:3578039 PMID:15888647 [IMP]) /// 0045892 // negative regulation of transcription, DNA-dependent (MGI:MGI:2388855 PMID:12397359 [IDA]) /// 0043153 // entrainment of circadian clock by photoperiod (MGI:MGI:3578039 PMID:15888647 [IMP]) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:5568183 PMID:24610784 [IMP])
Zfp819	- 7.5026 67671	1.591 56E- 09	MGI:19 21650	0045892 // negative regulation of transcription, DNA-dependent (MGI:MGI:5688249 PMID:25827285 [IDA]) /// 0043065 // positive regulation of apoptotic process (MGI:MGI:5688249 PMID:25827285 [IDA])
Clec4e	- 7.5019 86418	2.526 23E- 15	MGI:18 61232	0006955 // immune response (MGI:MGI:5009372 PMID:19171887 [IMP]) /// 0050715 // positive regulation of cytokine secretion (MGI:MGI:3817341 PMID:18776906 [IDA]) /// 0042742 // defense response to bacterium (MGI:MGI:5525050 PMID:23602766 [IMP] MGI:MGI:5013826) /// 0038094 // Fc-gamma receptor signaling pathway (MGI:MGI:5525050 PMID:23602766 [IDA]) /// 0002292 // T cell differentiation involved in immune response (MGI:MGI:5525050 PMID:23602766 [IMP] MGI:MGI:5013826) /// 0002376 // immune system process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0391) /// 0045087 // innate immune response (MGI:MGI:5525050 PMID:23602766 [IMP] MGI:MGI:5013826)
1700065 D16Rik	- 7.4616 81116	3.964 58E- 05	MGI:19 20660	0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])
Il19	- 7.4608 50519	8.574 05E- 07	MGI:18 90472	0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0006954 // inflammatory response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000172385) /// 2001237 // negative regulation of extrinsic apoptotic signaling pathway (MGI:MGI:5491082 PMID:23468852 [IDA]) /// 2001244 // positive regulation of intrinsic apoptotic signaling pathway (MGI:MGI:5491082 PMID:23468852 [IGI] MGI:MGI:3605069) /// 2001235 // positive regulation of apoptotic signaling pathway (MGI:MGI:2653146 PMID:12370360 [IDA]) /// 0042226 // interleukin-6 biosynthetic process (MGI:MGI:2653146 PMID:12370360 [IDA]) /// 0072593 // reactive oxygen species metabolic process (MGI:MGI:2653146 PMID:12370360 [IDA]) /// 0006955 // immune response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000172385) /// 0046427 // positive regulation of JAK-STAT cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN000172385)
Ankrd66	- 7.4362 19401	8.680 98E- 16		
Nfkb1	- 7.4303 68451	1.006 98E- 42	MGI:97 312	0010628 // positive regulation of gene expression (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70498) /// 0071347 // cellular response to interleukin-1 (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70498) /// 0071359 // cellular response to dsRNA (MGI:MGI:5604160 PMID:24114535 [IMP] MGI:MGI:1857225) /// 0006979 // response to oxidative stress (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70498) /// 0071407 // cellular response to organic cyclic compound (MGI:MGI:3850788 PMID:19414010 [ISO] UniProtKB:Q63369) /// 0045083 // negative regulation of interleukin-12 biosynthetic process (MGI:MGI:2679145 PMID:14568984 [IDA]) /// 1900127 // positive regulation of hyaluronan biosynthetic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P19838) /// 0006357 // regulation of transcription from RNA polymerase II promoter (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR030503) /// 0071316 // cellular response to nicotine (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P19838) /// 1901653 // cellular response to peptide (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70498) /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3531056 PMID:15728238 [IMP]) /// 0038061 // NIK/NF-kappaB cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0045892 // negative regulation of transcription, DNA-dependent (MGI:MGI:2679145 PMID:14568984 [IDA]) /// 0090263 // positive regulation of canonical Wnt receptor signaling pathway (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P19838) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:5544880 PMID:23776175 [ISO] UniProtKB:P19838) /// 0071354 // cellular response to interleukin-6 (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P19838) /// 0010956 // negative regulation of calcidiol 1-monooxygenase activity (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P19838) /// 0034097 // response to cytokine stimulus (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0033554 // cellular response to stress (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0006915 // apoptotic process (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0053) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4415769 PMID:19955433 [ISO] UniProtKB:P19838) /// 0006355 // regulation of

				<p>transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0805) /// 0071345 // cellular response to cytokine stimulus (MGI:MGI:3850788 PMID:19414010 [ISO] UniProtKB:Q63369) /// 1990416 /// 0043066 // negative regulation of apoptotic process (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70498) /// 0071222 // cellular response to lipopolysaccharide (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70498) /// 0045087 // innate immune response (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0071375 // cellular response to peptide hormone stimulus (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P19838) /// 0071322 // cellular response to carbohydrate stimulus (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70498) /// 0007249 // I-kappaB kinase/NF-kappaB cascade (MGI:MGI:4459044 GO_REF:0000033 [IBA] PANTHER:PTN001193216) /// 0071356 // cellular response to tumor necrosis factor (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70498) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P19838) /// 2000630 // positive regulation of miRNA metabolic process (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P19838) /// 0006355 // regulation of transcription, DNA-dependent (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000451 InterPro:IPR008967 InterPro:IPR011539) /// 0035994 // response to muscle stretch (MGI:MGI:4822295 PMID:20442316 [IDA]) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:3621346 PMID:16081776 [IDA]) /// 0007165 // signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR000488) /// 0045944 // positive regulation of transcription from RNA polymerase II promoter (MGI:MGI:4355633 PMID:19666510 [IDA]) /// 0045893 // positive regulation of transcription, DNA-dependent (MGI:MGI:4834177 GO_REF:0000096 [ISO] UniProtKB:P19838) /// 0006351 // transcription, DNA-dependent (MGI:MGI:1354194 GO_REF:0000004 [IEA] UniProtKB-KW:KW-0804) /// 0050728 // negative regulation of inflammatory response (MGI:MGI:3790904 PMID:18270204 [IMP] MGI:MGI:97312) /// 1904630 /// 0000122 // negative regulation of transcription from RNA polymerase II promoter (MGI:MGI:2154458 GO_REF:0000008 [ISO] UniProtKB:P19838) /// 0014070 // response to organic cyclic compound (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70498) /// 1902895 /// 1904632 /// 0001818 // negative regulation of cytokine production (MGI:MGI:3799438 PMID:18566389 [IMP]) /// 2000637 // positive regulation of gene silencing by miRNA (MGI:MGI:4417868 GO_REF:0000096 [ISO] RGD:70498) /// 0048535 // lymph node development (MGI:MGI:1353335 PMID:10687308 [TAS])</p>
Wsb1	- 7.4284 17687	1.277 66E- 25	MGI:19 26139	<p>0035556 // intracellular signal transduction (MGI:MGI:2152098 GO_REF:0000002 [IEA] InterPro:IPR001496) /// 0008150 // biological_process (MGI:MGI:2156816 GO_REF:0000015 [ND])</p>

Annex (5) Down-regulated genes in 7 dpi mouse ocular cells compared to 2 dpi mouse ocular cells due to infection by *P. aeruginosa* $\Delta wspF$

Appendix (6)

Control(MF)		
Live	Dead	L/D
1737930.00	512161.00	3.393327489
1625470.00	613698.00	2.648648032
1011920.00	271922.00	3.721361273
1216420.00	220266.00	5.522504608
1270740.00	291285.00	4.362531541
938432.00	225326.00	4.164774593
873104.00	156141.00	5.591766416
	Average(L/D)	4.200701993
Amikacin+Levofloxacin+DNase		
Live	Dead	L/D
1197880.00	992733.00	1.206648716
1922420.00	577581.00	3.32839896
2092640.00	586091.00	3.570503557
2089150.00	719573.00	2.903319052
2043130.00	752167.00	2.716324965
2382400.00	451395.00	5.277860854
2411320.00	507615.00	4.750293037
	Average(L/D)	3.393335592
Amikacin		
Live	Dead	L/D
684361.00	173658.00	3.940855014
1978370.00	937130.00	2.111094512
1609090.00	848323.00	1.896789313
2076210.00	635819.00	3.265410439
2674660.00	1563920.00	1.710228145
1627700.00	867890.00	1.875468089
2132460.00	956109.00	2.230352397
	Average(L/D)	2.432885416
Amikacin+Dnase		
Live	Dead	L/D
1632280.00	1229990.00	1.3270677
2123860.00	1089770.00	1.94890665

1767680.00	1495780.00	1.181778069
1503210.00	841669.00	1.785987128
1212500.00	1205870.00	1.005498105
1413960.00	1218300.00	1.160600837
1845540.00	780734.00	2.363852477
	Average(L/D)	1.539098709
Amikacin+Gati		
Live	Dead	L/D
1530060.00	1109040.00	1.379625622
920559.00	771148.00	1.193751394
1150080.00	1058870.00	1.086138997
1111050.00	1025600.00	1.083317083
1401390.00	1049970.00	1.334695277
1562290.00	978387.00	1.596801675
1687650.00	970611.00	1.738750127
	Average(L/D)	1.344725739
Amikacin+Gatifloxacin+DNase		
Live	Dead	L/D
811002.00	723548.00	1.120868277
1140060.00	1017760.00	1.120165854
1031950.00	809468.00	1.274849654
1206310.00	1287650.00	0.936830661
751063.00	680967.00	1.102935972
910202.00	999494.00	0.910662795
1317870.00	1300810.00	1.013114905
	Average(L/D)	1.068489731
Levofloxacin		
Live	Dead	L/D
1731570.00	1091690.00	1.58613709
2069700.00	1025420.00	2.018392464
1615020.00	968577.00	1.667415187
1724730.00	850611.00	2.027636605
3351650.00	1475550.00	2.2714581
1939310.00	1197470.00	1.619506125
1756450.00	1317190.00	1.333482641
	Average(L/D)	1.789146888
Levofloxacin+DNASE		
Live	Dead	L/D
1107910.00	1009900.00	1.097049213
1594890.00	1119250.00	1.424963145

1452670.00	963722.00	1.50735378
1564570.00	1057440.00	1.479582766
1515050.00	1073090.00	1.411857347
1657020.00	1418270.00	1.168338892
1394220.00	977628.00	1.426125275
	Average(L/D)	1.359324345
Amikacin+Levofloxacin		
Live	Dead	L/D
1370250.00	1149090.00	1.192465342
1730990.00	1497640.00	1.155811811
1426800.00	1219600.00	1.169891768
2020890.00	920015.00	2.196583751
1159800.00	782952.00	1.481316862
1374570.00	1060940.00	1.295615209
996043.00	731183.00	1.362234899
	Average(L/D)	1.407702806
Amikacin+Levofloxacin+DNase		
Live	Dead	L/D
1197880.00	1418620.00	0.844398077
1060100.00	1152080.00	0.920161794
1192400.00	1114890.00	1.069522554
1172070.00	764917.00	1.532283895
1362250.00	1347020.00	1.011306439
902145.00	924467.00	0.975854195
1041980.00	994145.00	1.048116723
	Average(L/D)	1.057377668
Gatifloxacin		
Live	Dead	L/D
1125610.00	807569.00	1.393825172
2033630.00	817869.00	2.486498449
1494520.00	937874.00	1.593518959
1579140.00	1137570.00	1.388169519
1640260.00	801559.00	2.0463372
1086380.00	492133.00	2.20749269
1736530.00	695412.00	2.497124007
	Average(L/D)	1.944709428
Gati and Dnase		
Live	Dead	L/D
1276950.00	1036810.00	1.231614278
1309100.00	1297240.00	1.009142487

1037730.00	1099430.00	0.943880011
981053.00	820355.00	1.195888365
1288920.00	1108620.00	1.162634627
1201620.00	596551.00	2.014278746
1136550.00	517750.00	2.195171415
	Average(L/D)	1.39322999

Author's Publication

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Yam JK ¶, **Aung TT** ¶, Chua SL, Cheng YY, Kohli GS, Zhou J, Constancias F, Liu Y, Cai Z, Salido MMS, Drautz-Moses DI, Rice SA, Schuster S, Wu B, Kjelleberg S, Nielsen TT, Beuerman RW, Givskov, Yang L. Cyclic-di-GMP is required for corneal infection by *Pseudomonas aeruginosa*, and modulates host immunity and antimicrobial resistance. Under Review in *Plos Pathogen*.

¶ These authors contributed equally to this work.

Posters and Talks

SGH 21st Annual Scientific Meeting, Singapore, April, 2015.

Oral presentation for YOUNG INVESTIGATOR'S AWARD (BASIC/TRANSLATIONAL):
Biofilm Flow Cell model for atypical mycobacteria and anti-mycobacterial drug discovery

7th ASM conferences on Biofilms, September, 2015.

Poster presentation: "Biofilms of pathogenic non-tuberculous mycobacteria targeted by new therapeutic approaches"

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