

xMWAS: R package for data integration and network analysis

Karan Uppal^{*1}

Clinical Biomarkers Laboratory, Division of Pulmonary Medicine, Department of Medicine, Emory University, Atlanta, Georgia 30322, USA
E-mail: kuppal2@emory.edu

Young-Mi Go

Clinical Biomarkers Laboratory, Division of Pulmonary Medicine, Department of Medicine, Emory University, Atlanta, Georgia 30322, USA

Dean P. Jones

Clinical Biomarkers Laboratory, Division of Pulmonary Medicine, Department of Medicine, Emory University, Atlanta, Georgia 30322, USA

¹ To whom correspondence should be addressed

xMWAS: an R package for data-driven integration and differential network analysis

Karan Uppal*, Young-Mi Go and Dean P. Jones

Clinical Biomarkers Laboratory, Department of Medicine, Emory University,
Atlanta, GA

*To whom correspondence should be addressed.

Abstract

Summary: Integrative omics is a central component of most systems biology studies. Computational methods are required for extracting meaningful relationships across different omics layers. Various tools have been developed to facilitate integration of paired heterogenous omics data; however most existing tools allow integration of only two omics datasets. Furthermore, existing data integration tools do not incorporate additional steps of identifying sub-networks or communities of highly connected entities and evaluating the topology of the integrative network under different conditions. Here we present xMWAS, an R package for data integration, network visualization, clustering, differential network analysis of data from biochemical and phenotypic assays, and two or more omics platforms.

Availability: <https://sourceforge.net/projects/xmwas/>

Contact: kuppal2@emory.edu

1 Introduction

Technological advances have led to a major paradigm shift where multi-assay molecular profiling of biological samples is increasingly being used to understand molecular mechanisms for diseases and host responses to environmental exposures (Hawkins 2010, Cancer Genome Atlas Network 2008). Most cellular processes in a biological system are dependent on complex molecular interactions (Barabasi 2011). Integrative omics allows researchers to address such complexity and answer challenging biological questions, such as function of genetic variants and unknown metabolites, mechanisms of gene regulation, signaling and metabolic pathway responses to infection and toxicity (Hawkins 2010, Chandler 2016, Uppal 2016).

Numerous data-driven/unsupervised and knowledge-based tools allow integration of data from different omics technologies and other molecular assays (Wanichthanarak 2015, Meng 2016). Most existing data integration tools allow integration of only two datasets and do not allow identification of community structure and evaluation of network changes between different conditions. Community detection reveals topological modules comprised of functionally related biomolecules (Barabasi 2011, Yang 2016). Differential network analysis (DiNA) allows characterization of

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nodes that undergo changes in topological characteristics between different conditions, e.g. healthy vs disease (Lichtblau 2016).

To advance these capabilities, we present, xMWAS, an R package that provides an automated workflow for integrative analysis of more than two datasets, differential network analysis, and community detection to improve our understanding of complex molecular interactions and disease mechanisms.

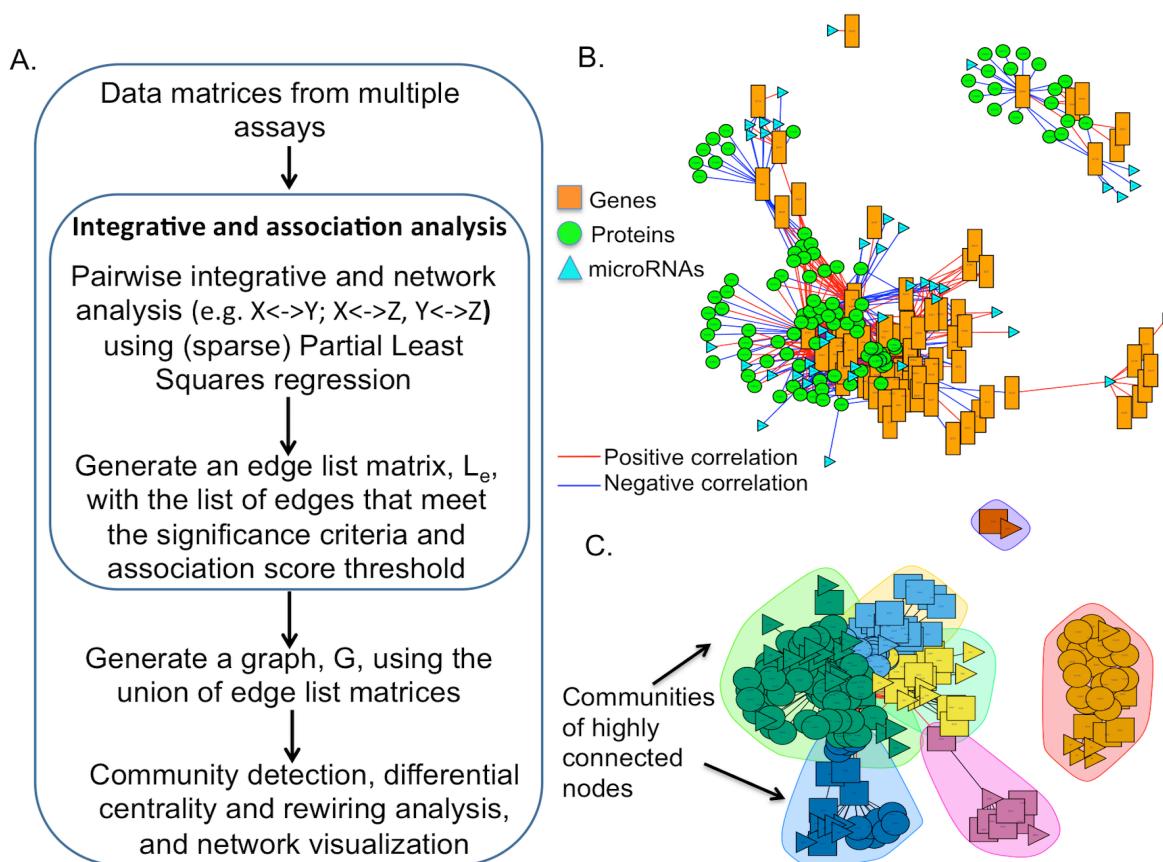


Fig. 1. xMWAS workflow. A. Pairwise data integration and association analysis is performed using (sparse) partial least squares regression. The edge list matrices of significant associations from each pairwise comparison are merged to generate a global association network. Community detection is performed using the multilevel algorithm. B. Illustration of association network for the NCI60 dataset (Meng 2016): microRNAs (triangle), protein (circle) and transcripts (rectangle). C. Identification of communities in the NCI60 integrated network using the multilevel community detection algorithm.

2 Implementation

xMWAS provides an automated framework for integrative and differential network analysis. Figure 1A provides an overview of different stages of xMWAS. In stage one, xMWAS uses dimension reduction techniques such as Partial Least Squares (PLS), sparse Partial Least Squares (sPLS), and multilevel sparse Partial Least Squares (msPLS; for repeated measures) regression for

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pairwise integrative and association analysis between data matrices (Le Cao 2009, Liquet 2012, Gonzalez 2012). sPLS and msPLS methods perform simultaneous data integration and variable selection using a LASSO penalty for the loading vectors, which reduces the complexity of the networks (Liquet 2012). R package *plsgenomics* is used to determine the optimal number of latent components. The *network()* function in the *mixOmics* package is used to generate the association matrix, A_{XY} , between matrices X and Y (Le Cao 2009, Gonzalez 2012). Student's t-test is used to evaluate the statistical significance of association scores. Only the associations that satisfy the user-defined thresholds, e.g. $|association\ score| > 0.7$ and $p\text{-value} < 0.01$, are used for downstream analysis. The resulting graph, $G_i = (V, E)$, where V is a set of nodes and E is a set of edges, is used to generate an edge list matrix, L_i , such that each row in L_i corresponds to an edge between nodes X_p and Y_q . The same process is repeated for generating edge list matrices from all pairwise association analyses between datasets, e.g. $L_i = \text{cor}(X, Y)$; $L_j = \text{cor}(Y, Z)$, and $L_k = \text{cor}(Y, Z)$.

In stage two, the union of the individual edge list matrices from pairwise integrative analysis of the n datasets is used to generate a combined edge list matrix, $L_e = \bigcup_{i=1}^n L_i$. Matrix L_e is used to generate the integrative network graph, $G = (V, E)$, where V corresponds to nodes and E corresponds to edges or connections between the nodes, representing positive or negative associations between multiple datasets (Figure 1B). Network graphics are generated using the *igraph* package in R.

In stage three, the multilevel community detection algorithm (Blondel 2008) is used to identify communities of nodes that are tightly connected with each other, but sparsely connected with the rest of the network (Figure 1C). Comparative studies for community detection algorithms show that the multilevel algorithm is suitable for both small and large networks with varying connectivity patterns (Yang 2016). The quality of the community structure is evaluated using the network modularity measure (Newman 2006).

Differential network analysis is performed using the differential betweenness centrality and differential eigenvector centrality methods to identify nodes that undergo changes in their topological characteristics (Odibat 2012, Lichtblau 2016). Additional description about the software input and output is provided in Supplementary Section S1.

3 Example

We tested xMWAS in a three-way integrative analysis using cytokine, transcriptome, and metabolome datasets from a recently published study to examine H1N1 influenza virus infection-altered metabolic response in mouse lung (Chandler 2016). For comparisons, we used data from all samples (Supplementary Figure S1A), only control samples (Supplementary Figure S1B), and only H1N1 influenza samples (Supplementary Figure S1C). Supplementary Section S2 shows that the various stages of xMWAS capture biologically meaningful information and provide deeper insights into the underlying biology, which cannot be obtained by analyzing and exploring the different layers individually.

4 Conclusion

xMWAS provides a platform-independent framework for integrative network analysis of two or more datasets, identification of modules of functionally related biomolecules, and differential network analysis. The results show that xMWAS can improve our understanding of disease pathophysiology and complex molecular interactions across various functional levels.

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Acknowledgements

The authors acknowledge members of the Clinical Biomarkers Laboratory, Emory University for testing and suggesting improvements to the software.

Funding

This project was funded by National Institutes of Health grants, ES025632, ES023485, ES019776, OD018006, HL095479, EY022618. The project was also funded in part by federal funds from the US National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services under contract # HHSN272201200031C.

Conflict of Interest: none declared.

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Supplementary Material

xMWAS: an R package for data-driven integration and differential network analysis

Karan Uppal*²

Clinical Biomarkers Laboratory, Division of Pulmonary Medicine, Department of Medicine,
Emory University, Atlanta, Georgia 30322, USA
E-mail: kuppal2@emory.edu

Young-Mi Go

Clinical Biomarkers Laboratory, Division of Pulmonary Medicine, Department of Medicine,
Emory University, Atlanta, Georgia 30322, USA

Dean P. Jones

Clinical Biomarkers Laboratory, Division of Pulmonary Medicine, Department of Medicine,
Emory University, Atlanta, Georgia 30322, USA

² To whom correspondence should be addressed

Supplementary Section S1. Description of input and output for xMWAS

The main input parameters include file paths or data matrices of input datasets, file with phenotypic labels (e.g. case, control), integration method (“pls”, “spl”), threshold for association score, and statistical significance. The software is designed to work with data from different sources and does not utilize any knowledgebase information for integration. For metabolomics studies, the software is designed to work with both targeted and untargeted datasets and does not require metabolite identification prior to integration. The output includes PDF of integrative network with cluster assignments, text files for association matrices and cluster assignments for each node and their centrality scores, and a GML format file that can be used for visualization with tools such as Cytoscape (Shannon 2003).

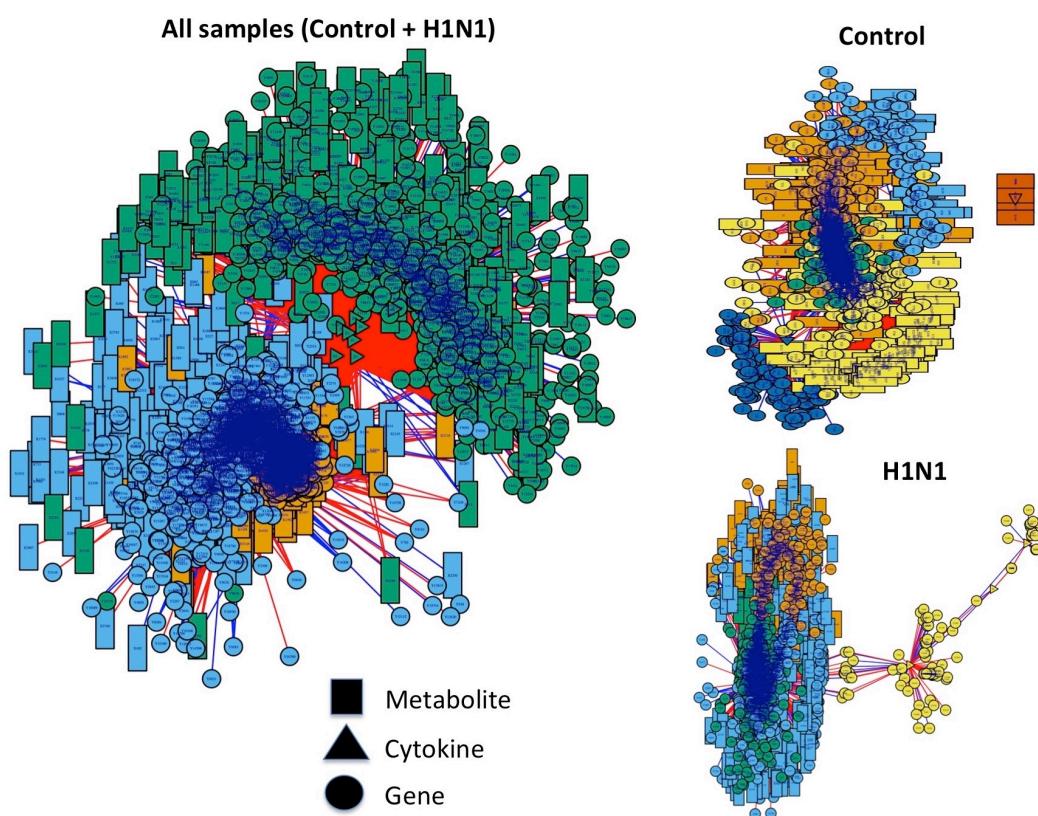


Figure S1. Integrative network analysis of cytokine, metabolome and transcriptome datasets from a study of H1N1 virus infection of mice. A. All samples; B. Only control samples; C. Only H1N1 infected samples. The results show that xMWAS analysis of the complex omics arrays allows identification and visualization of metabolite and transcript correlations with cytokines. The analysis further discriminates between correlations observed in controls from those observed in H1N1 virus infected mice and allows identification of nodes that undergo network changes. Details are provided in Supplementary Section S2.

Supplementary Section S2. Evaluation results using data from the H1N1 virus infection of mice

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Pathway analysis of metabolic features (*m/z* and retention time) and genes that were significantly associated with cytokines at $p<0.05$ across all samples was performed using Mummichog and MetaCore, respectively. Pathways related to immune response, lipid metabolism, amino acids metabolism, nitrogen metabolism, drug metabolism, vitamin metabolism, cytoskeleton remodeling, cell signaling, and energy metabolism were significantly enriched (Supplementary Tables S1 and S2). Previous studies have shown the role of these pathways in regulation of immune response and inflammation (Miyake 2000, Fortin 2009, Sadik 2012, Yin 2014, Chandler 2016)

Differential centrality analysis between control vs H1N1 samples showed dramatic change in the centrality of cytokines as well as genes and metabolites involved in immune response and defense mechanism (Supplementary Tables S3-6). Cytokines are known to be involved in the recruitment of the inflammatory cells and influence the adaptive immune response during influenza (Vareille 2011, Liu 2016, Chandler 2016).

Multilevel community detection identified four clusters in the integrative network generated using only H1N1 samples (Supplementary Figure S1C). Cluster 2 (blue), which comprised of four cytokines, 830 genes, and 437 metabolic features, was evaluated for significantly enriched pathways and biological processes. Pathway analysis of the metabolic features in this cluster showed enrichment of similar pathways as in the cytokine x metabolome association analysis across all samples described above (Supplementary Table S7). Pathway and process enrichment analysis using MetaCore showed enrichment of genes involved in immune responses, protein folding, signaling mechanisms, and various biological processes related to cilium movement, organization, assembly and organization (Supplementary Tables S8-S10). Previous studies have shown that the airway epithelium acts as a first layer of defense mechanism against respiratory viruses and that the respiratory viruses can lead to ciliary impairment (Vareille 2011).

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Supplementary Table S1. Pathway analysis of metabolic features (*m/z* and retention time) that were found to be significantly associated with the six cytokines at *p*<0.05 using Mummichog

Pathway Name	IL-1beta	IL-6	IL-10	TNFalpha	IP-1	IFNgamma
Carnitine shuttle	X	X	X	X	X	
Glycosphingolipid metabolism	X	X	X	X	X	
Vitamin D ₃ (cholecalciferol) metabolism	X	X	X	X	X	
Vitamin B ₆ (pyridoxine) metabolism			X	X	X	X
Biopterin metabolism	X	X		X	X	
Saturated fatty acids beta-oxidation			X	X	X	
Vitamin E metabolism	X		X	X		
Nitrogen metabolism		X			X	
Urea cycle/amino group metabolism					X	X
Drug metabolism - cytochrome P450					X	X
Tryptophan metabolism					X	X
Arginine and proline metabolism						X
Bile acid biosynthesis				X		
Fatty acid metabolism			X			
Limonene and pinene degradation			X			
Linoleate metabolism			X			
Tyrosine metabolism	X					

Supplementary Table S2. Pathway analysis of genes that were found to be significantly associated with the six cytokines at $p<0.05$ using MetaCore

Pathway Name	IL-1beta	IL-6	IL-10	TNFalpha	IP-1	IFNgamma
Immune response_Alternative complement pathway	x	x	x	x	x	x
GTP metabolism	x	x	x	x	x	
Cytoskeleton remodeling_TGF, WNT and cytoskeletal remodeling	x	x		x	x	x
Cytoskeleton remodeling_Cytoskeleton remodeling	x	x		x	x	x
Alternative complement cascade disruption in age-related macular degeneration	x	x		x	x	x
ATP metabolism	x	x	x	x	x	
Immune response_Lectin induced complement pathway		x	x		x	x
Regulation of lipid metabolism_Regulation of lipid metabolism by niacin and isoprenaline	x	x		x		
Development_Oligodendrocyte differentiation from adult stem cells			x		x	x
Cell adhesion_Chemokines and adhesion	x			x		
Expression targets of Tissue factor signaling in cancer	x			x		
Cell adhesion_ECM remodeling			x			x
Immune response_Classical complement pathway				x		x
Development_Regulation of epithelial-to-mesenchymal transition (EMT)					x	x
Protein folding and maturation_Insulin processing				x		
Glucocorticoid-induced elevation of intraocular pressure as glaucoma risk factor						x
Inhibition of neutrophil migration by proresolving lipid mediators in COPD						x

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Supplementary Table S3. Eigenvector centrality measures for cytokines with delta centrality (control vs H1N1) greater than 0.3

Name	All samples	Control	H1N1	Delta (Control vs H1N1)
IL-10	0.61	0.00	1.00	1.00
IL-1beta	0.66	0.00	0.98	0.98
TNF-alpha	0.66	0.00	0.88	0.88
IL-6	0.34	0.50	0.00	0.50

Supplementary Table S4. Pathway analysis of metabolic features with delta centrality (control vs H1N1) greater than 0.3 using Mummichog

Pathways	Overlap size	Pathway size	p
Carnitine shuttle	16	18	0.00065
Vitamin D3 (cholecalciferol) metabolism	10	10	0.00065
Phytanic acid peroxisomal oxidation	4	4	0.00115
De novo fatty acid biosynthesis	8	14	0.00134
Leukotriene metabolism	11	23	0.00174
Valine, leucine and isoleucine degradation	10	22	0.00278
Fatty acid activation	6	11	0.00288
Fatty Acid Metabolism	6	11	0.00288
Vitamin E metabolism	7	15	0.00474
Squalene and cholesterol biosynthesis	7	15	0.00474
Pyruvate Metabolism	7	15	0.00474
Omega-6 fatty acid metabolism	2	2	0.01496
Benzoate degradation via CoA ligation	2	2	0.01496
Fatty acid oxidation, peroxisome	2	2	0.01496
Di-unsaturated fatty acid beta-oxidation	2	2	0.01496
Prostaglandin formation from arachidonate	14	40	0.01604
Biopterin metabolism	5	12	0.01882
Bile acid biosynthesis	16	47	0.01928
Glycosphingolipid metabolism	8	22	0.02174
Vitamin B5 - CoA biosynthesis from pantothenate	3	6	0.02583
Tryptophan metabolism	16	49	0.03124
Saturated fatty acids beta-oxidation	2	3	0.03833
Glyoxylate and Dicarboxylate Metabolism	3	7	0.04628

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Supplementary Table S5. Pathway analysis of genes with delta centrality (control vs H1N1) greater than 0.3 using MetaCore. Only the top 20 significant pathways at FDR<0.1 are shown here.

Pathway Maps	Total	p	FDR	In D at a	Network Objects from Active Data
Expression targets of Tissue factor signaling in cancer	22	2.429E-04	5.928E-02	5	Tissue factor, PAR2, NFKBIE, PLAU (UPA), CSF1
Signal transduction_Soluble CXCL16 signaling	49	3.036E-04	5.928E-02	7	STAT3, HIF1A, I-kB, JAK2, P-selectin, CD163, NF-kB
Immune response_IL-12 signaling pathway	23	3.036E-04	5.928E-02	5	STAT3, IRF1, JAK2, P-selectin, Perforin
Immune response_IFN alpha/beta signaling pathway	24	3.752E-04	5.928E-02	5	IRF1, STAT2, PTP-1B, PML, USP18
Development_Leptin signaling via JAK/STAT and MAPK cascades	25	4.588E-04	5.928E-02	5	STAT3, HIF1A, JAK2, cPLA2, PTP-1B
Platelet activation during ADAM-TS13-deficient thrombotic microangiopathy development	28	7.946E-04	7.381E-02	5	Calpain 1(mu), P-selectin, Histone H4, CD36, Fc gamma RII alpha
Retinal ganglion cell damage in glaucoma	44	1.059E-03	7.381E-02	6	Calpain 1(mu), TNF-R1, P2X7, Sortilin, NF-kB, MAP1LC3B
Myeloid-derived suppressor cells and M2 macrophages in cancer	64	1.560E-03	7.381E-02	7	STAT3, IRF8, ARG1, HIF1A, NF-kB, IL4RA, CSF1
Chemotaxis_CCR1 signaling	48	1.684E-03	7.381E-02	6	STAT3, I-kB, cPLA2, CCR1, NF-kB, CCL7
Bacterial infections in CF airways	48	1.684E-03	7.381E-02	6	IRF1, IKK-epsilon, MyD88, JAK2, Cathepsin S, NF-kB
Immune response_CD40 signaling	65	1.709E-03	7.381E-02	7	STAT3, IRF1, CCL2, I-kB, JAK2, Lyn, NF-

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					kB
SLE genetic marker-specific pathways in antigen-presenting cells (APC)	84	1.813E-03	7.381E-02	8	IRF1, IKK-epsilon, IRF8, MyD88, I-kB, MICB, NF-kB, Fc gamma RII alpha
G-protein signaling_G-Protein alpha-q signaling cascades	34	1.973E-03	7.381E-02	5	I-kB, PKC-epsilon, RGS3, NF-kB, LARG
Development_GM-CSF signaling	50	2.085E-03	7.381E-02	6	STAT3, CCL2, I-kB, JAK2, Lyn, NF-kB
Transcription_Role of Akt in hypoxia induced HIF1 activation	21	2.118E-03	7.381E-02	4	Heme oxygenase 1, HIF1A, GLUT1, PGK1
Immune response_Inflammasome in inflammatory response	35	2.253E-03	7.381E-02	5	TNF-R1, P2X7, I-kB, Nod1, NF-kB
Development_Angiopoietin - Tie2 signaling	35	2.253E-03	7.381E-02	5	STAT3, I-kB, GRB7, NF-kB, NCK1
Signal transduction_NF-kB activation pathways	51	2.311E-03	7.381E-02	6	MyD88, TNF-R1, NF-kB2 (p52), I-kB, NF-kB2 (p100), NF-kB
Immune response_IL-15 signaling via JAK-STAT cascade	22	2.535E-03	7.381E-02	4	STAT3, IL-15, JAK2, STAT2
LRRK2 and immune function in Parkinson's disease	22	2.535E-03	7.381E-02	4	I-kB, JAK2, FCGR3A, NF-kB

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Supplementary Table S6. Process networks enrichment analysis of genes with delta centrali-ty (control vs H1N1) greater than 0.3 using MetaCore.

Process networks	Total	p	FDR	In Da-ta	Network Objects from Active Data
Development_Regulation of angiogenesis	222	5.828E-05	4.303E-03	23	Ephrin-A, STAT3, IL-15, CCL2, S2P, HIF1A, I-kB, JAK2, HNF4-alpha, Osteonectin, Prolyl endopeptidase, Ephrin-B2, Ephrin-B, CCR1, Galpha(q)-specific peptide GPCRs, NF-kB, Ephrin-A1, BTG1, Ihh, PKC, NCK1, Hedgehog, Syndecan-3
Immune re-sponse_Antigen presentation	197	8.134E-05	4.303E-03	21	STAT3, PSMB1, RFX5, TNF-R1, NF-kB2 (p52), I-kB, JAK2, PSMD3, IP-30, STAT2, Cathepsin S, MICB, AP-3 beta sub-units, PSMD14, NF-kB2 (p100), NFKBIE, NFKBIA, PSMB2, Legumain, NF-kB, TAP2 (PSF2)
Immune re-sponse_Phagosome in antigen presentation	243	8.663E-05	4.303E-03	24	PSMB1, Vinculin, NF-kB2 (p52), I-kB, PSMD3, CD63, Cathepsin S, FCGR3A, Lyn, Alpha-actinin, PSMD14, NF-kB2 (p100), NFKBIE, NFKBIA, VCP, PSMB2, Legumain, NF-kB, RalGDS, Alpha-actinin 3, TAP2 (PSF2), NCK1, FGR, Fc gamma RII alpha
Immune re-sponse_Phagocytosis	222	4.338E-04	1.616E-02	21	IL-15, Myosin I, Vinculin, NF-kB2 (p52), I-kB, MyHC, CD63, PKC-epsilon,

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					FCGR3A, Lyn, Alpha-actinin, NF-kB2 (p100), NFKBIE, NFKBIA, MRLC, NF-kB, Alpha-actinin 3, HDL proteins, NCK1, FGR, Fc gamma RII alpha
Inflammation_Interferon signaling	110	7.078E-04	2.109E-02	13	STAT3, IRF1, IRF8, CCL2, JAK2, STAT2, MICB, Pyrin (MEFV), PTP-1B, TAP2 (PSF2), PML, GBP2, CCL7
Development_Blood vessel morphogenesis	228	1.520E-03	3.632E-02	20	STAT3, FOXC2, Furin, PLGF, PDE, HIF1A, Neuregulin 1, Galphalpha(q)-specific nucleotide-like GPCRs, VEGF-D, Galphalpha(q)-specific amine GPCRs, MMP-19, CCR1, FOXC1/2, ErbB4, PGK1, Galphalpha(q)-specific peptide GPCRs, GRB7, NF-kB, NCK1, FGF1
Inflammation_Protein C signaling	108	1.932E-03	3.632E-02	12	Tissue factor, MyD88, NF-kB2 (p52), I-kB, PAR2, Alpha-actinin, NF-kB2 (p100), NFKBIE, NFKBIA, PLAU (UPA), NF-kB, Alpha-actinin 3
Cell adhesion_Synaptic contact	184	1.950E-03	3.632E-02	17	Ephrin-A, K(+) channel, subfamily J, Syntaxin 1A, GluR3, Synaptotagmin, GABA-A receptor beta-2 subunit, Ephrin-B2, Ephrin-B, Ephrin-B2 (CTF2), Alpha-actinin, SHANK, GABA-A receptor alpha-5 subunit, SHANK2, Neuroligin, Alpha-actinin 3, NCK1, Neuroligin 3

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Supplementary Table S7. Pathway analysis of the 437 metabolic features in cluster 2 in the H1N1 integrative network using Mummichog

Pathways	Overlap_size	Pathway_size	p
Carnitine shuttle	9	18	0.00036
Vitamin D ₃ (cholecalciferol) metabolism	6	10	0.00037
Linoleate metabolism	7	21	0.00050
Vitamin E metabolism	5	15	0.00081
Glycosphingolipid metabolism	6	22	0.00100
Bile acid biosynthesis	10	47	0.00108
Saturated fatty acids beta-oxidation	2	3	0.00305
Pyruvate Metabolism	3	15	0.01784
C21-steroid hormone biosynthesis and metabolism	9	64	0.02414

Supplementary Table S8. Pathway analysis of the 830 genes in cluster 2 in the H1N1 integrative network using MetaCore

Pathway	Total	p	FDR	In Data	Network Objects from Active Data
Protein folding and maturation_Insulin processing	20	2.16E-10	1.45E-07	9	Des (64,65) proinsulin, Split (32,33) proinsulin, Insulin processed, Di-arginyl insulin, Proinsulin C-peptide, Split (64,65) proinsulin, Insulin, Proinsulin, Des(31,32) proinsulin
Immune response_IL-15 signaling via JAK-STAT cascade	22	1.20E-04	3.02E-02	5	STAT3, IL-15, JAK2, sIL-15RA, IL-15RA
Immune response_Lectin induced complement pathway	50	1.38E-04	3.02E-02	7	C2, C2b, C4a, C4, C2a, C3 convertase (C2aC4b), C4b
Immune response_Classical complement pathway	53	2.00E-04	3.02E-02	7	C2, C2b, C4a, C4, C2a, C3 convertase (C2aC4b), C4b
Role of IL-23/ T17 pathogenic axis in psoriasis	54	2.25E-04	3.02E-02	7	STAT3, IL-15, sIL-15RA, IL-15RA, CD86, CD40(TNFRSF5), HLA-C
Main growth factor signaling cascades in multiple myeloma cells	41	3.26E-04	3.64E-02	6	STAT3, MEK1(MAP2K1), HIF1A, I-kB, FGFR3, PI3K reg class IA
Cell adhesion_Integrin inside-out signaling in neutrophils	77	3.84E-04	3.67E-02	8	MEK1(MAP2K1), ARF6, LTBR1, MEK1/2, Cytoshesin1, Lyn, Hck, GRO-1
Development_c-Kit ligand signaling pathway during hemopoiesis	61	4.84E-04	4.06E-02	7	STAT3, MGF, MEK1/2, DOK1, JAK2, Lyn, SLUG
Immune response_Fc gamma R-mediated phagocytosis in macrophages	46	6.16E-04	4.59E-02	6	ARF6, Vinculin, Lyn, Hck, Profilin, PI3K reg class IA
Immune response_CD40 signaling	65	7.15E-04	4.79E-02	7	STAT3, I-kB, JAK2, Lyn, A20, CD86, CD40(TNFRSF5)
Development_NOTCH-induced EMT	19	8.19E-04	4.85E-02	4	HEY1, VE-cadherin, NOTCH4, SLUG
Signal transduction_Soluble CXCL16 signaling	49	8.69E-04	4.85E-02	6	STAT3, HIF1A, I-kB, MEK1/2, JAK2, CD163
Development_GM-CSF sig-	50	9.68E-04	4.99E-02	6	STAT3, MEK1(MAP2K1),

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naling

I-kB, JAK2, Lyn, Hck

Supplementary Table S9. Process networks enrichment analysis of the 830 genes in cluster 2 in the H1N1 integrative network using MetaCore. Only the top 50 significantly enriched process networks are shown here.

Process networks	Total	p	FDR	In Data	Network Objects from Active Data
Immune response_Phagosome in antigen presentation	243	7.255E-05	1.110E-02	22	PSMA4, NFKBIB, ARF6, Vinculin, I-kB, PSMD3, Profilin II, Lyn, PSMA1, Alpha-actinin, PSMD14, Hck, TLR4, PSMA2, Profilin, PSMD12, HLA-C, HLA-B, Alpha-actinin 3, PI3K reg class IA (p55-gamma), NCK1, PI3K reg class IA
Immune response_Antigen presentation	197	2.965E-04	2.269E-02	18	PSMA4, STAT3, NFKBIB, RFX5, PSMD8, I-kB, JAK2, PSMD3, PSMA1, HLA-E, PSMD14, PSMA2, CD86, CD40(TNFRSF5), PSMD12, HLA-C, HLA-B, CD209
Inflammation_Interferon signaling	110	6.422E-04	3.275E-02	12	STAT3, MEK1(MAP2K1), MEK1/2, JAK2, MxA, Pyrin (MEFV), ISG20, CD86, SSAT, CD40(TNFRSF5), IFNAR2, SERPINB9
Signal transduction_Insulin signaling	171	1.428E-03	5.461E-02	15	Des (64,65) proinsulin, MEK1(MAP2K1), Split (32,33) proinsulin, Insulin processed, JAK2, Diargi-nyl insulin, Proinsulin C-peptide, PYGM, PKA-reg (cAMP-dependent), Split (64,65) proinsulin, Insulin, Proinsulin, Des(31,32) proinsulin, FADS2, PI3K reg class IA

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Cell adhesion_Synaptic contact	184	2.936E-03	7.812E-02	15	Syntaxin 4, Synaptotagmin II, Synaptotagmin, Profilin II, Ephrin-B2, Ephrin-B, Ephrin-B2 (CTF2), Alpha-actinin, SHANK, SynGAP, Profilin, SHANK2, Alpha-actinin 3, Syntenin 1, NCK1
Immune response_Phagocytosis	222	3.063E-03	7.812E-02	17	IL-15, NFKBIB, Vinculin, I-kB, MyHC, Profilin II, Lyn, Alpha-actinin, IL-15RA, Hck, TLR4, Profilin, Alpha-actinin 3, HDL proteins, PI3K reg class IA (p55-gamma), NCK1, PI3K reg class IA

Supplementary Table S10. GO processes analysis of the 830 genes in cluster 2 in the H1N1 integrative network using MetaCore. Only the top 50 significantly enriched GO processes are shown here.

GO Processes	Total	p	FDR	In Data	Network Objects from Active Data
cell projection assembly	367	1.09E-20	7.54E-17	51	FLJ13305, DNAH5, Dystrophin, CCDC39, SPEF2, ARMC4, DNAH1, SPAG17, Vinculin, IQCG, Rab8B, RABL2A, P2X7, DZIP1L, ATP6M, MIP-T3, LRRC50, MyHC, BBS9, WHDC1, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, MYH10, Dynein 2, cytoplasmic, heavy chain, CFA74, SPAG16, Alpha-actinin, RFX3, RAP2C, ABBA, KIAA1377(HIP5), CLR3, CYFIP1, HYDIN, TSGA2, CCDC176, DNAI1, DZIP, FGD3, Dynein, axonemal, intermediate chains, NME5, SNAP-29, Syntenin 1, LRGUK, NCK1, KAD7, C2orf39, RSPH4A, SNX10
cilium assembly	226	1.98E-19	5.75E-16	39	FLJ13305, DNAH5, Dystrophin, CCDC39, SPEF2, ARMC4, DNAH1, SPAG17, IQCG, Rab8B, RABL2A, DZIP1L, ATP6M, MIP-T3, LRRC50, BBS9, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, Dynein 2, cytoplasmic, heavy chain, CFA74, SPAG16, RFX3, KIAA1377(HIP5), CLR3, HYDIN, TSGA2, CCDC176, DNAI1, DZIP, Dynein, axonemal, inter-

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cilium organization	266	2.49E-19	5.75E-16	42	mediate chains, NME5, SNAP-29, LRGUK, KAD7, C2orf39, RSPH4A, SNX10 FLJ13305, DNAH5, Dystrophin, CCDC39, SPEF2, ARMC4, DNAH1, SPAG17, IQCG, Rab8B, RABL2A, DZIP1L, ATP6M, MIP-T3, MNS1, LRRC50, BBS9, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, ENO4, Dynein 2, cytoplasmic, heavy chain, CFA74, SPAG16, RFX3, KIAA1377(HIP5), CLR3, HYDIN, TSGA2, CCDC176, DNAI1, DZIP, Dynein, axonemal, intermediate chains, NME5, SNAP-29, LRGUK, KAD7, Nephrocystin-4, C2orf39, RSPH4A, SNX10
cilium morphogenesis	274	4.97E-18	8.60E-15	41	FLJ13305, DNAH5, Dystrophin, CCDC39, SPEF2, ARMC4, DNAH1, SPAG17, IQCG, Rab8B, RABL2A, DZIP1L, ATP6M, MIP-T3, LRRC50, BBS9, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, Alpha-parvin, Dynein 2, cytoplasmic, heavy chain, CFA74, SPAG16, RFX3, KIAA1377(HIP5), CLR3, Notch, HYDIN, TSGA2, CCDC176, DNAI1, DZIP, Dynein, axonemal, intermediate chains, NME5, SNAP-29, LRGUK, KAD7, C2orf39, RSPH4A, SNX10
cilium movement	61	1.46E-17	2.02E-14	21	DNAH5, CCDC39, ARMC4, DNAH1, SPAG17, Dynein, axonemal, light chains,

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cell projection organization	1348	2.17E-17	2.51E-14	98	LRRC50, DNAH6, Dynein, axonemal, heavy chains, CFA54, SPAG16, DNAH11, RFX3, Sp17, HYDIN, DNAI1, Dynein, axonemal, intermediate chains, NME5, KAD7, CABYR, RSPH4A FLJ13305, DNAH5, Dystrophin, C1orf88, CCDC39, SPEF2, OSF-2, MEK1(MAP2K1), ARMC4, SLIT3, DNAH1, SNX2, Hap-1, SNX1, Olfactory receptor, ARF6, SPAG17, Vinculin, APOD, HEY1, Dynein, axonemal, light chains, IQCG, Pleckstrin, Rab8B, RABL2A, P2X7, HES1, MEK1/2, B3GN1, ROBO1, DNAH9, JAK2, Islet-1, Galpha(q)-specific nucleotide-like GPCRs, DZIP1L, ATP6M, Rab-3, MIP-T3, MNS1, LRRC50, Ephrin-A receptor 5, FGFR3, MyHC, PMCA2b, Carbohydrate sulfotransferases, BBS9, WHDC1, Dynein, axonemal, heavy chains, RPGRIPI, Oxygen-regulated protein 1, CFA54, Alpha-parvin, ENO4, MYH10, Lyn, Ephrin-B2, Ephrin-B, Dynein 2, cytoplasmic, heavy chain, NPX1, CFA74, SPAG16, Alpha-actinin, RFX3, MENA, RAP2C, ABBA, Ephrin-A receptors, SHANK, SynGAP, KIAA1377(HIP5), CLR3, Notch, Galpha(q)-specific peptide GPCRs, GFRalpha1, CYFIP1, HYDIN, Rab-3A, TSGA2,
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						ATF/CREB, MAP-1B, CCDC176, DNAI1, DZIP, FGD3, HDL proteins, Dynein, axonemal, inter- mediate chains, NME5, SNAP-29, Phosphatase regulator (inhibitor), Syntenin 1, LRGUK, NCK1, KAD7, Nephrocys- tin-4, ABI2, C2orf39, RSPH4A, SNX10
cellular compo- nent assembly involved in morphogenesis	360	6.90E-16	6.83E-13	44	FLJ13305, DNAH5, Dystro- phin, CARP, CCDC39, SPEF2, ARMC4, DNAH1, SPAG17, IQCG, Rab8B, RABL2A, DZIP1L, ATP6M, MIP-T3, LRRC50, MyHC, BBS9, Dynein, axonemal, heavy chains, RPGRIP1L, Oxy- gen-regulated protein 1, CFA54, MYH10, Dynein 2, cytoplasmic, heavy chain, PKA-reg (cAMP- dependent), CFA74, SPAG16, Alpha-actinin, RFX3, KIAA1377(HIP5), CLR3, HYDIN, TSGA2, CCDC176, DNAI1, DZIP, Dynein, axonemal, inter- mediate chains, NME5, SNAP-29, LRGUK, KAD7, C2orf39, RSPH4A, SNX10	
axoneme assem- bly	66	1.47E-15	1.28E-12	20	DNAH5, CCDC39, SPEF2, ARMC4, DNAH1, SPAG17, IQCG, LRRC50, Dynein, axonemal, heavy chains, Oxygen-regulated protein 1, CFA74, SPAG16, HYDIN, TSGA2, DNAI1, Dynein, axonemal, intermediate chains, LRGUK, KAD7, C2orf39, RSPH4A	
cell part morpho- genesis	923	1.88E-14	1.45E-11	72	FLJ13305, DNAH5, Dystro- phin, CCDC39, PDIP38, SPEF2, OSF-2,	

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cell projection morphogenesis	889	2.84E-14	1.97E-11	70	PNPase(old-35), MEK1(MAP2K1), ARMC4, SLIT3, DNAH1, SNX2, SNX1, Olfactory receptor, SPAG17, Vincu- lin, Dynein, axonemal, light chains, IQCG, Rab8B, RABL2A, MEK1/2, B3GN1, ROBO1, Islet-1, Galpha(q)-specific nucleo- tide-like GPCRs, DZIP1L, ATP6M, Rab-3, MIP-T3, LRRC50, Ephrin-A recep- tor 5, FGFR3, MyHC, BBS9, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, Alpha-parvin, MYH10, Ephrin-B2, Ephrin-B, Dynein 2, cyto- plasmic, heavy chain, NPX1, CFA74, SPAG16, RFX3, MENA, Ephrin-A receptors, SHANK, KIAA1377(HIP5), CLR3, Notch, Galpha(q)-specific peptide GPCRs, CYFIP1, HYDIN, Rab-3A, TSGA2, ATF/CREB, MAP-1B, CCDC176, DNAI1, DZIP, Dynein, axonemal, inter- mediate chains, NME5, SNAP-29, LRGUK, KAD7, C2orf39, RSPH4A, SNX10
					FLJ13305, DNAH5, Dystro- phin, CCDC39, SPEF2, OSF-2, MEK1(MAP2K1), ARMC4, SLIT3, DNAH1, SNX2, SNX1, Olfactory receptor, SPAG17, Vincu- lin, Dynein, axonemal, light chains, IQCG, Rab8B, RABL2A, MEK1/2, B3GN1, ROBO1, Islet-1, Galpha(q)-specific nucleo- tide-like GPCRs, DZIP1L, ATP6M, Rab-3, MIP-T3,

xMWAS: R package for data integration and network analysis

cell morphogenesis	1193	9.55E-14	6.02E-11	83	LRRC50, Ephrin-A receptor 5, FGFR3, MyHC, BBS9, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, Alpha-parvin, MYH10, Ephrin-B2, Ephrin-B, Dynein 2, cytoplasmic, heavy chain, NPX1, CFA74, SPAG16, RFX3, MENA, Ephrin-A receptors, SHANK, KIAA1377(HIP5), CLR3, Notch, Galpha(q)-specific peptide GPCRs, CYFIP1, HYDIN, Rab-3A, TSGA2, ATF/CREB, MAP-1B, CCDC176, DNAI1, DZIP, Dynein, axonemal, intermediate chains, NME5, SNAP-29, LRGUK, KAD7, C2orf39, RSPH4A, SNX10
					FLJ13305, DNAH5, Dystrophin, CCDC39, SPEF2, OSF-2, MEK1(MAP2K1), ARMC4, SLIT3, DNAH1, SNX2, SNX1, Olfactory receptor, SPAG17, Vinculin, HEY1, Dynein, axonemal, light chains, IQCG, Rab8B, Ephrin-A receptor 1, HIF1A, RABL2A, FAT3, P2X7, NOTCH4, HES1, MEK1/2, B3GN1, ROBO1, Islet-1, Galpha(q)-specific nucleotide-like GPCRs, DZIP1L, ATP6M, Rab-3, MIP-T3, LRRC50, Ephrin-A receptor 5, FGFR3, MyHC, PMCA2b, BBS9, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, Alpha-parvin, CAP2, MYH10, Ephrin-B2, Ephrin-B, Dynein 2, cytoplasmic, heavy chain,

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						NPX1, CFA74, SPAG16, Alpha-actinin, RFX3, SLUG, MENA, Ephrin-A receptors, SHANK, TMEM100, KIAA1377(HIP5), CLR3, Notch, Galpha(q)-specific peptide GPCRs, CYFIP1, HYDIN, Rab-3A, TSGA2, ATF/CREB, MAP-1B, CCDC176, DNAI1, DZIP, Dynein, axonemal, inter- mediate chains, NME5, SNAP-29, LRGUK, ILPIP, KAD7, C2orf39, RSPH4A, SNX10
microtubule bun- dle formation	95	2.91E-13	1.68E-10	21	DNAH5, CCDC39, SPEF2, ARMC4, DNAH1, SPAG17, IQCG, LRRC50, Dynein, axonemal, heavy chains, Oxygen-regulated protein 1, CFA74, SPAG16, HYDIN, TSGA2, MAP-1B, DNAI1, Dynein, axonemal, intermediate chains, LRGUK, KAD7, C2orf39, RSPH4A	
cilium or flagel- lum-dependent cell motility	29	3.90E-13	1.77E-10	13	DNAH5, CCDC39, DNAH1, DNAH6, Dynein, ax- onemal, heavy chains, CFA54, SPAG16, DNAH11, RFX3, Sp17, DNAH3, DNAH2, C2orf39	
cellular compo- nent morpho- genesis	1316	3.93E-13	1.77E-10	87	FLJ13305, DNAH5, Dystro- phin, CARP, CCDC39, PDIP38, SPEF2, OSF-2, PNPase(old-35), MEK1(MAP2K1), ARMC4, SLIT3, DNAH1, SNX2, SNX1, Olfactory receptor, SPAG17, Vincu- lin, HEY1, Dynein, ax- onemal, light chains, IQCG, Rab8B, Ephrin-A receptor 1, HIF1A, RABL2A, FAT3, P2X7, NOTCH4, HES1, MEK1/2, B3GN1,	

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microtubule-based movement	297	4.07E-13	1.77E-10	36	ROBO1, Islet-1, Galpha(q)-specific nucleotide-like GPCRs, DZIP1L, ATP6M, Rab-3, MIP-T3, LRRC50, Ephrin-A receptor 5, FGFR3, MyHC, PMCA2b, BBS9, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, Alpha-parvin, CAP2, MYH10, Ephrin-B2, Ephrin-B, Dynein 2, cytoplasmic, heavy chain, NPX1, PKA-reg (cAMP-dependent), CFA74, SPAG16, Alpha-actinin, RFX3, SLUG, MENA, Ephrin-A receptors, SHANK, TMEM100, KIAA1377(HIP5), CLR3, Notch, Galpha(q)-specific peptide GPCRs, CYFIP1, HYDIN, Rab-3A, TSGA2, ATF/CREB, MAP-1B, CCDC176, DNAI1, DZIP, Dynein, axonemal, intermediate chains, NME5, SNAP-29, LRGUK, ILPIP, KAD7, C2orf39, RSPH4A, SNX10
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organelle assembly	692	4.08E-13	1.77E-10	58	DNAH12, KAD7, CABYR, RSPH4A, TCTE3 FLJ13305, DNAH5, Dystro- phin, CARP, CCDC39, WIPI1, Rab20, SPEF2, ARMC4, DNAH1, SPAG17, CHMP6, Synap- totagmin, IQCG, Rab8B, RABL2A, P2X7, FLJ32658, DZIP1L, ATP6M, MIP-T3, LRRC50, MyHC, CD34, BBS9, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, MYH10, Dynein 2, cytoplasmic, heavy chain, PKA-reg (cAMP- dependent), CFA74, VTA1, SPAG16, Alpha-actinin, RFX3, KIF3B, SHANK, RPS27, KIAA1377(HIP5), CLR3, Trp53inp2, HYDIN, TSGA2, CCDC176, CCDC52, DNAI1, DZIP, Dynein, axonemal, inter- mediate chains, NME5, SNAP-29, LRGUK, KAD7, MAP1LC3B, C2orf39, RSPH4A, SNX10
single-organism organelle organization	1928	6.04E-13	2.46E-10	112	Bomapin, STAT3, FLJ13305, DNAH5, Dystrophin, CARP, C2CD4D, MPV17L, CCDC39, WIPI1, Rab20, PDIP38, SPEF2, PNPase(old-35), MEK1(MAP2K1), ARMC4, DNAH1, ASCT1 (SLC1A4), Syntaxin 4, ARF6, SPAG17, CHMP6, Synaptotagmin II, Synapto- tagmin, Dynein, axonemal, light chains, IQCG, Pleck- strin, Rab8B, VIPAR, ALPK1, RABL2A, FLJ32658, MEK1/2, ALKBH7, JAK2, DZIP1L,

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movement of cell or subcellular component	1795	1.04E-12	3.99E-10	106	ATP6M, Rab-3, MIP-T3, MNS1, LRRC50, MyHC, Carbohydrate sulfotransferases, YSK4, BBS9, WHDC1, WRCH-1, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, Alpha-parvin, ENO4, CAP2, MYH10, Profilin II, MRE11, Dynein 2, cytoplasmic, heavy chain, PKA-reg (cAMP-dependent), CFA74, SPAG16, Alpha-actinin, RFX3, MENA, KIF3B, Bim, SHANK, RPS27, GMIP, NMT1, KIAA1377(HIP5), GRO-1, SPATA18, CLR3, Gal-pha(q)-specific peptide GPCRs, Huntingtin, Profilin, HYDIN, Rab-3A, TSGA2, FGF10, ATF/CREB, EPS8, MAP1B, CCDC176, CCDC52, DNAI1, DZIP, FGD3, N-myristoyltransferase, PI4KII, Dynein, axonemal, intermediate chains, NUAK2, FAT1, ANKFY1, NME5, SNAP-29, Phosphatase regulator (inhibitor), Syntenin 1, LRGUK, VAMP4, NCK1, Beta aducin, KAD7, BET1, Nephrocystin-4, ABI2, MAP1LC3B, C2orf39, RSPH4A, Alpha-internexin, SNX10, beta-MHC, KIF21A, CD84, STAT3, DNAH5, Dystrophin, CCDC39, MEK1(MAP2K1), ARMC4, SLIT3, DNAH1, PVR, PLET1, LYST, Hap-1, MGF, Olfactory receptor,
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anatomical structure formation involved in	1410	6.56E-12	2.39E-09	88	ARF6, LTBR1, SPAG17, Vinculin, DHSO, Dynein, axonemal, light chains, PDE, HIF1A, RABL2A, FAT3, HES1, MEK1/2, B3GN1, ROBO1, DNAH9, JAK2, Islet-1, Galpha(q)-specific nucleotide-like GPCRs, MIP-T3, LRRC50, Ephrin-A receptor 5, DNAH6, MyHC, CD34, Carbohydrate sulfotransferases, Dynein, axonemal, heavy chains, CFA54, Alpha-parvin, ENO4, MYH10, Lyn, Ephrin-B2, Ephrin-B, Dynein 2, cytoplasmic, heavy chain, STRBP, CAPZA1, SPAG16, Alpha-actinin, DNAH11, GRO-3, RFX3, SLUG, MENA, Ephrin-A receptors, Sp17, KIF3B, DAGK, CCR1, Hck, GRO-1, SPP lyase, CAPZA, CLR3, Notch, SLAM, Galpha(q)-specific peptide GPCRs, Huntington, GFRalpha1, HYDIN, CCL27, FGF10, ATF/CREB, EPS8, C4orf31, DNAH3, MAP-1B, CAPZA2, DNAH2, DNAI1, Alpha-actinin 3, HDL proteins, Dynein, axonemal, intermediate chains, FAT1, PLTP, NME5, Syntenin 1, NCK1, RANK(TNFRSF11A), DNAH12, KAD7, Nephrocystin-4, ABI2, CABYR, PI3K reg class IA, C2orf39, RSPH4A, CCNYL1, PSTPIP2, TCTE3
					FLJ13305, DNAH5, Dystrophin, CARP, IL-15, CCDC39, SF3B14a,

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morphogenesis						SPEF2, MEK1(MAP2K1), ARMC4, DNAH1, SPAG17, EPAS1, APOD, HEY1, PDE, IQCG, Rab8B, Ephrin-A receptor 1, HIF1A, Polycystin, RABL2A, FAT3, NOTCH4, MEK1/2, MIRK, ROBO1, Apaf-1, Is- let-1, DMP4, DZIP1L, ATP6M, MIP-T3, LRRC50, MyHC, CD34, PMCA2b, BBS9, Dynein, axonemal, heavy chains, RPGRIP1L, Oxygen- regulated protein 1, CFA54, Alpha-parvin, MYH10, Ephrin-B2, Ephrin-B, Dynein 2, cytoplasmic, heavy chain, TRIM15, PKA-reg (cAMP- dependent), CFA74, SPAG16, Alpha-actinin, RFX3, SLUG, MENA, Ephrin-A receptors, Bim, FAIM2, SHANK, TMEM100, Insulin, KIAA1377(HIP5), DUSP5, CLR3, Notch, Galpha(q)- specific peptide GPCRs, Huntingtin, Profilin, HYDIN, TSGA2, SSAT, FGF10, ATF/CREB, C4orf31, CCDC176, DNAI1, DZIP, HDL pro- teins, Dynein, axonemal, intermediate chains, NME5, SNAP-29, LRGUK, KAD7, AL1A1, Perlecan, C2orf39, RSPH4A, SNX10
epithelial cilium movement	29	1.03E-11	3.55E-09	12	CCDC39, DNAH1, SPAG17, LRRC50, Dynein, ax- onemal, heavy chains, RFX3, Sp17, DNAI1, Dynein, axonemal, inter- mediate chains, NME5, KAD7, CABYR	

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intracellular signal transduction	2102	6.31E-11	2.08E-08	113	PSMA4, STAT3, G3BP2, Dystrophin, IL-15, Rab20, p200RhoGAP, MEK1(MAP2K1), AM-R, SP100, RIPK2, MDA-5, MGF, PRKAR2B, IL-31RA, ARF6, Guanylate cyclase, Sec3, PDE, PSMD8, Pleckstrin, Guanylate cyclase alpha, Galph(q)-specific Class A Orphan/other GPCRs, Rab8B, Polycystin, RABL2A, I-kB, HES1, MEK1/2, PPP4C, DOK1, Apaf-1, JAK2, PLEKHM1, SGK3, GUCY1A2, Galph(q)-specific nucleotide-like GPCRs, PSMD3, Rab-3, Ephrin-A receptor 5, FGFR3, Galectin-9, Neu-regulin 4, WRCH-1, ATP1A2, Oxygen-regulated protein 1, PKA-reg type II (cAMP-dependent), Lyn, PSMA1, Centaurin alpha 1, CENTA2, DMPK, RGS11, PKA-reg (cAMP-dependent), Alpha-actinin, IL-15RA, PDE2A, RAP2C, A20, AZI2, Ephrin-A receptors, NPR3, GSTO1, Bim, FNIP2, SHANK, SyngAP, DAGK, PSMD14, GMIP, TLR4, TMEM100, Insulin, PSMA2, GRO-1, DUSP5, TANK, Galph(q)-specific peptide GPCRs, GFRalpha1, CYFIP1, CD86, NUDT4, Rab-3A, TOX3, FGF10, CD40(TNFRSF5), PNPH, ATF/CREB, Rhov, ERK3, EPS8, C4orf31, PSMD12, ASB14, DGKH, RGS6, DIRAS2, CD209,
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positive regulation of molecular function	2442	9.59E-10	3.02E-07	122	HDL proteins, NUAK2, Phosphatase regulator (in- hibitor), Syntenin 1, ILPIP, IFNAR2, Protein p8, TRIM23, PLCL2, Nephro- cystin-4, ABI2, CABYR, PI3K reg class IA, RGS9, Galpha(s)-specific peptide GPCRs
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xMWAS: R package for data integration and network analysis

regulation of response to stimulus	4960	1.14E-09	3.42E-07	209	PSMD14, CREB3, GMIP, TLR4, RGSS22, Insulin, Fibulin-1, Pyrin (MEFV), PSMA2, GRO-1, DUSP5, TANK, Galpha(q)-specific peptide GPCRs, Huntington, GFRalpha1, Profilin, Rab-3A, NEK5, FGF10, CD40(TNFRSF5), ATF/CREB, FAM116B, PSMD12, SERINC5, GITRL, Glutaredoxin, FGD3, RGS6, DIRAS2, HDL proteins, Phosphatase regulator (inhibitor), ILPIP, NCK1, RANK(TNFRSF11A), Beta adducin, AL1A1, TRIM23, PLCL2, LULL1, PI3K reg class IA, RGS9, Galpha(s)-specific peptide GPCRs, MAP1LC3B, NPNT, Glutaredoxin 1 Bomapin, beta-MHC, PSMA4, CD84, FAM13A1, STAT3, G3BP2, PODN, Dystrophin, CARP, MPV17L, IL-15, WFDC1, H-2L(d), p200RhoGAP, FLJ20898, OSF-2, REV-ERBalpha, NFKBIB, TR-alpha, MHC Class I alpha chain, PNPase(old-35), MEK1(MAP2K1), C2, DOT1, SLIT3, SP100, PVR, RIPK2, MDA-5, DENND1A, Hap-1, MGF, SNX1, IL-31RA, Syntaxin 4, Trim30, ARF6, Guanyl-ate cyclase, PRAM-1, APOD, EFP, HEY1, Vsm-RhoGEF, Synaptotagmin, Dynein, axonemal, light chains, PDE, TREML2, ACP33, PSMD8, Pleckstrin, Galpha(q)-specific Class A Orphan/other
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xMWAS: R package for data integration and network analysis

GPCRs, CD300LG,
ZNF364, FLJ32810,
ALPK1, HIF1A, Fibulin-5,
Peregrin, P2X7, I-kB, ORP-
family, NOTCH4, HES1,
MEK1/2, ATF-3, PPP4C,
DENND1B, SAMHD1,
DOK1, C3orf58, ROBO1,
Apaf-1, JAK2, SGK3,
ORP8, ARHGEF19, Islet-1,
DMP4, Galpha(q)-specific
nucleotide-like GPCRs,
PSMD3, MIP-T3, Cytohe-
sin1, Ephrin-A receptor 5,
FGFR3, MyHC, TRIB2,
CD34, Galectin-9, Carbo-
hydrate sulfotransferases,
Neuregulin 4, Ceb1,
TRAFD1, PLEKHG1,
WRCH-1, Krm1,
RPGrip1L, C4B protein,
Lyn, PSMA1, HLA-E,
Ephrin-B2, DMPK,
MRE11, Ephrin-B, Dynein
2, cytoplasmic, heavy
chain, hRap1, CysLT2 re-
ceptor, RGS11, TRIM15,
HA12 (rodent), Alpha-
actinin, GRO-3, TOP3A,
SLUG, MENA, PDE2A,
Coagulation factor X, Orex-
in receptor 1, A20, Ephrin-
A receptors, GSTO1, Bim,
FAIM2, SCAI, SHANK,
SynGAP, Fibrinogen gam-
ma, DAGK, PSMD14, IL-1
alpha, CREB3, CCR1, Hck,
GMIP, TLR4, C4,
RGSS22, NMT1,
TMEM100, Insulin, Fibu-
lin-1, Pyrin (MEFV),
PSMA2, ADAR1, GRO-1,
DUSP5, CD276, TANK,
BTNL2, Asporin, Notch,
Orexin receptor, SLAM,
Galpha(q)-specific peptide
GPCRs, Huntingtin,

microtubule-based process	696	3.79E-09	1.09E-06	50	CYFIP1, HA11, CD86, CCL27, FGF10, CD40(TNFRSF5), PNPH, ATF/CREB, Rhov, RNF34, EPS8, PSMD12, CQ087, GITRL, Glutaredoxin, HLA-C, PEAR1, FGD3, PCPH, N-myristoyltransferase, PIP1, RGS6, DIRAS2, HLA-B, Alpha-actinin 3, CD209, HDL proteins, BCAP, NME5, Phosphatase regulator (inhibitor), Syntenin 1, MPP1, PI3K reg class IA (p55-gamma), ILPIP, NCK1, RANK(TNFRSF11A), USP18, IFNAR2, GREM2, Thyroid hormone receptor, PLCL2, Nephrocystin-4, PI3K reg class IA, RGS9, CD300LF, IPP-2, Gal-pha(s)-specific peptide GPCRs, DUSP18, TIG2, DDX60, NPNT, SERPINB9, Glutaredoxin 1 KIF21A, DNAH5, CCDC39, SPEF2, MEK1(MAP2K1), ARMC4, DNAH1, LYST, Hap-1, SPAG17, Dynein, axonemal, light chains, IQCG, HIF1A, FLJ32658, MEK1/2, DNAH9, MIP-T3, LRRC50, DNAH6, MyHC, Dynein, axonemal, heavy chains, Oxygen-regulated protein 1, CFA54, Dynein 2, cytoplasmic, heavy chain, CFA74, SPAG16, DNAH11, RFX3, Sp17, KIF3B, KIAA1377(HIP5), Huntington, HYDIN, TSGA2, FGF10, DNAH3, MAP-1B, DNAH2, CCDC52, DNAI1, Dynein, axonemal,
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xMWAS: R package for data integration and network analysis

regulation of transport	2558	4.23E-09	1.17E-06	124	PAM, CD84, G3BP2, Dystrophin, CARP, C2CD4D, NHE3, MPV17L, OSF-2, REV-ERBalpha, CLCN7, NFKBIB, TR-alpha, MHC Class I alpha chain, MEK1(MAP2K1), C2, SP100, ELMOD1, Hap-1, ARG1, Olfactory receptor, Syntaxin 4, ARF6, CHMP6, Guanylate cyclase, Sec3, PRAM-1, APOD, Synaptotagmin II, Synaptotagmin, PDE, PSMD8, Galpha(q)-specific Class A Orphan/other GPCRs, Rab8B, KCNRG, Tbc1d9, HIF1A, Polycystin, P2X7, I-kB, ORP-family, HES1, MEK1/2, DGAT1, SLC24A6, JAK2, SGK3, ORP8, PDE1, Islet-1, Galpha(q)-specific nucleotide-like GPCRs, Rab-3, Ephrin-A receptor 5, MyHC, CD34, Galectin-9, PMCA2b, WRCH-1, ATP1A2, C4B protein, Profilin II, Lyn, HLA-E, DMPK, PKI, TRIM15, WWP2, Bestrophin-4, Alpha-actinin, RFX3, SLUG, PDE2A, ATP4A, Ephrin-A receptors, GSTO1, KCNE4, Bim, SHANK, Fibrinogen gamma, IL-1 alpha, CREB3, CCR1, Hck, TLR4, C4, NMT1, Insulin, Fibulin-1, CD276, IDH2, BTNL2, Notch, SLAM, Galpha(q)-specific peptide GPCRs, Huntingtin, Profilin, NUDT4, Rab-3A,
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xMWAS: R package for data integration and network analysis

phosphorus metabolic process	2600	5.92E-09	1.54E-06	125	FGF10, CD40(TNFRSF5), ATF/CREB, DNAJC13, SCN3A, MAP-1B, Glu- taredoxin, N- myristoyltransferase, HLA- B, CHD7, HDL proteins, PLTP, ANKFY1, Phospha- tase regulator (inhibitor), Syntenin 1, UGCG, PI3K reg class IA (p55-gamma), PARP-10, VAMP4, RANK(TNFRSF11A), Thyroid hormone receptor, PI3K reg class IA, Gal- pha(s)-specific peptide GPCRs, TIG2, MAP1LC3B, Glutaredoxin 1 beta-MHC, RPS6KL1, PSMA4, STAT3, GNPTA, CTP synthase, IL-15, DDHD1, MEK1(MAP2K1), PLB1, PHEX, Stk33, RIPK2, KIAA1274, LYST, MGF, PRKAR2B, IL-31RA, Mdh1b, Guanylate cyclase, Glycogen phosphorylase, CDP-diacylglycerol syn- thase, DHSO, PDE, PSMD8, Pleckstrin, Guanylate cyclase alpha, Ephrin-A receptor 1, ALPK1, Polycystin, P2X7, MEK1/2, PPP4C, MIRK, SAMHD1, DOK1, JAK2, SGK3, GUCY1A2, PDE1, DMP4, Galpha(q)-specific nucleotide-like GPCRs, PSMD3, Ephrin-A receptor 5, FGFR3, IDH1, MyHC, TRIB2, Galectin-9, PMCA2b, Neuregulin 4, YSK4, PGS1, ATP1A2, NNTM, PKA-reg type II (cAMP-dependent), ENO4, ATP6V1B2, MANA, Lyn,
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xMWAS: R package for data integration and network analysis

regulation of cell communication	4033	5.99E-09	1.54E-06	175	PSMA1, DMPK, PKI, CDS2, PKA-reg (cAMP-dependent), PKIB, Alpha-actinin, PDE2A, Ephrin-A receptors, NPR3, AKD1, FNIP2, SHANK, SynGAP, DAGK, PSMD14, Hck, TLR4, Insulin, PBEF, PSMA2, DUSP5, NT5C3, IDH2, Galpha(q)-specific peptide GPCRs, GFRalpha1, CD86, NUDT4, FLAD1, NEK5, MOK, FGF10, PNPH, ATF/CREB, ERK3, PSMD12, SERINC5, ADSSL1, LDHB, MTHFD2L, ATP6V1B, PDE1B, DGKH, PCPH, PI4KII, AGPHD1, TXL-2, HDL proteins, PPP1R3B, BCAP, NUAK2, C9orf98, NME5, Phosphatase regulator (inhibitor), MPP1, LRGUK, PI3K reg class IA (p55-gamma), ILPIP, NCK1, KAD7, AL1A1, ABI2, PI3K reg class IA, DUSP18, FRK
					PSMA4, CD84, FAM13A1, STAT3, G3BP2, PODN, Dystrophin, CARP, MPV17L, IL-15, p200RhoGAP, FLJ20898, OSF-2, REV-ERBalpha, NFKBIB, TR-alpha, MEK1(MAP2K1), DOT1, SLIT3, SP100, RIPK2, DENND1A, Hap-1, MGF, SNX1, IL-31RA, Syntaxin 4, Trim30, ARF6, Guanylate cyclase, APOD, EFP, HEY1, Vsm-RhoGEF, Synaptotagmin, Dynein, axonemal, light chains, PDE, PSMD8, Pleckstrin, Galpha(q)-specific Class A

Orphan/other GPCRs,
Rab8B, ZNF364,
FLJ32810, HIF1A, Pere-
grin, P2X7, I-kB, ORP-
family, NOTCH4, HES1,
MEK1/2, ATF-3, DOK1,
C3orf58, SLC24A6,
ROBO1, Apaf-1, JAK2,
SGK3, ORP8, ARHGEF19,
PDE1, Islet-1, DMP4, Gal-
pha(q)-specific nucleotide-
like GPCRs, PSMD3, Rab-
3, MIP-T3, Cytohesin1,
Ephrin-A receptor 5,
FGFR3, TRIB2, Galectin-9,
PMCA2b, Neuregulin 4,
PLEKHG1, WRCH-1,
Krm1, ATP1A2,
RPGRIP1L, Profilin II,
Lyn, PSMA1, DMPK,
MRE11, Dynein 2, cyto-
plasmic, heavy chain,
hRap1, CysLT2 receptor,
RGS11, TRIM15, Alpha-
actinin, TOP3A, RFX3,
SLUG, Coagulation factor
X, Orexin receptor 1, A20,
Ephrin-A receptors,
GSTO1, Bim, FAIM2,
SCAI, SHANK, SynGAP,
Fibrinogen gamma, DAGK,
PSMD14, IL-1 alpha,
CREB3, CCR1, GMIP,
TLR4, RGSS22, NMT1,
TMEM100, Insulin, Fibu-
lin-1, PSMA2, ADAR1,
DUSP5, TANK, BTNL2,
Asporin, Notch, Orexin re-
ceptor, SLAM, Galphag(q)-
specific peptide GPCRs,
Huntingtin, CD86, Profilin,
Rab-3A, FGF10,
CD40(TNFRSF5),
ATF/CREB, Rhov, RNF34,
EPS8, MAP-1B, PSMD12,
CQ087, GITRL,
Calsyntenin-2, Glutaredox-

xMWAS: R package for data integration and network analysis

regulation of localization	3402	7.46E-09	1.85E-06	153	in, PEAR1, SHANK2, FGD3, PCPH, N-myristoyltransferase, PIP1, RGS6, DIRAS2, CHD7, Alpha-actinin 3, HDL proteins, BCAP, NME5, Phosphatase regulator (inhibitor), Syntenin 1, ILPIP, NCK1, RANK(TNFRSF11A), USP18, IFNAR2, GREM2, Thyroid hormone receptor, PLCL2, Nephrocystin-4, PI3K reg class IA, RGS9, IPP-2, Galphas-specific peptide GPCRs, DUSP18, DDX60, NPNT, Glutaredoxin 1
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like GPCRs, Rab-3,
LRRC50, Ephrin-A receptor 5, MyHC, CD34, Galec-tin-9, PMCA2b, Carbohydrate sulfotransferases, Neuregulin 4, WRCH-1, ATP1A2, Dynein, axonemal, heavy chains, C4B protein, Profilin II, Lyn, HLA-E, DMPK, PKI, TRIM15, WWP2, Bestrophin-4, Alpha-actinin, DNAH11, GRO-3, RFX3, SLUG, PDE2A, RAP2C, ATP4A, Coagulation factor X, Ephrin-A receptors, GSTO1, KCNE4, Bim, SCAI, SHANK, Fibrinogen gamma, IL-1 alpha, CREB3, CCR1, Hck, TLR4, PLEKHM2, C4, NMT1, Insulin, Fibulin-1, GRO-1, CD276, IDH2, BTNL2, CLR3, Notch, SLAM, Galph(a(q)-specific peptide GPCRs, Huntingtin, Trp53inp2, Profilin, NUDT4, Rab-3A, CCL27, FGF10, CD40(TNFRSF5), ATF/CREB, DNAJC13, SCN3A, MAP-1B, GITRL, Glutaredoxin, N-myristoyltransferase, HLA-B, CHD7, HDL proteins, PLTP, ANKFY1, Phosphatase regulator (inhibitor), Syntenin 1, MPP1, UGCG, PI3K reg class IA (p55-gamma), PARP-10, VAMP4, NCK1, RANK(TNFRSF11A), Thyroid hormone receptor, PI3K reg class IA, Galph(a(s)-specific peptide GPCRs, TIG2, MAP1LC3B, Glutaredoxin

xMWAS: R package for data integration and network analysis

locomotion	1497	8.10E-09	1.93E-06	83	CD84, DNAH5, CCDC39, MEK1(MAP2K1), SLIT3, DNAH1, PVR, PLET1, LYST, MGF, Olfactory receptor, DHSO, PDE, Galpha(q)-specific Class A Orphan/other GPCRs, HIF1A, RABL2A, FAT3, HES1, MEK1/2, B3GN1, ROBO1, JAK2, Islet-1, Galpha(q)-specific nucleotide-like GPCRs, Ephrin-A receptor 5, DNAH6, MyHC, CD34, Galectin-9, PMCA2b, Carbohydrate sulfotransferases, ATP1A2, Dynein, axonemal, heavy chains, CFA54, Alpha-parvin, ENO4, MYH10, Lyn, Ephrin-B2, Ephrin-B, SPAG16, DNAH11, GRO-3, RFX3, SLUG, MENA, Ephrin-A receptors, Sp17, SHANK, DAGK, CREB3, CCR1, CCR9, Hck, GRO-1, SPP lyase, CLR3, Notch, SLAM, Galpha(q)-specific peptide GPCRs, GFRalpha1, CCL27, FGF10, ATF/CREB, EPS8, C4orf31, DNAH3, DNAH2, DNAI1, HDL proteins, Dynein, axonemal, intermediate chains, FAT1, PLTP, Syntenin 1, NCK1, RANK(TNFRSF11A), Nephrocystin-4, ABI2, PI3K reg class IA, TIG2, C2orf39, CCNYL1, PSTPIP2
regulation of signaling	4089	9.74E-09	2.25E-06	176	PSMA4, CD84, FAM13A1, STAT3, G3BP2, PODN, Dystrophin, CARP, MPV17L, IL-15, p200RhoGAP, FLJ20898, OSF-2, REV-ERBalpha,

NFKBIB, TR-alpha,
MEK1(MAP2K1), DOT1,
SLIT3, SP100, RIPK2,
DENND1A, Hap-1, MGF,
SNX1, IL-31RA, Syntaxin
4, Trim30, ARF6, Guanyl-
ate cyclase, APOD, EFP,
HEY1, Vsm-RhoGEF,
Synaptotagmin, Dynein,
axonemal, light chains,
PDE, PSMD8, Pleckstrin,
Galpha(q)-specific Class A
Orphan/other GPCRs,
Rab8B, ZNF364,
FLJ32810, HIF1A, Pere-
grin, P2X7, I-kB, ORP-
family, NOTCH4, HES1,
MEK1/2, ATF-3, DOK1,
C3orf58, SLC24A6,
ROBO1, Apaf-1, JAK2,
SGK3, ORP8, ARHGEF19,
PDE1, Islet-1, DMP4, Gal-
pha(q)-specific nucleotide-
like GPCRs, PSMD3, Rab-
3, MIP-T3, Cytohesin1,
Ephrin-A receptor 5,
FGFR3, TRIB2, Galectin-9,
Ca-ATPase3, PMCA2b,
Neuregulin 4, PLEKHG1,
WRCH-1, Krm1, ATP1A2,
RPGRIP1L, Profilin II,
Lyn, PSMA1, DMPK,
MRE11, Dynein 2, cyto-
plasmic, heavy chain,
hRap1, CysLT2 receptor,
RGS11, TRIM15, Alpha-
actinin, TOP3A, RFX3,
SLUG, Coagulation factor
X, Orexin receptor 1, A20,
Ephrin-A receptors,
GSTO1, Bim, FAIM2,
SCAI, SHANK, SynGAP,
Fibrinogen gamma, DAGK,
PSMD14, IL-1 alpha,
CREB3, CCR1, GMIP,
TLR4, RGSS22, NMT1,
TMEM100, Insulin, Fibu-

xMWAS: R package for data integration and network analysis

phosphate-containing compound metabolic process	2595	1.85E-08	3.97E-06	123	lin-1, PSMA2, ADAR1, DUSP5, TANK, BTNL2, Asporin, Notch, Orexin receptor, SLAM, Galpha(q)-specific peptide GPCRs, Huntington, CD86, Profilin, Rab-3A, FGF10, CD40(TNFRSF5), ATF/CREB, Rhov, RNF34, EPS8, MAP-1B, PSMD12, CQ087, GITRL, Calsyntenin-2, Glutaredoxin, PEAR1, SHANK2, FGD3, PCPH, N-myristoyltransferase, PIP1, RGS6, DIRAS2, CHD7, Alpha-actinin 3, HDL proteins, BCAP, NME5, Phosphatase regulator (inhibitor), Syntenin 1, ILPIP, NCK1, RANK(TNFRSF11A), USP18, IFNAR2, GREM2, Thyroid hormone receptor, PLCL2, Nephrocystin-4, PI3K reg class IA, RGS9, IPP-2, Galpha(s)-specific peptide GPCRs, DUSP18, DDX60, NPNT, Glutaredoxin 1 beta-MHC, RPS6KL1, PSMA4, STAT3, GNPTA, CTP synthase, IL-15, MEK1(MAP2K1), PLB1, Stk33, RIPK2, KIAA1274, LYST, MGF, PRKAR2B, IL-31RA, Mdh1b, Guanylate cyclase, Glycogen phosphorylase, CDP-diacylglycerol synthase, DHSO, PDE, PSMD8, Pleckstrin, Guanylate cyclase alpha, Ephrin-A receptor 1, ALPK1, Polycystin, P2X7, MEK1/2, PPP4C, MIRK, SAMHD1, DOK1, JAK2, SGK3,
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regulation of molecular function	3799	1.86E-08	3.97E-06	165	GUCY1A2, PDE1, DMP4, Galpha(q)-specific nucleotide-like GPCRs, PSMD3, Ephrin-A receptor 5, FGFR3, IDH1, MyHC, TRIB2, Galectin-9, PMCA2b, Neuregulin 4, YSK4, PGS1, ATP1A2, NNTM, PKA-reg type II (cAMP-dependent), ENO4, ATP6V1B2, MANA, Lyn, PSMA1, DMPK, PKI, CDS2, PKA-reg (cAMP-dependent), PKIB, Alpha-actinin, PDE2A, Ephrin-A receptors, NPR3, AKD1, FNIP2, SHANK, SynGAP, DAGK, PSMD14, Hck, TLR4, Insulin, PBEF, PSMA2, DUSP5, NT5C3, IDH2, Galpha(q)-specific peptide GPCRs, GFRalpha1, CD86, NUDT4, FLAD1, NEK5, MOK, FGF10, PNPH, ATF/CREB, ERK3, PSMD12, SERINC5, ADSSL1, LDHB, MTHFD2L, ATP6V1B, PDE1B, DGKH, PCPH, PI4KII, AGPHD1, TXL-2, HDL proteins, PPP1R3B, BCAP, NUAK2, C9orf98, NME5, Phosphatase regulator (inhibitor), MPP1, LRGUK, PI3K reg class IA (p55-gamma), ILPIP, NCK1, KAD7, AL1A1, ABI2, PI3K reg class IA, DUSP18, FRK, Bomapin, PSMA4, CD84, FAM13A1, STAT3, PODN, Dystrophin, C1orf88, WFDC1, p200RhoGAP, NFKBIB, TR-alpha, MEK1(MAP2K1), DOT1,
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xMWAS: R package for data integration and network analysis

DNAJB11, SP100,
ELMOD1, RIPK2,
DENND1A, Hap-1, MGF,
PRKAR2B, Syntaxin 4,
EFP, HEY1, Vsm-
RhoGEF, Dynein, ax-
onemal, light chains, PDE,
PSMD8, Pleckstrin, Gal-
pha(q)-specific Class A Or-
phan/other GPCRs, Ephrin-
A receptor 1, KCNRG,
FLJ32810, Tbc1d9, HIF1A,
Polycystin, LDB2, P2X7, I-
kB, ORP-family, HES1,
MEK1/2, MAPRE3(EB3),
DENND1B, TRIM14,
ROBO1, Apaf-1, JAK2,
SGK3, ORP8, SMIF,
ARHGEF19, Islet-1, Gal-
pha(q)-specific nucleotide-
like GPCRs, PSMD3, Rab-
3, MIP-T3, Cytohesin1,
Ephrin-A receptor 5,
FGFR3, SERPINB7, Sor-
tilin, MyHC, TRIB2,
Spp24, Galectin-9, Neureg-
ulin 4, ITIH2, Ceb1,
PLEKHG1, ATP1A2,
MUL, Antileukoproteinase
1, PKA-reg type II (cAMP-
dependent), CAP2, C4B
protein, Profilin II, Lyn,
PSMA1, Centaurin alpha 1,
CENTA2, DMPK, MRE11,
hRap1, PKI, RGS11,
TRIM15, PKA-reg (cAMP-
dependent), ELL, WWP2,
PKIB, Alpha-actinin,
RAP2C, A20, Ephrin-A re-
ceptors, NPR3, GSTO1,
Bim, SHANK, SynGAP,
DAGK, PSMD14, CREB3,
Hck, GMIP, TLR4, C4,
RGSS22, Insulin, Fibulin-1,
Pyrin (MEFV), PSMA2,
ADAR1, GRO-1, DUSP5,
TANK, Asporin, Notch,

xMWAS: R package for data integration and network analysis

regulation of signal transduction	3625	1.93E-08	3.97E-06	159	SLAM, Galph(q)-specific peptide GPCRs, Huntingtin, GFRalpha1, Mitd1, Profilin, Rab-3A, NEK5, FGF10, CD40(TNFRSF5), ATF/CREB, FAM116B, RNF34, PSMD12, SERINC5, GITRL, Glutaredoxin, AGAL, FGD3, RGS6, DIRAS2, HDL proteins, PPP1R3B, Phosphatase regulator (inhibitor), PI3K reg class IA (p55-gamma), PARP-10, ILPIP, NCK1, RANK(TNFRSF11A), Beta adducin, GREM2, AL1A1, Thyroid hormone receptor, TRIM23, PLCL2, LULL1, PI3K reg class IA, RGS9, IPP-2, Galph(s)-specific peptide GPCRs, DUSP18, MAP1LC3B, CCNYL1, NPNT, SERPINB9, Glutaredoxin 1
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HES1, MEK1/2, ATF-3,
DOK1, C3orf58, ROBO1,
Apaf-1, JAK2, SGK3,
ORP8, ARHGEF19, Islet-1,
DMP4, Galpha(q)-specific
nucleotide-like GPCRs,
PSMD3, MIP-T3, Cytohe-
sin1, FGFR3, TRIB2, Ga-
lectin-9, Neuregulin 4,
PLEKHG1, WRCH-1,
Krm1, RPGRIP1L, Lyn,
PSMA1, DMPK, MRE11,
Dynein 2, cytoplasmic,
heavy chain, hRap1,
CysLT2 receptor, RGS11,
TRIM15, Alpha-actinin,
TOP3A, SLUG, Coagula-
tion factor X, Orexin recep-
tor 1, A20, Ephrin-A recep-
tors, GSTO1, Bim, FAIM2,
SCAI, SHANK, SynGAP,
Fibrinogen gamma, DAGK,
PSMD14, IL-1 alpha,
CREB3, CCR1, GMIP,
TLR4, RGSS22, NMT1,
TMEM100, Insulin, Fibu-
lin-1, PSMA2, ADAR1,
DUSP5, TANK, BTNL2,
Asporin, Notch, Orexin re-
ceptor, SLAM, Galpha(q)-
specific peptide GPCRs,
Huntingtin, CD86, FGF10,
CD40(TNFRSF5),
ATF/CREB, Rhov, RNF34,
EPS8, PSMD12, CQ087,
GITRL, Glutaredoxin,
PEAR1, FGD3, PCPH, N-
myristoyltransferase, PIP1,
RGS6, DIRAS2, Alpha-
actinin 3, HDL proteins,
BCAP, NME5, Phosphatase
regulator (inhibitor),
Syntenin 1, ILPIP, NCK1,
RANK(TNFRSF11A),
USP18, IFNAR2, GREM2,
Thyroid hormone receptor,
PLCL2, Nephrocystin-4,

xMWAS: R package for data integration and network analysis

immune system process	3048	1.95E-08	3.97E-06	139	PI3K reg class IA, RGS9, IPP-2, Galpha(s)-specific peptide GPCRs, DUSP18, DDX60, NPNT, Glu- taredoxin 1 PSMA4, CD84, CTP syn- thase, IL-15, H-2L(d), Mca32, SPEF2, TR-alpha, MHC Class I alpha chain, MEK1(MAP2K1), C2, SP100, RIPK2, MDA-5, LYST, MGF, IL-31RA, LTBR1, EPAS1, EFP, PDE, TREML2, ACP33, PSMD8, Pleckstrin, Gal- pha(q)-specific Class A Or- phan/other GPCRs, Rab8B, CD300LG, HIF1A, SUSD2, ADAMDEC1, P2X7, I-kB, ORP-family, NOTCH4, HES1, MEK1/2, DENND1B, SAMHD1, TRIM14, JAK2, MR1, PDE1, DMP4, Galpha(q)- specific nucleotide-like GPCRs, PSMD3, FLVCR, Rab-3, MxA, Ku70, MyHC, CD34, Galectin-9, Carbohydrate sulfotransfer- ases, Ceb1, Antileukopro- teinase 1, TFE3, C4B pro- tein, Lyn, PSMA1, HLA-E, Ephrin-B2, Ephrin-B, Dynein 2, cytoplasmic, heavy chain, CysLT2 re- ceptor, TRIM15, CAPZA1, HA12 (rodent), Alpha- actinin, GRO-3, MENA, PDE2A, A20, OASL, AZI2, Ephrin-A receptors, KIF3B, Bim, Fibrinogen gamma, PSMD14, IL-1 al- pha, CCR1, CCR9, Hck, TLR4, C4, Insulin, Pyrin (MEFV), PSMA2, ADAR1, GRO-1, CD276, SPP lyase, TANK, Galectin-8,
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xMWAS: R package for data integration and network analysis

single-organism cellular process	14419	2.55E-08	5.05E-06	482	CAPZA, Notch, SLAM, Galpha(q)-specific peptide GPCRs, ISG20, CYFIP1, HA11, CD86, CCL27, TAPBPL, FGF10, CD40(TNFRSF5), PNPH, ATF/CREB, EPS8, PSMD12, SERINC5, ADSSL1, CAPZA2, GITRL, HLA-C, PDE1B, HLA-B, Artemis, CHD7, PI4KII, CD209, HDL pro- teins, BCAP, OSTM1 (grey-lethal), NCK1, RANK(TNFRSF11A), Beta adducin, IFNAR2, KAD7, Thyroid hormone receptor, PLCL2, RPESP, PI3K reg class IA, CD300LF, DDX60, FRK, SERPINB9, SNX10 Bomapin, beta-MHC, RPS6KL1, PAM, KIF21A, PSMA4, CD84, FAM13A1, B4GT4, STAT3, G3BP2, FLJ13305, PODN, DNAH5, Dystrophin, GNPTA, CARP, CTP syn- thase, C2CD4D, NHE3, MPV17L, IL-15, OLFML2A, C1orf88, CCDC39, H-2L(d), Mca32, WIPI1, Trehalase, DPYD, Rab20, PDIP38, p200RhoGAP, SPEF2, FLJ20898, OSF-2, REV- ERBalpha, HDAC11, NFKBIB, STOML3, ZNF281, TR-alpha, MHC Class I alpha chain, PNPase(old-35), GPR141, MEK1(MAP2K1), C2, ARMC4, DOT1, SLIT3, PLB1, AM-R, DNAH1, PHEX, DNAJB11, SNX2, SP100, PVR, PLET1, RIPK2, MDA-5, ASCT1
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(SLC1A4), ZNF313,
LYST, Hap-1, MGF,
SNX1, PRKAR2B, ARG1,
IL-31RA, Olfactory receptor,
Syntaxin 4, ARF6,
LTBR1, SPAG17,
SCPEP1, CHMP6, Mdh1b,
Guanylate cyclase, EPAS1,
DMKN, Sec3, PRAM-1,
Vinculin, APOD, EFP,
Glycogen phosphorylase,
HEY1, CEP78, Synaptotagmin II, VE-cadherin,
NCKX3, Synaptotagmin,
CD-MPR, CDP-diacylglycerol synthase,
DHSO, HIST3H2A,
Dynein, axonemal, light chains, PDE, IQCG,
TREML2, MGAT4A,
ACP33, KCNQ1OT1,
PSMD8, Pleckstrin,
LRP12, Guanylate cyclase alpha, Galpha(q)-specific
Class A Orphan/other GPCRs, Rab8B, HPLC2,
Ephrin-A receptor 1, VIPAR, FLJ32810,
ALPK1, HIF1A, Polycystin, Fibulin-5, Tmem195,
RABL2A, FAT3, P2X7, I-kB, ORP-family, NOTCH4,
HES1, FLJ32658, Vitrin, MEK1/2, DGAT1, ATF-3,
Olr1598, PPP4C, MIRK, OLAH, MAPRE3(EB3),
DENND1B, SAMHD1, VN1R4, B3GN1, DOK1,
C3orf58, Egflam, ALKBH7, SLC24A6,
ROBO1, DNAH9, Apaf-1, HAT1, JAK2, PLEKHM1,
MR1, SGK3, ORP8, SMIF, GUCY1A2, ARHGEF19,
ZCCHC14, PDE1, Islet-1, DMP4, Galpha(q)-specific
nucleotide-like GPCRs,

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WDR93, PSMD3, FLVCR,
DZIP1L, ATP6M, Rab-3,
MIP-T3, Cytohesin1,
MNS1, LRRC50, Ephrin-A
receptor 5, MxA, FGFR3,
FANCM, DNAH6,
DYDC1, IDH1, RETSAT,
Ku70, Sortilin, MyHC, V-
ATPase E subunit, OGFR,
CD34, Spp24, Galectin-9,
Ca-ATPase3, PCDHB8,
NHLRC2, PMCA2b, Car-
bohydrate sulfotransferases,
Neuregulin 4, Ceb1, Scd2,
YSK4, BBS9, PGS1,
TRAP25, WHDC1,
WRCH-1, Krm1, ATP1A2,
Dynein, axonemal, heavy
chains, RPGRIP1L, Oxy-
gen-regulated protein 1,
NNTM, CFA54, Alpha-
parvin, PKA-reg type II
(cAMP-dependent), ENO4,
CAP2, MYH10,
ATP6V1B2, VANGL1,
MANA, Profilin II, Lyn,
PSMA1, Centaurin alpha 1,
CENTA2, HLA-E, Ephrin-
B2, DMPK, PRIC285,
MRE11, Ephrin-B, Dynein
2, cytoplasmic, heavy
chain, PYGM, LMLN,
NPX1, STRBP, CNDP2,
PKI, CysLT2 receptor,
RGS11, CDS2, TRIM15,
G-protein alpha-14,
CAPZA1, PKA-reg
(cAMP-dependent), HA12
(rodent), CFA74,
KIAA1340, VTA1,
SPAG16, Alpha-actinin, c-
Maf, DNAH11, IL-15RA,
GRO-3, TOP3A, RFX3,
SLUG, MENA, PDE2A,
RAP2C, ATP4A, Orexin
receptor 1, A20, OASL,
AZI2, ABBA, Ephrin-A re-

ceptors, GALRL, NPR3,
GSTO1, Sp17, AKD1,
KCNE4, KIF3B, Bim,
SLC4A11, FAIM2, FNIP2,
SHANK, SynGAP, Fibrin-
ogen gamma, DAGK,
PSMD14, IL-1 alpha,
CREB3, CCR1, CCR9,
RPS27, TFIIF, beta subunit,
Hck, GMIP, TLR4, NAR4,
SCO2, NMT1, TMEM100,
Insulin, Fibulin-1, PBEF,
PSMA2, GNT-IV, Ces1
(mouse), ADAR1,
KIAA1377(HIP5), GRO-1,
DUSP5, CD276, SPP lyase,
TANK, Galectin-8, NT5C3,
PADI6, IDH2, SPATA18,
CAPZA, CLR3, Asporin,
FLJ46266, Notch, Orexin
receptor, SLAM,
APBA2BP, MCFD2, Gal-
pha(q)-specific peptide
GPCRs, ISG20, Huntingtin,
GFRalpha1, CYFIP1,
HA11, CD86, Mitd1,
POLR2G, Trp53inp2, Pro-
filin, NUDT4, HYDIN,
Rab-3A, CCL27, TOX3,
TSGA2, ACADM, CBR1,
FLAD1, ES130 (p180),
MOK, FGF10,
CD40(TNFRSF5),
OR52N5, PNPH, T6441,
ATF/CREB, Rhov, RNF34,
ERK3, DNAJC13, EPS8,
C4orf31, SCN3A, DNAH3,
MAP-1B, PSMD12,
SERINC5, ADSSL1,
CQ087, LDHB, CAPZA2,
FADS2, MTHFD2L,
GITRL, CCDC176,
Calsyntenin-2, SETDB2,
ASB14, Glutaredoxin,
DNAH2, MMSA, HLA-C,
PEAR1, ATP6V1B,
CCDC52, DNAI1,

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SHANK2, AGAL, DZIP,
CGI-128, ZNF541, AL3A1,
Heme oxygenase 2,
PDE1B, WDT2, FGD3,
DGKH, PCPH, N-
myristoyltransferase,
PCDHB16, RGS6, GPR35,
DIRAS2, HLA-B,
ATP6V1E, Artemis,
CHD7, Alpha-actinin 3,
PI4KII, FBX6, AGPHD1,
TXL-2, ANKRD28,
CD209, HDL proteins,
PPP1R3B, SIX5, BCAP,
Dynein, axonemal, inter-
mediate chains, NUAK2,
C9orf98, FAT1, NRIF2,
PLTP, ANKFY1, NME5,
SNAP-29, Phosphatase
regulator (inhibitor),
OSTM1 (grey-lethal),
Syntenin 1, ATP8B3,
MPP1, UGCG, LRGUK,
PI3K reg class IA (p55-
gamma), PARP-10,
VAMP4, ILPIP, NCK1,
RANK(TNFRSF11A),
P2Y4, NABP1, DNAH12,
Beta adducin, IFNAR2,
GREM2, KAD7, Protein
p8, AL1A1, Thyroid hor-
mone receptor, BET1,
TRIM23, UOX, PLCL2,
Nephrocystin-4, DIP13 be-
ta, GSTT2, ACSS1, PTER,
ABI2, TSNAXIP1,
CABYR, LULL1,
KIAA0317, PI3K reg class
IA, RGS9, CD300LF,
HPSE2, IPP-2, Galpha(s)-
specific peptide GPCRs,
C8orf34, DUSP18, TIG2,
MAP1LC3B, Perlecan,
C2orf39, FAM188A,
RSPH4A, Olfr554,
CCNYL1, NPNT, Alpha-
internexin, MCEE, FRK,

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					PSTPIP2, SERPINB9, Glutaredoxin 1, SNX10, TCTE3
negative regulation of intracellular transport	156	2.67E-08	5.07E-06	20	CD84, G3BP2, NFKBIB, TR-alpha, SP100, APOD, PDE, Polycystin, I-kB, Galectin-9, PKI, TRIM15, SLUG, PDE2A, CREB3, ATF/CREB, MAP-1B, HDL proteins, PARP-10, Thyroid hormone receptor
localization of cell	1212	2.78E-08	5.07E-06	70	CD84, DNAH5, CCDC39, MEK1(MAP2K1), SLIT3, DNAH1, PVR, PLET1, LYST, MGF, DHSO, PDE, HIF1A, RABL2A, FAT3, HES1, MEK1/2, ROBO1, JAK2, Islet-1, Galpha(q)-specific nucleotide-like GPCRs, DNAH6, MyHC, CD34, Carbohydrate sulfotransferases, Dynein, axonemal, heavy chains, CFA54, Alpha-parvin, ENO4, MYH10, Lyn, Ephrin-B2, Ephrin-B, SPAG16, DNAH11, GRO-3, RFX3, SLUG, Ephrin-A receptors, Sp17, DAGK, CCR1, Hck, GRO-1, SPP lyase, CLR3, Notch, SLAM, Galpha(q)-specific peptide GPCRs, GFRalpha1, CCL27, FGF10, EPS8, C4orf31, DNAH3, DNAH2, DNAI1, HDL proteins, Dynein, axonemal, intermediate chains, FAT1, PLTP, Syntenin 1, NCK1, RANK(TNFRSF11A), Nephrocystin-4, ABI2, PI3K reg class IA, C2orf39, CCNYL1, PSTPIP2
cell motility	1212	2.78E-08	5.07E-06	70	CD84, DNAH5, CCDC39, MEK1(MAP2K1), SLIT3, DNAH1, PVR, PLET1,

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single-organism process	16117	3.41E-08	6.05E-06	526	LYST, MGF, DHSO, PDE, HIF1A, RABL2A, FAT3, HES1, MEK1/2, ROBO1, JAK2, Islet-1, Galpha(q)-specific nucleotide-like GPCRs, DNAH6, MyHC, CD34, Carbohydrate sulfotransferases, Dynein, axonemal, heavy chains, CFA54, Alpha-parvin, ENO4, MYH10, Lyn, Ephrin-B2, Ephrin-B, SPAG16, DNAH11, GRO-3, RFX3, SLUG, Ephrin-A receptors, Sp17, DAGK, CCR1, Hck, GRO-1, SPP lyase, CLR3, Notch, SLAM, Galpha(q)-specific peptide GPCRs, GFRalpha1, CCL27, FGF10, EPS8, C4orf31, DNAH3, DNAH2, DNAI1, HDL proteins, Dynein, axonemal, intermediate chains, FAT1, PLTP, Syntenin 1, NCK1, RANK(TNFRSF11A), Nephrocystin-4, ABI2, PI3K reg class IA, C2orf39, CCNYL1, PSTPIP2, Bomarin, beta-MHC, RPS6KL1, PAM, KIF21A, PSMA4, CD84, FAM13A1, B4GT4, STAT3, G3BP2, EG1, FLJ13305, PODN, DNAH5, Dystrophin, GNPTA, MCT8, CARP, CTP synthase, C2CD4D, NHE3, MPV17L, IL-15, OLFML2A, C1orf88, CCDC39, DDHD1, H-2L(d), Mca32, WIPI1, Trehalase, DPYD, Rab20, PDIP38, p200RhoGAP, SF3B14a, SPEF2, FLJ20898, OSF-2, REV-ERBalpha, HDAC11,
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NFKBIB, STOML3,
ZNF281, TR-alpha, MHC
Class I alpha chain,
PNPase(old-35), GPR141,
MEK1(MAP2K1), CTRL,
C2, ARMC4, DOT1,
SLIT3, C10orf58, PLB1,
AM-R, DNAH1, PHEX,
DNAJB11, SNX2, SP100,
PVR, PLET1, ELMOD1,
RIPK2, MDA-5, ASCT1
(SLC1A4), ZNF313,
LYST, DENND1A, Hap-1,
MGF, SNX1, MAD,
PRKAR2B, ARG1, IL-
31RA, Olfactory receptor,
Syntaxin 4, ARF6, LTBR1,
TMEM2, SPAG17,
SCPEP1, CHMP6, Mdh1b,
Guanylate cyclase, EPAS1,
DMKN, Sec3, PRAM-1,
Vinculin, APOD, EFP,
Glycogen phosphorylase,
HEY1, Vsm-RhoGEF,
CEP78, Synaptotagmin II,
ASCC3, VE-cadherin,
NCKX3, Synaptotagmin,
CD-MPR, CDP-
diacylglycerol synthase,
DHSO, HIST3H2A,
Dynein, axonemal, light
chains, PDE, IQCG,
TREML2, MGAT4A,
ACP33, KCNQ1OT1,
PSMD8, Pleckstrin,
LRP12, Spermine oxidase,
Guanylate cyclase alpha,
Galpha(q)-specific Class A
Orphan/other GPCRs,
Rab8B, HPLC2,
CD300LG, Ephrin-A recep-
tor 1, VIPAR, FLJ32810,
ALPK1, NAT-1, HIF1A,
Polycystin, LDB2, Fibulin-
5, Tmem195, RABL2A,
FAT3, P2X7, I-kB, ORP-
family, NOTCH4, HES1,

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FLJ32658, Vitrin, MEK1/2,
DGAT1, ATF-3, Olr1598,
PPP4C, C20orf26, PAFAH
gamma, MIRK, OLAH,
MAPRE3(EB3),
DENND1B, SAMHD1,
VN1R4, B3GN1, DOK1,
C3orf58, Egflam,
ALKBH7, SLC24A6,
ROBO1, DNAH9, Apaf-1,
HAT1, JAK2, PLEKHM1,
MR1, SGK3, ORP8, SMIF,
GUCY1A2, DUS4L,
ARHGEF19, ZCCHC14,
PDE1, Islet-1, DMP4, Gal-
pha(q)-specific nucleotide-
like GPCRs, WDR93,
PSMD3, FLVCR, DZIP1L,
ATP6M, Rab-3, MIP-T3,
Cytohesin1, MNS1,
LRRC50, Ephrin-A recep-
tor 5, MxA, FGFR3,
FANCM, DNAH6,
DYDC1, IDH1, RETSAT,
SERPINB7, Ku70, Sortilin,
MyHC, V-ATPase E subu-
nit, OGFR, CD34, Spp24,
Galectin-9, Ca-ATPase3,
PCDHB8, Adipophilin,
NHLRC2, PMCA2b, Car-
bohydrate sulfotransferases,
Neuregulin 4, Ceb1, Scd2,
YSK4, BBS9, PGS1,
TRAP25, WHDC1,
WRCH-1, Krm1, ATP1A2,
Dynein, axonemal, heavy
chains, RPGRIP1L, Oxy-
gen-regulated protein 1,
NNTM, CFA54, Alpha-
parvin, PKA-reg type II
(cAMP-dependent), ENO4,
CAP2, MYH10,
ATP6V1B2, VANGL1,
C4B protein, MANA, Pro-
filin II, Lyn, PSMA1, Cen-
taurin alpha 1, CENTA2,
HLA-E, Ephrin-B2,

DMPK, RNPEP, PRIC285,
MRE11, Ephrin-B, Dynein
2, cytoplasmic, heavy
chain, PYGM, LMLN,
NPX1, STRBP, CNDP2,
PKI, CysLT2 receptor,
RGS11, CDS2, TRIM15,
G-protein alpha-14,
CAPZA1, PKA-reg
(cAMP-dependent), HA12
(rodent), ELL, CFA74,
KIAA1340, VTA1,
SPAG16, Alpha-actinin,
CREG2, c-Maf, DNAH11,
IL-15RA, GRO-3, TOP3A,
RFX3, SLUG, MENA,
PDE2A, RAP2C, ATP4A,
Coagulation factor X, Orex-
in receptor 1, A20, OASL,
AZI2, ABBA, Ephrin-A re-
ceptors, GALRL, NPR3,
GSTO1, Sp17, AKD1,
KCNE4, KIF3B, Bim,
SLC4A11, FAIM2, FNIP2,
SHANK, Tryptase delta,
SynGAP, Fibrinogen gam-
ma, DAGK, PSMD14, IL-1
alpha, CREB3, CHST2,
CCR1, CCR9, SULT1D1,
RPS27, TFIIF, beta subunit,
Hck, Hapl4, GMIP, TLR4,
NAR4, C4, SCO2, NMT1,
TMEM100, CYP2S1, Insu-
lin, Fibulin-1, PBEF,
PSMA2, GNT-IV, Ces1
(mouse), ADAR1,
KIAA1377(HIP5), GRO-1,
DUSP5, CD276, SPP lyase,
TANK, Galectin-8, NT5C3,
PHTF1, HYEP, PADI6,
IDH2, SPATA18, CAPZA,
CLR3, Asporin, FLJ46266,
DSCR2, Notch, Orexin re-
ceptor, SLAM, APBA2BP,
MCFD2, CAC, Galph(q)-
specific peptide GPCRs,
ISG20, PLEKHA5, Hun-

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tingtin, GFRalpha1,
CYFIP1, HA11, CD86,
Mitd1, POLR2G,
Trp53inp2, Profilin,
NUDT4, HYDIN, Rab-3A,
CCL27, TOX3, TSGA2,
SSAT, ACADM, CBR1,
FLAD1, ES130 (p180),
MOK, FGF10,
CD40(TNFRSF5),
OR52N5, PNPH, T6441,
ATF/CREB, Rhov, RNF34,
ERK3, DNAJC13, EPS8,
C4orf31, SCN3A, DNAH3,
MAP-1B, PSMD12,
SERINC5, ADSSL1,
CQ087, LDHB, CAPZA2,
FADS2, MTHFD2L,
GITRL, CCDC176,
Calsyntenin-2, SETDB2,
ASB14, Glutaredoxin,
DNAH2, MMSA, HLA-C,
PEAR1, ATP6V1B,
CCDC52, DNAI1,
SHANK2, AGAL, DZIP,
CGI-128, ZNF541, AL3A1,
Heme oxygenase 2,
PDE1B, WDT2, FGD3,
DGKH, PCPH, N-
myristoyltransferase,
PCDHB16, PIP1, RGS6,
GPR35, DIRAS2, HLA-B,
ATP6V1E, Artemis,
CHD7, Alpha-actinin 3,
PI4KII, FBX6, AGPHD1,
TXL-2, ANKRD28,
CD209, HDL proteins,
PPP1R3B, SIX5, BCAP,
Dynein, axonemal, intermediate chains, NUAK2,
C9orf98, FAT1, NRIF2,
PLTP, ANKFY1, NME5,
SNAP-29, Phosphatase
regulator (inhibitor),
OSTM1 (grey-lethal),
Syntenin 1, TRIML1,
ATP8B3, MPP1, UGCG,

					LRGUK, PI3K reg class IA (p55-gamma), PARP-10, VAMP4, ILPIP, NCK1, RANK(TNFRSF11A), P2Y4, NABP1, DNAH12, Beta adducin, IFNAR2, GREM2, KAD7, Protein p8, AL1A1, Thyroid hor- mone receptor, BET1, TRIM23, UOX, PLCL2, Nephrocystin-4, DIP13 be- ta, GSTT2, ACSS1, Lrig3, PTER, STOX2, ABI2, TSNAXIP1, CABYR, ULL1, KIAA0317, ANKFN1, PI3K reg class IA, RGS9, CD300LF, HPSE2, IPP-2, Galpha(s)- specific peptide GPCRs, C8orf34, DUSP18, TIG2, MAP1LC3B, Perlecan, C2orf39, FAM188A, RSPH4A, Olfr554, CCNYL1, NPNT, Alpha- internexin, MCEE, FRK, RNF22, PSTPIP2, SERPINB9, Glutaredoxin 1, SNX10, TCTE3
negative regula- tion of protein import	92	5.89E-08	9.96E-06	15	G3BP2, NFKB1B, TR-alpha, APOD, PDE, Polycystin, I- kB, PKI, SLUG, PDE2A, CREB3, ATF/CREB, HDL proteins, PARP-10, Thyroid hormone receptor
negative regula- tion of protein import into nu- cleus	92	5.89E-08	9.96E-06	15	G3BP2, NFKB1B, TR-alpha, APOD, PDE, Polycystin, I- kB, PKI, SLUG, PDE2A, CREB3, ATF/CREB, HDL proteins, PARP-10, Thyroid hormone receptor
negative regula- tion of nucleo- cytoplasmic transport	106	6.58E-08	1.09E-05	16	G3BP2, NFKB1B, TR-alpha, SP100, APOD, PDE, Poly- cystin, I-kB, PKI, SLUG, PDE2A, CREB3, ATF/CREB, HDL proteins, PARP-10, Thyroid hor- mone receptor
regulation of im- mune system process	2131	7.05E-08	1.14E-05	104	Bomarin, PSMA4, CD84, IL- 15, H-2L(d), Mca32, REV- ERBalpha, MHC Class I alpha chain, C2, C10orf58, PVR, RIPK2, MDA-5, LYST, MGF, IL-31RA, Syntaxin 4, Trim30, ARF6, PRAM-1, APOD, PDE, TREML2, ACP33, PSMD8, CD300LG, ALPK1, HIF1A, P2X7, I-

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cellular developmental process	4943	8.59E-08	1.34E-05	200	kb, HEST, DENND1B, SAMHD1, JAK2, Gal- pha(q)-specific nucleotide- like GPCRs, PSMD3, MIP- T3, FGFR3, MyHC, CD34, Galectin-9, Carbohydrate sulfotransferases, Ceb1, TRAFD1, CCDC88, TFE3, C4B protein, Lyn, PSMA1, HLA-E, Ephrin-B2, Ephrin- B, TRIM15, PKA-reg (cAMP-dependent), HA12 (rodent), IL-15RA, GRO-3, MENA, A20, PSMD14, IL- 1 alpha, CREB3, CCR1, Hck, GMIP, TLR4, C4, In- sulin, PSMA2, ADAR1, GRO-1, CD276, TANK, Galectin-8, BTNL2, Notch, SLAM, Galpha(q)-specific peptide GPCRs, CYFIP1, HA11, CD86, CCL27, TAPBPL, FGF10, CD40(TNFRSF5), PNPH, ATF/CREB, PSMD12, GITRL, HLA-C, HLA-B, CD209, HDL proteins, BCAP, MPP1, NCK1, USP18, IFNAR2, PLCL2, PI3K reg class IA, CD300LF, TIG2, DDX60, SERPINB9
					STAT3, FLJ13305, DNAH5, Dystrophin, GNPTA, CARP, IL-15, CCDC39, H- 2L(d), PDIP38, SPEF2, FLJ20898, OSF-2, REV- ERBalpha, HDAC11, ZNF281, TR-alpha, MHC Class I alpha chain, PNPase(old-35), MEK1(MAP2K1), ARMC4, SLIT3, DNAH1, SNX2, PLET1, ZNF313, Hap-1, MGF, SNX1, IL- 31RA, Olfactory receptor, ARF6, SPAG17, EPAS1, DMKN, Vinculin, APOD, HEY1, Synaptotagmin II, Synaptotagmin, Dynein, axonemal light chains, PDE, IQCG, Pleckstrin, Rab8B, Ephrin-A receptor 1, VIPAR, HIF1A, RABL2A, FAT3, P2X7, ORP-family, NOTCH4, HES1, FLJ32658, MEK1/2, ATF-3, MIRK, B3GN1, ROBO1, Apaf-1, JAK2, ORP8, PDE1, Islet-1, DMP4, Galpha(q)-specific nucleotide-like GPCRs, FLVCR, DZIP1L, ATP6M, Rab-3, MIP-T3, LRRK50, Ephrin-A receptor 5, FGFR3, Ku70, Sortilin, MyHC, CD34, Galectin-9, PMCA2b, Carbohydrate sulfotransferases, Ceb1, BBS9, Dynein, axonemal heavy chains, RPGRIP1L, Oxygen-regulated protein 1, CFA54, Alpha-parvin,

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localization	6321	8.71E-08	1.34E-05	244	CAP2, MYH10, Lyn, Ephrin-B2, Ephrin-B, Dynein 2, cytoplasmic, heavy chain, NPX1, STRBP, TRIM15, PKA-reg (cAMP-dependent), HA12 (rodent), CFA74, SPAG16, Alpha-actinin, c-Maf, IL-15RA, RFX3, SLUG, MENA, PDE2A, RAP2C, A20, AZI2, Ephrin-A receptors, FAIM2, SHANK, SynGAP, Fibrinogen gamma, DAGK, IL-1 alpha, CCR1, CCR9, Hck, TLR4, TMEM100, Insulin, ADAR1, KIAA1377(HIP5), SPP lyase, Galectin-8, IDH2, SPATA18, CAPZA, CLR3, FLJ46266, Notch, SLAM, Galpha(q)-specific peptide GPCRs, Huntington, GFRalpha1, CYFIP1, HA11, CD86, Trp53inp2, HYDIN, Rab-3A, TSGA2, ACADM, CBRI, ES130 (p180), FGF10, T6441, ATF/CREB, ERK3, DNAJC13, C4orf31, MAP1B, CCDC176, Glutaredoxin, MMSA, HLA-C, DNAI1, DZIP, ZNF541, PDE1B, WDT2, RGS6, HLA-B, Artemis, CHD7, Alpha-actinin 3, HDL proteins, SIX5, Dynein, axonemal, intermediate chains, NME5, SNAP-29, Phosphatase regulator (inhibitor), OSTM1 (grey-lethal), LRGUK, ILPIP, NCK1, RANK(TNFRSF11A), KAD7, Protein p8, Thyroid hormone receptor, PLCL2, Nephrocystin-4, PTER, ABI2, TSNAZIP1, CABYR, PI3K reg class IA, CD300LF, TIG2, Perlecan, C2orf39, RSPH4A, NPNT, Alpha-internexin, FRK, SNX10, SLCO6A1, PAM, Clcal (rodent), CD84, STAT3, G3BP2, DNAH5, Dystrophin, GNPTA, MCT8, SNX5, C2CD4D, NHE3, MPV17L, CCDC39, Mca32, WIP11, Rab20, CLCN7, NFKBIB, TR-alpha, PNPase(old-35), MEK1(MAP2K1), SLIT3, DNAH1, SNX2, PVR, PLET1, ELMOD1, ASCT1 (SLC1A4), LYST, DENND1A, Hap-1, MGF, SNX1, Olfactory receptor, Syntaxin 4, ARF6, CHMP6, Guanylate cyclase, Sec3, Vinculin, APOD, Synaptotagmin II, NCKX3, Synaptotagmin,
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CD-MPR, DHSO, Dynein, axonemal light chains, PDE, Pleckstrin, LRP12, Galpha(q)-specific Class A Orphan/other GPCRs, Rab8B, CD300LG, VIPAR, Tbc1d9, HIF1A, SUSD2, Polycystin, Fibulin-5, RABL2A, FAT3, P2X7, I-kB, ORP-family, HES1, FLJ32658, MEK1/2, DGAT1, DENND1B, C3orf58, ALKBH7, SLC24A6, ROBO1, JAK2, PLEKHM1, SGK3, ORP8, SMIF, Islet-1, Galpha(q)-specific nucleotide-like GPCRs, FLVCR, ATP6M, Rab-3, GOLT1A, MIP-T3, Cytohesin1, FAM38B, DNAH6, SERPINB7, Sorbin, MyHC V-ATPase E subunit, CD34, Spp24, Galectin-9, Ca-ATPase3, Adipophilin, PMCA2b, Carbohydrate sulfotransferases, BBS9, C9orf72, UGRP1, WHDC1, ATP1A2, Dynein, axonemal, heavy chains, NNTM, CFA54, Alpha-parvin, ENO4, MYH10, ATP6V1B2, C4B protein, Lyn, Ephrin-B2, CCDC46, Ephrin-B, Dynein 2, cytoplasmic, heavy chain, hRap1, NPX1, NIPA2, VTA1, SPAG16, Bestrophin-4, Alpha-actinin, DNAH11, GRO-3, MEX3D, RFX3, SLUG, MENA, PDE2A, ATP4A, Coagulation factor X, A20, Ephrin-A receptors, NPR3, Sp17, KCNE4, KIF3B, Bim, SLC4A11, SHANK, SynGAP, Fibrinogen gamma, DAGK, CREB3, CCR1, RPS27, Hck, TLR4, PLEKHM2, C4, SCQ2, NMT1, Insulin, ADAR1, GRO-1, SPP lyase, PADI6, IMP2, CLR3, Asporin, Notch, SLAM, APBA2BP, MCFD2, CAC, Galpha(q)-specific peptide GPCRs, Huntingtin, GFRalpha1, CYFIP1, Mitd1, Profilin, NUDT4, Rab-3A, CCL27, DHX38, ES130 (p180), FGF10, PNPH, ATF/CREB, DNAJC13, EPS8, C4orf31, SCN3A, DNAH3, MAP-1B, SERINC5, CD163, FADS2, Glutaredoxin, DNAH2, PEAR1, ATP6V1B, CCDC52, DNAI1, DZIP, WDT2, N-myristoyltransferase, ATP6V1E, MARCH5, PI4KII, ANKRD28, CD209, HDL proteins, Dynein, axonemal, inter-

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axonemal dynein complex assembly	30	1.11E-07	1.68E-05	9	mediate chains, FATT, PLTP, ANKFY1, SNAP-29, Phosphatase regulator (inhibitor), OSTM1 (grey-lethal), Syntenin 1, ATP8B3, VAMP4, ILPIP, NCK1, RANK(TNFRSF11A), P2Y4, Beta adducin, Thyroid hormone receptor, BET1, NXT2, Nephrocystin-4, GPP130, ABI2, RPESP, LULL1, PI3K reg class IA, Galpha(s)-specific peptide GPCRs, DUSP18, TIG2, Perlecan, C2orf39, UBAP1, CCNYL1, NPNT, RNF22, PSTPIP2, Glutaredoxin 1, SNX10, TCTE3
regulation of innate immune response	514	1.43E-07	2.05E-05	38	PSMA4, REV-ERBalpha, MHC Class I alpha chain, PVR, RIPK2, MDA-5, Trim30, ARF6, PSMD8, I-kB, SAMHD1, JAK2, PSMD3, Galectin-9, TRAFD1, Lyn, PSMA1, HLA-E, TRIM15, A20, PSMD14, CCR1, Hck, TLR4, Insulin, PSMA2, ADAR1, TANK, Galpha(q)-specific peptide GPCRs, CD86, PSMD12, HLA-B, CD209, BCAP, USP18, IFNAR2, DDX60, SERPINB9
regulation of defense response	1116	1.48E-07	2.05E-05	64	Bomarin, PSMA4, IL-15, WFDC1, REV-ERBalpha, MHC Class I alpha chain, C2, PVR, RIPK2, MDA-5, Trim30, ARF6, APOD, Synaptotagmin, PDE, PSMD8, Galpha(q)-specific Class A Orphan/other GPCRs, ALPK1, I-kB, SAMHD1, JAK2, Islet-1, Galpha(q)-specific nucleotide-like GPCRs, PSMD3, MIP-T3, Galectin-9, Carbohydrate sulfotransferases, Ceb1, TRAFD1, C4B protein, Lyn, PSMA1, HLA-E, TRIM15, PDE2A, A20, SHANK, PSMD14, CREB3, CCR1, Hck, GMIP, TLR4, C4, Insulin, Pyrin (MEFV), PSMA2, ADAR1, CD276, TANK, Galpha(q)-specific peptide GPCRs, CD86, ATF/CREB, PSMD12, GITRL, HLA-B, CD209, HDL proteins, BCAP, RANK(TNFRSF11A), USP18, IFNAR2, DDX60, SERPINB9
developmental	7554	1.49E-07	2.05E-05	281	beta-MHC, PAM, STAT3,

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process	EG1, FLJ13305, DNAH5, Dystrophin, GNPTA, CARP, MPV17L, IL-15, CCDC39, H-2L(d), Treha- lase, DPYD, PDIP38, SF3B14a, SPEF2, FLJ20898, OSF-2, REV- ERBalpha, HDAC11, ZNF281, TR-alpha, MHC Class I alpha chain, PNPase(fold-35), MEK1(MAP2K1), ARMC4, SLIT3, DNAH1, PHEX, SNX2, PLET1, ZNF313, Hap-1, MGF, SNX1, MAD, ARG1, IL- 31RA, Olfactory receptor, ARF6, TMEM2, SPAG17, Guanylate cyclase, EPAS1, DMKN, Vinculin, APOD, HEY1, Vsm-RhoGEF, Synaptotagmin II, VE- cadherin, Synaptotagmin, Dynein, axonemal, light chains, PDE, IQCG, Pfeck- strin, Galpha(q)-specific Class A Orphan/other GPCRs, Rab8B, Ephrin-A receptor 1, VIPAR, NAT-1, HIF1A, Polycystin, LDB2, RABL2A, FAT3, P2X7, I- kB, ORP-family, NOTCH4, HES1, FLJ32658, MEK1/2, ATF-3, PAFAH gamma, MIRK, B3GN1, C3orf58, ROBO1, Apaf-1, JAK2, ORP8, PDE1, Islet-1, DMP4, Galpha(q)-specific nucleotide-like GPCRs, FLVCR, DZIP1L, ATP6M, Rab-3, MIP-T3, MNS1, LRRC50, Ephrin-A recep- tor 5, FGFR3, IDH1, Ku70, Sortilin, MyHC, CD34, Spp24, Galectin-9, PCDHBB8, PMCA2b, Car- bohydrate sulfotransferases, Neuregulin 4, Ceb1, Scd2, BBS9, TRAP25, Krm1, Dynein, axonemal, heavy chains, RPGRIP1L, Oxy- gen-regulated protein I, CFA54, Alpha-parvin, CAP2, MYH10, VANGL1, Lyn, CENTA2, HLA-E, Ephrin-B2, RNPEP, MRE11, Ephrin-B, Dynein 2, cytoplasmic, heavy chain, NPX1, STRBP, TRIM15, PKA-reg (cAMP- dependent), HA12 (rodent), ELL, CFA74, SPAG16, Alpha-actinin, c-Maf, DNAH11, IL-15RA, RFX3, SLUG, MENA, PDE2A, RAP2C, A20, AZI2, Ephrin-A receptors, NPR3, KIF3B, Bim, FAIM2, SHANK, Tryptase delta, SynGAP, Fibrinogen gam- ma, DAGK, IL-1 alpha, CHST2, CCR1, CCR9, Hck, HaplN4, TLR4, SC02,
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cilium-dependent cell motility	16	1.49E-07	2.05E-05	7	NMT1, TMEM100, Insulin, Fibulin-1, PBEF, ADAR1, KIAA1377(HIP5), GRO-1, DUSP5, SPP lyase, Galec-tin-8, HYEP, IDH2, IMP2, SPATA18, CAPZA, CLR3, Asporin, FLJ46266, DSCR2, Notch, SLAM, MCFD2, Galpha(q)-specific peptide GPCRs, PLEKHA5, Huntington, GFRalpha1, CYFIP1, HA11, CD86, POLR2G, Trp53inp2, Profilin, HYDIN, Rab-3A, TSGA2, SSAT, ACADM, CBR1, ES130 (p180), FGF10, CD40(TNFRSF5), T6441, ATF/CREB, ERK3, DNAJC13, C4orf31, SCN3A, MAP-1B, SERINC5, CCDC176, SETDB2, Glutaredoxin, MMSA, HLA-C, ATP6V1B, DNAI1, SHANK2, AGAL, DZIP, ZNF541, AL3A1, PDE1B, WDT2, N-myristoyltransferase, PCDHB16, PIP1, RGS6, HLA-B, Artemis, CHD7, Alpha-actinin 3, HDL proteins, SIX5, Dynein, axonemal, intermediate chains, C9orf98, FAT1, NME5, SNAP-29, Phosphatase regulator (inhibitor), OSTM1 (grey-lethal), TRIML1, UGCG, LRGUK, ILPIP, NCK1, RANK(TNFRSF11A), Beta adducin, GREM2, KAD7, Protein p8, AL1A1, Thyroid hormone receptor, PLCL2, Nephrocystin-4, Lrig3, PTER, STOX2, ABI2, TSNAZXP1, CABYR, PI3K reg class IA, RGS9, CD300LF, Galpha(s)-specific peptide GPCRs, TIG2, Perlecan, C2orf39, RSPH4A, NPNT, Alpha-internexin, FRK, RNF22, Glutaredoxin 1, SNX10
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References for Supplementary Material

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