

**Supplementary Table 1** Functional analysis of genes that are differentially expressed in the mouse brain following reovirus infection at early times post infection<sup>a</sup>

General function	Specific function	Biological process	Gene symbol	Description	3D	6D	8D	
Immune response	Transcription	Interferon type 1 biosynthetic process	Irf9	Interferon regulatory factor 9	4.0	5.6	9.2	
			Irf7	Interferon regulatory factor 7	11.7	24.7	65.0	
		Cytokine and chemokine signaling	STAT1	Signal transducer and activator of transcription 1	8.4	11.8	33.9	
			Stat2	Signal transducer and activator of transcription 2	1.8	0	6.3	
			Nmi	N-myc (and Stat1) interactor	2.0	2.8	9.7	
		PML body	Pml	Promyocytic leukemia	9.5	0	11.3	
			Sp100	Nuclear antigen Sp100	0	35.5	81.1	
		Endopeptidase	Antigen presentation	Psmb8	Proteasome (prosome, macropain) subunit, beta type 8 (large multifunctional protease 7)	7.2	14.3	92.3
				Psmb9	Proteasome (prosome, macropain) subunit, beta type 9 (large multifunctional protease 2)	1.3	5.2	27.3
				Ctss	Cathepsin C	1.5	1.6	4.2
	MHC class II presentation	Antigen presentation	Ctss					
	MHC class I presentation	Antigen presentation	H2-K1	Histocompatibility 2, K1, K region	1.5	3.5	19.6	
			H2-T10	Histocompatibility 2, T region locus 10	2.4	0	21.7	
			H2-T23	Histocompatibility 2, T region locus 23	4.3	0	64.7	
			B2M	Beta-2 microglobulin	2.6	3.7	9.6	
			Fcg	Fc receptor, IgG, high affinity 1	1.9	0	17.1	
			Fcer1g	Fc receptor, IgE, high affinity 1 gamma polypeptide	0	1.9	9.4	
			Tapbp	TAP binding protein	1.9	0	12.7	
	GTP binding	Interferon induced	Gbp2	Guanylate nucleotide binding protein 2	8.9	53.6	111.4	
			Gbp3	Guanylate nucleotide binding protein 3	5.2	14.2	36.8	
			Gbp6	Guanylate nucleotide binding protein 6	6.5	10.1	32.9	
			Irgm1	Immunity related GTPase family M1	7.2	8.8	41.4	
			Mpa2l	Macrophage activation like 2	9.2	13.4	83.6	
			Igtp	Interferon gamma induced GTPase	15.6	18.5	163.1	
	GTPase	Interferon induced	Mx1	Myxovirus (influenza virus) resistance 1	7.0	0	84.2	
			Mx2	Myxovirus (influenza virus) resistance 2	31.9	38.1	129.7	
			Iigp1	Interferon inducible GTPase 1	25.6	22.2	295.5	
			Iigp2	Interferon inducible GTPase 2	9.7	10.7	96.2	
			Tgtp	T cell specific GTPase	16.9	31.3	508.4	
			Oas1b		5.3	0	24.9	
Oas1g			2'-5'oligoadenylate synthetase 1b	5.8	12.4	33.7		
Oas2			2'-5'oligoadenylate synthetase 1g	2.8	0	20.7		
Oas1			2'-5'oligoadenylate synthetase 2	3.3	0	29.0		
Oasl2			2'-5'oligoadenylate synthetase-like 1	32.9	80.3	259.6		
RNA binding	Interferon induced	Oasl2	2'-5'oligoadenylate synthetase-like 2					
		Ifit1	Interferon-induced protein with tetraco peptide repeats 1	46.6	104.9	233.9		
		Ifit2	Interferon-induced protein with tetraco peptide repeats 2	2.7	0	25.8		
DNA binding	Interferon induced	Ifit1	Interferon-induced protein with tetraco peptide repeats 1	46.6	104.9	233.9		
		Ifit2	Interferon-induced protein with tetraco peptide repeats 2	2.7	0	25.8		

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			Ifit3	Interferon-induced protein with tetraco peptide repeats 3	14.6	25.2	127.7	
	Helicase	Interferon induced	Ifih1	Interferon-induced protein with helicase C domain 1	6.7	9.7	45.1	
			Interferon type I biosynthetic process	Dhx58	DEXH (Asp-glu-X-His) box polypeptide 58	7.7	27.8	49.0
				Ddx58	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58	4.9	0	11.9
	Protein binding	NC	Ifi203	Interferon-activated gene 203	0	3.3	15.7	
				Pyhin1	Pyrin and HIN domain family, member 1	5.1	0	81.5
	Receptor activity	Tlr signaling	TLR3	Toll-like receptor 3	2.5	0	8.8	
				Interferon induced	Ifitm1	Interferon-induced transmembrane protein 1	0	1.9
			Ifitm3	Interferon-induced transmembrane protein 3	6.3	9.3	20.9	
		Cell adhesion	Lgals9	Lectin, galactosidase-binding, soluble 9	4.4	6.1	22.6	
			Lgals3bp	Lectin, galactosidase-binding, soluble, 3 binding protein	8.2	12.9	34.5	
			Icam1	Intercellular adhesion molecule 1	0	2.2	10.0	
		NC	Itgb2	Integrin beta 2	0	1.3	7.7	
			Ly6e	Lymphocyte antigen 6 complex, locus e	1.6	2.5	5.0	
	Exonuclease	Interferon induced	Isg20	Interferon-stimulated protein	4.5	0	33.6	
	Kinase	Interferon induced	Eif2ak2	Eukaryotic translation initiation factor 2-alpha kinase 2	3.3	0	10.8	
	Cytokine/chemokine	Chemotaxis	Ccl12	Chemokine (C-C motif) ligand 12	0	20.5	53.2	
				Cxcl10	Chemokine (C-X-C motif) ligand 10	23.1	0	248.8
			Cxcl11	Chemokine (C-X-C motif) ligand 11	7.5	0	198.6	
		Apoptosis	Tnfsf10	Tumor necrosis factor (ligand) superfamily, member 10	1.7	2.1	10.8	
	Peptidase	Complement activation	C2	Complement component 2 (within H2-S)	0	3.5	10.7	
	Phosphate transport	Complement activation	C1qb	Complement component 1, q subcomponent, beta polypeptide	1.8	0	7.5	
				C1qa	Complement component 1, q subcomponent, alpha polypeptide	1.6	1.9	5.2
				C1qc	Complement component 1, q subcomponent, C chain	1.5	2.1	7.9
	Complement binding	Complement activation	Serping1	Serine (or cysteine) peptidase inhibitor, clade G member 1	0	1.8	18.3	
	Poly-A-polymerase	NC	Parp 9	Poly (ADP-ribose) polymerase family, member 9	8.3	11.7	46.4	
	Catalytic activity	Virus response	Rsad2	Radical S-adenosyl methionine domain containing 2	6.7	0	70.8	
	NC	IFN induced	Ifi44	Interferon-induced protein 44	17.5	33.4	152.2	
		Interferon induced	Ifi47	Interferon gamma inducible protein 47	7.7	11.9	154.9	
	NC	NC	Ifi202b	Interferon-activated 202B	21.9	35.5	353.8	
	NC	Natural killer cell mediated cytotoxicity	Plac8	Placenta specific 8	6.1	17.6	93.1	
				Cd48	CD48 antigen	0	1.9	8.4
			Tyrobp	TYRO protein tyrosine kinase binding protein	0	1.4	3.2	
Defense response	GPI anchored	Cell proliferation	Ly6a	Lymphocyte antigen 6 complex, locus A	4.3	14.7	45.5	
	Macrophage associated	NC	Mpeg1	Macrophage expressed gene 1	1.1	0	8.9	
	Lysozyme activity	Defense response to bacteria	Lyz2	Lysozyme 2	2.0	2.3	14.5	
			Lyz1	Lysozyme 1	2	2.9	15.2	

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Ubiquitin cycle	Ubiquitin ligase	Interferon induced NC Protein modification	Dtx31	Deltrex 3-like ( <i>Drosophila</i> )	3.9	5.9	21.6
			Herc5	Hect domain and RLD5	2.9	0	25.9
			Trim25	Tripartate motif protein 25	2.1	2.6	7.5
			Trim21	Tripartate motif protein 21	3.2	2.5	12.7
			Ube2L6	Ubiquitin conjugating enzymeE2L6	0	2.6	15.7
	Ubiquitin activating Peptidase	Protein modification Interferon induced NC	Ube1l		4.8	2.9	24.4
Signal transduction	Receptor	NC	Ms4a4d	Membrane-spanning 4-domains, subfamily A, member 4d	1.6	3.2	24.3
			Ms4a4c	Membrane-spanning 4-domains, subfamily A, member4c	0	11.2	116.6
			Ms4a4b	Membrane-spanning 4-domains, subfamily A, member 4b	2.1	2.2	25.0
	Transmembrane receptor protein tyrosine kinase activity	NC	Pik3ap1	Phosphoinositide 3 kinase adaptor protein 1	1.5	2.1	12.6
Chaperone Metabolism	ATP binding	Protein folding	Tor3a	Torsin family 3, member A	2.8	0	15.9
	Phospholipase	Lipid catabolism	Pld4	Phospholipase D family member 4	0	1.6	4.2
	Acyltransferase activity	Lipid metabolism	Lpcat1	Lysophosphatidylcholine acetyltransferase 1	-2.2	0	0
domain containing NC	Inflammatory response	Protein binding	Apoptosis	Pycard	PYD and CARD		
	1.6	0	8.4				
	P53 signal transduction	Apoptosis	Nupr1	Nuclear protein 1	0	1.6	3.1
	Poly-A-polymerase	Transcription regulation NC	Parp14		5.6	6.8	47.7
	Transcriptional regulation	IL6 biosynthetic process	Parp12	CCAAT enhancer binding protein	4.6	6.3	22.4
	Apoptosis	Interferon induced	Cebpb (C/EBP), beta XAF-1	XIAP associated factor 1	0	1.4	4.7
	Caspase activity	Apoptosis	Casp 4	Casapse 4	14.1	17.8	65.3
	P53 signaling	Apoptosis	Casp 5	Shisa homolog 5	0	48.3	198.4
	Ras protein signal transduction	Cytokine-cytokine receptor interaction	Csf1	Colony-stimulating factor 1	1.4	0	2.8
	Helicase	NC	Mov10	Moloney leukemia virus 10	0	2.0	4.1
	Protein transport	NC	Mitd1	RMIT, microtubule interacting and transport, domain containing 1	1.3	0	3.3
	GTP binding	G protein coupled receptor protein signaling	Tgm2	Transglutaminase 2, C polypeptide	1.9	0	4.7
	GTPase	Small GTPase mediated signal transduction	Rac2	Ras-related C3 botulinum substrate 2	0	1.2	8.6
	GTP cyclohydrolase I activity	Neuromuscular process	Gch1	GTP cyclohydrolase 1	0	1.5	4.4
	Ferroxidase activity	Oxidation/reduction	Cp	Ceruloplasmin	0	1.5	5.0
Iron ion binding	Oxidation/reduction	Cyba	Cytochrome b-245, alpha polypeptide	0	1.7	6.4	
Transport Receptor	NC	Apod Rtp4	Apolipoprotein D Receptor transporter protein 4	0	1.4	4.5	
				1.8	2.9	7.5	
				15.3	32.3	58.7	

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General function	Specific function	Biological process	Gene symbol	Description	3D	6D	8D
	Protein/nucleic acid binding	Interferon-induced Interferon induced NC	Trim 34	Tripartite motif protein 34	2.3	0	7.7
			Trim 30	Tripartite motif protein 30	3.4	2.8	23.4
			Phf20l1	PHD finger protein 20-like 1	3.0	4.3	13.2
	Actin binding	NC	Brd4	Bromodomain containing 4	12.0	21.9	114.3
			Plec1	Plectin 1	2.5	0	23.5
			Lcp-1	Lymphocyte cytosolic protein 1	0	1.8	6.8
		Regulation of actin cytoskeleton	Arpc1b	Actin-related protein 2/3 complex, subunit 1b	0	1.3	2.9
	NC	Interferon induced	Ifi35	Interferon-induced protein 35	6.2	9.7	56.1
		Cell-cell adhesion	Itgal	Integrin alpha L	0	1.7	4.3
		NC	CD52	CD52 antigen	0	4.1	27.1
			Epsti1	Epithelial stromal interaction 1 (breast)	7.2	1.9	31.1
			D12Ert647e	DNA segment, Chr 12, ERATO Doi 668 expressed	3.2	4.3	3.4
			Samd9l	Sterile alpha motif domain containing 9 like	2.6	3.5	21.7
			Phf11	PHD finger protein 11	4.8	0	39.3
			Slfn2	Schlafen 2	4.0	0	27.6
			Slfn8	Schlafen 8	6.9	0	56.7
			Rnf213	Ring finger protein 213	4	1.4	24.9
			RIKEN cDNA 9830115L13 gene	3.6	4.2	18.0	
			RIKEN cDNA	0610037M15Rik	3.2	20.3	
				0	2.6	2.8	9.7
			BC006779	0610037M15 gene cDNA sequence BC006779			
			Ddx60	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60	17.4	9.6	54.6
				Expressed sequence	1.5	0	5.0
			Al413194	Al413194	8.5	11.4	33.7
				Predicted gene			
			100042856	100042856			
				Predicted gene 677168	15.5	49.8	167.3
				Transmembrane protein	0	2.4	8.5
			677168 Tmem140	140			
				Apolipoprotein L9a	0	4.6	35.9
			Apol 9a	NLR family CARD containing 5	0	4.6	55.3
			Nlrc5	Probe set ID:1438027	4.8	3.8	33.0
Probe set ID: 1442201	2.4						
Probe set ID: 1447213	0	5.6		20.2			
		3.2		6.7			

<sup>a</sup>Identified genes were differentially regulated in the brains of reovirus infected mice at day 3 and/or day 6 post infection. Probe sets from Table 1 representing the same gene were combined and the fold increases for these probe sets were averaged. All genes that were not differentially regulated by at least 2-fold at any day post infection were excluded from the table. All identified differentially regulated genes (except one) were up-regulated in reovirus-infected, compared to mock-infected, animals, with a false detection rate (FDR) of 0.1 and  $P < .002$ . These genes were also up-regulated at day 8 post infection.