

Online resources (Acta Neuropathologica)

Astroglial calcium signalling and homeostasis in Tuberous Sclerosis Complex

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Online Resource 1 Clinical informations on TSC (n=21) and control cortex (n=15) cohort.

	Diagnose	Gender	Seizure Onset (years)	Age at the time of operation (years)	Duration (years)	Area of Resection	Mutation
1 ^a	TSC	f	0	13	13	F	TSC2
2 ^a	TSC	m	0	2	2	F	TSC2
3 ^a	TSC	f	20	21	1	T	TSC1
4 ^a	TSC	m	6	14	8	F	TSC1
5 ^a	TSC	m	0	4	4	T	TSC1
6 ^a	TSC	f	0	2	2	T	TSC1
7 ^a	TSC	m	0	2	2	F	TSC2
8 ^a	TSC	m	0	2	2	F	TSC2
9 ^a	TSC	m	0	1	1	F	TSC2
10 ^a	TSC	m	0	0	0	F	TSC2
11 ^a	TSC	m	0	5	5	F	TSC2
12 ^a	TSC	m	0	0	0	F	TSC2
13 ^a	TSC	m	2	3	1	F	TSC1
14 ^a	TSC	f	0	8	8	F	TSC2
15 ^a	TSC	f	8	9	1	F	TSC2
16 ^a	TSC	v	0	0	0	F	TSC2
17 ^a	TSC	f	26	30	4	T	TSC1
18 ^a	TSC	f	0	0	0	T	TSC2
19 ^a	TSC	f	0	17	17	P	TSC2
20 ^a	TSC	f	5	11	6	T	TSC2
21 ^a	TSC	m	0	4	4	F	TSC2
22 ^a	Control	f	NA	0	NA	C	NA
23 ^a	Control	m	NA	10	NA	C	NA
24 ^a	Control	f	NA	0	NA	C	NA
25 ^a	Control	f	NA	2	NA	C	NA
26 ^a	Control	m	NA	15	NA	C	NA
27 ^a	Control	m	NA	13	NA	C	NA
28 ^a	Control	f	NA	0	NA	C	NA
29 ^a	Control	m	NA	10	NA	C	NA
30 ^a	Control	f	NA	17	NA	C	NA
31 ^a	Control	f	NA	17	NA	C	NA
32 ^a	Control	f	NA	61	NA	C	NA
33 ^a	Control	f	NA	44	NA	C	NA
34 ^a	Control	m	NA	60	NA	C	NA
35 ^a	Control	f	NA	39	NA	C	NA
36 ^a	Control	m	NA	49	NA	C	NA
37 ^b	Control	m	NA	12	NA	C	NA
38 ^b	Control	f	NA	16	NA	C	NA

39 ^b	Control	f	NA	5	NA	C	NA
40 ^b	TSC	m	0	2	2	F	TSC2
41 ^b	TSC	m	0	5	5	F	TSC2
42 ^b	TSC	f	0	8	8	F	TSC2
43 ^b	TSC	f	0	0	0	T	TSC2
44 ^b	TSC	f	0	17	17	P	TSC2
45 ^c	TLE-HS	m	2	34	32	T	HS2
46 ^c	TSC	m	8	13	5	P	TSC2

a=patients involved in the BulkRNASeq; b= patients involved in the single-cell RNASeq; c=patients subjected to EM; m=male; f=female; TSC=Tuberous Sclerosis Complex; TLE-HS=Temporal Lobe Epilepsy with Hippocampal Sclerosis; HS2=Hippocampal Sclerosis type 2; F=Frontal; T=Temporal; P=Parietal; C=Cortex.

Online Resource 2 Marker genes for scRNA-seq cell type clustering annotation

Cell type	Marker genes
Glutamatergic neurons	SLC17A7, SATB2, SLC17A6, NMDAR1
GABAergic neurons	GAD1, GAD2
Astrocytes	GFAP, ALDH1L1, AQP4, GLT1, S100B
Microglia	PTPRC, ITGAM, P2RY12, TMEM119
Oligodendrocytes	OLIG1, GLDN11, MOG, MBP
OPCs	PDGFRA, CSPG4
Endothelial cells	CLDN5, FOXJ1, PDGFRB

Online Resource 3 Bulk RNASeq analysis of control cortex and TSC cohort. a-b. Principal components analysis (PCA) of the whole transcriptome profile was performed for each sample in control and TSC cohort. Each point represented a different sample. PCA did not identify pathology or surgical area of resection as discriminating features in the cohort. X-axis: the first principal component (PC1); y-axis: the second principal component (PC2). **c.** Volcano plot showing the differentially expressed genes (DEGs) ($p_{adj} < 0.05$) between control cortex (n=15) and TSC (n=21) tissue. A total of 2766 mRNAs were found to be upregulated and 1780 downregulated in TSC compared to control tissue. **d.** Supervised clustering heatmap visualizing the expression of the relevant Ca^{2+} -related genes in control tissues and TSC cortical tubers. Adjusted p-value: * $p_{adj} \leq 0.05$; ** $p_{adj} \leq 0.01$; *** $p_{adj} \leq 0.001$; **** $p_{adj} \leq 0.0001$).

Online Resource 4 Significantly enriched GO Biological processes (BP) pathways of upregulated genes in TSC patients' tissue

ID	Description	pvalue	p.adjust
GO:0042119	neutrophil activation	7.95356377776396e-25	4.71089582556959e-21
GO:0002283	neutrophil activation involved in immune response	2.37831563027281e-24	7.04338173905292e-21

GO:00433 12	neutrophil degranulation	4.20064916883927e -24	8.29348167567833e -21
GO:00024 46	neutrophil mediated immunity	6.77615207245481e -24	1.00337871812875e -20
GO:00706 61	leukocyte proliferation	3.25156159283991e -20	3.85179986287816e -17
GO:00071 59	leukocyte cell-cell adhesion	7.89953519280749e -20	7.79815782449979e -17
GO:00421 10	T cell activation	1.32272139425595e -19	1.11921125973972e -16
GO:00706 63	regulation of leukocyte proliferation	2.94480356273144e -19	2.18025893775729e -16
GO:00329 43	mononuclear cell proliferation	4.53695297324811e -19	2.98581916228317e -16
GO:00329 44	regulation of mononuclear cell proliferation	5.92466859301897e -19	3.50918120764514e -16
GO:00466 51	lymphocyte proliferation	8.12430847894113e -19	4.37457082916076e -16
GO:00506 70	regulation of lymphocyte proliferation	1.41734527641908e -18	6.99578006019183e -16
GO:19030 39	positive regulation of leukocyte cell-cell adhesion	2.95661860842203e -18	1.34708092443721e -15
GO:00420 98	T cell proliferation	2.1230050032022e- 17	8.47775493492529e -15
GO:19030 37	regulation of leukocyte cell-cell adhesion	2.14699179510179e -17	8.47775493492529e -15
GO:00018 19	positive regulation of cytokine production	2.49455561279002e -17	9.23453305909707e -15
GO:00713 46	cellular response to interferon-gamma	3.76029581234342e -17	1.31013129979471e -14
GO:00508 67	positive regulation of cell activation	6.30257509507081e -17	2.07389734933913e -14
GO:00457 85	positive regulation of cell adhesion	7.38573742499244e -17	2.3024064614858e- 14
GO:00343 41	response to interferon-gamma	1.58528598169896e -16	4.69482443480148e -14
GO:19021 05	regulation of leukocyte differentiation	2.34115732771376e -16	6.60317850097553e -14
GO:00508 63	regulation of T cell activation	3.90372410427708e -16	1.05098899407423e -13
GO:00508 70	positive regulation of T cell activation	5.4759278738299e- 16	1.4101704694215e- 13
GO:00026 96	positive regulation of leukocyte activation	1.8407663654474e- 15	4.54285799272707e -13
GO:00224 09	positive regulation of cell-cell adhesion	4.68815910257158e -15	1.11071865458126e -12
GO:00072 49	I-kappaB kinase/NF-kappaB signaling	4.99600148143403e -15	1.1381275682513e- 12
GO:19021 07	positive regulation of leukocyte differentiation	5.68865841384996e -15	1.20335442090119e -12
GO:19037 08	positive regulation of hemopoiesis	5.68865841384996e -15	1.20335442090119e -12
GO:00329 46	positive regulation of mononuclear cell proliferation	9.0105505316081e- 15	1.8403272689212e- 12
GO:00603 33	interferon-gamma-mediated signaling pathway	1.04996812035856e -14	2.07298705896124e -12
GO:00421 29	regulation of T cell proliferation	1.80955170079618e -14	3.45741120123089e -12

GO:0022407	regulation of cell-cell adhesion	3.05665329883226e-14	5.55435852501408e-12
GO:0050671	positive regulation of lymphocyte proliferation	3.09461136798015e-14	5.55435852501408e-12
GO:0070665	positive regulation of leukocyte proliferation	8.16664884451953e-14	1.42267826782615e-11
GO:0002697	regulation of immune effector process	1.14314395917265e-13	1.93452619147989e-11
GO:1903131	mononuclear cell differentiation	1.89502506671047e-13	3.11784263059059e-11
GO:0042102	positive regulation of T cell proliferation	2.61772041932091e-13	4.19047514692913e-11
GO:0043122	regulation of I-kappaB kinase/NF-kappaB signaling	8.42875177669645e-13	1.31377623087824e-10
GO:0002221	pattern recognition receptor signaling pathway	1.82666003055339e-12	2.77418137460711e-10
GO:0002683	negative regulation of immune system process	2.5789777704367e-12	3.75288265797246e-10
GO:0043123	positive regulation of I-kappaB kinase/NF-kappaB signaling	2.5978083568609e-12	3.75288265797246e-10
GO:0002224	toll-like receptor signaling pathway	4.00146314394573e-12	5.64301576228347e-10
GO:0051251	positive regulation of lymphocyte activation	4.5270918792736e-12	6.23580586068314e-10
GO:0002819	regulation of adaptive immune response	7.16126483138208e-12	9.64003899915365e-10
GO:1903557	positive regulation of tumor necrosis factor superfamily cytokine production	7.91486840417187e-12	1.04177256795356e-09
GO:0071706	tumor necrosis factor superfamily cytokine production	1.27584701395252e-11	1.64279170948712e-09
GO:0032760	positive regulation of tumor necrosis factor production	1.40793038475822e-11	1.74151166662743e-09
GO:0046634	regulation of alpha-beta T cell activation	1.41132128985508e-11	1.74151166662743e-09
GO:0030098	lymphocyte differentiation	1.60976335945233e-11	1.94584252612982e-09
GO:0002237	response to molecule of bacterial origin	1.77845113859007e-11	2.1067532187738e-09
GO:1903555	regulation of tumor necrosis factor superfamily cytokine production	2.27200413988865e-11	2.63864323932558e-09
GO:0042063	gliogenesis	4.21853222933616e-11	4.80507046045348e-09
GO:0032640	tumor necrosis factor production	5.12401772093999e-11	5.72633150209954e-09
GO:0002573	myeloid leukocyte differentiation	9.27442259849265e-11	1.01726676020133e-08
GO:0046631	alpha-beta T cell activation	1.11145092512274e-10	1.19453157123955e-08
GO:0002685	regulation of leukocyte migration	1.13239438864348e-10	1.19453157123955e-08
GO:0032680	regulation of tumor necrosis factor production	1.14955764917533e-10	1.19453157123955e-08
GO:0002822	regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	1.27935442016217e-10	1.30414123780628e-08
GO:0046635	positive regulation of alpha-beta T cell activation	1.31404899503929e-10	1.30414123780628e-08
GO:0050866	negative regulation of cell activation	1.32109529408031e-10	1.30414123780628e-08

GO:0002699	positive regulation of immune effector process	1.77712378945827e-10	1.7255580663871e-08
GO:0032635	interleukin-6 production	1.81848109031955e-10	1.73723604805849e-08
GO:1903706	regulation of hemopoiesis	1.96961587053037e-10	1.85175155573831e-08
GO:0032675	regulation of interleukin-6 production	2.56495425230062e-10	2.37378500568384e-08
GO:0045619	regulation of lymphocyte differentiation	2.72820753140144e-10	2.48602664746011e-08
GO:0030217	T cell differentiation	3.10671936314492e-10	2.77649114342353e-08
GO:0019882	antigen processing and presentation	3.14072103004181e-10	2.77649114342353e-08
GO:0002695	negative regulation of leukocyte activation	3.6068533660015e-10	3.14167536570984e-08
GO:0032609	interferon-gamma production	4.04728283232637e-10	3.47421104577813e-08
GO:0042116	macrophage activation	4.13971944046911e-10	3.50279403512836e-08
GO:0046633	alpha-beta T cell proliferation	6.4495937181605e-10	5.38041459051614e-08
GO:0032496	response to lipopolysaccharide	6.74527188493481e-10	5.54892296867623e-08
GO:0002703	regulation of leukocyte mediated immunity	7.51450581850734e-10	6.09704355657794e-08
GO:0032755	positive regulation of interleukin-6 production	1.26978522315222e-09	1.01634295631495e-07
GO:0045621	positive regulation of lymphocyte differentiation	1.33950515679899e-09	1.05785187249606e-07
GO:0032649	regulation of interferon-gamma production	1.72952876525788e-09	1.34789458902926e-07
GO:0002755	MyD88-dependent toll-like receptor signaling pathway	1.77100666109683e-09	1.36229512385409e-07
GO:0001774	microglial cell activation	2.14138779746229e-09	1.62608204158579e-07
GO:0045582	positive regulation of T cell differentiation	2.38294351010367e-09	1.78660435573975e-07
GO:0045580	regulation of T cell differentiation	2.51109668434932e-09	1.85915320767513e-07
GO:0051250	negative regulation of lymphocyte activation	3.41166243920669e-09	2.49472550955817e-07
GO:0046640	regulation of alpha-beta T cell proliferation	8.78248735450346e-09	6.3437405610639e-07
GO:0032663	regulation of interleukin-2 production	9.28300190109869e-09	6.61899246784713e-07
GO:0060326	cell chemotaxis	9.38705668241024e-09	6.61899246784713e-07
GO:0048002	antigen processing and presentation of peptide antigen	1.10525882773665e-08	7.7017035725696e-07
GO:0007162	negative regulation of cell adhesion	1.2375898061523e-08	8.52354002539547e-07
GO:0098581	detection of external biotic stimulus	1.35366291901002e-08	9.21579938999579e-07
GO:0050764	regulation of phagocytosis	1.37765632772185e-08	9.27256639670059e-07
GO:0032729	positive regulation of interferon-gamma production	1.56789317025717e-08	1.04344171319475e-06

GO:0071216	cellular response to biotic stimulus	1.60234924878366e-08	1.05452384450507e-06
GO:0050729	positive regulation of inflammatory response	1.95337891396726e-08	1.26290269525714e-06
GO:0032623	interleukin-2 production	1.96162498672391e-08	1.26290269525714e-06
GO:0010001	glial cell differentiation	2.13638657258311e-08	1.36062555585051e-06
GO:0030198	extracellular matrix organization	2.17917240083264e-08	1.37311043937572e-06
GO:0043062	extracellular structure organization	2.44336254159008e-08	1.52337224566716e-06
GO:0002460	adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	2.52086618324238e-08	1.55532191701506e-06
GO:0046394	carboxylic acid biosynthetic process	2.62295750372633e-08	1.60162652521351e-06
GO:0045229	external encapsulating structure organization	3.06597579841462e-08	1.82715839576169e-06
GO:0032677	regulation of interleukin-8 production	3.09429164806969e-08	1.82715839576169e-06
GO:0016053	organic acid biosynthetic process	3.09590906141486e-08	1.82715839576169e-06
GO:0050766	positive regulation of phagocytosis	3.11570146837635e-08	1.82715839576169e-06
GO:0002763	positive regulation of myeloid leukocyte differentiation	3.50309180012952e-08	2.01444783807448e-06
GO:0031663	lipopolysaccharide-mediated signaling pathway	3.50309180012952e-08	2.01444783807448e-06
GO:0032637	interleukin-8 production	3.72663064139475e-08	2.12238781624818e-06
GO:0002698	negative regulation of immune effector process	3.9158285084611e-08	2.20890021482049e-06
GO:0002821	positive regulation of adaptive immune response	4.77975330845704e-08	2.67079989113123e-06
GO:0007272	ensheathment of neurons	4.87996243688093e-08	2.67629791793016e-06
GO:0008366	axon ensheathment	4.87996243688093e-08	2.67629791793016e-06
GO:0071219	cellular response to molecule of bacterial origin	4.96342238479657e-08	2.69709640230735e-06
GO:0002824	positive regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	5.1866652352571e-08	2.79278347167526e-06
GO:0009595	detection of biotic stimulus	7.17350764915123e-08	3.82780953206511e-06
GO:0002761	regulation of myeloid leukocyte differentiation	9.79233463625319e-08	5.1785712545114e-06
GO:0042552	myelination	1.06670110338381e-07	5.59121295163034e-06
GO:0002478	antigen processing and presentation of exogenous peptide antigen	1.10645971464263e-07	5.74873762265642e-06
GO:0001818	negative regulation of cytokine production	1.21820324252573e-07	6.27427635259124e-06
GO:0032757	positive regulation of interleukin-8 production	1.28681271582844e-07	6.57051009987228e-06
GO:0071222	cellular response to lipopolysaccharide	1.43335723185008e-07	7.25621784978465e-06

GO:0019884	antigen processing and presentation of exogenous antigen	1.52104578694666e-07	7.63487643736023e-06
GO:0070664	negative regulation of leukocyte proliferation	1.79439822199438e-07	8.93127787300228e-06
GO:0046638	positive regulation of alpha-beta T cell differentiation	1.98585157168294e-07	9.80183238256505e-06
GO:0007015	actin filament organization	2.07798213934988e-07	1.00958334311851e-05
GO:0046641	positive regulation of alpha-beta T cell proliferation	2.07950646396181e-07	1.00958334311851e-05
GO:0002687	positive regulation of leukocyte migration	2.10019832555812e-07	1.01133940506347e-05
GO:0002286	T cell activation involved in immune response	2.45061249050141e-07	1.17056272429354e-05
GO:0002718	regulation of cytokine production involved in immune response	2.4844119846628e-07	1.17721377481262e-05
GO:0031349	positive regulation of defense response	2.88954946071226e-07	1.35516070183305e-05
GO:0002285	lymphocyte activation involved in immune response	2.90571347514431e-07	1.35516070183305e-05
GO:0050868	negative regulation of T cell activation	4.05322502933988e-07	1.87556655068595e-05
GO:0050852	T cell receptor signaling pathway	4.2188136826412e-07	1.937056855991e-05
GO:0002705	positive regulation of leukocyte mediated immunity	4.27118913736713e-07	1.94601948158658e-05
GO:0050672	negative regulation of lymphocyte proliferation	4.47026376068117e-07	2.0211734545431e-05
GO:0031099	regeneration	4.64317320183553e-07	2.0834480965509e-05
GO:0030888	regulation of B cell proliferation	4.8526648210482e-07	2.16107772444124e-05
GO:0009615	response to virus	4.93190629662607e-07	2.17997619365046e-05
GO:0032612	interleukin-1 production	5.20979323357925e-07	2.28574854240666e-05
GO:0002291	T cell activation via T cell receptor contact with antigen bound to MHC molecule on antigen presenting cell	5.43310239052168e-07	2.36619598963676e-05
GO:2001185	regulation of CD8-positive, alpha-beta T cell activation	5.69056069173258e-07	2.46023291803884e-05
GO:0032945	negative regulation of mononuclear cell proliferation	5.79414309886351e-07	2.48686301264989e-05
GO:0048709	oligodendrocyte differentiation	6.18720028240861e-07	2.63645951602203e-05
GO:0036037	CD8-positive, alpha-beta T cell activation	8.8827872636807e-07	3.75805349734148e-05
GO:1901222	regulation of NIK/NF-kappaB signaling	9.47017246717908e-07	3.9781440796526e-05
GO:0034612	response to tumor necrosis factor	1.39563927208624e-06	5.78067930669009e-05
GO:0070371	ERK1 and ERK2 cascade	1.39563927208624e-06	5.78067930669009e-05
GO:0043372	positive regulation of CD4-positive, alpha-beta T cell differentiation	1.44061253079337e-06	5.88484993521027e-05
GO:0032611	interleukin-1 beta production	1.44066054466569e-06	5.88484993521027e-05
GO:0030595	leukocyte chemotaxis	1.51141060409745e-06	6.13156507401998e-05

GO:005077	negative regulation of immune response	1.58408062976615e-06	6.38265957149992e-05
GO:0030316	osteoclast differentiation	1.74706200010455e-06	6.95658355100821e-05
GO:0043087	regulation of GTPase activity	1.75001004406589e-06	6.95658355100821e-05
GO:1902563	regulation of neutrophil activation	1.80719927500233e-06	7.13602753722587e-05
GO:0002706	regulation of lymphocyte mediated immunity	1.82315521240663e-06	7.15135650535394e-05
GO:0051090	regulation of DNA-binding transcription factor activity	1.89193333383574e-06	7.37231653704547e-05
GO:0071356	cellular response to tumor necrosis factor	2.08365009186578e-06	8.06631339485034e-05
GO:0048017	inositol lipid-mediated signaling	2.1454737970421e-06	8.19963337469959e-05
GO:0007265	Ras protein signal transduction	2.14577608151011e-06	8.19963337469959e-05
GO:0002367	cytokine production involved in immune response	2.18492604888748e-06	8.295716017667e-05
GO:0006909	phagocytosis	2.25612215235731e-06	8.5114722983518e-05
GO:0016042	lipid catabolic process	2.63613265529976e-06	9.88216058059525e-05
GO:0030225	macrophage differentiation	2.70978358966366e-06	0.000100893276145883
GO:0030099	myeloid cell differentiation	2.72546415386481e-06	0.000100893276145883
GO:0046637	regulation of alpha-beta T cell differentiation	2.777318909225e-06	0.000100920612879385
GO:1901224	positive regulation of NIK/NF-kappaB signaling	2.777318909225e-06	0.000100920612879385
GO:2000514	regulation of CD4-positive, alpha-beta T cell activation	2.777318909225e-06	0.000100920612879385
GO:0002886	regulation of myeloid leukocyte mediated immunity	2.88408148163047e-06	0.000104161064729861
GO:0030866	cortical actin cytoskeleton organization	2.93773508302337e-06	0.000105455787253015
GO:0002831	regulation of response to biotic stimulus	2.98395751833643e-06	0.000106469761331968
GO:0002709	regulation of T cell mediated immunity	3.07543552207644e-06	0.000109076674235082
GO:0021782	glial cell development	3.20473975908893e-06	0.000112986152339784
GO:0046683	response to organophosphorus	3.31644387247714e-06	0.000116232526962616
GO:0043300	regulation of leukocyte degranulation	3.45517244583202e-06	0.000120382272921547
GO:0002429	immune response-activating cell surface receptor signaling pathway	3.65849876710076e-06	0.000125984233706615
GO:0002757	immune response-activating signal transduction	3.65849876710076e-06	0.000125984233706615
GO:0051607	defense response to virus	3.71963401979461e-06	0.000126617197122089
GO:0140546	defense response to symbiont	3.71963401979461e-06	0.000126617197122089
GO:0014068	positive regulation of phosphatidylinositol 3-kinase signaling	3.86747460426152e-06	0.000130897440463091

GO:0032743	positive regulation of interleukin-2 production	3.91553858136967e-06	0.000131771221690071
GO:0050727	regulation of inflammatory response	4.19692151151021e-06	0.000140442746399294
GO:2000516	positive regulation of CD4-positive, alpha-beta T cell activation	4.3114062974334e-06	0.000143463255616281
GO:0045639	positive regulation of myeloid cell differentiation	4.40976492940067e-06	0.000145916411602459
GO:1903038	negative regulation of leukocyte cell-cell adhesion	4.61354557124718e-06	0.000151811280102761
GO:0043547	positive regulation of GTPase activity	4.90579957861993e-06	0.00015927644723292
GO:0032490	detection of molecule of bacterial origin	4.91893350471218e-06	0.00015927644723292
GO:0022408	negative regulation of cell-cell adhesion	4.92836078963593e-06	0.00015927644723292
GO:0042590	antigen processing and presentation of exogenous peptide antigen via MHC class I	4.94797675010254e-06	0.00015927644723292
GO:0032732	positive regulation of interleukin-1 production	5.01895430716358e-06	0.000160687926277459
GO:0042554	superoxide anion generation	5.22783727145401e-06	0.000166475699778613
GO:0051056	regulation of small GTPase mediated signal transduction	5.49018638564525e-06	0.000173895047926079
GO:0071674	mononuclear cell migration	5.65636459114165e-06	0.000178205571666666
GO:0045123	cellular extravasation	6.05064056732819e-06	0.000187053525264154
GO:0002483	antigen processing and presentation of endogenous peptide antigen	6.06352808555082e-06	0.000187053525264154
GO:0034138	toll-like receptor 3 signaling pathway	6.06352808555082e-06	0.000187053525264154
GO:0098543	detection of other organism	6.06352808555082e-06	0.000187053525264154
GO:0002456	T cell mediated immunity	6.55267423235681e-06	0.000201095800405437
GO:0051092	positive regulation of NF-kappaB transcription factor activity	6.64544547239007e-06	0.000202891616149311
GO:0002576	platelet degranulation	6.71614113123458e-06	0.000203998481642577
GO:0032722	positive regulation of chemokine production	6.9262352554364e-06	0.000209306588867091
GO:0097529	myeloid leukocyte migration	6.98117840559559e-06	0.000209896039067729
GO:0002474	antigen processing and presentation of peptide antigen via MHC class I	7.69775219089013e-06	0.000230271647609304
GO:0050851	antigen receptor-mediated signaling pathway	8.21336529176333e-06	0.000244461118709117
GO:0072593	reactive oxygen species metabolic process	8.3633160905443e-06	0.000247679606021469
GO:0010038	response to metal ion	8.57329624869725e-06	0.000251384325153633
GO:0032956	regulation of actin cytoskeleton organization	8.57329624869725e-06	0.000251384325153633
GO:0032731	positive regulation of interleukin-1 beta production	9.51500370081421e-06	0.000277622497142476
GO:0006636	unsaturated fatty acid biosynthetic process	9.69183214392082e-06	0.000280023033114356

GO:0043370	regulation of CD4-positive, alpha-beta T cell differentiation	9.69183214392082e-06	0.000280023033114356
GO:0006633	fatty acid biosynthetic process	9.75636171875489e-06	0.000280519079903812
GO:0032642	regulation of chemokine production	1.0462462123277e-05	0.00029936793795251
GO:0048771	tissue remodeling	1.05246979709311e-05	0.000299700894624159
GO:0002577	regulation of antigen processing and presentation	1.09829802634581e-05	0.000310428692316354
GO:0032602	chemokine production	1.10077738599523e-05	0.000310428692316354
GO:0048732	gland development	1.10586618400727e-05	0.000310428692316354
GO:2000379	positive regulation of reactive oxygen species metabolic process	1.13760781013188e-05	0.00031702553812797
GO:1905523	positive regulation of macrophage migration	1.14007157895083e-05	0.00031702553812797
GO:0046632	alpha-beta T cell differentiation	1.15802640088121e-05	0.000320513568804645
GO:0002711	positive regulation of T cell mediated immunity	1.29984538941761e-05	0.000356969962546856
GO:1903053	regulation of extracellular matrix organization	1.30179827638225e-05	0.000356969962546856
GO:0072330	monocarboxylic acid biosynthetic process	1.44893050943779e-05	0.000395484580986178
GO:0031343	positive regulation of cell killing	1.52529931929778e-05	0.000414419626981686
GO:0071260	cellular response to mechanical stimulus	1.57281066587869e-05	0.000425377058173493
GO:0045807	positive regulation of endocytosis	1.62894758935653e-05	0.000438557116898125
GO:0030865	cortical cytoskeleton organization	1.64236169538888e-05	0.000440167797365987
GO:0002888	positive regulation of myeloid leukocyte mediated immunity	1.69815322069787e-05	0.000451038633461591
GO:0016045	detection of bacterium	1.69815322069787e-05	0.000451038633461591
GO:1905517	macrophage migration	1.72757329064017e-05	0.000455363884471937
GO:0034142	toll-like receptor 4 signaling pathway	1.72981384444008e-05	0.000455363884471937
GO:0048015	phosphatidylinositol-mediated signaling	1.76095294092424e-05	0.000461509923411252
GO:0022010	central nervous system myelination	1.89913135074965e-05	0.000493357675021499
GO:0032291	axon ensheathment in central nervous system	1.89913135074965e-05	0.000493357675021499
GO:0002479	antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-dependent	1.97024307841756e-05	0.000507598260076025
GO:0031341	regulation of cell killing	1.97108897210005e-05	0.000507598260076025
GO:0050730	regulation of peptidyl-tyrosine phosphorylation	2.15638187246739e-05	0.000552911248078975
GO:0006801	superoxide metabolic process	2.23104059235444e-05	0.0005695885098498
GO:1905521	regulation of macrophage migration	2.26656639725088e-05	0.000576174797035063

GO:0051591	response to cAMP	2.33350722010351e-05	0.000590656549772355
GO:0071675	regulation of mononuclear cell migration	2.37003154222356e-05	0.000597348801046389
GO:0045651	positive regulation of macrophage differentiation	2.45744062348249e-05	0.000616755119190118
GO:0006643	membrane lipid metabolic process	2.48773116711635e-05	0.000619110575749166
GO:0008154	actin polymerization or depolymerization	2.48773116711635e-05	0.000619110575749166
GO:0007229	integrin-mediated signaling pathway	2.85129220874446e-05	0.000705030229364593
GO:0035710	CD4-positive, alpha-beta T cell activation	2.85678296551582e-05	0.000705030229364593
GO:0019883	antigen processing and presentation of endogenous antigen	2.89107446911909e-05	0.000710532534464414
GO:0002281	macrophage activation involved in immune response	3.07913637054474e-05	0.000735456002754019
GO:0032930	positive regulation of superoxide anion generation	3.07913637054474e-05	0.000735456002754019
GO:0070372	regulation of ERK1 and ERK2 cascade	3.10510920822397e-05	0.000735456002754019
GO:0031589	cell-substrate adhesion	3.11835061829084e-05	0.000735456002754019
GO:0097191	extrinsic apoptotic signaling pathway	3.13843860088568e-05	0.000735456002754019
GO:0014074	response to purine-containing compound	3.13925326195148e-05	0.000735456002754019
GO:0048260	positive regulation of receptor-mediated endocytosis	3.14043783813478e-05	0.000735456002754019
GO:0046598	positive regulation of viral entry into host cell	3.15081116619695e-05	0.000735456002754019
GO:0075294	positive regulation by symbiont of entry into host	3.15081116619695e-05	0.000735456002754019
GO:0098883	synapse pruning	3.15081116619695e-05	0.000735456002754019
GO:2000392	regulation of lamellipodium morphogenesis	3.15081116619695e-05	0.000735456002754019
GO:0030890	positive regulation of B cell proliferation	3.15154226220897e-05	0.000735456002754019
GO:1903306	negative regulation of regulated secretory pathway	3.15390553266117e-05	0.000735456002754019
GO:0050920	regulation of chemotaxis	3.19039885287028e-05	0.000741048329629437
GO:0002688	regulation of leukocyte chemotaxis	3.24189432270605e-05	0.000747149419197975
GO:0032652	regulation of interleukin-1 production	3.24189432270605e-05	0.000747149419197975
GO:0051924	regulation of calcium ion transport	3.25842937207378e-05	0.000748049502743915
GO:0001959	regulation of cytokine-mediated signaling pathway	3.31023264320181e-05	0.0007570080287909
GO:0002449	lymphocyte mediated immunity	3.40025171150873e-05	0.000774603495664086
GO:0045920	negative regulation of exocytosis	3.65402582055127e-05	0.00082922585958334
GO:0071496	cellular response to external stimulus	3.75507651175833e-05	0.000848905274013151

GO:0050921	positive regulation of chemotaxis	3.85153124891963e-05	0.000865189370081622
GO:0046456	icosanoid biosynthetic process	3.85632270304826e-05	0.000865189370081622
GO:0010959	regulation of metal ion transport	4.05068631188783e-05	0.000905366604728741
GO:0042100	B cell proliferation	4.09664902277949e-05	0.00091219744969635
GO:0006631	fatty acid metabolic process	4.1792939324555e-05	0.00092711453040951
GO:0001910	regulation of leukocyte mediated cytotoxicity	4.61908235384745e-05	0.00102053292514275
GO:0033559	unsaturated fatty acid metabolic process	4.63487011418875e-05	0.00102053292514275
GO:0032651	regulation of interleukin-1 beta production	4.86491159328579e-05	0.00106721745803821
GO:0031295	T cell costimulation	4.96187667446881e-05	0.00108447216025383
GO:0006665	sphingolipid metabolic process	5.04375770187316e-05	0.00109675401642086
GO:0043302	positive regulation of leukocyte degranulation	5.05510461730364e-05	0.00109675401642086
GO:0046467	membrane lipid biosynthetic process	5.53948200999143e-05	0.00119310370709743
GO:1903900	regulation of viral life cycle	5.53948200999143e-05	0.00119310370709743
GO:0014015	positive regulation of gliogenesis	5.66130774119639e-05	0.00121492484605457
GO:0032088	negative regulation of NF-kappaB transcription factor activity	5.87798884138076e-05	0.00125687104359199
GO:0032970	regulation of actin filament-based process	5.97951391421173e-05	0.00127398060841281
GO:0060759	regulation of response to cytokine stimulus	6.37296740428562e-05	0.00135294214822881
GO:0062207	regulation of pattern recognition receptor signaling pathway	6.83183245999233e-05	0.00144517655930481
GO:0034154	toll-like receptor 7 signaling pathway	6.87329610821299e-05	0.00144527508733823
GO:0043367	CD4-positive, alpha-beta T cell differentiation	6.88110036517611e-05	0.00144527508733823
GO:0002704	negative regulation of leukocyte mediated immunity	6.97689809218824e-05	0.0014550763169025
GO:0002720	positive regulation of cytokine production involved in immune response	6.97689809218824e-05	0.0014550763169025
GO:0043903	regulation of biological process involved in symbiotic interaction	7.32211089627537e-05	0.00152171448556628
GO:0001913	T cell mediated cytotoxicity	7.51369884891691e-05	0.00155064941749599
GO:0033628	regulation of cell adhesion mediated by integrin	7.51369884891691e-05	0.00155064941749599
GO:0032753	positive regulation of interleukin-4 production	7.85155678755566e-05	0.0016147489879407
GO:0001914	regulation of T cell mediated cytotoxicity	7.90662080934029e-05	0.00162044688767206
GO:0031294	lymphocyte costimulation	8.04035851688064e-05	0.00164151258274871
GO:0042113	B cell activation	8.06483473881265e-05	0.00164151258274871

GO:1901264	carbohydrate derivative transport	8.34511849275143e-05	0.00169225852436224
GO:0044282	small molecule catabolic process	8.37129406783955e-05	0.00169225852436224
GO:0072673	lamellipodium morphogenesis	8.67776008433031e-05	0.00174231772811825
GO:0090594	inflammatory response to wounding	8.67776008433031e-05	0.00174231772811825
GO:0032928	regulation of superoxide anion generation	8.74619538996331e-05	0.00174423283820716
GO:0150146	cell junction disassembly	8.74619538996331e-05	0.00174423283820716
GO:0001909	leukocyte mediated cytotoxicity	9.11121950145982e-05	0.00181093131232035
GO:0001916	positive regulation of T cell mediated cytotoxicity	9.60689835952581e-05	0.00190306551784185
GO:0032330	regulation of chondrocyte differentiation	9.78538213614761e-05	0.00193196061308008
GO:0006066	alcohol metabolic process	9.94758848854248e-05	0.00195548774219396
GO:0050792	regulation of viral process	9.97057737873671e-05	0.00195548774219396
GO:0048525	negative regulation of viral process	0.000101122234774069	0.00197672276094658
GO:0050731	positive regulation of peptidyl-tyrosine phosphorylation	0.000101503411520018	0.00197764706063509
GO:0002700	regulation of production of molecular mediator of immune response	0.000102673313969967	0.00199388209391513
GO:0045622	regulation of T-helper cell differentiation	0.000107266480153849	0.00207627242467729
GO:0002294	CD4-positive, alpha-beta T cell differentiation involved in immune response	0.00011021323454588	0.00211659840778397
GO:0042130	negative regulation of T cell proliferation	0.00011021323454588	0.00211659840778397
GO:0014066	regulation of phosphatidylinositol 3-kinase signaling	0.000110421899038536	0.00211659840778397
GO:0002708	positive regulation of lymphocyte mediated immunity	0.000111252266625895	0.00212563604911347
GO:0001912	positive regulation of leukocyte mediated cytotoxicity	0.0001141011139166	0.00216609262092315
GO:0031529	ruffle organization	0.0001141011139166	0.00216609262092315
GO:0071887	leukocyte apoptotic process	0.000115428396516888	0.00218428879415185
GO:0033627	cell adhesion mediated by integrin	0.000116327919136112	0.00219430020714393
GO:2001236	regulation of extrinsic apoptotic signaling pathway	0.000122980885338402	0.00231243105987097
GO:0046686	response to cadmium ion	0.000126855528107578	0.00237773826892779
GO:0032479	regulation of type I interferon production	0.000127389841130657	0.00238022091172519
GO:0110053	regulation of actin filament organization	0.000129071456175583	0.00240405734254082
GO:0097530	granulocyte migration	0.000133615324537574	0.00248088892550487
GO:0062197	cellular response to chemical stress	0.000135302217155813	0.00249509244636835

GO:0002495	antigen processing and presentation of peptide antigen via MHC class II	0.000135715772896846	0.00249509244636835
GO:0002287	alpha-beta T cell activation involved in immune response	0.000136065314904099	0.00249509244636835
GO:0002293	alpha-beta T cell differentiation involved in immune response	0.000136065314904099	0.00249509244636835
GO:0045577	regulation of B cell differentiation	0.000137355903026674	0.00251098460995985
GO:0033630	positive regulation of cell adhesion mediated by integrin	0.000138814934193735	0.00252984878532151
GO:0002292	T cell differentiation involved in immune response	0.000141952526234805	0.00257909451806366
GO:0032735	positive regulation of interleukin-12 production	0.00014373921155803	0.00260356987785386
GO:0034109	homotypic cell-cell adhesion	0.000145302258453907	0.00262385755128808
GO:0032606	type I interferon production	0.000146650857920772	0.00264016118986241
GO:0019885	antigen processing and presentation of endogenous peptide antigen via MHC class I	0.000148818550742259	0.00264700383197117
GO:0031643	positive regulation of myelination	0.000148818550742259	0.00264700383197117
GO:0034134	toll-like receptor 2 signaling pathway	0.000148818550742259	0.00264700383197117
GO:0150078	positive regulation of neuroinflammatory response	0.000148818550742259	0.00264700383197117
GO:0032613	interleukin-10 production	0.000157855828095588	0.00279934152637776
GO:0002504	antigen processing and presentation of peptide or polysaccharide antigen via MHC class II	0.000159109454388162	0.00281315014430174
GO:2000106	regulation of leukocyte apoptotic process	0.000174349518878946	0.00306897773098399
GO:0034162	toll-like receptor 9 signaling pathway	0.000174615143566032	0.00306897773098399
GO:0030183	B cell differentiation	0.000178854247290411	0.00313418256420446
GO:0042088	T-helper 1 type immune response	0.000190392439722236	0.00331221460807792
GO:0046636	negative regulation of alpha-beta T cell activation	0.000190392439722236	0.00331221460807792
GO:0001516	prostaglandin biosynthetic process	0.000192804507678313	0.00331221460807792
GO:0046457	prostanoid biosynthetic process	0.000192804507678313	0.00331221460807792
GO:0032060	bleb assembly	0.000192928252538727	0.00331221460807792
GO:0043301	negative regulation of leukocyte degranulation	0.000192928252538727	0.00331221460807792
GO:1902946	protein localization to early endosome	0.000192928252538727	0.00331221460807792
GO:0038061	NIK/NF-kappaB signaling	0.000194396284790501	0.00332777223934721
GO:0045730	respiratory burst	0.000196651246795143	0.00335667243448885
GO:0030278	regulation of ossification	0.000205207692340213	0.00348265089321228
GO:1903509	liposaccharide metabolic process	0.000205207692340213	0.00348265089321228

GO:0045649	regulation of macrophage differentiation	0.000213082850332513	0.00360597063576992
GO:0031960	response to corticosteroid	0.000221620608002532	0.00373976883532478
GO:0042093	T-helper cell differentiation	0.000240182375658685	0.00404147787223406
GO:0035589	G protein-coupled purinergic nucleotide receptor signaling pathway	0.000246190048335844	0.00413083188751617
GO:0031641	regulation of myelination	0.000249450110522734	0.00417370905261626
GO:0002825	regulation of T-helper 1 type immune response	0.000251350524583149	0.0041818796547921
GO:0034123	positive regulation of toll-like receptor signaling pathway	0.000251350524583149	0.0041818796547921
GO:0051091	positive regulation of DNA-binding transcription factor activity	0.000254977444374896	0.00423034006451684
GO:0071320	cellular response to cAMP	0.000259027274625839	0.00428552666929844
GO:0019058	viral life cycle	0.000263450917572971	0.00434657321667049
GO:0033209	tumor necrosis factor-mediated signaling pathway	0.000266039009745497	0.00435373002329559
GO:0032673	regulation of interleukin-4 production	0.000266089864668749	0.00435373002329559
GO:0035590	purinergic nucleotide receptor signaling pathway	0.000266089864668749	0.00435373002329559
GO:0043030	regulation of macrophage activation	0.000280424312752306	0.00457562866234686
GO:0046486	glycerolipid metabolic process	0.000284586106976363	0.00463077887807966
GO:0046849	bone remodeling	0.000288850609736578	0.00468729359306781
GO:0034446	substrate adhesion-dependent cell spreading	0.000292403763283139	0.00473198767739353
GO:0070265	necrotic cell death	0.0002938038692767	0.00474169023903513
GO:0007040	lysosome organization	0.000300194912791069	0.00481452310586111
GO:0080171	lytic vacuole organization	0.000300194912791069	0.00481452310586111
GO:0034121	regulation of toll-like receptor signaling pathway	0.000300755284343848	0.00481452310586111
GO:0006672	ceramide metabolic process	0.000309706692018685	0.0049444548162444
GO:0032331	negative regulation of chondrocyte differentiation	0.00031756758157789	0.00505632469270387
GO:0031334	positive regulation of protein-containing complex assembly	0.000320842196821307	0.00509356869104934
GO:0045454	cell redox homeostasis	0.000323480564025545	0.00509356869104934
GO:0000768	syncytium formation by plasma membrane fusion	0.000324206550147831	0.00509356869104934
GO:0006968	cellular defense response	0.000324206550147831	0.00509356869104934
GO:0140253	cell-cell fusion	0.000324206550147831	0.00509356869104934
GO:0048839	inner ear development	0.00033217986432702	0.00520502999049985

GO:0030148	sphingolipid biosynthetic process	0.000338212276546833	0.00528557074930578
GO:0032615	interleukin-12 production	0.000345554132274786	0.00535789823419779
GO:0032653	regulation of interleukin-10 production	0.000345554132274786	0.00535789823419779
GO:0032655	regulation of interleukin-12 production	0.000345554132274786	0.00535789823419779
GO:0032703	negative regulation of interleukin-2 production	0.00035440245424269	0.00546259085718899
GO:0061037	negative regulation of cartilage development	0.00035440245424269	0.00546259085718899
GO:0001885	endothelial cell development	0.000357498579285353	0.00546259085718899
GO:0061035	regulation of cartilage development	0.000357498579285353	0.00546259085718899
GO:0072678	T cell migration	0.000357498579285353	0.00546259085718899
GO:0031532	actin cytoskeleton reorganization	0.000359729081266215	0.00546259085718899
GO:0002724	regulation of T cell cytokine production	0.000361528890092535	0.00546259085718899
GO:0032633	interleukin-4 production	0.000361528890092535	0.00546259085718899
GO:0045589	regulation of regulatory T cell differentiation	0.000361528890092535	0.00546259085718899
GO:0050869	negative regulation of B cell activation	0.000361528890092535	0.00546259085718899
GO:0007398	ectoderm development	0.000381563125541419	0.00573603652939549
GO:1903975	regulation of glial cell migration	0.000381563125541419	0.00573603652939549
GO:0006690	icosanoid metabolic process	0.000385818773004998	0.00576832199768899
GO:0045657	positive regulation of monocyte differentiation	0.000386632421590837	0.00576832199768899
GO:2001269	positive regulation of cysteine-type endopeptidase activity involved in apoptotic signaling pathway	0.000386632421590837	0.00576832199768899
GO:0002690	positive regulation of leukocyte chemotaxis	0.000398930416260598	0.00593684637063197
GO:0007599	hemostasis	0.000400527749033627	0.00594567884091773
GO:2000377	regulation of reactive oxygen species metabolic process	0.000410690048674476	0.00608129289574731
GO:0150076	neuroinflammatory response	0.000415423958716674	0.00613605014333881
GO:0038065	collagen-activated signaling pathway	0.000419784362747145	0.00616968431898595
GO:0060099	regulation of phagocytosis, engulfment	0.000419784362747145	0.00616968431898595
GO:0050817	coagulation	0.000431298474505678	0.00632171630910003
GO:0033077	T cell differentiation in thymus	0.000433330545584098	0.00632171630910003
GO:0042246	tissue regeneration	0.000433330545584098	0.00632171630910003
GO:0008360	regulation of cell shape	0.000443457491269675	0.00645355951054124

GO:0001503	ossification	0.000444581810878511	0.00645406388684662
GO:0006664	glycolipid metabolic process	0.000449089315221534	0.00648769759526133
GO:0022612	gland morphogenesis	0.000449089315221534	0.00648769759526133
GO:0006816	calcium ion transport	0.000453061729551175	0.00652915966941997
GO:0050864	regulation of B cell activation	0.000454808390456247	0.00653842256473872
GO:0007204	positive regulation of cytosolic calcium ion concentration	0.000456318557726008	0.00654424895256936
GO:0051928	positive regulation of calcium ion transport	0.000477276288024734	0.00681182519029036
GO:0072676	lymphocyte migration	0.000477276288024734	0.00681182519029036
GO:0036336	dendritic cell migration	0.000490367438793972	0.00698184216340553
GO:0006949	syncytium formation	0.000497635047294356	0.00706832706264861
GO:0018212	peptidyl-tyrosine modification	0.000502007501871257	0.00711337424302261
GO:0019886	antigen processing and presentation of exogenous peptide antigen via MHC class II	0.000513311910154874	0.00725619676335875
GO:0070527	platelet aggregation	0.000515646786546718	0.00727184742075288
GO:0046513	ceramide biosynthetic process	0.000521352126028377	0.00732610482618883
GO:0007596	blood coagulation	0.00052196796161602	0.00732610482618883
GO:0014013	regulation of gliogenesis	0.000543927235538173	0.00761626717752388
GO:0030041	actin filament polymerization	0.000561588871355391	0.00784502567225939
GO:0051048	negative regulation of secretion	0.000564167760325189	0.00786250739860258
GO:0016485	protein processing	0.000569401907149323	0.00791682510808788
GO:0032495	response to muramyl dipeptide	0.000577630573302609	0.00801242596175961
GO:0051403	stress-activated MAPK cascade	0.00058876920667508	0.00813865535360903
GO:0150077	regulation of neuroinflammatory response	0.000589478836180698	0.00813865535360903
GO:0070374	positive regulation of ERK1 and ERK2 cascade	0.000593761978574967	0.00817872604441751
GO:0009100	glycoprotein metabolic process	0.000599282208075895	0.00823561141167872
GO:0008202	steroid metabolic process	0.000613411222000957	0.00841026543498071
GO:0001676	long-chain fatty acid metabolic process	0.000620917353279371	0.00843403327605299
GO:0071248	cellular response to metal ion	0.000620983295573195	0.00843403327605299
GO:0034599	cellular response to oxidative stress	0.000623913259515427	0.00843403327605299
GO:0045670	regulation of osteoclast differentiation	0.000624710670558784	0.00843403327605299

GO:0071677	positive regulation of mononuclear cell migration	0.000624710670558784	0.00843403327605299
GO:0014065	phosphatidylinositol 3-kinase signaling	0.000625112376867679	0.00843403327605299
GO:0051017	actin filament bundle assembly	0.000625112376867679	0.00843403327605299
GO:0051897	positive regulation of protein kinase B signaling	0.00063021733504254	0.00848358471694764
GO:0031579	membrane raft organization	0.000653612177100537	0.00877855992055891
GO:0050798	activated T cell proliferation	0.000666822032367731	0.00887615731045286
GO:0035666	TRIF-dependent toll-like receptor signaling pathway	0.000666873206677616	0.00887615731045286
GO:0050901	leukocyte tethering or rolling	0.000666873206677616	0.00887615731045286
GO:0051125	regulation of actin nucleation	0.000666873206677616	0.00887615731045286
GO:0002532	production of molecular mediator involved in inflammatory response	0.000668409866154948	0.00887666286375731
GO:0045591	positive regulation of regulatory T cell differentiation	0.000678789622005689	0.0089343798469771
GO:0071361	cellular response to ethanol	0.000678789622005689	0.0089343798469771
GO:1901201	regulation of extracellular matrix assembly	0.000678789622005689	0.0089343798469771
GO:1905153	regulation of membrane invagination	0.000678789622005689	0.0089343798469771
GO:1904064	positive regulation of cation transmembrane transport	0.000681089886109108	0.00894477914728214
GO:0034340	response to type I interferon	0.000685224908218622	0.00895935349090265
GO:1902106	negative regulation of leukocyte differentiation	0.000685224908218622	0.00895935349090265
GO:0018108	peptidyl-tyrosine phosphorylation	0.000694728537820608	0.00906360601213978
GO:0007033	vacuole organization	0.000698995212899964	0.00909137764199477
GO:0033004	negative regulation of mast cell activation	0.000704531882099544	0.00909137764199477
GO:0035672	oligopeptide transmembrane transport	0.000704531882099544	0.00909137764199477
GO:0038063	collagen-activated tyrosine kinase receptor signaling pathway	0.000704531882099544	0.00909137764199477
GO:1905668	positive regulation of protein localization to endosome	0.000704531882099544	0.00909137764199477
GO:1902903	regulation of supramolecular fiber organization	0.000743839758925792	0.00954688369649884
GO:0019722	calcium-mediated signaling	0.000744666599321706	0.00954688369649884
GO:1901136	carbohydrate derivative catabolic process	0.000744666599321706	0.00954688369649884
GO:0051384	response to glucocorticoid	0.000750602984245328	0.00959142193051144
GO:0007520	myoblast fusion	0.000754618034715234	0.00959142193051144
GO:0046596	regulation of viral entry into host cell	0.000754618034715234	0.00959142193051144

GO:19053 14	semi-lunar valve development	0.00075461803471 5234	0.00959142193051 144
GO:00434 33	negative regulation of DNA-binding transcription factor activity	0.00077428918675 2628	0.00982037441784 972
GO:00193 18	hexose metabolic process	0.00080906741029 7633	0.01023954331451 47
GO:00510 47	positive regulation of secretion	0.00081857007504 3174	0.01033771973236 83
GO:00190 79	viral genome replication	0.00082581442980 5667	0.01040534278714 82
GO:00970 28	dendritic cell differentiation	0.00083423713280 0248	0.01040534278714 82
GO:00023 69	T cell cytokine production	0.00083454142847 4412	0.01040534278714 82
GO:00031 76	aortic valve development	0.00083454142847 4412	0.01040534278714 82
GO:00066 91	leukotriene metabolic process	0.00083454142847 4412	0.01040534278714 82
GO:00450 66	regulatory T cell differentiation	0.00083454142847 4412	0.01040534278714 82
GO:00463 95	carboxylic acid catabolic process	0.00083622204401 1912	0.01040534278714 82
GO:00160 54	organic acid catabolic process	0.00084885000888 6252	0.01051828159546 71
GO:00456 37	regulation of myeloid cell differentiation	0.00084885000888 6252	0.01051828159546 71
GO:00462 09	nitric oxide metabolic process	0.00085781356498 0124	0.01060716021999 43
GO:00022 30	positive regulation of defense response to virus by host	0.00089262020620 1093	0.01101456141943 56
GO:00464 70	phosphatidylcholine metabolic process	0.00090368701866 6666	0.01112492492888 25
GO:00358 21	modulation of process of other organism	0.00090680687062 1711	0.01112492492888 25
GO:00027 19	negative regulation of cytokine production involved in immune response	0.00090719884191 2923	0.01112492492888 25
GO:00456 87	positive regulation of glial cell differentiation	0.00095668520439 2232	0.01166152597641 05
GO:00622 08	positive regulation of pattern recognition receptor signaling pathway	0.00095668520439 2232	0.01166152597641 05
GO:00060 22	aminoglycan metabolic process	0.00095686335041 9639	0.01166152597641 05
GO:00161 25	sterol metabolic process	0.00096391358335 2263	0.01172332680532 95
GO:00615 72	actin filament bundle organization	0.00096716426815 7631	0.01173875811536 4
GO:20001 16	regulation of cysteine-type endopeptidase activity	0.00097018154725 0559	0.01175129919093 06
GO:00226 04	regulation of cell morphogenesis	0.00098203029259 3895	0.01187054167966 05
GO:00321 47	activation of protein kinase activity	0.00099009532901 5545	0.01194365505857 24
GO:20010 57	reactive nitrogen species metabolic process	0.00100745866487 764	0.01212840990258 18
GO:00716 21	granulocyte chemotaxis	0.00102462982849 711	0.01229140876556 16
GO:00602 84	regulation of cell development	0.00102824498785 819	0.01229140876556 16

GO:0071241	cellular response to inorganic substance	0.00102867023729891	0.0122914087655616
GO:0006692	prostanoid metabolic process	0.00103552472970036	0.0122914087655616
GO:0006693	prostaglandin metabolic process	0.00103552472970036	0.0122914087655616
GO:0052372	modulation by symbiont of entry into host	0.00103552472970036	0.0122914087655616
GO:0061028	establishment of endothelial barrier	0.00103552472970036	0.0122914087655616
GO:0048708	astrocyte differentiation	0.00104850593099267	0.0124206012585392
GO:0048713	regulation of oligodendrocyte differentiation	0.00107616314053842	0.0126591329933516
GO:0030199	collagen fibril organization	0.00107719112420213	0.0126591329933516
GO:0045071	negative regulation of viral genome replication	0.00107719112420213	0.0126591329933516
GO:0061756	leukocyte adhesion to vascular endothelial cell	0.00107719112420213	0.0126591329933516
GO:0031098	stress-activated protein kinase signaling cascade	0.00107994878262088	0.0126664091870563
GO:0045576	mast cell activation	0.00108883536696755	0.0127453989694641
GO:0070304	positive regulation of stress-activated protein kinase signaling cascade	0.00112533638729194	0.0131466813055822
GO:0045088	regulation of innate immune response	0.001166528429185	0.0135036975680187
GO:0090322	regulation of superoxide metabolic process	0.00117740672507943	0.0135036975680187
GO:2000515	negative regulation of CD4-positive, alpha-beta T cell activation	0.00117740672507943	0.0135036975680187
GO:0001776	leukocyte homeostasis	0.0011788011967687	0.0135036975680187
GO:1903707	negative regulation of hemopoiesis	0.0011829278930598	0.0135036975680187
GO:1902905	positive regulation of supramolecular fiber organization	0.00118636487289768	0.0135036975680187
GO:0001771	immunological synapse formation	0.00119237444336887	0.0135036975680187
GO:0006857	oligopeptide transport	0.00119237444336887	0.0135036975680187
GO:0036109	alpha-linolenic acid metabolic process	0.00119237444336887	0.0135036975680187
GO:0060100	positive regulation of phagocytosis, engulfment	0.00119237444336887	0.0135036975680187
GO:0072683	T cell extravasation	0.00119237444336887	0.0135036975680187
GO:1903054	negative regulation of extracellular matrix organization	0.00119237444336887	0.0135036975680187
GO:1903977	positive regulation of glial cell migration	0.00119237444336887	0.0135036975680187
GO:1905155	positive regulation of membrane invagination	0.00119237444336887	0.0135036975680187
GO:1905666	regulation of protein localization to endosome	0.00119237444336887	0.0135036975680187
GO:2001198	regulation of dendritic cell differentiation	0.00119237444336887	0.0135036975680187

GO:0014003	oligodendrocyte development	0.00120179667808256	0.0135327789435039
GO:0046006	regulation of activated T cell proliferation	0.00120179667808256	0.0135327789435039
GO:0097178	ruffle assembly	0.00120179667808256	0.0135327789435039
GO:0001911	negative regulation of leukocyte mediated cytotoxicity	0.00121029274732487	0.0135768256484947
GO:0045624	positive regulation of T-helper cell differentiation	0.00121029274732487	0.0135768256484947
GO:0097305	response to alcohol	0.00125110181472026	0.0140080832676523
GO:0009395	phospholipid catabolic process	0.00127582022382052	0.0142450478613143
GO:0006687	glycosphingolipid metabolic process	0.00127948091545149	0.0142450478613143
GO:0050848	regulation of calcium-mediated signaling	0.00127948091545149	0.0142450478613143
GO:0002702	positive regulation of production of molecular mediator of immune response	0.00128425637623642	0.014271389336676
GO:0045471	response to ethanol	0.00130049115293242	0.01442473614011
GO:0080164	regulation of nitric oxide metabolic process	0.0013058533227248	0.0144571387485962
GO:0006694	steroid biosynthetic process	0.00136421433831273	0.0150470047035872
GO:0046578	regulation of Ras protein signal transduction	0.00136421433831273	0.0150470047035872
GO:0043010	camera-type eye development	0.00140861912112531	0.015507901588151
GO:0002832	negative regulation of response to biotic stimulus	0.0014677724041456	0.0161291576062234
GO:0045124	regulation of bone resorption	0.00149668644784478	0.0164164330196011
GO:0045685	regulation of glial cell differentiation	0.00151275131219707	0.016539334317789
GO:0006979	response to oxidative stress	0.00151347614388682	0.016539334317789
GO:0030851	granulocyte differentiation	0.001532136218552	0.0167124177209641
GO:0051235	maintenance of location	0.00154405404254554	0.016811456055142
GO:0030100	regulation of endocytosis	0.00154935050046197	0.0168322521852857
GO:0008347	glial cell migration	0.00156074299551668	0.0168322521852857
GO:2000179	positive regulation of neural precursor cell proliferation	0.00156074299551668	0.0168322521852857
GO:0002643	regulation of tolerance induction	0.00156301514467451	0.0168322521852857
GO:0034375	high-density lipoprotein particle remodeling	0.00156301514467451	0.0168322521852857
GO:0045953	negative regulation of natural killer cell mediated cytotoxicity	0.00156301514467451	0.0168322521852857
GO:0043280	positive regulation of cysteine-type endopeptidase activity involved in apoptotic process	0.00165031489192438	0.0177293675895796
GO:0002507	tolerance induction	0.00165230641726286	0.0177293675895796

GO:0008064	regulation of actin polymerization or depolymerization	0.00167956696018285	0.017989285904454
GO:1903055	positive regulation of extracellular matrix organization	0.00168641283572326	0.0180300058230846
GO:1904407	positive regulation of nitric oxide metabolic process	0.00173279758110325	0.0184925406718461
GO:0007160	cell-matrix adhesion	0.00180207985831751	0.0191973363324004
GO:0030168	platelet activation	0.00180817215760729	0.0192276547387935
GO:0060337	type I interferon signaling pathway	0.00182215549765201	0.0193416254705966
GO:0031331	positive regulation of cellular catabolic process	0.00183887155976143	0.0194668273998558
GO:0030832	regulation of actin filament length	0.00184052394798569	0.0194668273998558
GO:0002707	negative regulation of lymphocyte mediated immunity	0.00184871130638119	0.019494410678144
GO:2000401	regulation of lymphocyte migration	0.00184971446920765	0.019494410678144
GO:0001906	cell killing	0.00188590437235893	0.0198338405931501
GO:0046850	regulation of bone remodeling	0.00189640180258262	0.0198338405931501
GO:0097300	programmed necrotic cell death	0.00189640180258262	0.0198338405931501
GO:0001921	positive regulation of receptor recycling	0.00190201273964363	0.0198338405931501
GO:0010935	regulation of macrophage cytokine production	0.00190201273964363	0.0198338405931501
GO:0043374	CD8-positive, alpha-beta T cell differentiation	0.00190201273964363	0.0198338405931501
GO:0048880	sensory system development	0.0019220775099571	0.0199373788763744
GO:0048545	response to steroid hormone	0.00192540616533617	0.0199373788763744
GO:0071214	cellular response to abiotic stimulus	0.00192540616533617	0.0199373788763744
GO:0104004	cellular response to environmental stimulus	0.00192540616533617	0.0199373788763744
GO:0002691	regulation of cellular extravasation	0.00196880588891513	0.0203157443903211
GO:0002756	MyD88-independent toll-like receptor signaling pathway	0.00196880588891513	0.0203157443903211
GO:0060395	SMAD protein signal transduction	0.00197254865036719	0.020318966358478
GO:0032874	positive regulation of stress-activated MAPK cascade	0.0020068263294366	0.0206361672730086
GO:2001056	positive regulation of cysteine-type endopeptidase activity	0.00202285212637072	0.0207649101291053
GO:0009636	response to toxic substance	0.00203297026398914	0.02081161279599
GO:1990266	neutrophil migration	0.00203442914213713	0.02081161279599
GO:0090527	actin filament reorganization	0.00204002536683836	0.0208328797375579
GO:0006766	vitamin metabolic process	0.00204814779298305	0.0208600505528359

GO:0003158	endothelium development	0.00204972976899383	0.0208600505528359
GO:0009612	response to mechanical stimulus	0.0020724464763592	0.0210190076703348
GO:0043583	ear development	0.0020724464763592	0.0210190076703348
GO:0071357	cellular response to type I interferon	0.00207889971913494	0.0210484154468996
GO:0019216	regulation of lipid metabolic process	0.00210035038704209	0.0212293094581063
GO:0052548	regulation of endopeptidase activity	0.00212124262827191	0.0214039524484745
GO:0045069	regulation of viral genome replication	0.00213306347762413	0.02148662411219
GO:0150063	visual system development	0.00215669401212258	0.0216877735718201
GO:2001233	regulation of apoptotic signaling pathway	0.00225056189658443	0.0225067082524719
GO:0002716	negative regulation of natural killer cell mediated immunity	0.00225219548916882	0.0225067082524719
GO:0010829	negative regulation of glucose transmembrane transport	0.00225219548916882	0.0225067082524719
GO:0031102	neuron projection regeneration	0.00225713062670409	0.0225067082524719
GO:0031638	zymogen activation	0.00225713062670409	0.0225067082524719
GO:0043303	mast cell degranulation	0.00226584869720946	0.0225556669471793
GO:0001889	liver development	0.00227864080750015	0.022637877341815
GO:0048678	response to axon injury	0.00228839025789354	0.022637877341815
GO:0002820	negative regulation of adaptive immune response	0.00228939532800053	0.022637877341815
GO:0032608	interferon-beta production	0.00228939532800053	0.022637877341815
GO:0002407	dendritic cell chemotaxis	0.00229911985868525	0.0226961448716545
GO:1903532	positive regulation of secretion by cell	0.00230826565254976	0.0227485149085727
GO:0046579	positive regulation of Ras protein signal transduction	0.00243672703250351	0.0239348826094831
GO:0070227	lymphocyte apoptotic process	0.00243672703250351	0.0239348826094831
GO:0008625	extrinsic apoptotic signaling pathway via death domain receptors	0.00245349761168386	0.0240259307871312
GO:0048872	homeostasis of number of cells	0.00245410908766071	0.0240259307871312
GO:0010950	positive regulation of endopeptidase activity	0.00247734710356824	0.0242034440458365
GO:0005996	monosaccharide metabolic process	0.00248041373220037	0.0242034440458365
GO:0014902	myotube differentiation	0.00249528912486794	0.0243085484976855
GO:1903531	negative regulation of secretion by cell	0.00252899220002796	0.024596421676134
GO:0045824	negative regulation of innate immune response	0.00257028404949205	0.0249570367625269

GO:0030001	metal ion transport	0.00261368537324406	0.025336920565834
GO:0043281	regulation of cysteine-type endopeptidase activity involved in apoptotic process	0.00266910013597558	0.0258141976562171
GO:0045428	regulation of nitric oxide biosynthetic process	0.00267841102576491	0.0258141976562171
GO:1902041	regulation of extrinsic apoptotic signaling pathway via death domain receptors	0.00267841102576491	0.0258141976562171
GO:0032689	negative regulation of interferon-gamma production	0.00268414933887089	0.0258141976562171
GO:0051817	modulation of process of other organism involved in symbiotic interaction	0.00268471142262869	0.0258141976562171
GO:0042493	response to drug	0.00273678354391641	0.0262505736208984
GO:1902743	regulation of lamellipodium organization	0.00274680761667849	0.0262505736208984
GO:0002279	mast cell activation involved in immune response	0.00275668694786405	0.0262505736208984
GO:0002448	mast cell mediated immunity	0.00275668694786405	0.0262505736208984
GO:0002823	negative regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	0.00275668694786405	0.0262505736208984
GO:0045581	negative regulation of T cell differentiation	0.00275668694786405	0.0262505736208984
GO:0052547	regulation of peptidase activity	0.00279532481824382	0.0265573606867265
GO:0046718	viral entry into host cell	0.0028023552978565	0.0265573606867265
GO:0061008	hepaticobiliary system development	0.0028023552978565	0.0265573606867265
GO:0002828	regulation of type 2 immune response	0.00282159570795797	0.0266969830323244
GO:0120254	olefinic compound metabolic process	0.00282917647216302	0.0267229314520303
GO:0002753	cytoplasmic pattern recognition receptor signaling pathway	0.00283336163293518	0.0267229314520303
GO:0002827	positive regulation of T-helper 1 type immune response	0.00289016499090796	0.0268735435496826
GO:0010934	macrophage cytokine production	0.00289016499090796	0.0268735435496826
GO:0030852	regulation of granulocyte differentiation	0.00289016499090796	0.0268735435496826
GO:0032933	SREBP signaling pathway	0.00289016499090796	0.0268735435496826
GO:0034638	phosphatidylcholine catabolic process	0.00289016499090796	0.0268735435496826
GO:0045064	T-helper 2 cell differentiation	0.00289016499090796	0.0268735435496826
GO:0045579	positive regulation of B cell differentiation	0.00289016499090796	0.0268735435496826
GO:0097202	activation of cysteine-type endopeptidase activity	0.00289016499090796	0.0268735435496826
GO:2001044	regulation of integrin-mediated signaling pathway	0.00289016499090796	0.0268735435496826
GO:0050854	regulation of antigen receptor-mediated signaling pathway	0.00300940139102473	0.0279383768636982

GO:0048259	regulation of receptor-mediated endocytosis	0.00310486915317159	0.0287795618063151
GO:0042092	type 2 immune response	0.0031412201056129	0.0289171155569467
GO:0002064	epithelial cell development	0.00314413489366642	0.0289171155569467
GO:0034764	positive regulation of transmembrane transport	0.00314413489366642	0.0289171155569467
GO:0034767	positive regulation of ion transmembrane transport	0.00314413489366642	0.0289171155569467
GO:0002726	positive regulation of T cell cytokine production	0.00315388429001985	0.0289171155569467
GO:0007252	I-kappaB phosphorylation	0.00315388429001985	0.0289171155569467
GO:0043691	reverse cholesterol transport	0.00315388429001985	0.0289171155569467
GO:0034113	heterotypic cell-cell adhesion	0.00316219492192061	0.0289485015804263
GO:0034103	regulation of tissue remodeling	0.00321583666525824	0.029367080956296
GO:0030324	lung development	0.00321783480341653	0.029367080956296
GO:0006650	glycerophospholipid metabolic process	0.00323958310463187	0.029520078044207
GO:0043406	positive regulation of MAP kinase activity	0.00325274666864858	0.0295425629669371
GO:0044242	cellular lipid catabolic process	0.00325274666864858	0.0295425629669371
GO:0010952	positive regulation of peptidase activity	0.00326534488098767	0.0295425629669371
GO:0030834	regulation of actin filament depolymerization	0.00327619821185392	0.0295425629669371
GO:0070228	regulation of lymphocyte apoptotic process	0.00327619821185392	0.0295425629669371
GO:0019932	second-messenger-mediated signaling	0.00327984654500599	0.0295425629669371
GO:0006809	nitric oxide biosynthetic process	0.0032819527996361	0.0295425629669371
GO:0031100	animal organ regeneration	0.0032819527996361	0.0295425629669371
GO:0032535	regulation of cellular component size	0.00329434299845325	0.0296090949618188
GO:0014009	glial cell proliferation	0.00333040768725196	0.0298426697906102
GO:2001238	positive regulation of extrinsic apoptotic signaling pathway	0.00333040768725196	0.0298426697906102
GO:1901654	response to ketone	0.00338692781524383	0.0302600033782279
GO:0002645	positive regulation of tolerance induction	0.00341785282121129	0.0302600033782279
GO:0019371	cyclooxygenase pathway	0.00341785282121129	0.0302600033782279
GO:0032493	response to bacterial lipoprotein	0.00341785282121129	0.0302600033782279
GO:0032957	inositol trisphosphate metabolic process	0.00341785282121129	0.0302600033782279
GO:0045628	regulation of T-helper 2 cell differentiation	0.00341785282121129	0.0302600033782279

GO:0046643	regulation of gamma-delta T cell activation	0.00341785282121129	0.0302600033782279
GO:0051132	NK T cell activation	0.00341785282121129	0.0302600033782279
GO:0008630	intrinsic apoptotic signaling pathway in response to DNA damage	0.0034321281539559	0.030341037396837
GO:0009101	glycoprotein biosynthetic process	0.00344287426752802	0.0303906770291632
GO:0045669	positive regulation of osteoblast differentiation	0.00350841691282469	0.0309231449027688
GO:0003180	aortic valve morphogenesis	0.0036107220495858	0.0317304253704698
GO:0097421	liver regeneration	0.0036107220495858	0.0317304253704698
GO:0051604	protein maturation	0.00363591139871488	0.0319044492067974
GO:0050767	regulation of neurogenesis	0.00365708632061279	0.0320427844334165
GO:0051651	maintenance of location in cell	0.00368966676702749	0.0322804966929155
GO:2000403	positive regulation of lymphocyte migration	0.00390605601860343	0.034123259289363
GO:0001501	skeletal system development	0.00395669787721055	0.034514759244062
GO:0070231	T cell apoptotic process	0.00399676037809458	0.0348129584109621
GO:0031342	negative regulation of cell killing	0.00403626644708607	0.0350026444598694
GO:0036152	phosphatidylethanolamine acyl-chain remodeling	0.00403626644708607	0.0350026444598694
GO:0051016	barbed-end actin filament capping	0.00403626644708607	0.0350026444598694
GO:0006026	aminoglycan catabolic process	0.00407322793187025	0.035271533684894
GO:0051960	regulation of nervous system development	0.00412785004895899	0.035672932490006
GO:0010810	regulation of cell-substrate adhesion	0.00413162783861964	0.035672932490006
GO:0060541	respiratory system development	0.00414743175362762	0.0357572609559481
GO:0046890	regulation of lipid biosynthetic process	0.00415935680789819	0.0358079511238096
GO:0002693	positive regulation of cellular extravasation	0.00421699021224933	0.0360421833003647
GO:0002830	positive regulation of type 2 immune response	0.00421699021224933	0.0360421833003647
GO:0045779	negative regulation of bone resorption	0.00421699021224933	0.0360421833003647
GO:0071501	cellular response to sterol depletion	0.00421699021224933	0.0360421833003647
GO:0071800	podosome assembly	0.00421699021224933	0.0360421833003647
GO:0045655	regulation of monocyte differentiation	0.00430699095172959	0.0367583680217498
GO:0045453	bone resorption	0.00434430215054448	0.0369798401010366
GO:0032231	regulation of actin filament bundle assembly	0.00434542777483057	0.0369798401010366

GO:0051701	biological process involved in interaction with host	0.00445705059648964	0.0378753381391795
GO:0043491	protein kinase B signaling	0.00453046555155482	0.0384440508049559
GO:1901889	negative regulation of cell junction assembly	0.00456288891569698	0.0386637926290032
GO:0051058	negative regulation of small GTPase mediated signal transduction	0.00458343286554954	0.0387823898037856
GO:0030323	respiratory tube development	0.00460455977785458	0.0389055742713733
GO:0051480	regulation of cytosolic calcium ion concentration	0.00461795350914881	0.0389631604482741
GO:0002833	positive regulation of response to biotic stimulus	0.00468441746088668	0.0394677163880964
GO:0050688	regulation of defense response to virus	0.00471003193668327	0.0396271578991122
GO:0097581	lamellipodium organization	0.00472010798000012	0.0396556022206251
GO:0007566	embryo implantation	0.00476602902522444	0.0399846882668617
GO:0030279	negative regulation of ossification	0.0048108593704158	0.0401334085224969
GO:0032733	positive regulation of interleukin-10 production	0.0048108593704158	0.0401334085224969
GO:0045429	positive regulation of nitric oxide biosynthetic process	0.0048108593704158	0.0401334085224969
GO:0048246	macrophage chemotaxis	0.0048108593704158	0.0401334085224969
GO:0052126	movement in host environment	0.00484899437251899	0.0403946465097468
GO:0002062	chondrocyte differentiation	0.00487250840876023	0.0404199822200096
GO:0007200	phospholipase C-activating G protein-coupled receptor signaling pathway	0.00487250840876023	0.0404199822200096
GO:2001237	negative regulation of extrinsic apoptotic signaling pathway	0.00487250840876023	0.0404199822200096
GO:0044409	entry into host	0.00489123219799096	0.0405185570751055
GO:0010720	positive regulation of cell development	0.00496669628658561	0.0410862319908472
GO:0030500	regulation of bone mineralization	0.004990554977422	0.0412260211035851
GO:0043112	receptor metabolic process	0.00502063497884813	0.0414167423115842
GO:0010803	regulation of tumor necrosis factor-mediated signaling pathway	0.00505704148806928	0.0416590496993524
GO:0032102	negative regulation of response to external stimulus	0.00517853315681938	0.0426006276220016
GO:0002675	positive regulation of acute inflammatory response	0.0052156952666685	0.0427874834688055
GO:0045672	positive regulation of osteoclast differentiation	0.0052156952666685	0.0427874834688055
GO:1901605	alpha-amino acid metabolic process	0.00528964450681489	0.0431608543113772
GO:0071900	regulation of protein serine/threonine kinase activity	0.00530781909425687	0.0431608543113772
GO:0000187	activation of MAPK activity	0.00535232966796554	0.0431608543113772

GO:0002863	positive regulation of inflammatory response to antigenic stimulus	0.00535593920629111	0.0431608543113772
GO:0016554	cytidine to uridine editing	0.00535593920629111	0.0431608543113772
GO:0032494	response to peptidoglycan	0.00535593920629111	0.0431608543113772
GO:0035739	CD4-positive, alpha-beta T cell proliferation	0.00535593920629111	0.0431608543113772
GO:0046185	aldehyde catabolic process	0.00535593920629111	0.0431608543113772
GO:0046642	negative regulation of alpha-beta T cell proliferation	0.00535593920629111	0.0431608543113772
GO:0048266	behavioral response to pain	0.00535593920629111	0.0431608543113772
GO:0061517	macrophage proliferation	0.00535593920629111	0.0431608543113772
GO:0071801	regulation of podosome assembly	0.00535593920629111	0.0431608543113772
GO:2000561	regulation of CD4-positive, alpha-beta T cell proliferation	0.00535593920629111	0.0431608543113772
GO:0001894	tissue homeostasis	0.00536542336804726	0.043167343908802
GO:0002260	lymphocyte homeostasis	0.00537860878012761	0.043167343908802
GO:1900024	regulation of substrate adhesion-dependent cell spreading	0.00537860878012761	0.043167343908802
GO:0006644	phospholipid metabolic process	0.00539723752511127	0.0432582379719
GO:1990868	response to chemokine	0.00541669583741496	0.0432970167948837
GO:1990869	cellular response to chemokine	0.00541669583741496	0.0432970167948837
GO:0030038	contractile actin filament bundle assembly	0.00545121314543012	0.0434556331902861
GO:0043149	stress fiber assembly	0.00545121314543012	0.0434556331902861
GO:0043277	apoptotic cell clearance	0.00564899124757577	0.0449113760528742
GO:0071715	icosanoid transport	0.00564899124757577	0.0449113760528742
GO:0051057	positive regulation of small GTPase mediated signal transduction	0.00569931949401965	0.0450703226063007
GO:0034368	protein-lipid complex remodeling	0.00569942117712632	0.0450703226063007
GO:0034369	plasma lipoprotein particle remodeling	0.00569942117712632	0.0450703226063007
GO:0055094	response to lipoprotein particle	0.00569942117712632	0.0450703226063007
GO:0006907	pinocytosis	0.00575211678045179	0.0453658957265193
GO:1904996	positive regulation of leukocyte adhesion to vascular endothelial cell	0.00575211678045179	0.0453658957265193
GO:0015748	organophosphate ester transport	0.00578513594319112	0.0455656385525545
GO:0048247	lymphocyte chemotaxis	0.0058610792504635	0.0461024865876431
GO:0002701	negative regulation of production of molecular mediator of immune response	0.00587225998742013	0.0461291722884475

GO:0046330	positive regulation of JNK cascade	0.00589106914733952	0.0462156325293933
GO:0010759	positive regulation of macrophage chemotaxis	0.00594456521608163	0.0463895385702918
GO:0030889	negative regulation of B cell proliferation	0.00594456521608163	0.0463895385702918
GO:0043217	myelin maintenance	0.00594456521608163	0.0463895385702918
GO:2001267	regulation of cysteine-type endopeptidase activity involved in apoptotic signaling pathway	0.00594456521608163	0.0463895385702918
GO:0045446	endothelial cell differentiation	0.00599106097342605	0.046690860717898
GO:0062013	positive regulation of small molecule metabolic process	0.00620365800222348	0.0482835276185882
GO:0051051	negative regulation of transport	0.00621172514694652	0.0482835276185882
GO:2001259	positive regulation of cation channel activity	0.00622582757989111	0.0483297205186043
GO:2001234	negative regulation of apoptotic signaling pathway	0.00642864119705051	0.0498387981807987

Online Resource 5 Significantly enriched GO Molecular Function (MF) pathways of upregulated genes in TSC patients tissue

ID	Description	pvalue	p.adjust
GO:0140375	immune receptor activity	4.07185839582541e-09	4.3894633506998e-06
GO:0030246	carbohydrate binding	1.44485229317616e-07	7.78775386021951e-05
GO:0019955	cytokine binding	4.4140516446089e-07	0.00015861158909628
GO:0038024	cargo receptor activity	3.57705682633559e-06	0.000964016814697441
GO:0032395	MHC class II receptor activity	1.79349875956133e-05	0.00386678332561424
GO:0004896	cytokine receptor activity	3.97017322369383e-05	0.00672337722410337
GO:0023023	MHC protein complex binding	4.74054357896313e-05	0.00672337722410337
GO:0016798	hydrolase activity, acting on glycosyl bonds	4.98951927577245e-05	0.00672337722410337
GO:0004620	phospholipase activity	5.88254558664445e-05	0.00674063038522638
GO:0005178	integrin binding	6.54331815732763e-05	0.00674063038522638
GO:0016298	lipase activity	6.87819427063916e-05	0.00674063038522638
GO:0035325	Toll-like receptor binding	9.67247550402919e-05	0.00868910716111956
GO:0005149	interleukin-1 receptor binding	0.000215884971924427	0.0158322521862987
GO:0023026	MHC class II protein complex binding	0.000215884971924427	0.0158322521862987
GO:0030695	GTPase regulator activity	0.000226198829338703	0.0158322521862987
GO:1901981	phosphatidylinositol phosphate binding	0.000234987045436715	0.0158322521862987
GO:0052740	1-acyl-2-lysophosphatidylserine acylhydrolase activity	0.000259081783815633	0.0164288331148972
GO:0017124	SH3 domain binding	0.000307919869085699	0.0184409788263547
GO:0044548	S100 protein binding	0.000342753824939306	0.0184744311642286
GO:0045028	G protein-coupled purinergic nucleotide receptor activity	0.000342753824939306	0.0184744311642286
GO:0005044	scavenger receptor activity	0.000396208053871929	0.020338680098759
GO:0042605	peptide antigen binding	0.00042197803333555	0.0206211012078031
GO:0038187	pattern recognition receptor activity	0.000472123819765255	0.0206211012078031
GO:0035091	phosphatidylinositol binding	0.000488993342544647	0.0206211012078031
GO:0016175	superoxide-generating NAD(P)H oxidase activity	0.00051648398201362	0.0206211012078031
GO:0042608	T cell receptor binding	0.00051648398201362	0.0206211012078031

GO:0052739	phosphatidylserine 1-acylhydrolase activity	0.00051648398201362	0.0206211012078031
GO:0005543	phospholipid binding	0.000561617749953876	0.0210789409527151
GO:0019956	chemokine binding	0.000570174480771412	0.0210789409527151
GO:0008081	phosphoric diester hydrolase activity	0.000586612456940123	0.0210789409527151
GO:0005126	cytokine receptor binding	0.000628383820483608	0.0218515405961719
GO:0003779	actin binding	0.000678828567363725	0.0219974736415149
GO:0019865	immunoglobulin binding	0.000681645892491063	0.0219974736415149
GO:0001540	amyloid-beta binding	0.000693797869955016	0.0219974736415149
GO:0050664	oxidoreductase activity, acting on NAD(P)H, oxygen as acceptor	0.000935030806828316	0.0272685190752939
GO:0008970	phospholipase A1 activity	0.000936243208986949	0.0272685190752939
GO:0016004	phospholipase activator activity	0.000936243208986949	0.0272685190752939
GO:0030247	polysaccharide binding	0.000961227945140229	0.0272685190752939
GO:0001637	G protein-coupled chemoattractant receptor activity	0.00132697907889172	0.0357620861761318
GO:0004950	chemokine receptor activity	0.00132697907889172	0.0357620861761318
GO:0030169	low-density lipoprotein particle binding	0.00143843289126104	0.0378202599214487
GO:0004602	glutathione peroxidase activity	0.00170915467360924	0.0438683032893039
GO:0016614	oxidoreductase activity, acting on CH-OH group of donors	0.00198664122158299	0.049804633415499

Online Resource 6 Significantly enriched GO Cellular Components (CC) pathways of upregulated genes in TSC patients tissue

ID	Description	pvalue	p.adjust
GO:0030667	secretory granule membrane	1.04702468773677e-15	6.51249355772272e-13
GO:0045335	phagocytic vesicle	6.97887731854525e-14	2.17043084606757e-11
GO:0042611	MHC protein complex	6.63626924599969e-13	1.03690663924726e-10
GO:0005765	lysosomal membrane	8.33526237337026e-13	1.03690663924726e-10
GO:0098852	lytic vacuole membrane	8.33526237337026e-13	1.03690663924726e-10
GO:0005766	primary lysosome	3.84650978364361e-12	3.41789869346618e-10
GO:0042582	azurophil granule	3.84650978364361e-12	3.41789869346618e-10
GO:0005774	vacuolar membrane	7.57866287808744e-12	5.89241038771299e-10
GO:0030139	endocytic vesicle	9.47059698682447e-12	6.5452348064498e-10
GO:0030055	cell-substrate junction	8.53433963318989e-11	5.30835925184411e-09
GO:0070820	tertiary granule	1.2829950366789e-10	7.25475375285704e-09
GO:0005925	focal adhesion	4.3981631644794e-10	2.20836894725157e-08
GO:0062023	collagen-containing extracellular matrix	4.6155621084036e-10	2.20836894725157e-08
GO:0042581	specific granule	6.17700912559207e-10	2.74435691151305e-08
GO:0005775	vacuolar lumen	9.16826703336206e-10	3.80177472983413e-08
GO:0042613	MHC class II protein complex	2.48410961139636e-09	9.65697611430334e-08
GO:0034774	secretory granule lumen	4.14029973121224e-09	1.47381168885477e-07
GO:0071556	integral component of luminal side of endoplasmic reticulum membrane	4.50199712029593e-09	1.47381168885477e-07
GO:0098553	luminal side of endoplasmic reticulum membrane	4.50199712029593e-09	1.47381168885477e-07
GO:0060205	cytoplasmic vesicle lumen	7.11216710828294e-09	2.21188397067599e-07
GO:0031983	vesicle lumen	9.27474669663636e-09	2.74709164062277e-07
GO:0070821	tertiary granule membrane	1.26609871007225e-08	3.57960635302246e-07
GO:0045121	membrane raft	2.65846781941985e-08	6.88986243199644e-07

GO:0098857	membrane microdomain	2.65846781941985e-08	6.88986243199644e-07
GO:0035579	specific granule membrane	3.32389187925041e-08	8.26984299557503e-07
GO:0030670	phagocytic vesicle membrane	4.4848397539295e-08	1.07291166420929e-06
GO:0005769	early endosome	7.1082569406625e-08	1.63753178410818e-06
GO:0005788	endoplasmic reticulum lumen	8.73629853139938e-08	1.94070631661801e-06
GO:0030666	endocytic vesicle membrane	1.1192556628314e-07	2.40061042165907e-06
GO:0098576	luminal side of membrane	2.33842559889498e-07	4.84833574170893e-06
GO:0030176	integral component of endoplasmic reticulum membrane	3.2118871018652e-07	6.4444960560005e-06
GO:0009897	external side of plasma membrane	8.97184422251851e-07	1.74390222075204e-05
GO:0035577	azurophil granule membrane	1.08180327948104e-06	2.03903527223395e-05
GO:0031227	intrinsic component of endoplasmic reticulum membrane	1.24725612803937e-06	2.28174503423672e-05
GO:0043202	lysosomal lumen	1.59234541704593e-06	2.82982528400734e-05
GO:0035578	azurophil granule lumen	1.78284665997456e-06	3.08036284028939e-05
GO:0045178	basal part of cell	4.31295248309411e-06	7.25042282293117e-05
GO:0009925	basal plasma membrane	1.22924002666287e-05	0.00020120718331166
GO:0005884	actin filament	1.48713376105644e-05	0.000237178769071052
GO:0030027	lamellipodium	3.91691348427422e-05	0.000609080046804641
GO:0001772	immunological synapse	5.00384665325744e-05	0.00075912015081125
GO:0012507	ER to Golgi transport vesicle membrane	5.32930984668173e-05	0.000789245410627627
GO:0001726	ruffle	7.84575981001642e-05	0.0011348982794954
GO:0016323	basolateral plasma membrane	0.000100694441172749	0.00142345323657841
GO:0042383	sarcolemma	0.000149662956164924	0.0020496100652436
GO:0031252	cell leading edge	0.00015157887942316	0.0020496100652436
GO:0032432	actin filament bundle	0.000168684537840943	0.00223237835185248
GO:0031091	platelet alpha granule	0.00017371475551348	0.00225105370686218
GO:0042641	actomyosin	0.000204590116310109	0.00254635746357644
GO:0055037	recycling endosome	0.000204691114435405	0.00254635746357644
GO:0008305	integrin complex	0.000216631274718151	0.00264205201715078
GO:0098636	protein complex involved in cell adhesion	0.000222603176686623	0.00266267645959768
GO:0101002	ficolin-1-rich granule	0.000251312156120166	0.00294936153031591
GO:0001725	stress fiber	0.000280889083379422	0.0031766001793091
GO:0097517	contractile actin filament bundle	0.000280889083379422	0.0031766001793091
GO:0002102	podosome	0.000394169385871354	0.00437809567878539
GO:0031901	early endosome membrane	0.000409580095270067	0.00446945296943827
GO:0045177	apical part of cell	0.000538956988541735	0.00577984908401654
GO:0005802	trans-Golgi network	0.000619212272355883	0.00652796666788745
GO:0042470	melanosome	0.000666259339470768	0.0067936608057511
GO:0048770	pigment granule	0.000666259339470768	0.0067936608057511
GO:0030134	COPII-coated ER to Golgi transport vesicle	0.000750577660587178	0.0074649573784107
GO:0043020	NADPH oxidase complex	0.000756096969195939	0.0074649573784107
GO:0030175	filopodium	0.00107613705512479	0.010458707004494
GO:0031301	integral component of organelle membrane	0.00109482167109357	0.0104766012218492
GO:0005912	adherens junction	0.00119005320972773	0.0112153499462219
GO:0001931	uropod	0.00127802418630292	0.0115207397663829
GO:0031254	cell trailing edge	0.00127802418630292	0.0115207397663829
GO:0071203	WASH complex	0.00127802418630292	0.0115207397663829
GO:0001891	phagocytic cup	0.00135623286310097	0.0120510977264115

GO:0005911	cell-cell junction	0.00146601808565117	0.0128431443559863
GO:0101003	ficolin-1-rich granule membrane	0.00149066853450633	0.012877719839763
GO:0030662	coated vesicle membrane	0.00157656541535097	0.0134332012102508
GO:0043034	costamere	0.0016882760590991	0.0141906447129681
GO:0055038	recycling endosome membrane	0.0017404669136791	0.0144342722707787
GO:0030669	clathrin-coated endocytic vesicle membrane	0.00192614016882858	0.0157639366448866
GO:0032588	trans-Golgi network membrane	0.00213008270031145	0.0172066420726457
GO:0097197	tetraspanin-enriched microdomain	0.00216404493533801	0.0172568711510287
GO:0016324	apical plasma membrane	0.00220956330191973	0.0173968148581528
GO:0098858	actin-based cell projection	0.00243074522996339	0.0188990441629653
GO:0030665	clathrin-coated vesicle membrane	0.00266710185013595	0.0204807080343773
GO:0044853	plasma membrane raft	0.00293469245312199	0.0222607159249009
GO:0005902	microvillus	0.00299579895213815	0.0224504451593968
GO:0033270	paranode region of axon	0.00362119960061825	0.0268141208521971
GO:0005581	collagen trimer	0.00421213734163727	0.0308229344293928
GO:1904724	tertiary granule lumen	0.00434811942974872	0.0312440363151238
GO:0005604	basement membrane	0.00437014655854625	0.0312440363151238
GO:0030133	transport vesicle	0.00443313893923877	0.0313342320478013
GO:0005767	secondary lysosome	0.00450294165179782	0.0314699967125646
GO:0035580	specific granule lumen	0.00488381149879041	0.0337525639138626
GO:0031300	intrinsic component of organelle membrane	0.00679028827115368	0.0464127396116219

Online Resource 7 Significantly enriched GO Biological Processes (BP) pathways of downregulated genes in TSC patients tissue

ID	Description	pvalue	p.adjust
GO:0050804	modulation of chemical synaptic transmission	1.33599654194654e-08	3.24089753725737e-05
GO:0099177	regulation of trans-synaptic signaling	1.43339121506297e-08	3.24089753725737e-05
GO:0023061	signal release	3.93986177799222e-07	0.00059386849866936
GO:0006836	neurotransmitter transport	1.54135721862852e-06	0.00174250433565954
GO:0032409	regulation of transporter activity	4.20081751079842e-06	0.00306025815119743
GO:0022898	regulation of transmembrane transporter activity	4.43197492673336e-06	0.00306025815119743
GO:0060079	excitatory postsynaptic potential	5.61923940961924e-06	0.00306025815119743
GO:0032412	regulation of ion transmembrane transporter activity	6.15417805730906e-06	0.00306025815119743
GO:0007269	neurotransmitter secretion	7.23561336284971e-06	0.00306025815119743
GO:0099643	signal release from synapse	7.23561336284971e-06	0.00306025815119743
GO:0035249	synaptic transmission, glutamatergic	7.44423698875978e-06	0.00306025815119743
GO:0051966	regulation of synaptic transmission, glutamatergic	1.02966592628816e-05	0.00360028660868988
GO:0099565	chemical synaptic transmission, postsynaptic	1.03502268715101e-05	0.00360028660868988
GO:0046888	negative regulation of hormone secretion	1.42502565663603e-05	0.00460283287093437
GO:0061337	cardiac conduction	1.53291797781881e-05	0.00462123673046443
GO:0031644	regulation of nervous system process	1.84528899875828e-05	0.00521524803274058
GO:0001505	regulation of neurotransmitter levels	1.963413405247e-05	0.00522267965795703
GO:0008016	regulation of heart contraction	2.36989180337864e-05	0.00595369485271012

GO:0098815	modulation of excitatory postsynaptic potential	3.4571694839448e-05	0.00822806337178862
GO:2000311	regulation of AMPA receptor activity	3.96183218159035e-05	0.00895770256257579
GO:1904062	regulation of cation transmembrane transport	4.77072684132743e-05	0.00982352380347624
GO:2001257	regulation of cation channel activity	4.77924643247406e-05	0.00982352380347624
GO:2000463	positive regulation of excitatory postsynaptic potential	5.17351797089088e-05	0.00984284637271247
GO:0042391	regulation of membrane potential	5.40146686302315e-05	0.00984284637271247
GO:0099601	regulation of neurotransmitter receptor activity	5.44164439004449e-05	0.00984284637271247
GO:0060078	regulation of postsynaptic membrane potential	6.22187282424914e-05	0.0108212726581748
GO:0009914	hormone transport	6.74038069166979e-05	0.0112888894399003
GO:0035637	multicellular organismal signaling	0.00010238243112039	0.016534762625943
GO:0010975	regulation of neuron projection development	0.000107195771815004	0.0167151475912913
GO:0050808	synapse organization	0.000118585078806478	0.01769222571133
GO:0051668	localization within membrane	0.00012128681933906	0.01769222571133
GO:0019935	cyclic-nucleotide-mediated signaling	0.0001383672836761	0.0195530267744789
GO:0060047	heart contraction	0.000184001309363777	0.0252137551800909
GO:0035418	protein localization to synapse	0.000218382075304397	0.0290448160154848
GO:0046879	hormone secretion	0.000246739402799447	0.0318787308416885
GO:0048568	embryonic organ development	0.000263943342381169	0.0331542165068791
GO:0000381	regulation of alternative mRNA splicing, via spliceosome	0.000282060029807531	0.0344723095889096
GO:0003015	heart process	0.000310901361397677	0.0359828172496826
GO:0050773	regulation of dendrite development	0.000314981016157931	0.0359828172496826
GO:0010469	regulation of signaling receptor activity	0.000318291174256369	0.0359828172496826
GO:1903522	regulation of blood circulation	0.000327075348708414	0.0360740177282792
GO:0001704	formation of primary germ layer	0.000440030653083436	0.0473766336486499

Online Resource 8 Significantly enriched GO Molecular Functions (MF) pathways of downregulated genes in TSC patients tissue

ID	Description	pvalue	p.adjust
GO:0005245	voltage-gated calcium channel activity	9.60333889213829e-07	0.000770187779149491
GO:0022843	voltage-gated cation channel activity	3.1644816813178e-06	0.00126895715420844
GO:0005262	calcium channel activity	7.95845254838171e-05	0.0212755964793404
GO:0072349	modified amino acid transmembrane transporter activity	0.000135483981204829	0.0271645382315683
GO:0005261	cation channel activity	0.000207146770224205	0.0332263419439625
GO:0015085	calcium ion transmembrane transporter activity	0.000331984333309968	0.0355652933112278
GO:0005104	fibroblast growth factor receptor binding	0.000385260254393058	0.0355652933112278
GO:0005244	voltage-gated ion channel activity	0.000399111770325499	0.0355652933112278
GO:0022832	voltage-gated channel activity	0.000399111770325499	0.0355652933112278

Online Resource 9 Significantly enriched GO Cellular Components (CC) pathways of downregulated genes in TSC patients tissue

ID	Description	pvalue	p.adjust
GO:0098984	neuron to neuron synapse	4.61687428684333e-07	0.000202434933791588
GO:0099572	postsynaptic specialization	7.30812035348692e-07	0.000202434933791588
GO:0014069	postsynaptic density	1.59805187332176e-06	0.000295106912606751
GO:0032279	asymmetric synapse	2.23167155524426e-06	0.000309086510401329
GO:0098978	glutamatergic synapse	9.25085120384402e-06	0.00102499431338592
GO:0043197	dendritic spine	1.68031748671255e-05	0.00126451093950171
GO:0034703	cation channel complex	1.68761777380091e-05	0.00126451093950171
GO:0044309	neuron spine	1.82600857689778e-05	0.00126451093950171
GO:0043025	neuronal cell body	8.96707573240998e-05	0.0054792239500706
GO:0097060	synaptic membrane	9.89029593875559e-05	0.0054792239500706
GO:1990351	transporter complex	0.000127387353855138	0.00641569036688604
GO:1902495	transmembrane transporter complex	0.000144078865110255	0.00654100586844213
GO:0098793	presynapse	0.000153489307382216	0.00654100586844213
GO:0005891	voltage-gated calcium channel complex	0.000204830233652694	0.00810542496025662
GO:0044305	calyx of Held	0.000256601893067274	0.00900229112734998
GO:0034704	calcium channel complex	0.000261081375360611	0.00900229112734998
GO:0034702	ion channel complex	0.000276243590550451	0.00900229112734998
GO:0098878	neurotransmitter receptor complex	0.000598202674308234	0.0184113489759312
GO:1990454	L-type voltage-gated calcium channel complex	0.000844344748760604	0.0246193153059671
GO:0098831	presynaptic active zone cytoplasmic component	0.00118260464885611	0.0327581487733143
GO:0098798	mitochondrial protein-containing complex	0.00149083494522769	0.0393296456979114
GO:0031234	extrinsic component of cytoplasmic side of plasma membrane	0.00161782054350234	0.0404399980119315
GO:0019898	extrinsic component of membrane	0.00167891688497189	0.0404399980119315

Online Resource 10 Ca²⁺ signaling-related genes of interest identified by gene symbol and ENSEMBL ID.

Protein	Gene Symbol	Ensembl ID
General Ca²⁺ Homeostasis		
PMCA1-4	<i>ATP2B1</i>	ENSG00000070961
	<i>ATP2B2</i>	ENSG00000157087
	<i>ATP2B3</i>	ENSG00000067842
	<i>ATP2B4</i>	ENSG00000058668
SERCA1-3	<i>ATP2A1</i>	ENSG00000196296
	<i>ATP2A2</i>	ENSG00000174437
	<i>ATP2A3</i>	ENSG00000074370
NCX1-3	<i>SLC8A1</i>	ENSG00000183023
	<i>SLC8A2</i>	ENSG00000118160
	<i>SLC8A3</i>	ENSG00000100678
NHE1	<i>SLC9A1</i>	ENSG00000090020
Ca²⁺ channels, metabotropic and SOCE		
IP ₃ R1-3	<i>ITPR1</i>	ENSG00000150995
	<i>ITPR2</i>	ENSG00000123104
	<i>ITPR3</i>	ENSG00000096433
RyR1-3	<i>RYR1</i>	ENSG00000196218
	<i>RYR2</i>	ENSG00000198626

	<i>RYR3</i>	ENSG00000198838
STIM1-2	<i>STIM1</i>	ENSG00000167323
	<i>STIM2</i>	ENSG00000109689
ORAI1-3	<i>ORAI1</i>	ENSG00000276045
	<i>ORAI2</i>	ENSG00000160991
	<i>ORAI3</i>	ENSG00000175938
TRPC1,3,4 (Ca ²⁺ permeable)	<i>TRPC1</i>	ENSG00000144935
	<i>TRPC3</i>	ENSG00000138741
	<i>TRPC4</i>	ENSG00000133107
ER Ca²⁺ homeostasis		
Calreticulins	<i>CALR</i>	ENSG00000179218
	<i>CALR3</i>	ENSG00000269058
Calnexin	<i>CANX</i>	ENSG00000127022
BiP/GRP78	<i>HSPA5</i>	ENSG00000044574
Mitochondrial Ca²⁺ homeostasis		
VDAC1	<i>VDAC1</i>	ENSG00000213585
GRP75	<i>HSPA9</i>	ENSG00000113013
MCU complex	<i>MCU</i>	ENSG00000156026

Online Resource 11 UMAP plot of scRNA-seq data with 7 clusters. Each point represents an individual cell, and the color scheme distinguishes cell types. The spatial arrangement reflects the underlying gene expression patterns, revealing distinct clusters corresponding to cell populations in both control and TSC.

Online Resource 12 Significantly differentially expressed proteins in TSC primary culture astrocytes

Peak Name	p-value	Log (Fold Change)	neglog
Q9HA92	4.0768e-08	2	7.38968059368076
Q9UGT4	9.3034e-08	2	7.03135830613554
P29972	2.4036e-05	2	4.6191378046588
Q9UMS6	0.00081	2	3.09151498112135
Q8IVN3	0.03096	2	1.50919904798915
Q15847	0.00463	1.85967144273677	2.33441900898205
P26447	4.7431e-10	1.79374709559554	9.32393771890909
P15090	0.00048	1.63086071796027	3.31875876262441
P35749	0.00801	1.51030413157874	2.09636748391576
P50238	0.03218	1.49913169641163	1.49241396023699
P07197	0.01783	1.41984679683655	1.74884865682465
Q14BN4	0.0011	1.29912048033143	2.95860731484178
O14683	0.00434	1.26078658508732	2.36251027048749
Q9UBY9	5.3537e-06	1.23989816803744	5.27134596859827
P48307	0.00323	1.20940684416246	2.4907974776689
P48960	7.3829e-05	1.13678848823982	4.13177301397525
O95810	2.7803e-07	1.1265108000119	6.5559083402995
Q99685	0.00715	1.07996350821451	2.14569395819892
P05413	1.4041e-05	1.04181012187158	4.85260196065235
Q12929	9e-04	1.03621382765784	3.04575749056068
Q96A00	0.0175	0.957540386073922	1.75696195131371
P01889	0.00244	0.851850602528915	2.61261017366127
P00813	0.00045	0.811751931702616	3.34678748622466
P27658	0.001	0.784366700075886	3

P23497	0.00034	0.782350500062995	3.46852108295774
Q9BUP0	0.01198	0.761639383490376	1.92154318194671
P61769	0.03644	0.726828416163769	1.43842163169904
Q6NZI2	0.00128	0.714333708312105	2.89279003035213
Q16799	0.0014	0.69953233326808	2.85387196432176
Q9BUH8	0.00075	0.696842794749936	3.1249387366083
P15559	0.04805	0.649921546448693	1.31830660799544
Q9H098	0.02471	0.640384743172495	1.60712725459792
Q969G5	0.00164	0.635237936108073	2.7851561519523
Q9NZN4	0.00972	0.615743802044935	2.01233373507373
P0C7U3	0.01906	0.611819532782861	1.71987710369769
P09497-2	0.0012	0.600995887422807	2.92081875395238
P42224	0.015	0.59821125267767	1.82390874094432
P29536	0.00141	0.588249982733639	2.85078088734462
P55201	0.00063	0.566225841136549	3.20065945054642
P27105	0.00031	0.561052491427051	3.50863830616573
Q14847	1.9871e-05	0.560898972111135	4.70178027664691
P21589	0.00112	0.545629295425041	2.95078197732982
P05204	0.02879	0.545374763844125	1.54075833512192
Q9NZN3	0.00041	0.511555039191916	3.38721614328026
Q9BWT7	0.00635	0.50923199903341	2.19722627470802
Q96B97	0.01516	0.494565101812481	1.81930079870397
Q6UVK1	0.00026	0.491017854511005	3.58502665202918
Q9BRF8	0.03575	0.47067652154677	1.4467239538629
P02461	0.01605	0.470338473311634	1.79452496325911
P06396	0.01413	0.469111810027899	1.84985783815144
O95602	0.00231	0.430953528099113	2.63638802010786
P17813	0.01111	0.398113789562407	1.95428594105913
O00151	0.00181	0.396387712899563	2.74232142513082
Q8IVM0	0.00271	0.394397543363471	2.56703070912559
P04439	0.00054	0.387531946090577	3.26760624017703
Q9Y639	0.01659	0.384000053664212	1.78015361397564
Q14764	0.03932	0.36829883038091	1.4053864908399
P02545	1.297e-06	0.367316739933413	5.88706002391592
O94875	0.02251	0.36435933769562	1.64762450499948
Q15746	0.0081	0.362568374038302	2.09151498112135
Q13683-3	0.02927	0.360570644843012	1.53357727756621
P15144	0.00942	0.359824553618525	2.02594909720712
P39060	0.00515	0.359508000199637	2.28819277095881
Q03135	0.04532	0.358215528433426	1.34371009880864
P18065	0.00764	0.347943682753973	2.11690664142431
Q04446	0.0402	0.346875110801855	1.39577394691553
Q8WWW9	0.0021	0.343769052570045	2.67778070526608
O95817	0.00902	0.326847371296255	2.04479346245806
P06703	0.0285	0.325676512668286	1.54515513999149
Q00577	0.02059	0.321273104079878	1.68634365338197
Q9BRK5	0.04426	0.320961227410534	1.35398859040876
Q96Q80-4	0.03416	0.316485627023464	1.46648213798303
P63313	0.04833	0.315776640740411	1.31578320486112
P21926	0.01065	0.309502976094745	1.97265039222524
Q09666	0.00121	0.295265623648132	2.91721462968355

Q9Y6G9	0.00664	0.294394675816786	2.17783192063198
P04792	0.00284	0.292146946742978	2.54668165995296
P54652	0.02473	0.289171854155962	1.6067758836387
P02042	0.03874	0.287361728628042	1.41184038361691
P42892	0.04906	0.273128040607493	1.30927245612963
Q9UGH3	0.02049	0.270324248134186	1.68845804159881
P09382	0.01487	0.265625478995363	1.82768903147805
P46976	0.04896	0.254247387546831	1.3101585908625
Q8NBV4	0.0029	0.23366424837032	2.53760200210104
P48637	0.01871	0.226455722366603	1.72792621249999
Q99575	0.03574	0.210170918378437	1.44684545183037
Q9Y281	0.0022	0.209735645427755	2.65757731917779
Q16270	0.03615	0.208957213556279	1.44189169836945
Q92882	8e-04	0.20611168606755	3.09691001300806
Q9UL46	0.00058	0.203116707758466	3.23657200643706
Q8IWE2	0.04625	0.189007254388208	1.33488826292495
P26885	0.03413	0.181982835247576	1.46686371172136
P13987	0.02139	0.17755717383353	1.66978921542847
Q92743	0.04028	0.177270012312993	1.39491053811842
Q15404	0.00465	0.176223125936187	2.33254704711005
P06576	0.01908	0.172207143339814	1.71942162963192
Q9UBC2	0.01696	0.172011067204336	1.77057415207931
O60664	0.03996	0.162991431825751	1.39837452044606
Q06323	0.00087	0.139203382398955	3.06048074738138
Q13642-1	0.02384	0.134456754575769	1.6226937489318
Q15942	0.01034	0.124031452408835	1.98547946124208
O75947	0.01535	0.114652423917978	1.81389162018679
P60903	0.04904	0.106948156143694	1.30944953848964
P60660	0.03696	0.104498887582815	1.43226803745193
O15511	0.03041	0.0903868984750699	1.51698357985587
Q99436	0.04195	-0.110563027512219	1.37726803483528
Q15370	0.03453	-0.118820543557663	1.46180342165055
P63104	0.00305	-0.130896232110636	2.51570016065321
P24539	0.0171	-0.13318082381023	1.76700388960785
Q15691	0.00267	-0.140750784457149	2.57348873863542
P61088	3e-04	-0.141578770633377	3.52287874528034
P27824	0.03378	-0.141720076629269	1.47134035476501
P62258	0.00478	-0.141746140270261	2.32057210338788
O60716	0.00157	-0.141946887328959	2.80410034759077
P53990	0.03867	-0.145148570001523	1.41262582792693
Q9HC38	0.01493	-0.149159775424219	1.82594019227497
O15173	0.01125	-0.154833686006199	1.94884747755262
Q7L1Q6	0.04141	-0.159136692686738	1.38289476949762
Q9UHX1	0.0447	-0.1618068535371	1.34969247686806
P61981	0.02521	-0.165948007430322	1.59842715432355
P63241	0.01638	-0.167630119043219	1.7856861025756
P35232	0.01011	-0.171978796045288	1.995248844409
P13473	0.01397	-0.177953061895383	1.85480359388582
P28072	0.02046	-0.182957700482508	1.68909437062386
Q13177	0.01029	-0.186180970682587	1.98758462523757
Q99623	0.02146	-0.186440232131475	1.66837028237007

P26368	0.03907	-0.189201931753633	1.40815658877522
P13667	0.03709	-0.191194613178209	1.43074316667139
Q9Y230	0.01065	-0.19211407117217	1.97265039222524
P00403	0.01864	-0.192532155505061	1.72955409198204
P11233	0.03609	-0.192619343987908	1.44261311794049
O75844	0.02685	-0.194798833405802	1.57105570996443
P37108	0.0222	-0.194982715929778	1.65364702554936
P60468	0.02311	-0.195897275330019	1.63620005452089
O15355	0.01976	-0.196233018475853	1.70421305974839
Q16643	0.00257	-0.197007444211891	2.59006687666871
P20340	0.03763	-0.199345461165932	1.42446578168014
P38646	0.03236	-0.201746749718078	1.48999148705977
Q07954	0.01915	-0.201761001841849	1.71783122169536
Q86Y82	0.04257	-0.202515510864899	1.37089634982286
A6NCE7	0.00277	-0.203391975200376	2.55752023093555
O60739	0.04437	-0.20749801368562	1.35291057128345
P50281	0.03786	-0.208348910765614	1.42181939037222
P68104	0.02104	-0.212920189724151	1.6769542645183
Q99426	0.02169	-0.219533380793996	1.66374044798581
Q86UP2	0.0236	-0.221019109216454	1.62708799702989
P26232	0.00183	-0.222861588081444	2.73754891026957
P46779	0.02785	-0.224649910153521	1.55517480049025
Q9UNF0	0.00215	-0.227798193697239	2.66756154008439
Q9UNM6	0.02202	-0.228668471374707	1.65718268536427
P18085	0.01888	-0.229545323987439	1.72399801003795
Q99729-2	0.00268	-0.229579599662652	2.57186520597121
Q9H3N1	0.01791	-0.230765147203873	1.74690441415097
P15586	0.03941	-0.231876157464593	1.4043935651344
Q07666	0.01944	-0.235853318151874	1.71130373940974
P07858	0.03468	-0.239704216193581	1.45992091119583
P27348	4.1859e-05	-0.24221367706832	4.37821115104916
Q96KP4	0.00112	-0.244909752689134	2.95078197732982
O43242	0.00707	-0.246619929899444	2.1505805862031
P60983	0.01993	-0.24777320552711	1.70049270129951
O94905	0.01079	-0.247927708839235	1.96697855531709
P09211	0.00013	-0.252448229004565	3.88605664769316
Q06830	4e-04	-0.253185203944578	3.39794000867204
P17174	0.00805	-0.254090450162694	2.09420411963213
Q12765	0.00553	-0.25446295490093	2.2572748686953
Q14108	0.02656	-0.259004325243594	1.57577192930402
P51149	0.01867	-0.259737442831016	1.72885568205092
Q96FQ6	0.03117	-0.26080075183913	1.50626319772316
P40429	0.00406	-0.263174881796053	2.39147396642281
Q6IAA8	0.0036	-0.263321191147381	2.44369749923271
O00264	0.00109	-0.263886761139938	2.96257350205938
O43237	0.01653	-0.265504475580668	1.78172714642855
Q99439	0.02608	-0.266844284638918	1.58369241294012
P62256	0.01657	-0.270435202679708	1.78067749158066
P51665	0.01491	-0.273216848438125	1.82652235654701
P60953	0.00905	-0.27386523073174	2.0433514207948
P06756	0.02061	-0.273944175687789	1.68592200822079

Q14019	0.03829	-0.274682917657263	1.41691463365231
P61916	0.03531	-0.279197218384775	1.4521022824369
P18124	0.00925	-0.284432657859781	2.03385826726097
P11766	0.00259	-0.288179347662035	2.58670023591875
P62877	0.00451	-0.289433594863826	2.34582345812204
Q9H0R8-2	0.00988	-0.28947349240992	2.00524305541237
Q9HDC9	0.00085	-0.289666658273303	3.07058107428571
Q9NZA1	4e-04	-0.292319033114065	3.39794000867204
P49591	0.02124	-0.298248411068964	1.67284548759057
Q96IZ0	0.01217	-0.298268988804781	1.91470942176993
P48723	0.00065	-0.30178303486807	3.18708664335714
P54577	0.00889	-0.303975763973758	2.05109823902979
P10619	0.01383	-0.305421018199567	1.85917781989069
P30626	0.00011	-0.305445328043638	3.95860731484178
Q13263	0.00434	-0.307104074825646	2.36251027048749
P61204	0.036	-0.307293192159587	1.44369749923271
O43681	0.00046	-0.309085524732653	3.33724216831843
P35221	2.9626e-06	-0.313674271950337	5.52832698149991
Q16881	0.0154	-0.314462119586921	1.81247927916354
P57058	0.00155	-0.314741976268442	2.80966830182971
P11279	0.00885	-0.314900294847161	2.05305672930217
P32119	0.00045	-0.32154962999293	3.34678748622466
Q15417	0.02116	-0.322487177693221	1.67448433663685
Q96A72	0.01341	-0.322733679174237	1.8725712221484
O95197	0.01833	-0.324474409687647	1.73683753503778
Q15388	0.00334	-0.324846167086982	2.47625353318844
P48147	0.0414	-0.326028134843669	1.3829996588791
P84085	0.00031	-0.326664889961416	3.50863830616573
Q5JWF2	0.00359	-0.33071230064526	2.44490555142168
O94760	0.0245	-0.33886422768855	1.61083391563547
P20700	0.00973	-0.340247156814433	2.01188715973165
Q8NFC6	0.00125	-0.340664500529761	2.90308998699194
Q96PU8	0.00161	-0.342612579327422	2.79317412396815
Q14192	0.00071	-0.346300008783728	3.14874165128092
Q9UMS4	0.00149	-0.347591824987684	2.82681373158773
P15121	0.04464	-0.3479504980357	1.35027581407048
P11166	0.02009	-0.349848599758398	1.69702006325175
Q9UMR2	0.01423	-0.3540767763862	1.84679509991572
P52306	0.03165	-0.358395110642719	1.49962628564663
Q9UHB6	0.00724	-0.361764625515131	2.14026143380285
P49419	0.00058	-0.362837480553171	3.23657200643706
P29323	0.01289	-0.364294029122552	1.8897470826466
Q9P0K7	0.04759	-0.370310521867872	1.32248429520124
Q15393	0.03705	-0.372406081745669	1.43121178768465
P15531	0.00129	-0.374487383374263	2.88941028970075
Q13151	0.03302	-0.378224846744173	1.48122293107323
O60637	0.00898	-0.379078606857665	2.0467236633327
Q16658	0.02862	-0.383757418393498	1.54333037057624
P30041	0.00116	-0.389043454968126	2.93554201077308
P13611	0.00917	-0.390867432055452	2.03763066432998
O75525	0.03376	-0.403888486693165	1.47159756204638

O95865	0.01203	-0.429403867368982	1.91973437266016
P53041	0.01679	-0.432545905347275	1.77494930386195
P46821	0.00105	-0.434588099020568	2.97881070093006
P07339	0.00764	-0.454953689325876	2.11690664142431
Q8WX93	0.02707	-0.456789997159961	1.56751174422949
P07099	0.02002	-0.458748665056213	1.6985359268567
P25205	0.0203	-0.471198051388552	1.69250396208679
P35052	0.00311	-0.472260010826086	2.50723961097316
O96019	0.00149	-0.480932253583836	2.82681373158773
Q9NVJ2	0.00044	-0.492198970908247	3.35654732351381
P20908	0.0055	-0.497533850436111	2.25963731050576
Q13885	0.00712	-0.49995797803848	2.14752000636314
P32322	0.03274	-0.518753002866988	1.48492132492408
P63172	0.00737	-0.521483715255785	2.13253251214095
Q00796	0.03305	-0.537061043659015	1.48082853617834
Q16527	0.00463	-0.572765672188757	2.33441900898205
Q9UKX5	0.00343	-0.580106937918487	2.46470587995723
P10253	0.04234	-0.58019806384605	1.37324914631661
O00483	0.01853	-0.60853182295702	1.7321245806811
O75369	0.01175	-0.621092638750147	1.92996213339224
P05090	0.03672	-0.623839866194265	1.4350973274708
Q15102	0.00188	-0.644108824574167	2.72584215073632
O00469	0.02173	-0.647345136557689	1.66294027367948
Q14315	0.00455	-0.658310191879942	2.34198860334289
P0C0L4	0.00042	-0.66169133564175	3.3767507096021
Q06033	0.00011	-0.661820340599306	3.95860731484178
Q8IZA3	0.00056	-0.667666959359367	3.2518119729938
Q9UBG0	1.2368e-05	-0.669497816532931	4.90770052342575
P24821-4	7.8302e-05	-0.675477553941165	4.10622714499351
O15061	0.04288	-0.685820619793169	1.36774522331529
Q9BRX8	0.03346	-0.691893560137774	1.47547406337362
Q8IV08	5.0325e-06	-0.694828016406243	5.29821621643931
P01023	0.00136	-0.702124693665469	2.86646109162978
Q9H2A2	0.00022	-0.70273373785165	3.65757731917779
Q15582	0.00189	-0.704838679092307	2.72353819582676
P78330	1.5835e-05	-0.708738927129822	4.80038193229207
P46926	0.02122	-0.708976550323341	1.67325462043468
P60891	0.01278	-0.718169234848181	1.89346914617762
P08195	8.008e-05	-0.742585688809685	4.09647593552874
Q96EM0	0.02103	-0.768275023890034	1.67716072731368
P30837	0.00335	-0.775772535979865	2.47495519296315
Q14195-2	0.00085	-0.783776274180144	3.07058107428571
P08729	0.00327	-0.795731315455881	2.48545224733971
P05783	0.0269	-0.799331449087839	1.57024771999759
P17661	0.02548	-0.79996230467405	1.59380057633669
Q9Y2J2	9.5997e-05	-0.800497931759896	4.01774233887505
P02511	0.01953	-0.80792680264585	1.70929775671215
O00592	0.00929	-0.808704462619558	2.03198428600636
P15311	0.00999	-0.813725279251067	2.00043451177402
P53801	0.00735	-0.844825086558271	2.13371266091581
P53985	0.00076	-0.85914815260585	3.11918640771921

Q9BVA1	0.03104	-0.885696856941491	1.50807828741385
Q04695	0.02819	-0.90170711597345	1.5499049241284
P28300	0.01037	-0.914447694627514	1.98422124361096
P24821	4.0315e-06	-0.949358757945034	5.39453333586463
P78386	0.00404	-0.949393278914015	2.39361863488939
Q9Y617	0.00285	-0.955027380443442	2.54515513999149
P35580	0.02565	-1.00537631750433	1.59091263055217
P04216	0.02118	-1.01398343408003	1.67407404422853
P09936	0.00044	-1.13096102441855	3.35654732351381
Q01650	4.3378e-05	-1.13704741599924	4.3627304755811
P49006	0.00599	-1.14701300798263	2.22257317761069
P05091	0.00287	-1.18466795827753	2.54211810326601
P54687	0.02659	-1.24866336127977	1.57528166266843
P12277	0.01265	-1.27702854407412	1.89790947448816
Q9P0M6	0.00218	-1.37703747285697	2.66154350639539
P19022	0.00139	-1.41940908819593	2.85698519974591
Q96CG8	0.03798	-1.56142849798896	1.420445039599
Q6DKJ4	0.00523	-1.65558114832841	2.28149831113273
P17301	0.00525	-1.69058533870335	2.27984069659404
Q9H4G4	2.4026e-05	-1.71901346283718	4.61931852726217
O60462	0.00592	-1.7782800971984	2.22767829327708
P40121	0.00622	-1.92626018566119	2.20620961530918
P12429	0.00039	-2	3.4089353929735
O75487	0.00244	-2	2.61261017366127
Q13308	0.00358	-2	2.44611697335613
P50479	0.00557	-2	2.25414480482627
P09455	0.01691	-2	1.77185639240226
P17677	0.02068	-2	1.6844494655781
Q56VL3	0.04497	-2.28093688186573	1.34707711243206
P21980	0.00949	-2.66725183595481	2.02273378757271
O15540	0.02078	-2.94169709266011	1.68235445677884
P14136	0.00957	-2.96593461871816	2.01908806222316

Online Resource 13 Significantly enriched pathways predicted via Ingenuity Pathway Analysis (IPA)

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio
Neutrophil degranulation	15,9	-1,85933936	0,0735
Phagosome Maturation	10,7		0,11
Caveolar-mediated Endocytosis Signaling	8,43		0,147
Protein Ubiquitination Pathway	6,99		0,0634
Microautophagy Signaling Pathway	6,8	-2,121320344	0,0828
Gene and protein expression by JAK-STAT signaling after IL-12 stimulation	6,35	1,133893419	0,189
Integrin Signaling	6,19	0	0,0676
Integrin cell surface interactions	5,77	-0,333333333	0,106
Germ Cell-Sertoli Cell Junction Signaling	5,64		0,0714
Virus Entry via Endocytic Pathways	5,42		0,084
Actin Cytoskeleton Signaling	5,41	-1,897366596	0,0581
RHO GTPases activate PAKs	5,2	-0,447213595	0,238
Vitamin-C Transport	4,99	-0,447213595	0,217
BAG2 Signaling Pathway	4,92	-1	0,0976

Hedgehog 'off' state	4,77	-1,889822365	0,0804
Signaling by ROBO receptors	4,65	-2,333333333	0,0776
Syndecan interactions	4,63	-1,341640786	0,185
Aryl Hydrocarbon Receptor Signaling	4,61		0,068
Semaphorin Neuronal Repulsive Signaling Pathway	4,61	0	0,068
Remodeling of Epithelial Adherens Junctions	4,61		0,106
PAK Signaling	4,56	-2,236067977	0,0756
MAPK6/MAPK4 signaling	4,55		0,087
RHO GDI Signaling	4,49	2,645751311	0,055
Ferroptosis Signaling Pathway	4,34	-1,666666667	0,0709
Regulation of RUNX2 expression and activity	4,32	-1,133893419	0,0959
Natural Killer Cell Signaling	4,26	-2,713602101	0,0564
COPI-mediated anterograde transport	4,26	-1,414213562	0,0792
Signaling by Rho Family GTPases	4,26	-3	0,0487
Triglyceride metabolism	4,19	1,341640786	0,152
Regulation of Apoptosis	4,18	-1,632993162	0,113
Extracellular matrix organization	4,11	-0,707106781	0,0755
Regulation of Actin-based Motility by Rho	4	-2	0,0727
Detoxification of Reactive Oxygen Species	3,94	-2,236067977	0,135
Metabolism of polyamines	3,92	-0,816496581	0,102
Assembly of collagen fibrils and other multimeric structures	3,84	0	0,0984
Collagen degradation	3,84	0	0,0984
ERK/MAPK Signaling	3,84	-0,377964473	0,0507
L1CAM interactions	3,66	-2,828427125	0,065
Epithelial Adherens Junction Signaling	3,63	-2,333333333	0,0573
Regulation of Insulin-like Growth Factor (IGF) transport and uptake by IGFbps	3,63	-0,707106781	0,0645
Smooth Muscle Contraction	3,62	0,447213595	0,116
MHC class II antigen presentation	3,59	-2,121320344	0,0635
Cellular response to heat stress	3,54	-0,377964473	0,0722
Mitotic Metaphase and Anaphase	3,54	-1,507556723	0,0468
Ephrin Receptor Signaling	3,48	-1,632993162	0,0498
ABC-family proteins mediated transport	3,43	-1,133893419	0,0693
Cellular response to hypoxia	3,35	-1,632993162	0,08
Ethanol Degradation II	3,34	-2	0,143
RHO GTPases activate PKNs	3,34	0	0,143
RAC Signaling	3,3	-1,341640786	0,0576
Myogenesis	3,28	-2	0,138
Post-translational protein phosphorylation	3,28	-1,133893419	0,0654
Paxillin Signaling	3,26	-2	0,0648
Signaling by VEGF	3,26	-1,133893419	0,0648
Histamine Degradation	3,24		0,231
Noradrenaline and Adrenaline Degradation	3,22	-2	0,133
Xenobiotic Metabolism AHR Signaling Pathway	3,22	-1,632993162	0,0759
Tumor Microenvironment Pathway	3,2	-2,121320344	0,05
RHO GTPases activate IQGAPs	3,16	-2	0,129
Signaling by NOTCH4	3,14	-1,632993162	0,0732
FAT10 Signaling Pathway	3,12		0,0909
HSP90 chaperone cycle for steroid hormone receptors in the presence of ligand	3,12	-0,447213595	0,0909
Sensory processing of sound by outer hair cells of the cochlea	3,12	-0,447213595	0,0909
Metabolism of nitric oxide: NOS3 activation and regulation	3,05		0,2

Hedgehog 'on' state	3,03	-1,632993162	0,0698
Hepatic Fibrosis / Hepatic Stellate Cell Activation	3,03		0,0474
Synthesis of DNA	3,01	-1,889822365	0,0588
Regulation of Cellular Mechanics by Calpain Protease	2,98		0,0682
TP53 Regulates Metabolic Genes	2,98	-2,449489743	0,0682
Fatty Acid α -oxidation	2,96		0,188
NIK-->noncanonical NF-kB signaling	2,95	-1,341640786	0,0833
Degradation of beta-catenin by the destruction complex	2,93	-1,632993162	0,0667
ILK Signaling	2,92	0,333333333	0,0457
Actin Nucleation by ARP-WASP Complex	2,9		0,0659
KEAP1-NFE2L2 pathway	2,9	-1,632993162	0,0659
ROBO SLIT Signaling Pathway	2,9	1,889822365	0,0565
EPH-Ephrin signaling	2,88	-0,816496581	0,0652
Putrescine Degradation III	2,88		0,176
Sertoli Cell-Sertoli Cell Junction Signaling	2,86	-3,16227766	0,0413
Antigen Presentation Pathway	2,83		0,105
Inhibition of Matrix Metalloproteases	2,83		0,105
Intra-Golgi and retrograde Golgi-to-ER traffic	2,83	-2,333333333	0,0443
NFE2L2 regulating anti-oxidant/detoxification enzymes	2,81		0,167
Hedgehog ligand biogenesis	2,79	-1,341640786	0,0769
CDC42 Signaling	2,74	-1,632993162	0,0354
Collagen biosynthesis and modifying enzymes	2,73	0,447213595	0,0746
Tryptophan Degradation X (Mammalian, via Tryptamine)	2,73		0,158
TNFR2 non-canonical NF-kB pathway	2,7	-1,341640786	0,0735
Ethanol Degradation IV	2,67		0,15
Autophagy	2,67	-1,133893419	0,0421
Aggrephagy	2,62	-1	0,093
DNA Replication Pre-Initiation	2,61	-1,632993162	0,0577
Fructose metabolism	2,61		0,333
Collagen chain trimerization	2,59	1	0,0909
Retinoid metabolism and transport	2,59	-2	0,0909
Chaperone Mediated Autophagy	2,55		0,136
Antioxidant Action of Vitamin C	2,5		0,055
Glycogen Biosynthesis II (from UDP-D-Glucose)	2,46		0,286
Thioredoxin Pathway	2,46		0,286
Dopamine Degradation	2,44		0,125
Glycogen metabolism	2,44		0,125
Renal Cell Carcinoma Signaling	2,4		0,0625
CLEAR Signaling Pathway	2,39	-1,264911064	0,0356
Huntington's Disease Signaling	2,39		0,0356
Serine biosynthesis	2,34		0,25
Mitotic G2-G2/M phases	2,32	-2,121320344	0,0402
Apoptotic execution phase	2,32	0	0,0769
Spliceosomal Cycle	2,29	-2	0,0755
Role of Osteoclasts in Rheumatoid Arthritis Signaling Pathway	2,26	0,632455532	0,0341
Axonal Guidance Signaling	2,23		0,0283
Regulation of mitotic cell cycle	2,22	-1,341640786	0,0568
TCR signaling	2,2	-1,632993162	0,0476
Serotonin Degradation	2,18	-2	0,0702
Oxidative Ethanol Degradation III	2,16		0,1
Interleukin-1 family signaling	2,16	-1,632993162	0,0469

Semaphorin Signaling in Neurons	2,13		0,0678
Interferon gamma signaling	2,1	2,236067977	0,0532
HGF Signaling	2,09		0,0451
RHO GTPases activate KTN1	2,06		0,182
Transcriptional regulation by RUNX3	2,06	-1,341640786	0,0521
Retinoate Biosynthesis I	2,04		0,0909
LPS/IL-1 Mediated Inhibition of RXR Function	2,02		0,0357
Semaphorin interactions	2,01	-1	0,0625
Gap junction trafficking and regulation	2,01		0,0882
Cell Cycle Checkpoints	2	-1,666666667	0,0331
Tryptophan catabolism	1,99		0,167
γ -glutamyl Cycle	1,99		0,167
S Phase	1,99	-1,341640786	0,05
Pulmonary Fibrosis Idiopathic Signaling Pathway	1,97	-1,264911064	0,0309
Class I MHC mediated antigen processing and presentation	1,96	-0,904534034	0,0293
Osteoarthritis Pathway	1,93		0,0345
C-type lectin receptors (CLRs)	1,91	-1,632993162	0,0414
Sertoli Cell-Germ Cell Junction Signaling Pathway (Enhanced)	1,9	0	0,034
Glucocorticoid Receptor Signaling	1,89		0,0257
Sensory processing of sound by inner hair cells of the cochlea	1,89	-1	0,058
Leukocyte Extravasation Signaling	1,88	-2,645751311	0,0366
Sorbitol Degradation I	1,88		1
Selenoamino acid metabolism	1,87	-2,236067977	0,0467
Dilated Cardiomyopathy Signaling Pathway	1,85	0	0,04
PTEN Regulation	1,85	-1,632993162	0,04
Translocation of SLC2A4 (GLUT4) to the plasma membrane	1,85	-2	0,0563
Phenylalanine Degradation IV (Mammalian, via Side Chain)	1,85		0,143
Ephrin B Signaling	1,83		0,0556
PTEN Signaling	1,83		0,0397
Transcriptional regulation by RUNX1	1,82	-1,632993162	0,0395
Neuroprotective Role of THOP1 in Alzheimer's Disease	1,8		0,0446
TCF dependent signaling in response to WNT	1,79	-1,133893419	0,0352
SRP-dependent cotranslational protein targeting to membrane	1,77	-2,236067977	0,0439
Coronavirus Replication Pathway	1,76		0,0714
Neuregulin Signaling	1,75		0,0435
Adenosine Nucleotides Degradation II	1,74		0,125
Triacylglycerol Degradation	1,73		0,0698
Inhibition of ARE-Mediated mRNA Degradation Pathway	1,71		0,0373
Signaling by MET	1,7	0	0,0506
IL-8 Signaling	1,7	-1,632993162	0,0337
Cachexia Signaling Pathway	1,7	-1,264911064	0,028
Glycosaminoglycan metabolism	1,68	-1	0,05
Cell surface interactions at the vascular wall	1,67	-1,889822365	0,0332
RHOA Signaling	1,65	-1	0,041
Deubiquitination	1,64	-2,121320344	0,0304
NRF2-mediated Oxidative Stress Response	1,64	-2	0,0327
Metabolism of Angiotensinogen to Angiotensins	1,64		0,111
Aldosterone Signaling in Epithelial Cells	1,61		0,0353
Signaling by the B Cell Receptor (BCR)	1,61	-0,816496581	0,0353
Purine Nucleotides Degradation II (Aerobic)	1,6		0,105
RHO GTPases Activate ROCKs	1,6		0,105

RHO GTPases activate CIT	1,6		0,105
Chaperone Mediated Autophagy Signaling Pathway	1,59	-0,301511345	0,0258
IL-17A Signaling in Fibroblasts	1,58	1	0,0465
Choline Degradation I	1,58		0,5
Formaldehyde Oxidation II (Glutathione-dependent)	1,58		0,5
Thyroid Hormone Biosynthesis	1,58		0,5
14-3-3-mediated Signaling	1,57		0,0391
ABRA Signaling Pathway	1,55	1	0,0455
Mitotic G1 phase and G1/S transition	1,54	-1,341640786	0,0382
Xenobiotic Metabolism Signaling	1,53		0,029
Xenobiotic Metabolism PXR Signaling Pathway	1,52	-1,632993162	0,0337
CCR3 Signaling in Eosinophils	1,52		0,0379
Response to elevated platelet cytosolic Ca ²⁺	1,52	-0,447213595	0,0379
Factors involved in megakaryocyte development and platelet production	1,5	1	0,044
Phagosome Formation	1,49	-1,807392228	0,0223
Insertion of tail-anchored proteins into the endoplasmic reticulum membrane	1,48		0,0909
Interconversion of nucleotide di- and triphosphates	1,48		0,0909
Cell junction organization	1,48	-1	0,0435
Sirtuin Signaling Pathway	1,46	0	0,0281
RHO GTPase cycle	1,45	-1,507556723	0,0244
Meiotic synapsis	1,45		0,0545
RHO GTPases Activate Formins	1,44	-1,341640786	0,036
Eukaryotic Translation Elongation	1,44	-2	0,0421
Wound Healing Signaling Pathway	1,42	0,377964473	0,0294
Glutathione Redox Reactions I	1,41		0,0833
Aspartate Biosynthesis	1,41		0,333
Glutamate Degradation II	1,41		0,333
Glutathione Biosynthesis	1,41		0,333
L-cysteine Degradation III	1,41		0,333
Lactose synthesis	1,41		0,333
N-acetylglucosamine Degradation I	1,41		0,333
PRPP Biosynthesis I	1,41		0,333
Serine Biosynthesis	1,41		0,333
Signaling by PDGF	1,39		0,0517
Apelin Liver Signaling Pathway	1,35		0,0769
Glutathione-mediated Detoxification	1,35		0,0769
ISGylation Signaling Pathway	1,35	1	0,0392
Gap Junction Signaling	1,35		0,0306
Hepatic Fibrosis Signaling Pathway	1,33	0	0,0242
Autism Signaling Pathway	1,33	-0,707106781	0,0264
PI3K/AKT Signaling	1,33		0,0303
Endometrial Cancer Signaling	1,32		0,0484
eNOS Signaling	1,32	-1	0,0333
D-glucuronate Degradation I	1,29		0,25
L-cysteine Degradation I	1,29		0,25
N-acetylglucosamine Degradation II	1,29		0,25
Oxidized GTP and dGTP Detoxification	1,29		0,25
Phenylethylamine Degradation I	1,29		0,25
Proline Biosynthesis I	1,29		0,25
Retinoate Biosynthesis II	1,29		0,25

IGF-1 Signaling	1,29		0,0377
Clathrin-mediated Endocytosis Signaling	1,26		0,029
HIF1 α Signaling	1,26	-0,816496581	0,029
Fc epsilon receptor (FCERI) signaling	1,26	-1,632993162	0,0291
Degradation of the extracellular matrix	1,25		0,0455
RAF/MAP kinase cascade	1,24	-1,889822365	0,0267
Agrin Interactions at Neuromuscular Junction	1,22		0,0441
Choline catabolism	1,2		0,2
Creatine-phosphate Biosynthesis	1,2		0,2
Formation of xylulose-5-phosphate	1,2		0,2
Lysine Degradation II	1,2		0,2
Lysine Degradation V	1,2		0,2
Proline Biosynthesis II (from Arginine)	1,2		0,2
Reelin signalling pathway	1,2		0,2
Superpathway of Serine and Glycine Biosynthesis I	1,2		0,2
CDK5 Signaling	1,2		0,0351
Granzyme A Signaling	1,18		0,0423
Interferon alpha/beta signaling	1,18		0,0423
Nonsense-Mediated Decay (NMD)	1,17	-2	0,0342
Neutrophil Extracellular Trap Signaling Pathway	1,17	-2,333333333	0,0234
Activation of Matrix Metalloproteinases	1,16		0,0606
Amyloid fiber formation	1,15		0,0411
Glioma Invasiveness Signaling	1,15		0,0411
Oxytocin Signaling Pathway	1,14	1,133893419	0,0254
HER-2 Signaling in Breast Cancer	1,12	0,447213595	0,0267
Selenocysteine Biosynthesis II (Archaea and Eukaryotes)	1,12		0,167
Serotonin Receptor Signaling	1,11	-1,897366596	0,0219
GP6 Signaling Pathway	1,09	1	0,032
Xenobiotic Metabolism CAR Signaling Pathway	1,09	-2,236067977	0,0286
Complement System	1,09		0,0556
Pancreatic Adenocarcinoma Signaling	1,08	0	0,0317
D-myo-inositol (1,4,5,6)-Tetrakisphosphate Biosynthesis	1,08	0	0,0282
D-myo-inositol (3,4,5,6)-tetrakisphosphate Biosynthesis	1,08	0	0,0282
Protein Sorting Signaling Pathway	1,08	-1,341640786	0,0282
Role of Osteoblasts in Rheumatoid Arthritis Signaling Pathway	1,08	-0,816496581	0,0261
Atherosclerosis Signaling	1,06		0,0312
NF- κ B Activation by Viruses	1,06		0,0375
Tight Junction Signaling	1,06		0,0279
Regulation of eIF4 and p70S6K Signaling	1,05		0,0276
Clathrin-mediated endocytosis	1,05	0	0,031
G Beta Gamma Signaling	1,05	-1	0,031
tRNA Charging	1,05		0,0526
Adenine and Adenosine Salvage III	1,05		0,143
Arginine Degradation VI (Arginase 2 Pathway)	1,05		0,143
Aspartate Degradation II	1,05		0,143
Erythrocytes take up oxygen and release carbon dioxide	1,05		0,143
Purine Ribonucleosides Degradation to Ribose-1-phosphate	1,05		0,143
IL-6 Signaling	1,03	0	0,0305
SNARE Signaling Pathway	1,02	-1	0,0303
Acute Phase Response Signaling	1,02		0,0272

Immunogenic Cell Death Signaling Pathway	1,01		0,0357
Miro GTPase Cycle	1		0,125
Superoxide Radicals Degradation	1		0,125
Intrinsic Prothrombin Activation Pathway	0,998		0,0488
3-phosphoinositide Degradation	0,993	0	0,0266
Neddylation	0,984	-1,632993162	0,0245
DAPI2 interactions	0,98		0,0476
Endothelin-1 Signaling	0,979		0,0263
Assembly and cell surface presentation of NMDA receptors	0,963		0,0465
Oncostatin M Signaling	0,963		0,0465
Vasopressin regulates renal water homeostasis via Aquaporins	0,963		0,0465
Agranulocyte Adhesion and Diapedesis	0,958		0,0259
D-myo-inositol-5-phosphate Metabolism	0,958	0	0,0259
PDGF Signaling	0,953		0,0337
Interleukin-9 signaling	0,951		0,111
Leucine Degradation I	0,951		0,111
Lysine catabolism	0,951		0,111
Reelin Signaling in Neurons	0,95		0,0286
Xenobiotic Metabolism General Signaling Pathway	0,95	0	0,0286
Elastic fibre formation	0,947		0,0455
TBC/RABGAPs	0,947		0,0455
Carboxyterminal post-translational modifications of tubulin	0,931		0,0444
Crosstalk between Dendritic Cells and Natural Killer Cells	0,931		0,033
Cellular Effects of Sildenafil (Viagra)	0,926		0,028
Fcy Receptor-mediated Phagocytosis in Macrophages and Monocytes	0,911		0,0323
TEC Kinase Signaling	0,908	-1	0,0212
Neurotransmitter clearance	0,908		0,1
Death Receptor Signaling	0,901		0,0319
Eukaryotic Translation Termination	0,901		0,0319
Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell	0,897	1,341640786	0,0248
ERBB Signaling	0,891		0,0316
3-phosphoinositide Biosynthesis	0,878	0	0,0244
Erythrocytes take up carbon dioxide and release oxygen	0,87		0,0909
Ephrin A Signaling	0,87		0,0408
Signaling by NOTCH3	0,87		0,0408
Protein folding	0,862		0,0306
Colorectal Cancer Metastasis Signaling	0,862	-1	0,0226
Netrin-1 signaling	0,856		0,04
RNA Polymerase I Transcription	0,856		0,04
Signaling by EGFR	0,856		0,04
TNFR1 Signaling	0,856		0,04
Aspartate and asparagine metabolism	0,835		0,0833
Assembly of RNA Polymerase I Complex	0,835		0,0833
Glycogen Degradation III	0,835		0,0833
UDP-N-acetyl-D-galactosamine Biosynthesis II	0,835		0,0833
Phase I - Functionalization of compounds	0,834		0,0297
Response of EIF2AK4 (GCN2) to amino acid deficiency	0,816		0,0291
Transport of inorganic cations/anions and amino acids/oligopeptides	0,807		0,0288
Guanosine Nucleotides Degradation III	0,803		0,0769

Passive transport by Aquaporins	0,803		0,0769
Processing of SMDT1	0,803		0,0769
Trafficking and processing of endosomal TLR	0,803		0,0769
Cargo recognition for clathrin-mediated endocytosis	0,798		0,0286
PD-1, PD-L1 cancer immunotherapy pathway	0,79		0,0283
CSDE1 Signaling Pathway	0,79		0,0364
E3 ubiquitin ligases ubiquitinate target proteins	0,79		0,0364
SPINK1 Pancreatic Cancer Pathway	0,79		0,0364
Signaling by PTK6	0,79		0,0364
Aspirin ADME	0,773		0,0714
Choline Biosynthesis III	0,773		0,0714
Glutamate and glutamine metabolism	0,773		0,0714
Urate Biosynthesis/Inosine 5'-phosphate Degradation	0,773		0,0714
Neurexins and neuroligins	0,766		0,0351
CNTF Signaling	0,755		0,0345
CXCR4 Signaling	0,747		0,0238
Platelet Adhesion to exposed collagen	0,746		0,0667
Prolactin receptor signaling	0,746		0,0667
Metabolism of water-soluble vitamins and cofactors	0,743		0,0339
IL-12 Signaling and Production in Macrophages	0,734	1,341640786	0,0217
Superpathway of Inositol Phosphate Compounds	0,723	0	0,0216
Glutaryl-CoA Degradation	0,721		0,0625
Granzyme B Signaling	0,721		0,0625
Parkinson's Signaling	0,721		0,0625
Kinesins	0,721		0,0328
NCAM signaling for neurite out-growth	0,721		0,0328
Heparan Sulfate Biosynthesis (Late Stages)	0,71		0,0323
FOXO-mediated transcription of cell cycle genes	0,697		0,0588
Isoleucine Degradation I	0,697		0,0588
Protein methylation	0,697		0,0588
Th1 Pathway	0,689		0,0252
Mitochondrial protein import	0,689		0,0312
Phospholipases	0,689		0,0312
IL-15 Production	0,682		0,025
p38 MAPK Signaling	0,682		0,025
AMPK Signaling	0,679	-1,341640786	0,0207
Macroautophagy	0,679		0,0308
RAB geranylgeranylation	0,679		0,0308
Thrombopoietin Signaling	0,679		0,0308
Branched-chain amino acid catabolism	0,675		0,0556
Methylglyoxal Degradation III	0,675		0,0556
Nicotinate metabolism	0,675		0,0556
Eukaryotic Translation Initiation	0,668		0,0246
Renin-Angiotensin Signaling	0,661		0,0244
CTLA4 Signaling in Cytotoxic T Lymphocytes	0,657	-1,133893419	0,0187
Docosahexaenoic Acid (DHA) Signaling	0,655	-0,447213595	0,0203
FOXO-mediated transcription	0,654		0,0526
Synaptogenesis Signaling Pathway	0,65	-2,449489743	0,0193
Role of JAK1 and JAK3 in γ c Cytokine Signaling	0,65		0,0294
Heparan Sulfate Biosynthesis	0,641		0,029
Phospholipase C Signaling	0,636	0,447213595	0,017

Inflammasome pathway	0,635		0,05
Interleukin-12 family signaling	0,635		0,05
Valine Degradation I	0,635		0,05
GNRH Signaling	0,633	-2	0,0213
ISG15 antiviral mechanism	0,623		0,0282
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	0,622		0,0211
Nucleotide salvage	0,616		0,0476
Synaptic adhesion-like molecules	0,616		0,0476
The Visual Cycle	0,616		0,0476
Dendritic Cell Maturation	0,614	1,889822365	0,0181
GM-CSF Signaling	0,614		0,0278
Growth Hormone Signaling	0,614		0,0278
Myelination Signaling Pathway	0,61	-1,632993162	0,0187
fMLP Signaling in Neutrophils	0,609		0,0229
Extra-nuclear estrogen signaling	0,606		0,0274
Iron homeostasis signaling pathway	0,603		0,0227
Role of PKR in Interferon Induction and Antiviral Response	0,603		0,0227
Cellular hexose transport	0,599		0,0455
NAD Salvage Pathway II	0,599		0,0455
ERK5 Signaling	0,597		0,027
Hypoxia Signaling in the Cardiovascular System	0,597		0,027
trans-Golgi Network Vesicle Budding	0,597		0,027
IL-7 Signaling Pathway	0,589		0,0267
Pulmonary Healing Signaling Pathway	0,588	-1	0,0203
Protein Kinase A Signaling	0,586	-1	0,0178
Gα12/13 Signaling	0,585		0,0222
Pyrimidine Deoxyribonucleotides De Novo Biosynthesis I	0,582		0,0435
Tryptophan Degradation III (Eukaryotic)	0,582		0,0435
Plasma lipoprotein assembly, remodeling, and clearance	0,581		0,0263
GDNF Family Ligand-Receptor Interactions	0,573		0,026
Macropinocytosis Signaling	0,573		0,026
Growth hormone receptor signaling	0,567		0,0417
IL-22 Signaling	0,567		0,0417
Interleukin-6 family signaling	0,567		0,0417
Sulfur amino acid metabolism	0,567		0,0417
Angiopoietin Signaling	0,565		0,0256
Costimulation by the CD28 family	0,565		0,0256
ID1 Signaling Pathway	0,564	-1	0,0198
DHCR24 Signaling Pathway	0,562		0,0216
Mitotic Prometaphase	0,559	-1	0,0197
Role of Tissue Factor in Cancer	0,559	-1	0,0197
Gαi Signaling	0,556		0,0214
Glucose metabolism	0,55		0,025
Neurotrophin/TRK Signaling	0,55		0,025
Insulin Secretion Signaling Pathway	0,549	-1,341640786	0,0185
BEX2 Signaling Pathway	0,543		0,0247
IL-3 Signaling	0,543		0,0247
Role of MAPK Signaling in the Pathogenesis of Influenza	0,543		0,0247
Pathogen Induced Cytokine Storm Signaling Pathway	0,541	0,816496581	0,0176
Fertilization	0,537		0,0385

Interleukin-20 family signaling	0,537		0,0385
Role of JAK1, JAK2 and TYK2 in Interferon Signaling	0,537		0,0385
FLT3 Signaling in Hematopoietic Progenitor Cells	0,528		0,0241
Effects of PIP2 hydrolysis	0,524		0,037
Activation of NMDA receptors and postsynaptic events	0,521		0,0238
JAK/STAT Signaling	0,521		0,0238
Transcriptional regulation of white adipocyte differentiation	0,521		0,0238
HIPPO signaling	0,514		0,0235
Regulation of the Epithelial Mesenchymal Transition in Development Pathway	0,514		0,0235
Molecular Mechanisms of Cancer	0,513	-2,496150883	0,0155
Keratinization	0,512	-2	0,0187
MTOR signalling	0,51		0,0357
Apelin Adipocyte Signaling Pathway	0,507		0,0233
Platelet homeostasis	0,507		0,0233
VEGF Family Ligand-Receptor Interactions	0,507		0,0233
LPS-stimulated MAPK Signaling	0,501		0,023
IL-10 Signaling	0,499		0,0199
EIF2 Signaling	0,499	-2	0,0184
Energy dependent regulation of mTOR by LKB1-AMPK	0,498		0,0345
RAB GEFs exchange GTP for GDP on RABs	0,488		0,0225
Unfolded protein response	0,488		0,0225
Mitophagy	0,486		0,0333
Nucleotide catabolism	0,486		0,0333
Protein ubiquitination	0,486		0,0333
Regulation of TP53 Activity through Acetylation	0,486		0,0333
Signaling by CSF3 (G-CSF)	0,486		0,0333
Thrombin Signaling	0,479		0,018
Cristae formation	0,474		0,0323
Signaling by CSF1 (M-CSF) in myeloid cells	0,474		0,0323
Ceramide Signaling	0,463		0,0215
G-protein beta:gamma signalling	0,463		0,0312
Class B/2 (Secretin family receptors)	0,457		0,0213
Activation of the pre-replicative complex	0,452		0,0303
Nucleotide Excision Repair	0,445		0,0208
Prolactin Signaling	0,445		0,0208
Salvage Pathways of Pyrimidine Ribonucleotides	0,445		0,0208
TGF- β Signaling	0,445		0,0208
IL-4 Signaling	0,445	0	0,0162
Cargo concentration in the ER	0,442		0,0294
Superpathway of Methionine Degradation	0,442		0,0294
Coagulation System	0,432		0,0286
GPVI-mediated activation cascade	0,432		0,0286
Metabolism of steroid hormones	0,432		0,0286
G α q Signaling	0,431		0,0181
Glycerophospholipid biosynthesis	0,429		0,0202
UVA-Induced MAPK Signaling	0,429		0,0202
Melanocyte Development and Pigmentation Signaling	0,423		0,02
IL-9 Signaling	0,422		0,0278
Interferon Signaling	0,422		0,0278
RHO GTPases Activate WASPs and WAVES	0,422		0,0278

Striated Muscle Contraction	0,422		0,0278
Th1 and Th2 Activation Pathway	0,419		0,0178
Sumoylation Pathway	0,418		0,0198
Erythropoietin Signaling Pathway	0,415		0,0176
Apoptosis Signaling	0,413		0,0196
WNT/ β -catenin Signaling	0,411		0,0175
Pancreatic Secretion Signaling Pathway	0,408	0	0,0165
Integration of energy metabolism	0,407		0,0194
Mitotic Prophase	0,407		0,0194
Cardiac Hypertrophy Signaling (Enhanced)	0,405	-0,447213595	0,0151
Pyrimidine Ribonucleotides Interconversion	0,404		0,0263
Granulocyte Adhesion and Diapedesis	0,399		0,0172
Sperm Motility	0,398		0,0163
Formation of Fibrin Clot (Clotting Cascade)	0,396		0,0256
α -Adrenergic Signaling	0,392		0,0189
Mechanisms of Viral Exit from Host Cells	0,379		0,0244
Pyrimidine Ribonucleotides De Novo Biosynthesis	0,379		0,0244
Transport of vitamins, nucleosides, and related molecules	0,379		0,0244
Dopamine-DARPP32 Feedback in cAMP Signaling	0,377		0,0167
Interleukin-4 and Interleukin-13 signaling	0,373		0,0182
Role of MAPK Signaling in Promoting the Pathogenesis of Influenza	0,373		0,0182
Formation of WDR5-containing histone-modifying complexes	0,371		0,0238
Retinol Biosynthesis	0,371		0,0238
Cardiac Hypertrophy Signaling	0,367		0,0157
Signaling by Retinoic Acid	0,364		0,0233
Signaling by SCF-KIT	0,364		0,0233
Binding and Uptake of Ligands by Scavenger Receptors	0,364		0,0179
Estrogen Receptor Signaling	0,363	-2	0,0149
Prostate Cancer Signaling	0,36		0,0177
MicroRNA Biogenesis Signaling Pathway	0,359		0,0162
Major pathway of rRNA processing in the nucleolus and cytosol	0,356		0,0161
Regulation of mRNA stability by proteins that bind AU-rich elements	0,356		0,0227
SUMOylation of transcription cofactors	0,356		0,0227
Bladder Cancer Signaling	0,355		0,0175
Systemic Lupus Erythematosus in T Cell Signaling Pathway	0,35	0,816496581	0,0147
GPER1 signaling	0,349		0,0222
iNOS Signaling	0,349		0,0222
Cholecystokinin/Gastrin-mediated Signaling	0,343		0,0171
Interleukin-2 family signaling	0,342		0,0217
Synaptic Long Term Depression	0,339		0,0157
ESR-mediated signaling	0,338		0,0169
MSP-RON Signaling in Macrophages Pathway	0,338		0,0169
Regulation of lipid metabolism by PPARalpha	0,334		0,0168
Regulation of the Epithelial Mesenchymal Transition by Growth Factors Pathway	0,33		0,0155
Apelin Muscle Signaling Pathway	0,329		0,0208
DNA Damage Bypass	0,329		0,0208
G alpha (z) signalling events	0,329		0,0208
XBP1(S) activates chaperone genes	0,329		0,0208

Adrenomedullin signaling pathway	0,327		0,0154
Coronavirus Pathogenesis Pathway	0,327		0,0154
Regulation of the Epithelial-Mesenchymal Transition Pathway	0,327		0,0154
NGF Signaling	0,326		0,0165
PFKFB4 Signaling Pathway	0,322		0,0204
Transcriptional activity of SMAD2/SMAD3:SMAD4 heterotrimer	0,322		0,0204
LXR/RXR Activation	0,319		0,0163
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	0,316		0,02
FAT10 Cancer Signaling Pathway	0,316		0,02
NR1H2 and NR1H3-mediated signaling	0,316		0,02
Opioid Signaling Pathway	0,313	-2	0,0145
UVC-Induced MAPK Signaling	0,31		0,0196
Cilium Assembly	0,309		0,0149
B-WICH complex positively regulates rRNA expression	0,304		0,0192
Melanoma Signaling	0,304		0,0192
Primary Immunodeficiency Signaling	0,304		0,0192
Synaptic Long Term Potentiation	0,3		0,0156
Signaling by TGF-beta Receptor Complex	0,298		0,0189
Endocannabinoid Developing Neuron Pathway	0,296		0,0155
mTOR Signaling	0,294		0,0146
Amino acids regulate mTORC1	0,287		0,0182
Intrinsic Pathway for Apoptosis	0,287		0,0182
The citric acid (TCA) cycle and respiratory electron transport	0,287		0,0182
Multiple Sclerosis Signaling Pathway	0,284		0,0143
Processing of Capped Intron-Containing Pre-mRNA	0,284	-2	0,0139
Complement cascade	0,283		0,015
Cell Cycle Control of Chromosomal Replication	0,282		0,0179
DNA Damage/Telomere Stress Induced Senescence	0,282		0,0179
CGAS-STING Signaling Pathway	0,279		0,0149
Th2 Pathway	0,276		0,0148
Insulin Receptor Signaling	0,273		0,0147
Cancer Drug Resistance by Drug Efflux	0,272		0,0172
EGF Signaling	0,272		0,0172
Role of JAK2 in Hormone-like Cytokine Signaling	0,272		0,0172
Signaling by ERBB4	0,272		0,0172
Adipogenesis pathway	0,27		0,0146
White Adipose Tissue Browning Pathway	0,27		0,0146
DNA Double Strand Break Response	0,267		0,0169
Polyamine Regulation in Colon Cancer	0,267		0,0169
GABA receptor activation	0,262		0,0167
PCP (Planar Cell Polarity) Pathway	0,262		0,0167
Visual phototransduction	0,262		0,0167
Role of Chondrocytes in Rheumatoid Arthritis Signaling Pathway	0,26		0,0143
Apelin Endothelial Signaling Pathway	0,257		0,0142
MSP-RON Signaling in Cancer Cells Pathway	0,257		0,0142
Cytoprotection by HMOX1	0,253		0,0161
T Cell Receptor Signaling	0,252	0,447213595	0,0131
Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells	0,251		0,0135
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	0,249		0,0134

Activation of IRF by Cytosolic Pattern Recognition Receptors	0,248		0,0159
SPINK1 General Cancer Pathway	0,248		0,0159
IL-2 Signaling	0,244		0,0156
NAD Signaling Pathway	0,243		0,0137
Pyridoxal 5'-phosphate Salvage Pathway	0,24		0,0154
RNA Polymerase II Transcription	0,237		0,0135
ERB2-ERBB3 Signaling	0,235		0,0152
Eicosanoid Signaling	0,231		0,0149
Phase II - Conjugation of compounds	0,231		0,0149
ERBB4 Signaling	0,227		0,0147
COPII-mediated vesicle transport	0,212		0,0139
Senescence-Associated Secretory Phenotype (SASP)	0,209		0,0137
GPCR-Mediated Integration of Enteroendocrine Signaling Exemplified by an L Cell	0,205		0,0135
Antiproliferative Role of Somatostatin Receptor 2	0,198		0,0132
Pre-NOTCH Expression and Processing	0,198		0,0132
Role of MAPK Signaling in Inhibiting the Pathogenesis of Influenza	0,198		0,0132
SUMOylation of DNA damage response and repair proteins	0,198		0,0132
ATM Signaling	0		0,0101
Activin Inhibin Signaling Pathway	0		0,00948
Acute Myeloid Leukemia Signaling	0		0,0109
Adrenergic Receptor Signaling Pathway (Enhanced)	0		0,00518
Airway Pathology in Chronic Obstructive Pulmonary Disease	0		0,00885
Allograft Rejection Signaling	0		0,012
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	0		0,00424
Amyotrophic Lateral Sclerosis Signaling	0		0,00862
Androgen Signaling	0		0,00599
Apelin Cardiomyocyte Signaling Pathway	0		0,01
Autoimmune Thyroid Disease Signaling	0		0,008
B Cell Development	0		0,00905
B Cell Receptor Signaling	0	0	0,0108
BMP signaling pathway	0		0,0112
Beta-catenin independent WNT signaling	0		0,0098
Breast Cancer Regulation by Stathmin1	0	1,341640786	0,00853
CCR5 Signaling in Macrophages	0		0,00338
CD28 Signaling in T Helper Cells	0		0,00958
CREB Signaling in Neurons	0		0,00503
Calcium Signaling	0		0,00948
Calcium-induced T Lymphocyte Apoptosis	0		0,00791
Cardiac conduction	0		0,00769

Cardiac β -adrenergic Signaling	0		0,0113
Chemokine Signaling	0		0,013
Chronic Myeloid Leukemia Signaling	0		0,00368
Circadian Rhythm Signaling	0		0,0076
Class A/1 (Rhodopsin-like receptors)	0		0,00315
Communication between Innate and Adaptive Immune Cells	0		0,00647
Corticotropin Releasing Hormone Signaling	0		0,0068
Dopamine Receptor Signaling	0		0,0127
Electron transport, ATP synthesis, and heat production by uncoupling proteins	0		0,00781
Endocannabinoid Neuronal Synapse Pathway	0		0,00676
Estrogen-Dependent Breast Cancer Signaling	0		0,0123
FAK Signaling	0	-0,632455532	0,0121
FXR/RXR Activation	0		0,0113
Factors Promoting Cardiogenesis in Vertebrates	0		0,00671
Fc Epsilon RI Signaling	0		0,00833
Fcgamma receptor (FCGR) dependent phagocytosis	0		0,00637
Fc γ RIIB Signaling in B Lymphocytes	0		0,00365
G Protein Signaling Mediated by Tubby	0		0,00376
G alpha (i) signalling events	0		0,00386
G alpha (s) signalling events	0		0,0069
G-Protein Coupled Receptor Signaling	0	-0,377964473	0,0101
GABA Receptor Signaling	0		0,00769
GABAergic Receptor Signaling Pathway (Enhanced)	0		0,00725
GPCR-Mediated Nutrient Sensing in Enteroendocrine Cells	0		0,00855
Generic Transcription Pathway	0		0,00234
Glioblastoma Multiforme Signaling	0		0,0118
Glioma Signaling	0		0,00806
Glutaminergic Receptor Signaling Pathway (Enhanced)	0	-2	0,0125
Graft-versus-Host Disease Signaling	0		0,00826
G α s Signaling	0		0,00806
HMGB1 Signaling	0		0,0124
HOTAIR Regulatory Pathway	0		0,0124
Hereditary Breast Cancer Signaling	0		0,00709
Human Embryonic Stem Cell Pluripotency	0		0,00503
ICOS-ICOSL Signaling in T Helper Cells	0		0,0066
IL-1 Signaling	0		0,0104

IL-13 Signaling Pathway	0		0,0085 5
IL-15 Signaling	0		0,0037 5
IL-17 Signaling	0		0,0055 2
Ion channel transport	0		0,0109
Kinetochore Metaphase Signaling Pathway	0		0,0093 5
Lipid Antigen Presentation by CD1	0		0,0047 2
Macrophage Alternative Activation Signaling Pathway	0		0,011
Macrophage Classical Activation Signaling Pathway	0		0,0055 6
Maturity Onset Diabetes of Young (MODY) Signaling	0		0,013
Mitochondrial Dysfunction	0	2	0,012
Mouse Embryonic Stem Cell Pluripotency	0		0,0095 2
NAFLD Signaling Pathway	0		0,0046 1
NER (Nucleotide Excision Repair, Enhanced Pathway)	0		0,0114
NF- κ B Signaling	0		0,0054 2
NOD1/2 Signaling Pathway	0		0,0114
NUR77 Signaling in T Lymphocytes	0		0,0109
Necroptosis Signaling Pathway	0		0,0131
Netrin Signaling	0		0,0116
Neuroinflammation Signaling Pathway	0	2	0,0129
Neurovascular Coupling Signaling Pathway	0		0,0091 3
Nitric Oxide Signaling in the Cardiovascular System	0		0,0087
Non-Small Cell Lung Cancer Signaling	0		0,0105
OX40 Signaling Pathway	0		0,0123
Orexin Signaling Pathway	0		0,0042 7
Ovarian Cancer Signaling	0		0,0063 3
Oxidative Phosphorylation	0		0,0093 5
Oxytocin in Brain Signaling Pathway	0		0,0102
P2Y Purigenic Receptor Signaling Pathway	0		0,0074 6
PEDF Signaling	0		0,0116
PI Metabolism	0		0,0122
PI3K Signaling in B Lymphocytes	0		0,0061 5
PKC θ Signaling in T Lymphocytes	0		0,0084 5
PPAR Signaling	0		0,0096 2
PPAR α /RXR α Activation	0		0,0109
RANK Signaling in Osteoclasts	0		0,0111
RAR Activation	0	-2	0,0096 6
Regulation of IL-2 Expression in Activated and Anergic T Lymphocytes	0		0,0038 2

Relaxin Signaling	0		0,00654
Role of BRCA1 in DNA Damage Response	0		0,0125
Role of Hypercytokinemia/hyperchemokinaemia in the Pathogenesis of Influenza	0		0,0125
Role of JAK family kinases in IL-6-type Cytokine Signaling	0		0,013
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	0		0,00625
Role of NANOG in Mammalian Embryonic Stem Cell Pluripotency	0		0,00806
Role of NFAT in Cardiac Hypertrophy	0		0,00901
Role of NFAT in Regulation of the Immune Response	0	0	0,00701
S100 Family Signaling Pathway	0	0	0,0107
SAPK/JNK Signaling	0		0,00662
STAT3 Pathway	0		0,00741
Senescence Pathway	0		0,00338
Signaling by NOTCH1	0		0,013
Signaling by NTRK1 (TRKA)	0		0,0123
Sphingolipid metabolism	0		0,0115
Sphingosine-1-phosphate Signaling	0		0,0084
Systemic Lupus Erythematosus Signaling	0		0,00676
Systemic Lupus Erythematosus in B Cell Signaling Pathway	0		0,00442
T Cell Exhaustion Signaling Pathway	0		0,011
T Helper Cell Differentiation	0		0,0112
TR/RXR Activation	0		0,00769
Telomerase Signaling	0		0,00935
Thyroid Cancer Signaling	0		0,013
Transcriptional Regulatory Network in Embryonic Stem Cells	0		0,0061
Transport of bile salts and organic acids, metal ions and amine compounds	0		0,012
Type I Diabetes Mellitus Signaling	0		0,00987
VEGF Signaling	0		0,0101
WNK Renal Signaling Pathway	0		0,01
cAMP-mediated signaling	0		0,00433
p70S6K Signaling	0		0,00625

Online Resource 14 Significantly enriched GO pathways of differentially expressed proteins.

#term ID	term description	genes mapped	enrichment score	direction	false discovery rate
GO:0005509	Calcium ion binding	88	0.076586	bottom	4.61e-07
GO:0140640	Catalytic activity, acting on a nucleic acid	69	615.908	top	4.61e-07
GO:0016462	Pyrophosphatase activity	124	552.731	top	7.46e-06

GO:0017111	Nucleoside-triphosphatase activity	118	551.794	top	1.08e-05
GO:0140098	Catalytic activity, acting on RNA	50	606.135	top	2.46e-05
GO:0004812	aminoacyl-tRNA ligase activity	21	671.755	top	0.00051
GO:0016874	Ligase activity	49	57.479	top	0.00051
GO:0140101	Catalytic activity, acting on a tRNA	23	635.538	top	0.00058
GO:0005524	ATP binding	193	344.703	top	0.0011
GO:0016884	Carbon-nitrogen ligase activity, with glutamine as amido-N-donor	4	949.327	top	0.0036
GO:0016887	ATP hydrolysis activity	67	563.654	top	0.0037
GO:0004386	Helicase activity	27	650.903	top	0.0092

Online Resource 15 Percentage of responding cells during Ca²⁺ imaging in the cytoplasm of control and TSC astrocytes. **a.** The percentage of responding control and TSC astrocytes upon DHPG stimulation. **b.** The percentage of responding control and TSC astrocytes upon glutamate stimulation. **c.** The percentage of responding control and TSC astrocytes upon ATP stimulation. Data are expressed as mean ± SEM; p-value: * p-value ≤ 0.05; ** p-value ≤ 0.01; *** p-value ≤ 0.001; **** p-value ≤ 0.0001. Mann–Whitney U-test.

Online Resource 16 Electron microscopy analysis of mitochondria morphology in healthy-appearing astrocytes and neurons in TLE control tissue and astrocytes and dysmorphic neurons in TSC tissue. **a-c.** Multiple parameters were considered in the analysis to describe mitochondria morphology. TSC astrocytes showed significant reduction in circularity, feret’s diameter and integrated density compared to control astrocytes. Data are expressed as mean ± SEM; Non-parametric Kruskal-Wallis H test was performed with correction for multiple comparisons. Significance is represented by p-value: * p-value ≤ 0.05; ** p-value ≤ 0.01; *** p-value ≤ 0.001; **** p-value ≤ 0.0001.