

Figure S1

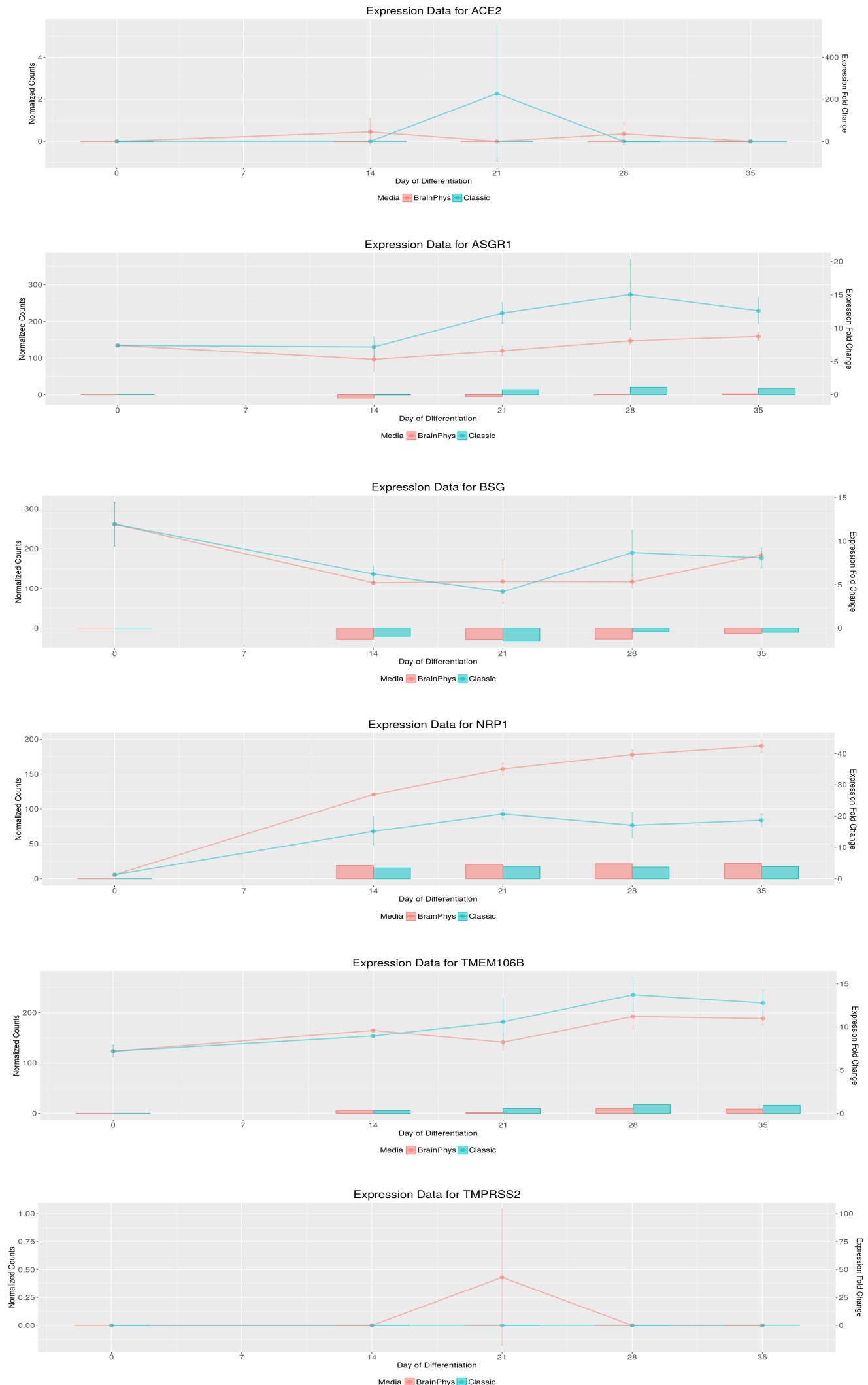


Figure S2

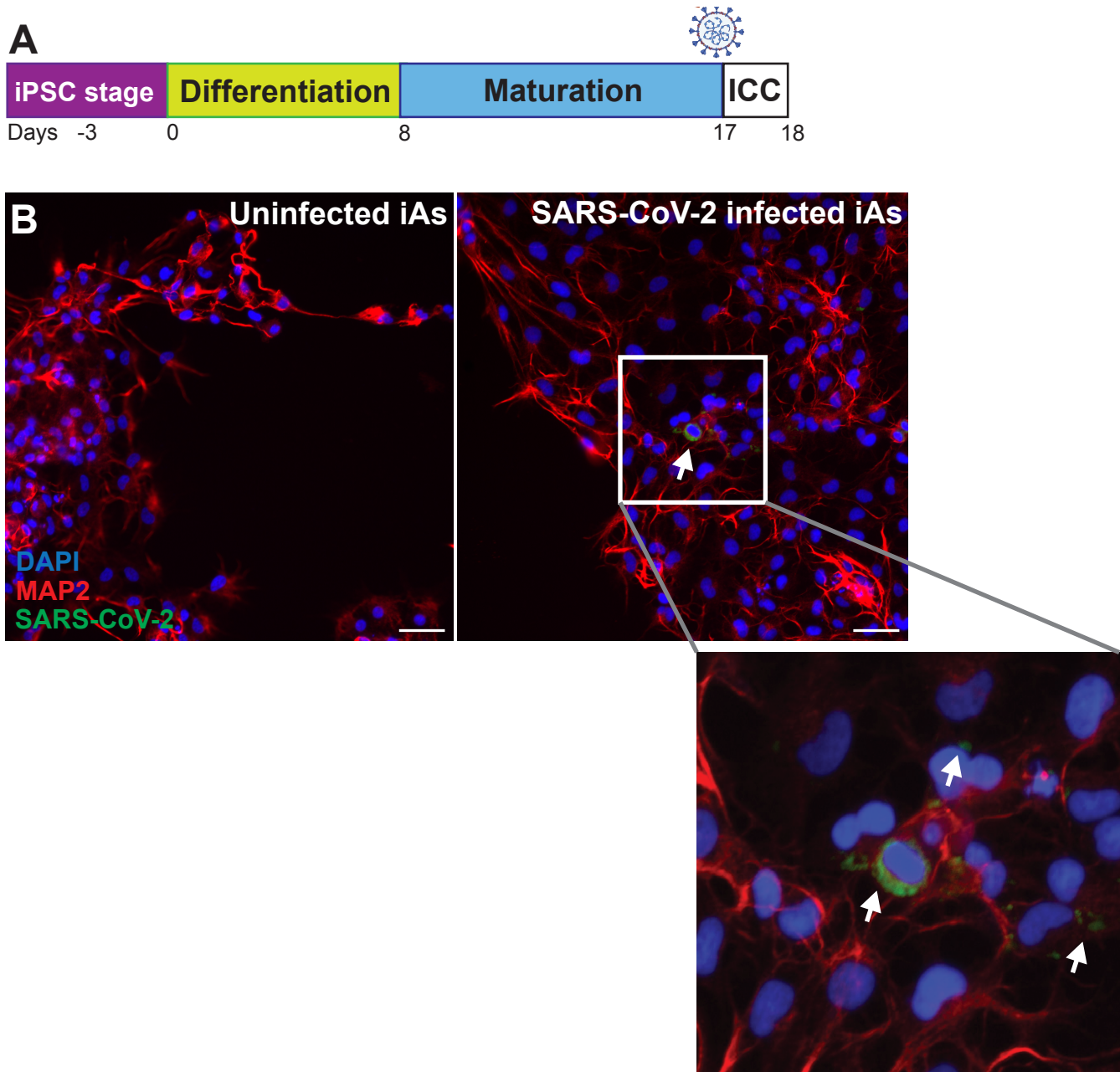


Figure S3

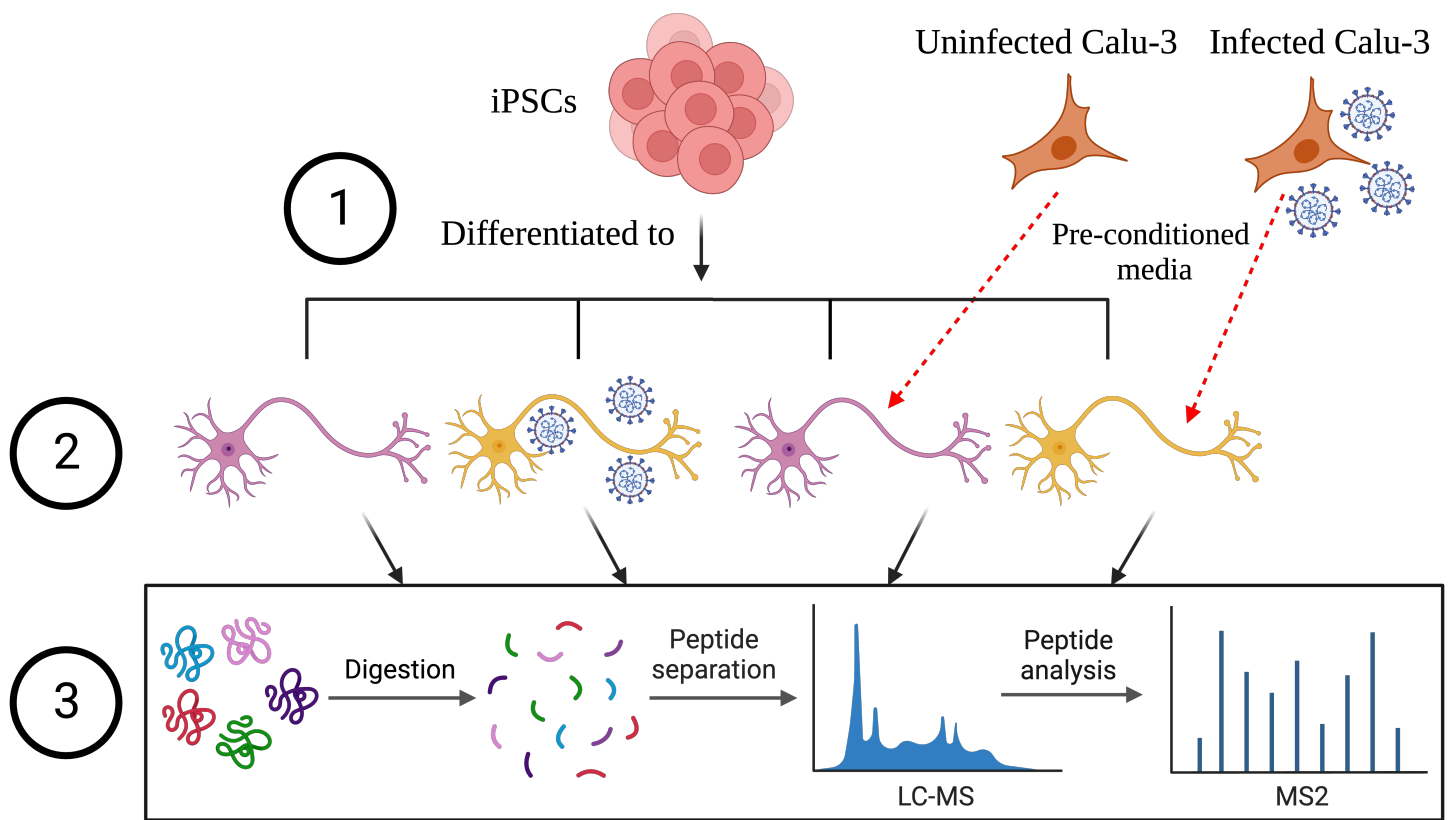


Figure S4

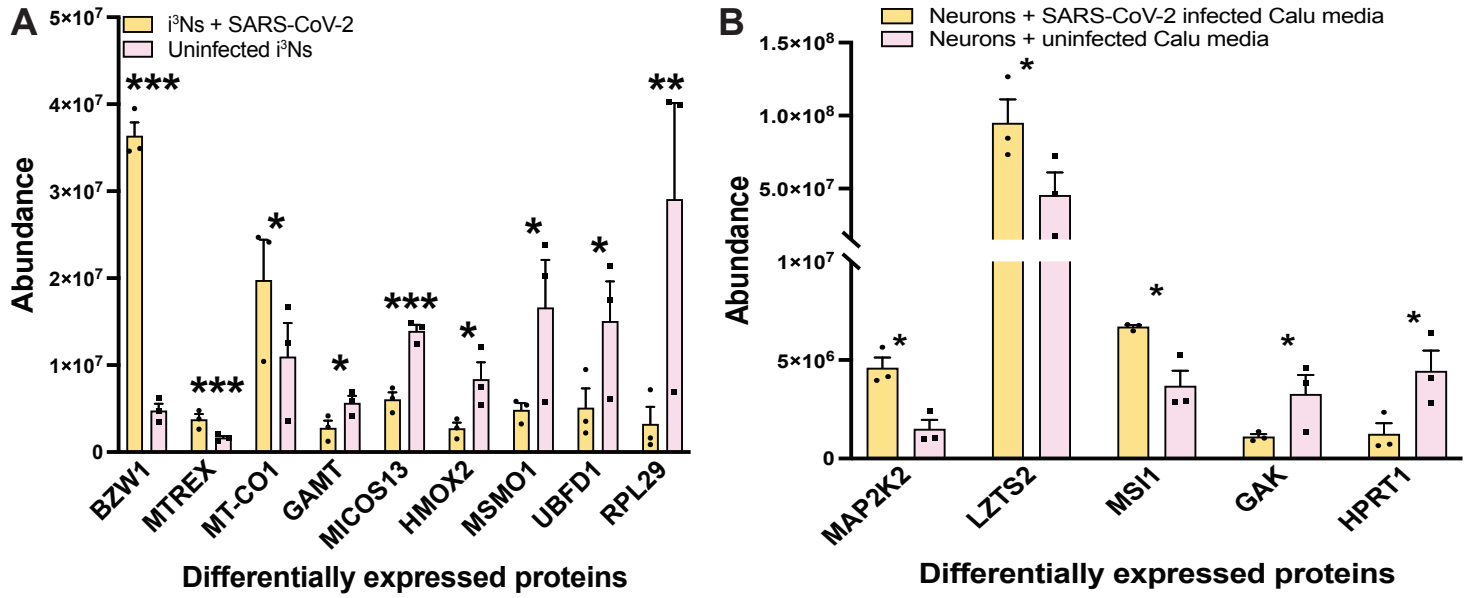
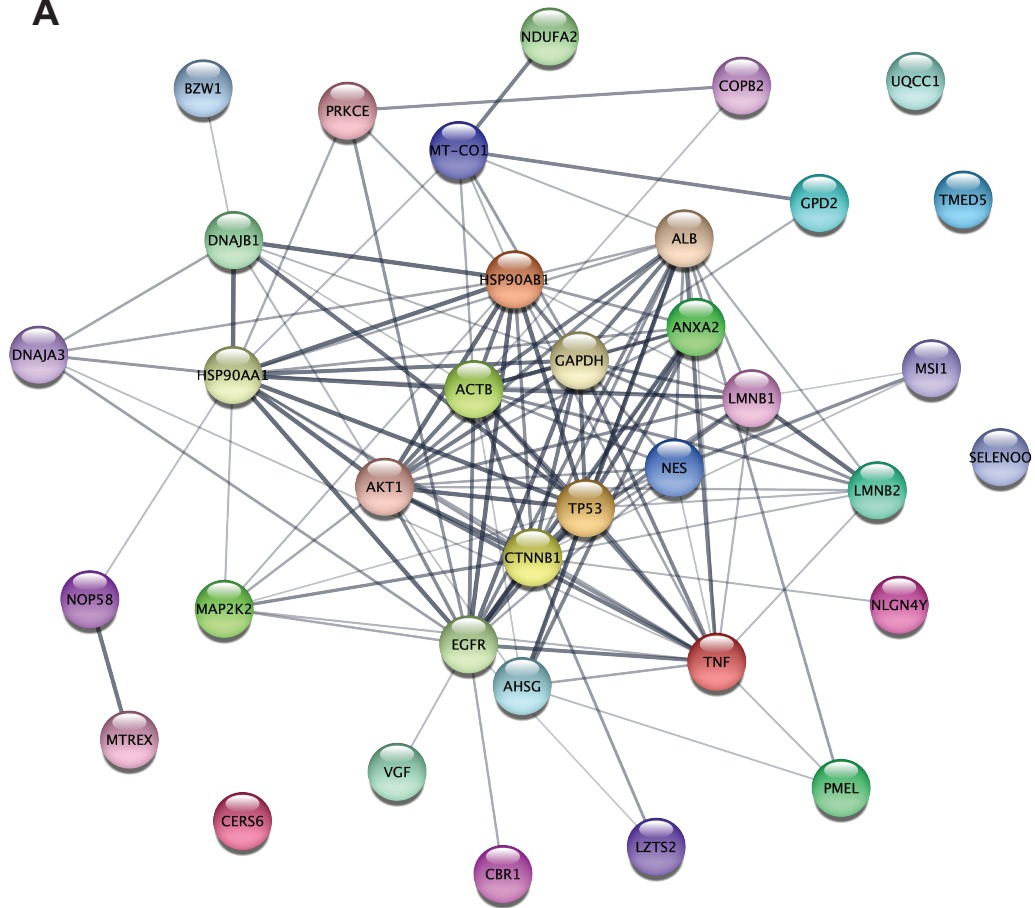


Figure S5

A



B

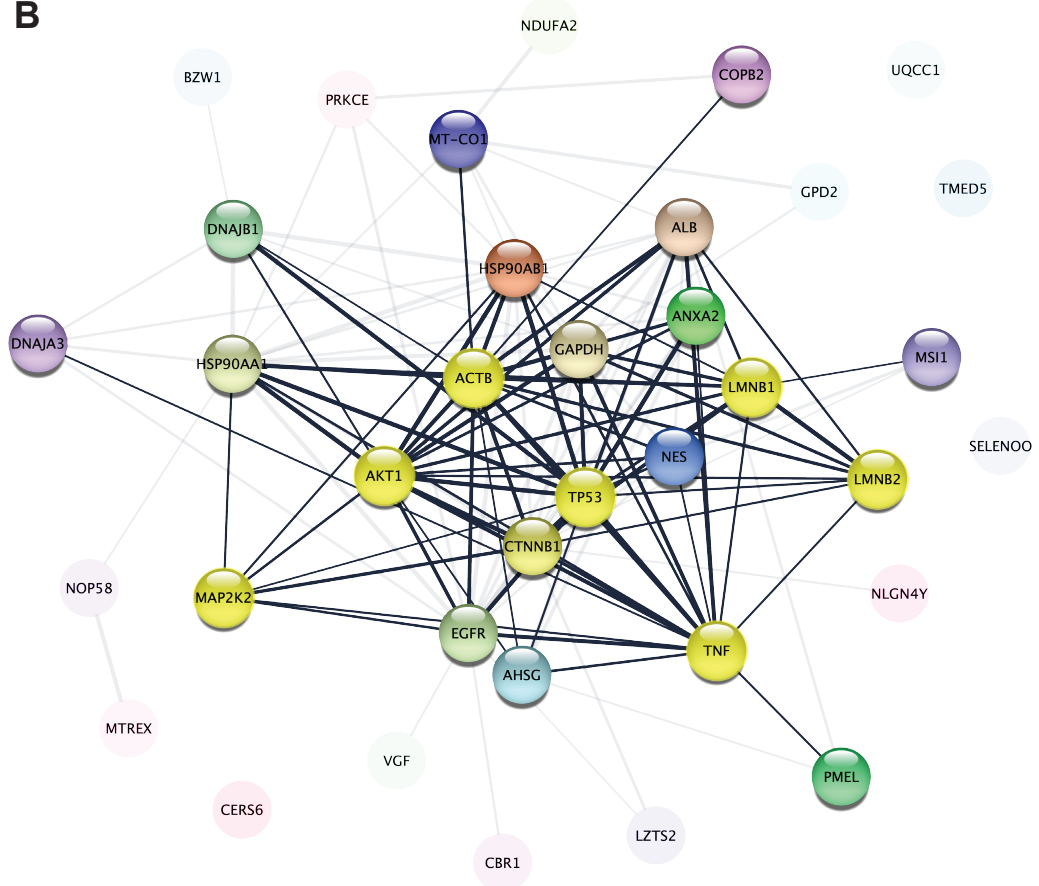
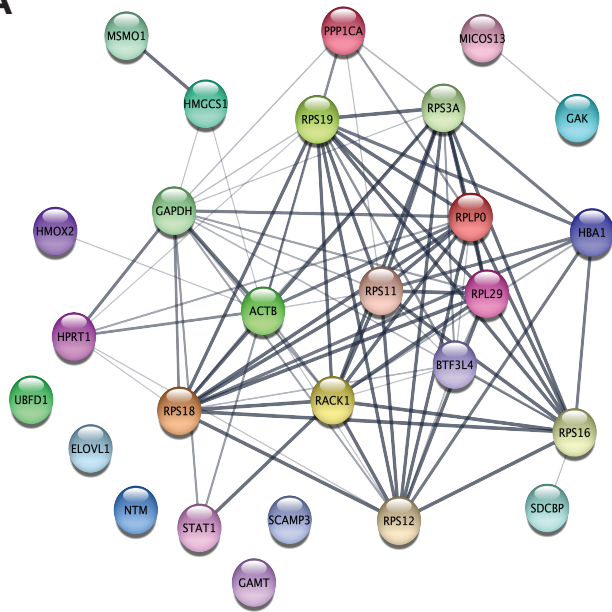
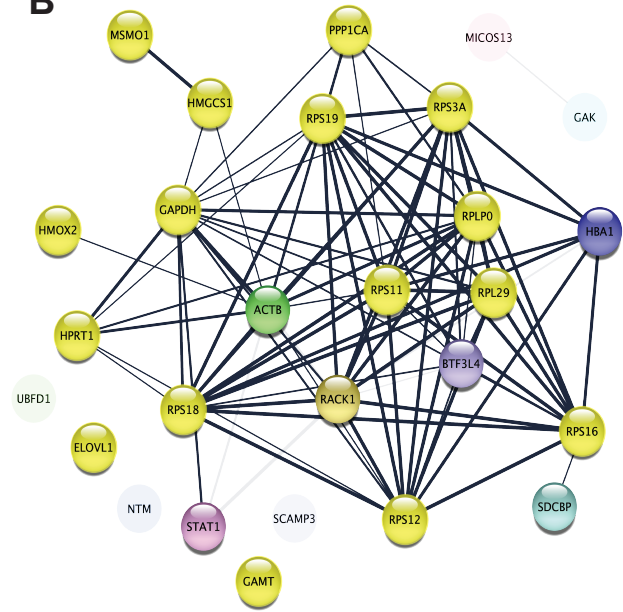


Figure S6

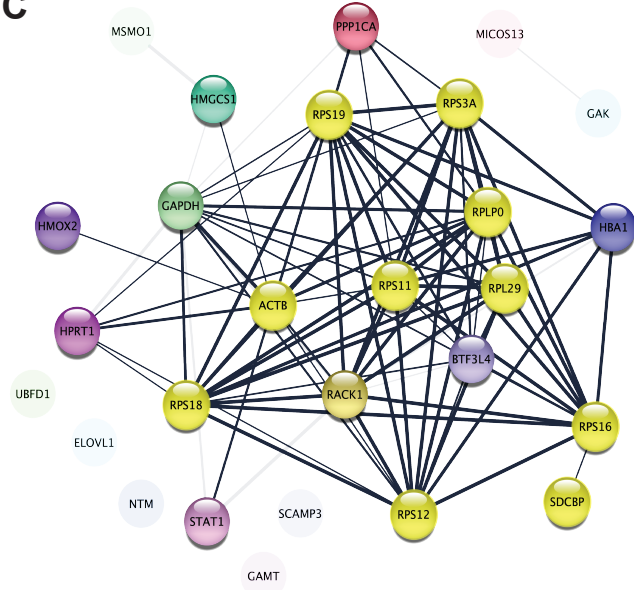
A



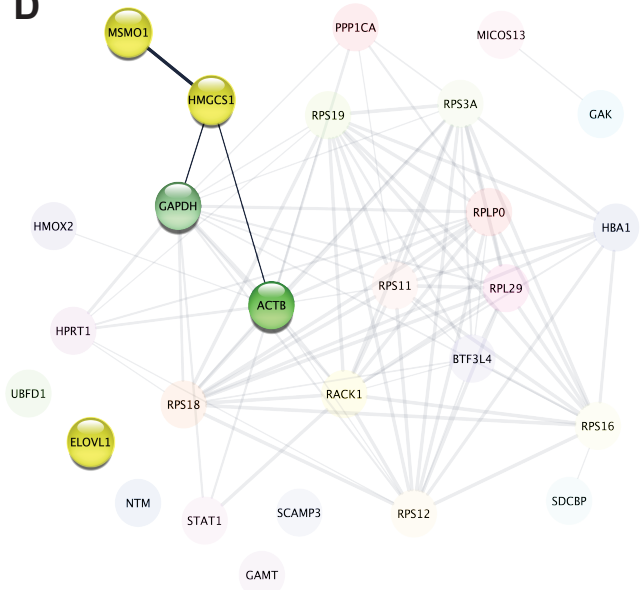
B



C



D



E

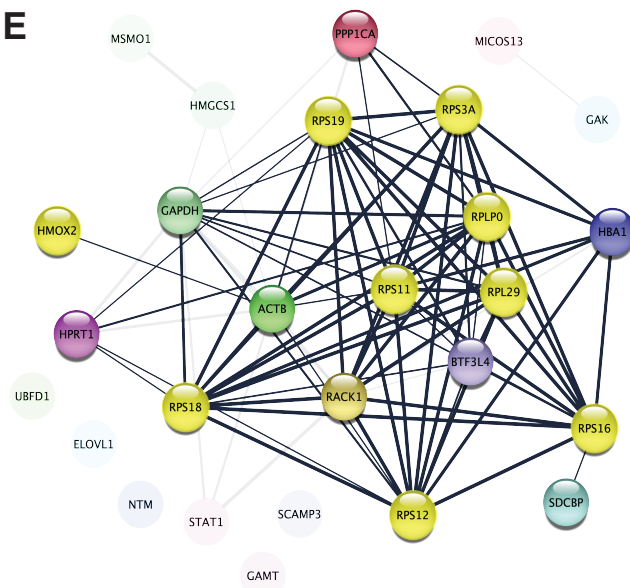


Table S1

Gene Symbol	Accession	Description	Coverage [%]	# Peptides	# AAs	MW [kDa]	Abundances (Neurons infected 10MOI),Exp_1	Abundances (Neurons infected 10MOI),Exp_2	Abundances (Neurons infected 10MOI),Exp_3	Abundances (Neurons uninfected, Exp_Rep_1)	Abundances (Neurons uninfected, Exp_Rep_2)	Abundances (Neurons uninfected, Exp_Rep_3)	P-VALUE (Neurons infected 10MOI) / (Neurons uninfected)	Fold change (Neurons infected 10MOI) / (Neurons uninfected)	Log2 Fold change (Neurons infected 10MOI) / (Neurons uninfected)
BZW1	Q7L1Q6	Basic leucine zipper and W2 domain-containing protein 1 OS=Homo sapiens OX=9606 GN=BZW1 PE=1 SV=1	9	2	419	48	39486128.3	34616019.3	34919740.4	6201765.6	4672663.43	3410889.53	0.000	8.004	2.973
MTREX	P42285	Exosome RNA helicase MTR4 OS=Homo sapiens OX=9606 GN=MTREX PE=1 SV=3	2	1	1042	117.7	4789450.76	2637481.57	3817221.27	2032091.45	1271455.72	1628985.98	0.000	2.258	1.173
MT-CO1	P00395	Cytochrome c oxidase subunit 1 OS=Homo sapiens OX=9606 GN=MT-CO1 PE=1 SV=1	6	1	513	57	24709217.6	10420581	24133118.9	16716230.4	3621365.45	12558610.7	0.023	2.093	1.007
VGF	O15240	Neurosecretory protein VGF OS=Homo sapiens OX=9606 GN=VGF PE=1 SV=2	6	2	615	67.2	7761896.05	7967594.75	9547882.34	4643209.68	3879001.67	4251967.79	0.002	1.991	0.983
NDUFA2	O43678	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 2 OS=Homo sapiens OX=9606 GN=NDUFA2 PE=1 SV=3	21	1	99	10.9	2672175.63	2117426.52	5029526.18	1019275.27	1192451.96	3332394.72	0.017	1.969	0.937
ANXA2	P07355	Annexin A2 OS=Homo sapiens OX=9606 GN=ANXA2 PE=1 SV=2	44	12	339	38.6	34276527.5	30773273.7	38066348	17168255.5	18478491.1	19360306.4	0.000	1.876	0.907
PRKCE	Q02156	Protein kinase C epsilon type OS=Homo sapiens OX=9606 GN=PRKCE PE=1 SV=1	3	1	737	83.6	210828543	310165728	291681870	139481579	178434549	127263210	0.008	1.847	0.867
GPD2	P43304	Glycerol-3-phosphate dehydrogenase, mitochondrial OS=Homo sapiens OX=9606 GN=GPD2 PE=1 SV=3	8	4	727	80.8	11413484.1	12591676.2	13149524.1	7869757.48	5511900.84	9462593.51	0.033	1.708	0.733
NLGN4Y	B4DH13	Neuroigin-4, Y-linked OS=Homo sapiens OX=9606 GN=NLGN4Y PE=1 SV=1	3	2	836	94.1	17819041.2	16585098.5	20763161.2	10074374.5	8235224.78	16576860.7	0.025	1.679	0.717
UQCCL1	Q9NVA1	Ubiquinol-cytochrome-c reductase complex assembly factor 1 OS=Homo sapiens OX=9606 GN=UQCCL1 PE=1 SV=3	3	1	299	34.6	3620803.88	6643312.84	4697289.26	2842521.23	3520293.11	2526488.8	0.018	1.673	0.720
NES	P48681	Nestin OS=Homo sapiens OX=9606 GN=NES PE=1 SV=2	2	2	1621	177.3	15177266.6	17211570.7	13043688.3	8992645.74	11069650.8	8018230.73	0.000	1.623	0.700
CBR1	P16152	Carbonyl reductase [NADPH] 1 OS=Homo sapiens OX=9606 GN=CBR1 PE=1 SV=3	5	1	277	30.4	14453136.2	8911700.71	13041726.2	9058721.79	6342068.59	7939479.53	0.001	1.548	0.627
TMED5	Q9Y3A6	Transmembrane emp24 domain-containing protein 5 OS=Homo sapiens OX=9606 GN=TMED5 PE=1 SV=1	13	2	229	26	52730652.6	43547293.2	61160430.4	28972625.5	34355348.2	40921677.9	0.017	1.528	0.593
STAT1	A0A669KB52	Signal transducer and activator of transcription OS=Homo sapiens OX=9606 GN=STAT1 PE=1 SV=1	3	1	636	74.2	1934368.47	4101113.5	4472186.42	4390522.16	5330106.64	7203409.25	0.032	0.610	-0.750
ELOVL1	Q9BW60	Elongation of very long chain fatty acids protein 1 OS=Homo sapiens OX=9606 GN=ELOVL1 PE=1 SV=1	5	1	279	32.6	680999.535	959414.616	644299.681	1371777.95	1499629.6	1056888.77	0.002	0.582	-0.787
NTM	F8W8Y1	Neurotrimin OS=Homo sapiens OX=9606 GN=NTM PE=1 SV=1	22	2	179	19.7	3234971.77	4522111.14	7371502.5	6049996.93	10005356.2	11273020	0.005	0.547	-0.887
HBA1	P69905	Hemoglobin subunit alpha OS=Homo sapiens OX=9606 GN=HBA1 PE=1 SV=2	28	3	142	15.2	144015582	149574201	176545366	234202829	325328369	389003680	0.002	0.510	-0.987
GAMT	A0A1W2PR3	Guanidinoacetate N-methyltransferase OS=Homo sapiens OX=9606 GN=GAMT PE=1 SV=1	7	1	213	23.8	1247650.41	2886592.4	4177745.19	4131471.03	5866569.04	6942449.91	0.017	0.465	-1.160
MICOS13	A0A140TA86	MICOS complex subunit MIC13 OS=Homo sapiens OX=9606 GN=MICOS13 PE=1 SV=1	37	2	140	15.4	4530397.16	7385723.86	6197023.83	12451770	14867775.4	14385952.6	0.001	0.431	-1.230
HMOX2	I3L4P8	Heme oxygenase 2 (Fragment) OS=Homo sapiens OX=9606 GN=HMOX2 PE=1 SV=8	12	1	130	15.1	3823451.9	2795420.41	1530055.18	5459667.15	12106288.4	7476229.88	0.044	0.379	-1.637
MSMO1	Q15800	Methylsterol monooxygenase 1 OS=Homo sapiens OX=9606 GN=MSMO1 PE=1 SV=1	5	1	293	35.2	5407125.7	5834836.15	3241866.24	20216718	23768156	5790270.14	0.013	0.357	-1.590
UBFD1	O14562	Ubiquitin domain-containing protein UBFD1 OS=Homo sapiens OX=9606 GN=UBFD1 PE=1 SV=2	4	1	309	33.4	3548875.91	2215916.93	9500912.01	21448638.8	6163848.17	17509686.5	0.030	0.356	-1.653
RPL29	A0A3B3ITT5	60S ribosomal protein L29 OS=Homo sapiens OX=9606 GN=RPL29 PE=1 SV=1	9	1	167	18.5	7178780.24	863801.931	1630011.9	40283875.7	6945582.96	39958680.5	0.006	0.114	-3.373

Table S2

Gene Symbol	Accession	Description	Coverage [%]	# Peptides	# AAs	MW [kDa]	Abundances (Neurons with infected Calu media,Exp_Rep_1	Abundances (Neurons with infected Calu media,Exp_Rep_2	Abundances (Neurons with infected Calu media,Exp_Rep_3	Abundances (Neurons with uninfected Calu media,Exp_Rep_1	Abundances (Neurons with uninfected Calu media,Exp_Rep_2	Abundances (Neurons with uninfected Calu media,Exp_Rep_3	P-VALUE: (Neurons with infected Calu media) / (Neurons with uninfected Calu media)	Fold change (Neurons with infected Calu media) / (Neurons with uninfected Calu media)	Log2 fold change (Neurons with infected Calu media) / (Neurons with uninfected Calu media)
MAP2K2	P36507	Dual specificity mitogen-activated protein kinase kinase 2 OS=Homo sapiens OX=9606 GN=MAP2K2 PE=1 SV=1	5	1	400	44.4	5653888.67	4159245.55	3970646.21	1042435.62	1003634.73	2434397.73	0.030	3.733	1.733
LZTS2	Q9BRK4	Leucine zipper putative tumor suppressor 2 OS=Homo sapiens OX=9606 GN=LZTS2 PE=1 SV=2	2	1	669	72.7	84517369.1	73340460	126646442	46195665	17830094.2	72053187.1	0.036	2.567	1.240
MSI1	Q43347	RNA-binding protein Musashi homolog 1 OS=Homo sapiens OX=9606 GN=MSI1 PE=1 SV=1	9	1	362	39.1	6804254.22	6760166.56	6476667.35	5243876.05	2846748.3	2934859.56	0.028	1.960	0.923
DNAJA3	Q96EY1	DnaJ homolog subfamily A member 3, mitochondrial OS=Homo sapiens OX=9606 GN=DNAJA3 PE=1 SV=2	5	1	480	52.5	6462586.9	5646233.87	2311836.1	2785893.25	2631984.59	1653034.78	0.015	1.955	0.930
SELENOO	Q9BVL4	Protein adenyltransferase SelO, mitochondrial OS=Homo sapiens OX=9606 GN=SELENOO PE=1 SV=3	6	2	669	73.4	2876831.92	5579663.14	3970370.77	1602161.92	3748370.02	1861917.56	0.005	1.806	0.833
CERS6	Q6ZMG9	Ceramide synthase 6 OS=Homo sapiens OX=9606 GN=CERS6 PE=1 SV=1	3	1	384	44.9	1388753.52	2674939.61	1714841.32	1079409.37	1094769.84	1026007.63	0.042	1.800	0.797
NOP58	Q9Y2X3	Nucleolar protein 58 OS=Homo sapiens OX=9606 GN=NOP58 PE=1 SV=1	16	6	529	59.5	8522768.54	15802475.4	8839014.1	3745806.47	10225516.4	6879113.32	0.041	1.702	0.727
VGf	O15240	Neurosecretory protein VGf OS=Homo sapiens OX=9606 GN=VGf PE=1 SV=2	6	2	615	67.2	5461131.39	8201110.46	6655932.54	3288199.73	6215759.67	3186210.25	0.019	1.690	0.730
COPB2	H0Y938	Coatomer subunit beta' OS=Homo sapiens OX=9606 GN=COPB2 PE=1 SV=2	5	2	898	101.5	13372858.1	11447768.9	12473261.2	9689714.9	6522807.11	7661504.21	0.003	1.588	0.657
DNAJB1	M0R080	DnaJ homolog subfamily B member 1 (Fragment) OS=Homo sapiens OX=9606 GN=DNAJB1 PE=1 SV=1	10	1	183	20.5	12334044.1	14624292	11305948.3	7223190.42	9347241.25	7776859.5	0.001	1.576	0.653
LMNB1	P20700	Lamin-B1 OS=Homo sapiens OX=9606 GN=LMNB1 PE=1 SV=2	41	19	586	66.4	84645294.1	90119621.9	81956084.5	48411104.8	51891289.9	66826146	0.021	1.570	0.633
AHSG	P02765	Alpha-2-HS-glycoprotein OS=Homo sapiens OX=9606 GN=AHSG PE=1 SV=2	7	4	367	39.3	6415775.49	6524458.67	10641872	4550059.88	5310860.46	5296049.54	0.046	1.549	0.603
LMNB2	Q03252	Lamin-B2 OS=Homo sapiens OX=9606 GN=LMNB2 PE=1 SV=4	17	9	620	69.9	35138942.9	33051307.3	33791618	17661152.9	24990270.3	25961846.2	0.042	1.538	0.590
PMEL	F8W1D1	Melanocyte protein PMEL (Fragment) OS=Homo sapiens OX=9606 GN=PMEL PE=1 SV=1	7	1	299	32.3	12761519.1	11846212.7	7162404.16	9120020.87	6392801.43	5712367.16	0.028	1.502	0.567
SCAMP3	O14828	Secretory carrier-associated membrane protein 3 OS=Homo sapiens OX=9606 GN=SCAMP3 PE=1 SV=3	14	3	347	38.3	13719353.4	9866450.06	10406195.5	16669116.1	17604646.3	17491095.8	0.023	0.659	-0.623
PPP1CA	P62136	Serine/threonine-protein phosphatase PP1-alpha catalytic subunit OS=Homo sapiens OX=9606 GN=PPP1CA PE=1 SV=1	41	9	330	37.5	11116841.8	11819417.5	9173960.17	18666180.7	16408816.3	15277357	0.002	0.639	-0.653
BTF3L4	Q96K17	Transcription factor BTF3 homolog 4 OS=Homo sapiens OX=9606 GN=BTF3L4 PE=1 SV=1	36	4	158	17.3	16903959.7	16751032	18495287.3	28894466	23514097.6	31721928.4	0.002	0.627	-0.680
HMGCS1	Q01581	Hydroxymethylglutaryl-CoA synthase, cytoplasmic OS=Homo sapiens OX=9606 GN=HMGCS1 PE=1 SV=2	22	9	520	57.3	18809078.4	21354662.2	18944774.2	37129943.3	33238420.8	31048987.9	0.002	0.586	-0.777
SDCBP	O00560	Syntenin-1 OS=Homo sapiens OX=9606 GN=SDCBP PE=1 SV=1	21	3	298	32.4	10957080.5	9677270.18	8881010.4	24410310.5	19712278.3	22097586.7	0.000	0.447	-1.170
GAK	O14976	Cyclin-G-associated kinase OS=Homo sapiens OX=9606 GN=GAK PE=1 SV=2	2	1	1311	143.1	1366859.65	1036911.65	905710.775	3859034.64	4592503.73	1349427.39	0.036	0.417	-1.410
HPRT1	P00492	Hypoxanthine-guanine phosphoribosyltransferase OS=Homo sapiens OX=9606 GN=HPRT1 PE=1 SV=2	5	1	218	24.6	725887.506	2345069.58	654027.274	2836594.42	4087270.98	6388343.84	0.048	0.311	-2.020

Table S3

Category	GO	Upregulated pathways in infected i3Ns	LogP	Hits
KEGG Pathway	hsa05208	Chemical carcinogenesis - reactive oxygen species	-4.4	CBR1 MT-CO1 NDUFA2 MAP2K2
GO Biological Processes	GO:0022904	respiratory electron transport chain	-3.9	GPD2 MT-CO1 NDUFA2
KEGG Pathway	hsa04071	Sphingolipid signaling pathway	-3.8	PRKCE MAP2K2 CERS6
KEGG Pathway	hsa04210	Apoptosis	-3.7	LMNB1 MAP2K2 LMNB2
GO Biological Processes	GO:0006091	generation of precursor metabolites and energy	-3.6	GPD2 MT-CO1 NDUFA2 VGF
GO Biological Processes	GO:0022900	electron transport chain	-3.4	GPD2 MT-CO1 NDUFA2
GO Biological Processes	GO:0061024	membrane organization	-3.4	ANXA2 LMNB1 DNAJA3 NLGN4Y LMNB2
GO Biological Processes	GO:0009266	response to temperature stimulus	-3.4	DNAJB1 VGF DNAJA3
GO Biological Processes	GO:1903034	regulation of response to wounding	-3.4	ANXA2 PRKCE MAP2K2
GO Biological Processes	GO:0045333	cellular respiration	-3.2	GPD2 MT-CO1 NDUFA2
GO Biological Processes	GO:0015980	energy derivation by oxidation of organic compounds	-2.8	GPD2 MT-CO1 NDUFA2
KEGG Pathway	hsa05010	Alzheimer disease	-2.4	MT-CO1 NDUFA2 MAP2K2
GO Biological Processes	GO:0007005	mitochondrion organization	-2.2	NDUFA2 DNAJA3 UQCC1
GO Biological Processes	GO:0099536	synaptic signaling	-2.2	PRKCE VGF NLGN4Y
KEGG Pathway	hsa05022	Pathways of neurodegeneration - multiple diseases	-2.1	MT-CO1 NDUFA2 MAP2K2
GO Biological Processes	GO:0050804	modulation of chemical synaptic transmission	-2.1	PRKCE VGF NLGN4Y
GO Biological Processes	GO:0099177	regulation of trans-synaptic signaling	-2.1	PRKCE VGF NLGN4Y
GO Biological Processes	GO:0010638	positive regulation of organelle organization	-2	ANXA2 PRKCE NES
Reactome Gene Sets	R-HSA-9006934	Signaling by Receptor Tyrosine Kinases	-2	PRKCE MAP2K2 VGF

Table S4**Upregulated Biological Processes in infected i3Ns**

	p-value	q-value
Protein Localization To Nuclear Envelope (GO:0090435)	5.82E-05	0.01277448
Nuclear Migration (GO:0007097)	0.000192831	0.01277448
Nuclear Envelope Organization (GO:0006998)	0.000218367	0.01277448
Postsynaptic Membrane Organization (GO:0001941)	0.000218367	0.01277448
Heterochromatin Formation (GO:0031507)	0.000786914	0.03682757
Membrane Assembly (GO:0071709)	0.001109993	0.03775719
Heterochromatin Organization (GO:0070828)	0.001169059	0.03775719
Membrane Organization (GO:0061024)	0.001290844	0.03775719
Nucleus Organization (GO:0006997)	0.001486539	0.03865002
Negative Regulation Of Gene Expression, Epigenetic (GO:0045814)	0.001992369	0.04662145
Positive Regulation Of Cellular Metabolic Process (GO:0031325)	0.002396892	0.05098843
Positive Regulation Of Cytoskeleton Organization (GO:0051495)	0.004708244	0.07917454
Mitochondrial Respiratory Chain Complex Assembly (GO:0033108)	0.006066898	0.07917454
rRNA Metabolic Process (GO:0016072)	0.006198298	0.07917454
Positive Regulation Of Vesicle Fusion (GO:0031340)	0.006483689	0.07917454
Regulation Of Plasma Membrane Repair (GO:1905684)	0.006483689	0.07917454
snoRNA Localization (GO:0048254)	0.006483689	0.07917454
ncRNA Processing (GO:0034470)	0.007438995	0.07917454
rRNA Processing (GO:0006364)	0.007583244	0.07917454
Peptidyl-Serine Autophosphorylation (GO:0036289)	0.009065844	0.07917454
Postsynaptic Membrane Assembly (GO:0097104)	0.009065844	0.07917454
Positive Regulation Of Fibroblast Migration (GO:0010763)	0.009065844	0.07917454
Endoplasmic Reticulum To Golgi Vesicle-Mediated Transport (GO:0006888)	0.009734268	0.07917454
Golgi Ribbon Formation (GO:0090161)	0.010354502	0.07917454

Regulation Of Vesicle Fusion (GO:0031338)	0.010354502	0.07917454
Vitamin K Metabolic Process (GO:0042373)	0.010354502	0.07917454
Cyclooxygenase Pathway (GO:0019371)	0.010354502	0.07917454
Presynaptic Membrane Assembly (GO:0097105)	0.010354502	0.07917454
Protein Localization To Nucleus (GO:0034504)	0.010900111	0.07917454
Quinone Metabolic Process (GO:1901661)	0.011641548	0.07917454
Negative Regulation Of Sodium Ion Transmembrane Transport (GO:1902306)	0.011641548	0.07917454
Postsynapse Assembly (GO:0099068)	0.011641548	0.07917454
Presynaptic Membrane Organization (GO:0097090)	0.011641548	0.07917454
Negative Regulation Of Inclusion Body Assembly (GO:0090084)	0.012926986	0.07917454
Regulation Of Inclusion Body Assembly (GO:0090083)	0.012926986	0.07917454
Positive Regulation Of Protein Depolymerization (GO:1901881)	0.012926986	0.07917454
Negative Regulation Of Sodium Ion Transmembrane Transporter Activity (GO:2000650)	0.012926986	0.07917454
Regulation Of Cytoplasmic Transport (GO:1903649)	0.014210816	0.07917454
Regulation Of Stress-Activated Protein Kinase Signaling Cascade (GO:0070302)	0.014210816	0.07917454
Mitochondrial Respiratory Chain Complex III Assembly (GO:0034551)	0.014210816	0.07917454
Respiratory Chain Complex III Assembly (GO:0017062)	0.014210816	0.07917454
Presynapse Organization (GO:0099172)	0.014210816	0.07917454
Negative Regulation Of Receptor Internalization (GO:0002091)	0.016773662	0.08987931
Ribosome Biogenesis (GO:0042254)	0.01716994	0.08987931
Peptidyl-Serine Phosphorylation (GO:0018105)	0.017800851	0.08987931
Membrane Raft Organization (GO:0031579)	0.018052682	0.08987931
Neuron Cell-Cell Adhesion (GO:0007158)	0.018052682	0.08987931
Regulation Of Cellular Response To Heat (GO:1900034)	0.019330102	0.0923111
Presynapse Assembly (GO:0099054)	0.019330102	0.0923111
Maturation Of 5.8S rRNA (GO:0000460)	0.020605924	0.09454483
Regulation Of Golgi Organization (GO:1903358)	0.020605924	0.09454483

Prostaglandin Biosynthetic Process (GO:0001516)	0.021880151	0.09660293
Toll-Like Receptor 4 Signaling Pathway (GO:0034142)	0.021880151	0.09660293
Response To Organophosphorus (GO:0046683)	0.023152783	0.09995444
Regulation Of Early Endosome To Late Endosome Transport (GO:2000641)	0.024423824	0.09995444
Receptor Clustering (GO:0043113)	0.024423824	0.09995444
Lipopolysaccharide-Mediated Signaling Pathway (GO:0031663)	0.025693274	0.09995444
Positive Regulation Of Protein Processing (GO:0010954)	0.025693274	0.09995444
Regulation Of Fibroblast Migration (GO:0010762)	0.025693274	0.09995444
Fc-gamma Receptor Signaling Pathway Involved In Phagocytosis (GO:0038096)	0.025693274	0.09995444
Endomembrane System Organization (GO:0010256)	0.026614404	0.09995444
Golgi Vesicle Transport (GO:0048193)	0.026866135	0.09995444
snRNA Metabolic Process (GO:0016073)	0.026961136	0.09995444
Regulation Of Translation (GO:0006417)	0.0281394	0.09995444
Fc Receptor Mediated Stimulatory Signaling Pathway (GO:0002431)	0.028227412	0.09995444
Regulation Of Neural Precursor Cell Proliferation (GO:2000177)	0.028227412	0.09995444
Response To Purine-Containing Compound (GO:0014074)	0.030755212	0.09995444
Fc-gamma Receptor Signaling Pathway (GO:0038094)	0.030755212	0.09995444
Neuromuscular Junction Development (GO:0007528)	0.030755212	0.09995444
ERK1 And ERK2 Cascade (GO:0070371)	0.030755212	0.09995444
Fat-Soluble Vitamin Metabolic Process (GO:0006775)	0.030755212	0.09995444
Negative Regulation Of Ion Transmembrane Transporter Activity (GO:0032413)	0.030755212	0.09995444
Camera-Type Eye Development (GO:0043010)	0.033276689	0.10360518
Negative Regulation Of Receptor-Mediated Endocytosis (GO:0048261)	0.033276689	0.10360518
Negative Regulation Of Catalytic Activity (GO:0043086)	0.033276689	0.10360518
Chaperone Cofactor-Dependent Protein Refolding (GO:0051085)	0.034535061	0.10360518
Myeloid Cell Development (GO:0061515)	0.034535061	0.10360518
Positive Regulation Of Response To Wounding (GO:1903036)	0.034535061	0.10360518
Positive Regulation Of Neural Precursor Cell Proliferation (GO:2000179)	0.037047083	0.1097344

Presynaptic Endocytosis (GO:0140238)	0.03955282	0.115692
'De Novo' Post-Translational Protein Folding (GO:0051084)	0.040803336	0.11646119
intra-Golgi Vesicle-Mediated Transport (GO:0006891)	0.042052286	0.11646119
ncRNA Catabolic Process (GO:0034661)	0.042052286	0.11646119
Positive Regulation Of Small Molecule Metabolic Process (GO:0062013)	0.042052286	0.11646119
Positive Regulation Of Organelle Organization (GO:0010638)	0.043299673	0.11646119
Positive Regulation Of Carbohydrate Metabolic Process (GO:0045913)	0.043299673	0.11646119
Mitochondrial Electron Transport, NADH To Ubiquinone (GO:0006120)	0.043299673	0.11646119
Regulation Of Receptor Internalization (GO:0002090)	0.045789763	0.11697245
Regulation Of Trans-Synaptic Signaling (GO:0099177)	0.045789763	0.11697245
Melanosome Organization (GO:0032438)	0.04703247	0.11697245
Regulation Of Sodium Ion Transmembrane Transporter Activity (GO:2000649)	0.04703247	0.11697245
Positive Regulation Of Signaling (GO:0023056)	0.04703247	0.11697245
Regulation Of Ossification (GO:0030278)	0.04703247	0.11697245
G2/M Transition Of Mitotic Cell Cycle (GO:0000086)	0.048273621	0.11697245
Response To cAMP (GO:0051591)	0.048273621	0.11697245
Positive Regulation Of ATP-dependent Activity (GO:0032781)	0.049513218	0.11697245
Positive Regulation Of Cytokinesis (GO:0032467)	0.049513218	0.11697245

Table S5

Upregulated Molecular Functions in infected i3Ns	p-value	q-value
ATPase Binding (GO:0051117)	0.00403523	0.09085148
Sphingosine N-acyltransferase Activity (GO:0050291)	0.00777557	0.09085148
Cadherin Binding (GO:0045296)	0.00796435	0.09085148
Endopeptidase Inhibitor Activity (GO:0004866)	0.00925288	0.09085148
Phospholipase Inhibitor Activity (GO:0004859)	0.01164155	0.09085148
MAP-kinase Scaffold Activity (GO:0005078)	0.01292699	0.09085148
Neurexin Family Protein Binding (GO:0042043)	0.01421082	0.09085148
MAP Kinase Kinase Activity (GO:0004708)	0.01805268	0.09085148
Protein Kinase C Activity (GO:0004697)	0.01805268	0.09085148
Oxidoreductase Activity, Acting On NAD(P)H, Quinone Or Similar Compound As Acceptor (GO:0016655)	0.0193301	0.09085148
Cadherin Binding Involved In Cell-Cell Adhesion (GO:0098641)	0.02188015	0.09348792
Actin Monomer Binding (GO:0003785)	0.0294921	0.10426696
Adenylyltransferase Activity (GO:0070566)	0.03201674	0.10426696
RNA Binding (GO:0003723)	0.03293571	0.10426696
Protein Serine/Threonine/Tyrosine Kinase Activity (GO:0004712)	0.03327669	0.10426696
snoRNA Binding (GO:0030515)	0.03955282	0.10526315
NADH Dehydrogenase (Ubiquinone) Activity (GO:0008137)	0.04205229	0.10526315
NADH Dehydrogenase (Quinone) Activity (GO:0050136)	0.04329967	0.10526315
Hsp70 Protein Binding (GO:0030544)	0.04329967	0.10526315
N-acyltransferase Activity (GO:0016410)	0.04703247	0.10526315
Peptidase Inhibitor Activity (GO:0030414)	0.04703247	0.10526315

Table S6

Category	GO	Downregulated pathways in infected i3Ns	LogP	Hits
GO Biological Processes	GO:0044283	small molecule biosynthetic process	-5.4	GAMT HMGCS1 HPRT1 MSMO1 ELOVL1
Reactome Gene Sets	R-HSA-556833	Metabolism of lipids	-3.2	HMGCS1 PPP1CA MSMO1 ELOVL1
GO Biological Processes	GO:0009150	purine ribonucleotide metabolic process	-3.1	HMGCS1 HPRT1 ELOVL1
GO Biological Processes	GO:0009259	ribonucleotide metabolic process	-3	HMGCS1 HPRT1 ELOVL1
GO Biological Processes	GO:0019693	ribose phosphate metabolic process	-3	HMGCS1 HPRT1 ELOVL1
GO Biological Processes	GO:0006979	response to oxidative stress	-2.9	HBA1 HMOX2 STAT1
GO Biological Processes	GO:0006163	purine nucleotide metabolic process	-2.8	HMGCS1 HPRT1 ELOVL1
WikiPathways	WP3888	VEGFA-VEGFR2 signaling	-2.8	PPP1CA SDCBP STAT1
GO Biological Processes	GO:0072521	purine-containing compound metabolic process	-2.7	HMGCS1 HPRT1 ELOVL1
GO Biological Processes	GO:1901615	organic hydroxy compound metabolic process	-2.7	HMGCS1 HPRT1 MSMO1
GO Biological Processes	GO:0009117	nucleotide metabolic process	-2.6	HMGCS1 HPRT1 ELOVL1
GO Biological Processes	GO:0006753	nucleoside phosphate metabolic process	-2.6	HMGCS1 HPRT1 ELOVL1
GO Biological Processes	GO:0032787	monocarboxylic acid metabolic process	-2.6	GAMT MSMO1 ELOVL1
GO Biological Processes	GO:0010035	response to inorganic substance	-2.5	HBA1 PPP1CA STAT1
GO Biological Processes	GO:0090407	organophosphate biosynthetic process	-2.5	HMGCS1 HPRT1 ELOVL1
GO Biological Processes	GO:0055086	nucleobase-containing small molecule metabolic process	-2.5	HMGCS1 HPRT1 ELOVL1
GO Biological Processes	GO:0008610	lipid biosynthetic process	-2.4	HMGCS1 MSMO1 ELOVL1
Reactome Gene Sets	R-HSA-2262752	Cellular responses to stress	-2	HBA1 HMOX2 RPL29
GO Biological Processes	GO:0043603	amide metabolic process	-2	HMGCS1 RPL29 ELOVL1

Table S7

Downregulated Biological Processes in infected i3Ns	p-value	q-value
Secondary Alcohol Biosynthetic Process (GO:1902653)	0.00018563	0.01928305
Cholesterol Biosynthetic Process (GO:0006695)	0.00020167	0.01928305
Sterol Biosynthetic Process (GO:0016126)	0.00025372	0.01928305
Cholesterol Metabolic Process (GO:0008203)	0.00145547	0.0589797
Monocarboxylic Acid Metabolic Process (GO:0032787)	0.00301943	0.0589797
Synaptic Vesicle Uncoating (GO:0016191)	0.00424314	0.0589797
Mesenchymal Cell Differentiation Involved In Kidney Development (GO:0072161)	0.00424314	0.0589797
Regulation Of Extracellular Exosome Assembly (GO:1903551)	0.00424314	0.0589797
Interleukin-27-Mediated Signaling Pathway (GO:0070106)	0.00424314	0.0589797
Interleukin-9-Mediated Signaling Pathway (GO:0038113)	0.00508974	0.0589797
Response To Lead Ion (GO:0010288)	0.00508974	0.0589797
Clathrin Coat Disassembly (GO:0072318)	0.00508974	0.0589797
GMP Biosynthetic Process (GO:0006177)	0.00508974	0.0589797
Substrate-Dependent Cell Migration, Cell Extension (GO:0006930)	0.00508974	0.0589797
Macrophage Derived Foam Cell Differentiation (GO:0010742)	0.00508974	0.0589797
Cellular Response To Interleukin-9 (GO:0071355)	0.00508974	0.0589797
Regulation Of Dopamine Metabolic Process (GO:0042053)	0.00593566	0.0589797
Foam Cell Differentiation (GO:0090077)	0.00593566	0.0589797
IMP Biosynthetic Process (GO:0006188)	0.00593566	0.0589797
Purine Ribonucleoside Monophosphate Catabolic Process (GO:0009169)	0.00593566	0.0589797
GMP Metabolic Process (GO:0046037)	0.00678091	0.0589797
Purine Nucleobase Metabolic Process (GO:0006144)	0.00762547	0.0589797
Type II Interferon-Mediated Signaling Pathway (GO:0060333)	0.00762547	0.0589797
Positive Regulation Of Mesenchymal Cell Proliferation (GO:0002053)	0.00762547	0.0589797
Alpha-Linolenic Acid Metabolic Process (GO:0036109)	0.00762547	0.0589797
Peptidyl-Serine Dephosphorylation (GO:0070262)	0.00762547	0.0589797

Cell Differentiation Involved In Metanephros Development (GO:0072202)	0.00762547	0.0589797
IMP Metabolic Process (GO:0046040)	0.00762547	0.0589797
Nitrogen Compound Transport (GO:0071705)	0.00828509	0.0589797
Oxygen Transport (GO:0015671)	0.00846937	0.0589797
Metanephric Mesenchyme Development (GO:0072075)	0.00846937	0.0589797
Heme Catabolic Process (GO:0042167)	0.00846937	0.0589797
Carbon Dioxide Transport (GO:0015670)	0.00931258	0.0589797
Golgi To Lysosome Transport (GO:0090160)	0.00931258	0.0589797
Purine Ribonucleoside Monophosphate Metabolic Process (GO:0009167)	0.00931258	0.0589797
Regulation Of Mesenchymal Cell Proliferation (GO:0010464)	0.00931258	0.0589797
Fatty Acid Elongation (GO:0030497)	0.01015513	0.05936843
Porphyrin-Containing Compound Catabolic Process (GO:0006787)	0.01015513	0.05936843
Cristae Formation (GO:0042407)	0.01015513	0.05936843
Clathrin Coat Assembly (GO:0048268)	0.01099699	0.05969797
Negative Regulation Of Receptor Internalization (GO:0002091)	0.01099699	0.05969797
Substrate-Dependent Cell Migration (GO:0006929)	0.01099699	0.05969797
Positive Regulation Of Exosomal Secretion (GO:1903543)	0.01183819	0.06276993
Gas Transport (GO:0015669)	0.01267871	0.06569877
acetyl-CoA Metabolic Process (GO:0006084)	0.01351856	0.06680742
Peptidyl-Threonine Dephosphorylation (GO:0035970)	0.01435773	0.06680742
Golgi To Vacuole Transport (GO:0006896)	0.01435773	0.06680742
Purine-Containing Compound Biosynthetic Process (GO:0072522)	0.01435773	0.06680742
Long-Chain fatty-acyl-CoA Biosynthetic Process (GO:0035338)	0.01435773	0.06680742
Regulation Of Exosomal Secretion (GO:1903541)	0.01519624	0.06793613
Response To Organophosphorus (GO:0046683)	0.01519624	0.06793613
Linoleic Acid Metabolic Process (GO:0043651)	0.01603407	0.06897676
Nucleotide Biosynthetic Process (GO:0009165)	0.01603407	0.06897676
Hydrogen Peroxide Catabolic Process (GO:0042744)	0.01687123	0.0712341

Positive Regulation Of Interferon-Alpha Production (GO:0032727)	0.01770773	0.07209575
Purine Nucleotide Biosynthetic Process (GO:0006164)	0.01770773	0.07209575
Cellular Response To Interferon-Beta (GO:0035458)	0.01854355	0.07315248
Long-Chain fatty-acyl-CoA Metabolic Process (GO:0035336)	0.0193787	0.07315248
Entrainment Of Circadian Clock By Photoperiod (GO:0043153)	0.0193787	0.07315248
Photoperiodism (GO:0009648)	0.02021319	0.07315248
Response To Purine-Containing Compound (GO:0014074)	0.02021319	0.07315248
Positive Regulation Of Cellular Response To Transforming Growth Factor Beta Stimulus (GO:1903846)	0.02021319	0.07315248
Positive Regulation Of Transforming Growth Factor Beta Receptor Signaling Pathway (GO:0030511)	0.02021319	0.07315248
fatty-acyl-CoA Biosynthetic Process (GO:0046949)	0.021047	0.07336286
Purine Ribonucleotide Catabolic Process (GO:0009154)	0.021047	0.07336286
Regulation Of Interferon-Alpha Production (GO:0032647)	0.02188015	0.07336286
Negative Regulation Of Receptor-Mediated Endocytosis (GO:0048261)	0.02188015	0.07336286
Positive Regulation Of Erythrocyte Differentiation (GO:0045648)	0.02188015	0.07336286
Chaperone Cofactor-Dependent Protein Refolding (GO:0051085)	0.02271263	0.07397829
Clathrin-Dependent Endocytosis (GO:0072583)	0.02271263	0.07397829
Positive Regulation Of Defense Response To Virus By Host (GO:0002230)	0.02354445	0.07455741
Protein Localization To Golgi Apparatus (GO:0034067)	0.02354445	0.07455741
Response To Interferon-Beta (GO:0035456)	0.02437559	0.07613199
Positive Regulation Of Phosphate Metabolic Process (GO:0045937)	0.02520608	0.07638245
Receptor Signaling Pathway Via STAT (GO:0097696)	0.02603589	0.07638245
acyl-CoA Metabolic Process (GO:0006637)	0.02603589	0.07638245
'De Novo' Post-Translational Protein Folding (GO:0051084)	0.02686504	0.07638245
Mitochondrial Membrane Organization (GO:0007006)	0.02686504	0.07638245
Negative Regulation Of Proteasomal Ubiquitin-Dependent Protein Catabolic Process (GO:0032435)	0.02686504	0.07638245
Very Long-Chain Fatty Acid Metabolic Process (GO:0000038)	0.02686504	0.07638245
Purine Nucleotide Metabolic Process (GO:0006163)	0.02852135	0.07638245
Inner Mitochondrial Membrane Organization (GO:0007007)	0.02852135	0.07638245

One-Carbon Compound Transport (GO:0019755)	0.02934851	0.07638245
Receptor Signaling Pathway Via JAK-STAT (GO:0007259)	0.03017501	0.07638245
Positive Regulation Of Myeloid Cell Differentiation (GO:0045639)	0.03017501	0.07638245
Regulation Of Erythrocyte Differentiation (GO:0045646)	0.03017501	0.07638245
Regulation Of Receptor Internalization (GO:0002090)	0.03017501	0.07638245
Negative Regulation Of Endothelial Cell Proliferation (GO:0001937)	0.03100085	0.07638245
Regulation Of Defense Response To Virus By Host (GO:0050691)	0.03100085	0.07638245
Type I Interferon-Mediated Signaling Pathway (GO:0060337)	0.03100085	0.07638245
Positive Regulation Of Exocytosis (GO:0045921)	0.03100085	0.07638245
Tumor Necrosis Factor-Mediated Signaling Pathway (GO:0033209)	0.03182602	0.07638245
Cellular Response To Type I Interferon (GO:0071357)	0.03182602	0.07638245
Response To cAMP (GO:0051591)	0.03182602	0.07638245
Response To Peptide (GO:1901652)	0.03182602	0.07638245
Negative Regulation Of Proteasomal Protein Catabolic Process (GO:1901799)	0.03265053	0.07674558
Negative Regulation Of Ubiquitin-Dependent Protein Catabolic Process (GO:2000059)	0.03265053	0.07674558
Synaptic Vesicle Endocytosis (GO:0048488)	0.03347438	0.07709252
Endothelial Cell Migration (GO:0043542)	0.03347438	0.07709252
Negative Regulation Of I-kappaB kinase/NF-kappaB Signaling (GO:0043124)	0.0351201	0.07928103
Organic Hydroxy Compound Biosynthetic Process (GO:1901617)	0.0351201	0.07928103
Regulation Of Cellular Component Size (GO:0032535)	0.03594198	0.08034089
Epithelial Cell Migration (GO:0010631)	0.03840364	0.08409095
Response To Hydrogen Peroxide (GO:0042542)	0.03840364	0.08409095
Positive Regulation Of Smooth Muscle Cell Proliferation (GO:0048661)	0.03922288	0.08409095
Positive Regulation Of Epithelial To Mesenchymal Transition (GO:0010718)	0.03922288	0.08409095
Unsaturated Fatty Acid Metabolic Process (GO:0033559)	0.04085939	0.08409095
Positive Regulation Of Pathway-Restricted SMAD Protein Phosphorylation (GO:0010862)	0.04085939	0.08409095
Interferon-Mediated Signaling Pathway (GO:0140888)	0.04085939	0.08409095
Steroid Biosynthetic Process (GO:0006694)	0.04167665	0.08409095

Positive Regulation Of Cell Death (GO:0010942)	0.04167665	0.08409095
Negative Regulation Of Cell Projection Organization (GO:0031345)	0.04167665	0.08409095
Blood Circulation (GO:0008015)	0.04167665	0.08409095
Protein Homotetramerization (GO:0051289)	0.04412453	0.08757379
Regulation Of Smooth Muscle Cell Proliferation (GO:0048660)	0.04493918	0.08757379
Negative Regulation Of Neuron Projection Development (GO:0010977)	0.04493918	0.08757379
Endoplasmic Reticulum Organization (GO:0007029)	0.04493918	0.08757379
Response To Peptide Hormone (GO:0043434)	0.04575318	0.08840445
post-Golgi Vesicle-Mediated Transport (GO:0006892)	0.04656653	0.0892199
Membrane Lipid Biosynthetic Process (GO:0046467)	0.04737922	0.09002051
Renal System Development (GO:0072001)	0.04819126	0.09080667
Regulation Of Cell Death (GO:0010941)	0.04900265	0.09157872
Sterol Metabolic Process (GO:0016125)	0.04981338	0.09160438

Table S8

Downregulated Molecular Functions in infected i3Ns	p-value	q-value
Cadherin Binding (GO:0045296)	0.00012828	0.00538758
Heme Binding (GO:0020037)	0.00243818	0.05120184
Oxidoreductase Activity, Acting On Paired Donors, With Incorporation Or Reduction Of Molecular Oxygen, Another Compound As One Donor, And Incorporation Of One Atom Of Oxygen (GO:0016716)	0.00424314	0.05940402
Tumor Necrosis Factor Receptor Binding (GO:0005164)	0.00762547	0.07108588
Fatty Acid Synthase Activity (GO:0004312)	0.00846937	0.07108588
RNA Polymerase II Core Promoter Sequence-Specific DNA Binding (GO:0000979)	0.01015513	0.07108588
Histone Acetyltransferase Binding (GO:0035035)	0.01435773	0.07537811
Cadherin Binding Involved In Cell-Cell Adhesion (GO:0098641)	0.01435773	0.07537811
Oxidoreductase Activity, Acting On Paired Donors, With Incorporation Or Reduction Of Molecular Oxygen, Reduced Flavin Or Flavoprotein As One Donor, And Incorporation Of One Atom Of Oxygen (GO:0016712)	0.021047	0.08386461
Tumor Necrosis Factor Receptor Superfamily Binding (GO:0032813)	0.02271263	0.08386461
Ubiquitin-Like Protein Ligase Binding (GO:0044389)	0.02452902	0.08386461
Frizzled Binding (GO:0005109)	0.02769353	0.08386461
Transcription Coactivator Binding (GO:0001223)	0.02852135	0.08386461
Core Promoter Sequence-Specific DNA Binding (GO:0001046)	0.02934851	0.08386461
Methyltransferase Activity (GO:0008168)	0.03100085	0.08386461
Promoter-Specific Chromatin Binding (GO:1990841)	0.0351201	0.08386461
Transcription Corepressor Binding (GO:0001222)	0.0351201	0.08386461
Cell-Cell Adhesion Mediator Activity (GO:0098632)	0.03594198	0.08386461
S-adenosylmethionine-dependent Methyltransferase Activity (GO:0008757)	0.04167665	0.09094938
Phosphoric Ester Hydrolase Activity (GO:0042578)	0.04330923	0.09094938
Protein Serine/Threonine Phosphatase Activity (GO:0004722)	0.04575318	0.09150636