

TABLE S1 GeneGo pathway analysis elucidates networks enriched in each cluster

(Clusters 1 and 2)

Cluster	Enrichment by Pathway Maps	Total Genes	Genes In Data	p-value	FDR	Network Objects from Active Data
Cluster 1: Stress Response / Inflammation (n=158)	ATP metabolism	106	5	4.40E-04	1.05E-01	PDE8B, WARS, PKM2, PAPS2, ENP1
	G-protein signaling_Rac3 regulation pathway	16	2	4.14E-03	3.68E-01	PAK1, DOCK7
	Glycolysis and gluconeogenesis (short map)	66	3	7.46E-03	3.68E-01	G3P2, PKM2, HXK3
	Apoptosis and survival_NO signaling in apoptosis	23	2	8.49E-03	3.68E-01	G3P2, PAK1
	Immune response_Inflammasome in inflammatory response	34	2	1.80E-02	3.68E-01	CARD5, Caspase-1
	Development_Activation of ERK by Kappa-type opioid receptor	36	2	2.01E-02	3.68E-01	PLA2, Pyk2(FAK2)
	G-protein signaling_G-Protein alpha-12 signaling pathway	37	2	2.12E-02	3.68E-01	PAK1, PDZ-RhoGEF
	Immune response_Role of Integrins in NK cells cytotoxicity	38	2	2.23E-02	3.68E-01	PAK1, Pyk2(FAK2)
	G-protein signaling_Regulation of p38 and JNK signaling mediated by G-proteins	39	2	2.34E-02	3.68E-01	PAK1, Pyk2(FAK2)
	Tryptophan metabolism	101	3	2.34E-02	3.68E-01	WARS, INDO, AL1A1
	<b>Total</b>	<b>In Data</b>	<b>p-value</b>	<b>FDR</b>	<b>Network Objects from Active Data</b>	
	Cell adhesion_Platelet aggregation	158	6	1.83E-03	1.92E-01	GAB3, Gab, PLA2, ENP1, Pyk2(FAK2), PLA2G7
	Proliferation_Positive regulation cell proliferation	221	6	9.43E-03	3.87E-01	G-protein alpha-15, TCIRG1 (Atp6i), Beta-arrestin1, PAK1, Pyk2(FAK2), VEGF-B
	Inflammation_Interferon signaling	110	4	1.27E-02	3.87E-01	INDO, IL18RAP, Caspase-1, SOCS3
	Proteolysis_Connective tissue degradation	119	4	1.65E-02	3.87E-01	Alpha 1-antitrypsin, Furin, ADAM15, Cystatin C
Apoptosis_Death Domain receptors & caspases in apoptosis	123	4	1.84E-02	3.87E-01	DR6(TNFRSF21), CARD5, Caspase-4, Caspase-1	
Immune response_BCR pathway	137	4	2.62E-02	4.58E-01	BCAP, PAK1, Oct-2, Fc gamma RII beta	
Immune response_Th17-derived cytokines	98	3	4.69E-02	7.04E-01	Calgranulin B, IL-17 receptor, SOCS3	
Muscle contraction_Nitric oxide signaling in the cardiovascular system	125	3	8.40E-02	8.36E-01	Beta-arrestin1, ERK1, Ca-ATPase2	
Proteolysis_Proteolysis in cell cycle and apoptosis	125	3	8.40E-02	8.36E-01	Cathepsin H, Caspase-4, Caspase-1	
Immune response_Phagocytosis	222	4	1.10E-01	8.36E-01	MFGES, PAK1, Pyk2(FAK2), Fc gamma RII beta	
<b>Total</b>	<b>In Data</b>	<b>p-value</b>	<b>FDR</b>	<b>Network Objects from Active Data</b>		
cellular response to zinc ion	17	4	4.07E-06	2.16E-03	Metallothionein-I, Metallothionein-IG, Metallothionein-II, Metallothionein-IA	
cellular response to cadmium ion	17	4	4.07E-06	2.16E-03	Metallothionein-I, Metallothionein-IG, Metallothionein-II, Metallothionein-IA	
apoptotic process	1325	19	1.11E-05	3.23E-03	GADD34, G3P2, DR6(TNFRSF21), CNB5, CARD5, Cathepsin H, PSMB8(LMP7), Phosphatase regulator (inhibitor), DAL1, Calgranulin B, PAK1, EBP50, PPM1F, Caspase-4, Caspase-1, Pyk2(FAK2), Cystatin C, GADD45 beta, PP2C	
negative regulation of growth	279	4	1.22E-05	3.23E-03	Metallothionein-I, Metallothionein-IG, Metallothionein-II, Metallothionein-IA	
plasma lipoprotein particle oxidation	2	2	4.34E-05	6.57E-03	PLA2, PLA2G7	
response to muscle inactivity	9	2	4.34E-05	6.57E-03	Pyruvate kinase, PKM2	
lipid oxidation	82	2	4.34E-05	6.57E-03	PLA2, PLA2G7	
inflammatory response	593	12	6.09E-05	8.07E-03	TLR5, CARD5, PLA2, INDO, Calgranulin B, Alpha 1-antitrypsin, IL18RAP, Caspase-4, JMDJ3, PLA2G7, AOA8, CD163	
response to lithium ion	60	4	8.16E-05	9.61E-03	Pyruvate kinase, PLA2, Ionotropic glutamate receptor, Pyk2(FAK2)	
positive regulation of adaptive immune response	128	3	9.76E-05	1.03E-02	CD74, CARD5, SASH3	
Cluster 2: Type I Interferon Response (n=246)	<b>Total</b>	<b>In Data</b>	<b>p-value</b>	<b>FDR</b>	<b>Network Objects from Active Data</b>	
	Immune response_IFN alpha/beta signaling pathway	24	9	2.54E-13	5.34E-11	ISG54, IFI6, STAT1, PML, STAT2, USP18, STAT1/STAT2, SOCS1, ISG15
	Immune response_Antiviral actions of Interferons	52	9	5.87E-10	6.16E-08	ADAR1, PKR, OAS2, OAS1, 2'-5'-oligoadenylate synthetase, INDO, STAT1, Mx, STAT2
	Immune response_Role of PKR in stress-induced antiviral cell response	57	6	1.03E-05	7.24E-04	IRF7, MyD88, IL-6, PKR, TLR2, STAT1
	Immune response_HMGB1/TLR signaling pathway	36	5	1.49E-05	7.83E-04	IRF7, MyD88, IL-6, IL1RN, TLR2
	Immune response_Innate immune response to RNA viral infection	28	4	1.01E-04	4.25E-03	IRF7, MDA-5, RIG-I, TBK1
	Immune response_IL-1 signaling pathway	44	4	6.02E-04	2.11E-02	MyD88, IL-6, Heme oxygenase 1, STAT1
	Bacterial infections in CF airways	48	4	8.40E-04	2.39E-02	MyD88, TLR2, STAT1, TBK1
	Immune response_Bacterial infections in normal airways	49	4	9.09E-04	2.39E-02	MyD88, IL-6, TLR2, STAT1
	Development_Prolectin receptor signaling	58	4	1.71E-03	3.98E-02	NMI, OAS1, STAT1, SOCS1
	Immune response_Antigen presentation by MHC class I	28	3	1.90E-03	3.98E-02	HSP90, Tapasin, PSMB8(LMP7)
	<b>Total</b>	<b>In Data</b>	<b>p-value</b>	<b>FDR</b>	<b>Network Objects from Active Data</b>	
	Inflammation_Interferon signaling	110	24	1.21E-22	1.39E-20	MICB, IFITM2, ISG54, IRF7, IFI56, PKR, IFI17, ISG20, Fc gamma RI, IFP 35, IFI27, IFI6, INDO, STAT1, Mx, PML, STAT2, CCL8, IFI44, GBP1, GBP2, STAT1/STAT2, SOCS1, ISG15
	Immune response_Innate immune response to RNA viral infection	84	15	4.84E-13	2.78E-11	IRF7, RPK3, MyD88, ADAR1, IL-6, PKR, MDA-5, RIG-I, 2'-5'-oligoadenylate synthetase, INDO, STAT1, Mx, STAT2, IP10, TBK1
	Protein folding_ER and cytoplasm	45	7	2.87E-06	1.10E-04	HSP90, Erp29, SCO2, ERO1Lalpha, ATF-6 alpha (50kDa), Glutaredoxin, ERO1
Inflammation_Inflammasome	118	10	6.15E-06	1.77E-04	IRF7, RPK3, MyD88, PKR, RPK2, MDA-5, RIG-I, INCA, TBK1, ISG15	
Inflammation_Innate inflammatory response	181	12	9.04E-06	2.08E-04	PLA2, IRF7, RPK3, MyD88, Beta-defensin 1, IL-6, RPK2, TLR2, APOBEC3G, IP10, TBK1, cPLA2	
Protein folding_Response to unfolded proteins	69	6	4.25E-04	8.14E-03	HSP90, Torsin B, ATF-6 alpha (50kDa), Glutaredoxin, HSP90 alpha, ERO1	
Inflammation_IL-12,15,18 signaling	59	5	1.46E-03	2.41E-02	IL-15, MyD88, IL-18BP, STAT1, STAT1/STAT2	
Proteolysis_Ubiquitin-proteasomal proteolysis	166	8	2.48E-03	3.56E-02	UBCH8, HSP90, BAP1, EFP, VHL, Glutaredoxin, PSMB8(LMP7), Bard1	
Apoptosis_Apoptotic mitochondria	77	5	4.72E-03	6.04E-02	Bak, SNAPalpha, RPK2, Glutaredoxin, Glutaredoxin 1	
Protein folding_Folding in normal condition	119	6	6.93E-03	7.97E-02	HSP90, ERO1Lalpha, ATF-6 alpha (50kDa), VHL, HSP90 alpha, ERO1	
<b>Total</b>	<b>In Data</b>	<b>p-value</b>	<b>FDR</b>	<b>Network Objects from Active Data</b>		
defense response to virus	197	38	1.95E-37	2.95E-34	OASL, UNC93B, FAM111A, IFITM2, ISG54, IRF7, IFI56, ADAR1, ZBP1, IL-6, PKR, IFI17, MDA-5, RIG-I, OAS2, APOBEC3F, EFP, ISG20, OAS1, 2'-5'-oligoadenylate synthetase, C6orf150, STAT1, Mx, RIG-G, PML, STAT2, APOBEC3G, Ceb1,	
type I interferon-mediated signaling pathway	87	24	5.96E-28	4.51E-25	OASL, IFITM2, ISG54, IRF7, IFI56, ADAR1, IFI17, OAS2, ISG20, IFP 35, IFI27, OAS1, IFI6, PSMB8(LMP7), 2'-5'-oligoadenylate synthetase, STAT1, Mx, RIG-G, STAT2, USP18, GBP2, STAT1/STAT2, SOCS1, ISG15	
response to virus	322	25	1.88E-21	9.48E-19	OASL, Galpha(i)-specific amine GPCRs, IFITM2, ISG54, IRF7, IFI56, MyD88, ADAR1, PKR, IFI17, MDA-5, RIG-I, OAS2, ISG20, IFP 35, OAS1, 2'-5'-oligoadenylate synthetase, Mx, RIG-G, IP10, Staf-50, CCL8, IFI44, TBK1, DDX60	
cytokine-mediated signaling pathway	439	32	2.73E-21	1.03E-18	UBCH8, OASL, IFITM2, ISG54, IRF7, IGFBP, IFI56, MyD88, ADAR1, IL-6, IFI17, OAS2, ISG20, Fc gamma RI, IFP 35, IFI27, OAS1, IFI6, PSMB8(LMP7), 2'-5'-oligoadenylate synthetase, STAT1, Mx, RIG-G, PML, STAT2, Ceb1, USP18, GBP1	
negative regulation of viral genome replication	46	14	2.93E-18	8.87E-16	OASL, FAM111A, IFITM2, IFI56, PKR, IFI17, APOBEC3F, ISG20, OAS1, 2'-5'-oligoadenylate synthetase, Mx, APOBEC3G, PL scramblase 1, ISG15	
innate immune response	985	40	1.67E-16	4.21E-14	UBCH8, HSP90, OASL, UNC93B, PLA2, IFITM2, ISG54, IRF7, RPK3, IFI56, MyD88, Beta-defensin 1, ADAR1, ZBP1, PKR, IFI17, RPK2, MDA-5, RIG-I, OAS2, APOBEC3F, EFP, ISG20, MOV-10, Fc gamma RI, OAS1, TLR2, HSP90 alpha, 2'-5'-	
immune response	1505	28	2.10E-12	4.53E-10	MICB, OASL, IL-15, IFITM2, Tapasin, IGFBP, MyD88, Beta-defensin 1, IL-6, OAS2, IL1RN, Fc gamma RI, Galpha(i)-specific Class A Orphan/other GPCRs, Fc gamma RII beta, IFP 35, OAS1, IFI6, TLR2, 2'-5'-oligoadenylate synthetase, Mx	
interferon-gamma-mediated signaling pathway	94	13	1.58E-11	2.98E-09	OASL, IRF7, IGFBP, OAS2, Fc gamma RI, OAS1, 2'-5'-oligoadenylate synthetase, STAT1, PML, GBP1, GBP2, STAT1/STAT2, SOCS1	
modulation by virus of host morphology or physiology	524	26	2.36E-11	3.97E-09	MICB, FAM111A, IRF7, RPK3, IFI56, DYNLT, ZBP1, PKR, MDA-5, RIG-I, EFP, Dynein, axonemal, light chains, Fc gamma RII beta, PSMB8(LMP7), Tctex-1, STAT1, PML, STAT2, APOBEC3G, Staf-50, TBK1, STAT1/STAT2, GCN5, LTRB(TNFR	
defense response to Gram-positive bacterium	66	9	2.58E-08	3.90E-06	PLA2, MyD88, IL-6, RPK2, GBP6, TLR2, GBP1, TBK1, GBP2	

# Table S1 (Continued)

## (Clusters 3 and 4)

Cluster	Enrichment by	Pathway Maps	Total	In Data	p-value	FDR	Network Objects from Active Data	
Cluster 3: Antigen presentation / Myeloid Precursor (n=146)	Enrichment by Pathway Maps	Signal transduction_Calcium signaling	45	3	1.18E-03	1.51E-01	Ca-ATPase2, Phospholamban, MEF2	
		PGE2 pathways in cancer	55	3	2.11E-03	1.51E-01	Tcf(Lef), Lef-1, PGE2R4	
		wtCFTR and deltaF508-CFTR traffic / Clathrin coated vesicles formation (normal and CF)	20	2	3.86E-03	1.84E-01	PICALM, Eps15	
		Immune response_Antigen presentation by MHC class I	28	2	7.50E-03	2.31E-01	Tapasin, MHC class I	
		Immune response_IL-6 signaling pathway	31	2	9.14E-03	2.31E-01	IL6RA, sIL6-RA	
		Glycogen metabolism	38	2	1.35E-02	2.31E-01	UGPA1, UGPA2	
		Regulation of lipid metabolism_PPAR regulation of lipid metabolism	42	2	1.64E-02	2.31E-01	Fatty acid-binding protein, ACADM	
		Vitamin B7 (biotin) metabolism	47	2	2.03E-02	2.31E-01	Histone H2, BPL1	
		Immune response_Function of ME2 in T lymphocytes	51	2	2.36E-02	2.31E-01	MEF2A, MEF2	
		Development_Beta-adrenergic receptors signaling via cAMP	52	2	2.45E-02	2.31E-01	Ca-ATPase2, Phospholamban	
		Enrichment by Process Networks	Immune response_Antigen presentation	197	5	6.89E-03	4.42E-01	HLA-C, Tapasin, MHC class I, TRAF6, HLA-Cw3
			Cardiac development_Wnt_beta-catenin, Notch, VEGF, IP3 and Integrin signaling	150	4	1.32E-02	4.42E-01	MEF2A, Tcf(Lef), Phospholamban, MEF2
	Development_Ossification and bone remodeling		157	4	1.54E-02	4.42E-01	Lef-1, Galpha(s)-specific prostanoid GPCRs, TRAF6, PGE2R4	
	Transcription_Chromatin modification		128	3	4.37E-02	7.60E-01	Histone H2, Histone H2B, SDS3	
	Immune response_Phagosome in antigen presentation		243	4	6.15E-02	7.60E-01	HLA-C, Tapasin, MHC class I, HLA-Cw3	
	Protein folding_Response to unfolded proteins		69	2	6.72E-02	7.60E-01	XPB1, HSP10 (mitochondrial)	
	Apoptosis_Apoptotic nucleus		159	3	7.40E-02	7.60E-01	Apaf-1, BAG5, Histone H2B	
	Inflammation_Complement system		73	2	7.41E-02	7.60E-01	C1qc, CR1	
	Inflammation_NK cell cytotoxicity		164	3	7.95E-02	7.60E-01	HLA-C, MHC class I, Histone H2B	
	Apoptosis_Endoplasmic reticulum stress pathway		87	2	1.00E-01	7.76E-01	Apaf-1, XPB1	
	Enrichment by GO Processes		antigen processing and presentation of peptide antigen via MHC class I	157	9	1.36E-07	5.74E-05	HLA-C, HLA-Cw4, ITGB5, Sec24, Tapasin, MHC class I, Sec24A, HLA-Cw7, HLA-Cw3
			antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-independent	24	5	1.68E-07	5.74E-05	HLA-C, HLA-Cw4, MHC class I, HLA-Cw7, HLA-Cw3
		immune response	1505	15	2.13E-07	5.74E-05	HLA-C, HLA-Cw4, C1qb, Tapasin, PRG2, C1qc, Tcf(Lef), MHC class I, Galpha(s)-specific prostanoid GPCRs, XPB1, TRAF6, HLA-Cw7, PGE2R4, Fc alpha receptor, HLA-Cw3	
		positive regulation of cell proliferation in bone marrow	6	3	1.54E-06	3.12E-04	Tcf(Lef), Lef-1, MEF2	
antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-dependent		111	7	2.45E-06	3.95E-04	HLA-C, HLA-Cw4, ITGB5, Tapasin, MHC class I, HLA-Cw7, HLA-Cw3		
antigen processing and presentation of exogenous peptide antigen via MHC class I		118	7	3.68E-06	4.95E-04	HLA-C, HLA-Cw4, ITGB5, Tapasin, MHC class I, HLA-Cw7, HLA-Cw3		
type 1 interferon-mediated signaling pathway		87	6	7.88E-06	9.09E-04	HLA-C, HLA-Cw4, MHC class I, SP100, HLA-Cw7, HLA-Cw3		
positive regulation of T cell mediated cytotoxicity		56	5	1.10E-05	1.11E-03	HLA-C, HLA-Cw4, MHC class I, HLA-Cw7, HLA-Cw3		
interferon-gamma-mediated signaling pathway		94	6	1.23E-05	1.11E-03	HLA-C, HLA-Cw4, MHC class I, SP100, HLA-Cw7, HLA-Cw3		
negative regulation of apoptotic process in bone marrow		3	2	2.92E-05	1.72E-03	Tcf(Lef), Lef-1		
Cluster 4: Innate Immune Response, IL-17/IL-1 Signaling (n=130)		Enrichment by Pathway Maps	Immune response_TLR2 and TLR4 signaling pathways	57	8	1.25E-10	2.80E-08	I-kB, COX-2 (PTGS2), TLR4, TAB2, TPL2(MAP3K8), IL-1 beta, IL-8, Pellino 1
			Immune response_MIF in innate immunity response	40	7	3.95E-10	4.42E-08	I-kB, COX-2 (PTGS2), TLR4, TAB2, C/EBPbeta, IL-1 beta, IL-8
	Immune response_HSP60 and HSP70/TLR signaling pathway		54	7	3.58E-09	2.67E-07	I-kB, CD83, TLR4, TAB2, TPL2(MAP3K8), IL-1 beta, IL-8	
	Immune response_Role of PKR in stress-induced antiviral cell response		57	7	5.29E-09	2.96E-07	I-kB, IRF1, TLR4, TAB2, IL-1 beta, IL-8, NFKBIA	
	Immune response_IL-1 signaling pathway		44	6	3.79E-08	1.70E-06	I-kB, IRF1, COX-2 (PTGS2), TAB2, IL-1 beta, IL-8	
	Immune response_TLR5, TLR7, TLR8 and TLR9 signaling pathways		48	6	6.51E-08	2.36E-06	I-kB, IRF1, TAB2, TPL2(MAP3K8), IL-1 beta, IL-8	
	Immune response_Bacterial infections in normal airways		49	6	7.39E-08	2.36E-06	I-kB, IRF1, TLR4, TAB2, IL-1 beta, IL-8	
	Apoptosis and survival_Role of PKR in stress-induced apoptosis		53	6	1.20E-07	3.35E-06	p21, I-kB, IRF1, TLR4, TAB2, NFKBIA	
	Immune response_TREM1 signaling pathway		59	6	2.30E-07	5.71E-06	I-kB, TLR4, TREM1, IL-1 beta, IL-8, NFKBIA	
	Immune response_IL-17 signaling pathways		60	6	2.55E-07	5.71E-06	I-kB, COX-2 (PTGS2), C/EBPbeta, IL-1 beta, IL-8, CCL7	
	Enrichment by Process Networks		Immune response_Th17-derived cytokines	98	9	1.33E-07	1.45E-05	I-kB, COX-2 (PTGS2), TIMP1, C/EBPbeta, IL-1 beta, C/EBP, IL-8, Mcl-1, CCL7
			Inflammation_TREM1 signaling	145	9	3.72E-06	2.03E-04	I-kB, CD83, TIMP1, TLR4, TREM1, IL-1 beta, IL-8, NFKBIA, CCL7
		Inflammation_IL-10 anti-inflammatory response	87	7	8.93E-06	3.25E-04	I-kB, TIMP1, TLR4, TREM1, IL-1 beta, IL-8, NFKBIA	
		Inflammation_MIF signaling	140	8	2.48E-05	6.75E-04	I-kB, COX-2 (PTGS2), TLR4, IL-1 beta, ETS, IL-8, NFKBIA, ETS2	
		Inflammation_IFN-gamma signaling	110	6	3.56E-04	7.75E-03	p21, I-kB, IRF1, TLR4, C/EBPbeta, NFKBIA	
		Development_Regulation of angiogenesis	223	8	6.31E-04	1.09E-02	p21, I-kB, PLAU (uPAR), HB-EGF, TAB2, IL-1 beta, IL-8, HIF1A	
		Cell adhesion_Platelet-endothelium-leucocyte interactions	174	7	7.19E-04	1.09E-02	I-kB, PLAU (uPAR), IL-1 beta, OBP22/MSR1(CD204), IL-8, PAI2, NFKBIA	
		Cell cycle_G1-S Interleukin regulation	128	6	7.98E-04	1.09E-02	p21, I-kB, JunB, IL-1 beta, IL-8, NFKBIA	
		Inflammation_Innate inflammatory response	181	7	9.08E-04	1.09E-02	I-kB, COX-2 (PTGS2), TLR4, TAB2, IL-1 beta, IL-8, NFKBIA	
		Proliferation_Negative regulation of cell proliferation	184	7	1.00E-03	1.09E-02	p21, CCL3L1, COX-2 (PTGS2), BTG3, IL-1 beta, IL-8, Oncostatin M	
		Enrichment by GO Processes	positive regulation of transcription from RNA polymerase II promoter	1023	22	2.46E-08	2.26E-05	NURR1, MaFb, I-kB, PIAS2, CCL3L1, IRF1, AXUD1, JunB, FOXP1, TLR4, DDX3X, C/EBPbeta, IL-1 beta, ETS, C/EBP, Oncostatin M, PSM09, FOXP1/2/4 proteins, NFKBIA, NOR1, ETS2, HIF1A
			immune response	1505	16	4.31E-08	2.26E-05	CCL3L1, E4BP4, CCL4L1, GPR65, TLR4, C/EBPbeta, IL-1 beta, ETS, CD1b, C/EBP, IL-8, Oncostatin M, EB12, chemokine (C-C motif) ligand 4-like 1, CCL14, CCL7
	negative regulation of apoptotic process		1022	18	6.08E-07	2.12E-04	p21, I-kB, PLAU (uPAR), TIMP1, DDX3X, Pim-3, C/EBPbeta, IL-1 beta, IEX1, C/EBP, PAI2, SON, PSM09, Mcl-1, NFKBIA, NOR1, Albumin, HIF1A	
	lipopolysaccharide-mediated signaling pathway		41	5	3.01E-06	7.88E-04	I-kB, CCL3L1, TLR4, IL-1 beta, NFKBIA	
positive regulation of transcription, DNA-dependent	1383		16	3.78E-06	7.92E-04	NURR1, I-kB, PIAS2, IRF1, FOXP1, C/EBPbeta, IL-1 beta, ETS, C/EBP, ID2, PSM09, Trp53inp2, FOXP1/2/4 proteins, NFKBIA, ETS2, HIF1A		
apoptotic process	1325		17	1.28E-05	1.81E-03	I-kB, AXUD1, GPR65, KLF11 (TIEG2), DDX3X, Pim-3, IL-1 beta, IEX1, GPR109A, G0/G1switch 2, Oncostatin M, PSM09, Mcl-1, TIEG, MCP1P, NFKBIA, FEM1B		
negative regulation of cell proliferation	802		13	1.60E-05	1.81E-03	p21, CCL3L1, IRF1, COX-2 (PTGS2), KLF11 (TIEG2), BTG3, IL-1 beta, ETS, C/EBP, IL-8, Oncostatin M, TIEG, Ctmn		
toll-like receptor signaling pathway	159		7	1.61E-05	1.81E-03	I-kB, Cathespins L, MKP-3, TLR4, TAB2, Pellino 1, NFKBIA		
toll-like receptor TLR6:TLR2 signaling pathway	98		6	1.73E-05	1.81E-03	I-kB, MKP-3, TLR4, TAB2, Pellino 1, NFKBIA		
toll-like receptor TLR1:TLR2 signaling pathway	98		6	1.73E-05	1.81E-03	I-kB, MKP-3, TLR4, TAB2, Pellino 1, NFKBIA		

Table S1 (Continued)

(Clusters 5 and 6)

	Total	In Data	p-value	FDR	Network Objects from Active Data
<b>Cluster 5: Hematopoiesis (n=75)</b>					
<b>Enrichment by Pathway Maps</b>					
Transcription_Transcription regulation of aminoacid metabolism	25	2	1.67E-03	1.56E-01	ALAS2, FECH
Apoptosis and survival_BAD phosphorylation	42	2	4.68E-03	1.66E-01	Bcl-XL, PP2C
Mitochondrial unsaturated fatty acid beta-oxidation	45	2	5.36E-03	1.66E-01	ACSL6, HADHB
Mitochondrial long chain fatty acid beta-oxidation	83	2	1.74E-02	1.89E-01	ACSL6, HADHB
Heme metabolism	105	2	2.71E-02	1.89E-01	ALAS2, FECH
Mechanism of Ploglitazone/ Metformin and Rosiglitazone/ Metformin cooperative action in Diabetes mellitus, Type 2	16	1	3.87E-02	1.89E-01	AdipoR1
Cell cycle_Cell cycle (generic schema)	21	1	5.05E-02	1.89E-01	E2F2
Transcription_CHREBP regulation pathway	21	1	5.05E-02	1.89E-01	Acyl-CoA synthetase
Development_Thrombopoietin signaling via JAK-STAT pathway	22	1	5.28E-02	1.89E-01	Bcl-XL
Immune response_IL-15 signaling via JAK-STAT cascade	23	1	5.52E-02	1.89E-01	Bcl-XL
<b>Enrichment by Process Networks</b>					
Cell cycle_G0-G1	71	3	9.52E-04	4.95E-02	E2F2, PP2C alpha, p18
Transport_Iron transport	108	2	3.61E-02	4.71E-01	PP2C alpha, FECH
Cell cycle_Core	115	2	4.05E-02	4.71E-01	E2F2, p18
DNA damage_Checkpoint	124	2	4.64E-02	4.71E-01	SNM1, GADD45 alpha
Development_Hemopoiesis, Erythropoietin pathway	136	2	5.47E-02	4.71E-01	Bcl-XL, HBG1
Response to hypoxia and oxidative stress	163	2	7.53E-02	4.71E-01	p18, GPX4 (PHGpx)
Cytoskeleton_Actin filaments	176	2	8.59E-02	4.71E-01	Tropomodulin, EPB41
Cytoskeleton_Regulation of cytoskeleton rearrangement	183	2	9.18E-02	4.71E-01	Tropomodulin, EPB41
Cell adhesion_Amyloid proteins	195	2	1.02E-01	4.71E-01	BACE2, Bcl-XL
Autophagy_Autophagy	55	1	1.43E-01	4.71E-01	Bcl-XL
<b>Enrichment by GO Processes</b>					
oxygen transport	20	4	5.08E-07	2.65E-04	HBG, HGBA, HBG1, Adult hemoglobin
fatty acid metabolic process	35	7	3.42E-06	8.93E-04	ACSL6, ACSM3, HADHB, Acyl-coenzyme A synthetase ACSM3, mitochondrial precursor, AdipoR1, Alpha-nuclein, Acyl-CoA synthetase
response to lead ion	35	4	5.29E-06	9.20E-04	ALAS2, Bcl-XS, Bcl-XL, FECH
apoptotic process in bone marrow	2	2	1.08E-05	1.41E-03	Bcl-XS, Bcl-XL
positive regulation of plasma membrane long-chain fatty acid transport	3	2	3.22E-05	2.74E-03	ACSL6, Acyl-CoA synthetase
suppression by virus of host apoptotic process	3	2	3.22E-05	2.74E-03	Bcl-XS, Bcl-XL
cell cycle arrest	194	6	3.67E-05	2.74E-03	ILP1P, PP2C alpha, p18, PP2C, Sestrin 3, GADD45 alpha
heme biosynthetic process	24	3	5.09E-05	2.80E-03	SLC25A39, ALAS2, FECH
protein heterooligomerization	160	5	5.22E-05	2.80E-03	HBG, HGBA, PINCH, HBG1, Adult hemoglobin
response to cycloheximide	7	2	6.43E-05	2.80E-03	Bcl-XS, Bcl-XL
<b>Cluster 6: Undefined (n=324)</b>					
<b>Enrichment by Pathway Maps</b>					
CFTR folding and maturation (normal and CF)	21	4	5.78E-05	1.20E-02	HSP70, HSP40, UGCGL1, HSP105
Transport_Clathrin-coated vesicle cycle	71	6	9.03E-05	1.20E-02	Rab11-FIP1, Syntaxin 5, GOS-28, SAR1, Syntaxin 12, Rab11-FIP2
Transcription_Transcription regulation of aminoacid metabolism	25	4	1.18E-04	1.20E-02	NFE2L1, NRF2, c-Myc, KEAP1
Apoptosis and survival_Role of IAP-proteins in apoptosis	31	4	2.81E-04	2.13E-02	HSP70, TNF-R1, c-IAP2, Bax
Apoptosis and survival_TNFR1 signaling pathway	43	4	1.00E-03	6.08E-02	Caspase-2, TNF-R1, c-IAP2, Bax
Development_G-CSF signaling	49	4	1.64E-03	7.25E-02	CXCR4, c-IAP2, c-Myc, IL8RB
Development_ERKS in cell proliferation and neuronal survival	23	3	1.67E-03	7.25E-02	Sequestosome 1(p62), Rap 1, c-Fos
Apoptosis and survival_Role of PKR in stress-induced apoptosis	53	4	2.19E-03	8.33E-02	TRAM, TNF-R1, TARBP2, c-Myc
Development_EGFR signaling via small GTPases	33	3	4.77E-03	1.44E-01	VAV-2, c-Myc, c-Fos
Apoptosis and survival_Caspase cascade	33	3	4.77E-03	1.44E-01	Caspase-2, TNF-R1, Bax
<b>Enrichment by Process Networks</b>					
Development_Blood vessel morphogenesis	228	11	5.76E-04	6.68E-02	Galpha(s)-specific nucleotide-like GPCRs, CRK, Galpha(i)-specific amine GPCRs, Galpha(q)-specific peptide GPCRs, PDE, CXCR4, PDE9A, Galpha(i)-specific peptide GPCRs, Galpha(q)-specific nucleotide-like GPCRs, c-Myc, c-Fos
Chemotaxis	137	8	9.89E-04	6.68E-02	CX3CR1, FPRL2, Galpha(q)-specific peptide GPCRs, FPR, NCAM1, Galpha(i)-specific peptide GPCRs, CCR7, IL8RB
Protein folding_Response to unfolded proteins	69	5	3.61E-03	1.63E-01	HSP70, HSP40, HSPA1A, HSP105, HSPA1B
Development_ERKS in cell proliferation and neuronal survival	24	3	5.27E-03	1.78E-01	Sequestosome 1(p62), c-Myc, c-Fos
Protein folding_Folding in normal condition	119	6	8.70E-03	2.35E-01	NFYC, HSP70, HSP40, HSPA1A, HSP105, HSPA1B
Reproduction_Feeding and Neurohormone signaling	211	8	1.36E-02	3.06E-01	HSP70, Galpha(q)-specific peptide GPCRs, Galpha(q)-specific Class A Orphan/other GPCRs, Galpha(i)-specific peptide GPCRs, c-Myc, c-Fos, LAMG1, Bax
Apoptosis_Anti-Apoptosis mediated by external signals via MAPK and JAK/STAT	179	7	1.76E-02	3.40E-01	CRK, VAV-2, c-IAP2, c-Myc, MEK4(MAP3K4), c-Fos, Bax
Inflammation_Inflammasome	118	5	3.17E-02	4.99E-01	TRAM, TNF-R1, TLR8, NALP12, Nod2 (CARD15)
Cell adhesion_Leucocyte chemotaxis	205	7	3.38E-02	4.99E-01	CX3CR1, Galpha(q)-specific peptide GPCRs, CXCR4, Galpha(i)-specific peptide GPCRs, CCR7, CaMK II delta, IL8RB
Apoptosis_Death Domain receptors & caspases in apoptosis	123	5	3.70E-02	4.99E-01	Caspase-2, TNF-R1, c-IAP2, NALP12, Nod2 (CARD15)
<b>Enrichment by GO Processes</b>					
regulation of vasodilation	64	10	6.77E-13	1.38E-09	Galpha(i)-specific amine GPCRs, Galpha(i)-specific nucleotide-like GPCRs, P2Y2, Guanylate cyclase, Galpha(q)-specific peptide GPCRs, Beta-2 adrenergic receptor, Beta-adrenergic receptor, Galpha(i)-specific peptide GPCRs, Galpha
G-protein coupled purinergic nucleotide receptor signaling pathway	18	7	2.75E-09	2.79E-06	Galpha(s)-specific nucleotide-like GPCRs, Galpha(i)-specific nucleotide-like GPCRs, P2Y2, P2Y10, Galpha(q)-specific Class A Orphan/other GPCRs, Galpha(q)-specific nucleotide-like GPCRs, GPR86
positive regulation of vasodilation	43	9	6.83E-09	4.62E-06	Galpha(s)-specific nucleotide-like GPCRs, Urocortin, Galpha(i)-specific amine GPCRs, Galpha(q)-specific peptide GPCRs, Beta-2 adrenergic receptor, Beta-adrenergic receptor, Galpha(i)-specific peptide GPCRs, Galpha(q)-specific nu
regulation of systemic arterial blood pressure by norepinephrine-epinephrine	17	4	3.78E-08	1.38E-05	Galpha(i)-specific amine GPCRs, Beta-2 adrenergic receptor, Beta-adrenergic receptor, Galpha(s)-specific amine GPCRs
positive regulation of the force of heart contraction by epinephrine	4	4	3.78E-08	1.38E-05	Galpha(i)-specific amine GPCRs, Beta-2 adrenergic receptor, Beta-adrenergic receptor, Galpha(s)-specific amine GPCRs
Inflammatory response	593	24	4.43E-08	1.38E-05	Galpha(s)-specific nucleotide-like GPCRs, K(+) channel, subfamily J, Urocortin, Galpha(i)-specific amine GPCRs, TRAM, Galpha(i)-specific nucleotide-like GPCRs, C/EBP, FPRL2, Galpha(q)-specific peptide GPCRs, TNF-R1, TLR8, Galpha
regulation of calcium ion transport	221	9	4.75E-08	1.38E-05	Galpha(s)-specific nucleotide-like GPCRs, Galpha(i)-specific amine GPCRs, Galpha(q)-specific peptide GPCRs, Beta-2 adrenergic receptor, CXCR4, Beta-adrenergic receptor, Galpha(i)-specific peptide GPCRs, Galpha(q)-specific nu
negative regulation of ossification	48	7	1.94E-07	4.00E-05	Galpha(i)-specific amine GPCRs, Galpha(i)-specific nucleotide-like GPCR, P2Y2, Beta-2 adrenergic receptor, Beta-adrenergic receptor, Galpha(q)-specific peptide GPCRs, Galpha(s)-specific amine GPCRs
microglial cell activation involved in immune response	11	5	2.25E-07	4.00E-05	CX3CR1, TLR8, Galpha(i)-specific peptide GPCRs, TLR6, Nod2 (CARD15)
negative regulation of urine volume	11	5	2.25E-07	4.00E-05	Galpha(i)-specific amine GPCRs, Galpha(q)-specific peptide GPCRs, Beta-2 adrenergic receptor, Beta-adrenergic receptor, Galpha(s)-specific amine GPCRs

Table S1 (Continued)

(Clusters 7 and 8)

	Total	In Data	p-value	FDR	Network Objects from Active Data
<b>Cluster 7: Cytotoxic Lymphocyte Proliferation (n=149)</b>					
<b>Enrichment by Pathway Maps</b>					
Immune response_Role of DAP12 receptors in NK cells	54	6	1.37E-06	2.65E-04	PI3K cat class IA, Lck, KIR2DL3, KIR2DL4, ZAP70, CD94
Cell cycle_Start of DNA replication in early S phase	32	5	1.95E-06	2.65E-04	MCM4, MCM3, HP1 alpha, Histone H1, Cyclin E
Cytoskeleton remodeling_Role of PDGFs in cell migration	24	4	1.72E-05	1.56E-03	PI3K cat class IA, PDGF receptor, Tiam1, PDGF-R-beta
Cell cycle_Transition and termination of DNA replication	28	4	3.25E-05	2.21E-03	TOP2 alpha, TOP2, Cyclin A, Brca1
G-protein signaling_H-RAS regulation pathway	37	4	1.00E-04	5.06E-03	PI3K cat class IA, Tiam1, PDGF-R-beta, Lck
Cell cycle_Regulation of G1/S transition (part 1)	38	4	1.12E-04	5.06E-03	PP2A regulatory, Cyclin A, Brca1, Cyclin E
Cell cycle_Chromosome condensation in prometaphase	21	3	3.45E-04	1.20E-02	TOP2, Cyclin A, Histone H1
Some pathways of EMT in cancer cells	51	4	3.54E-04	1.20E-02	PI3K cat class IA, PDGF receptor, Axin, PDGF-R-beta
Neurophysiological process_Dopamine D2 receptor transactivation of PDGFR in CNS	26	3	6.59E-04	1.99E-02	PDGF receptor, PP2A regulatory, PDGF-R-beta
Apoptosis and survival_Granzyme A signaling	30	3	1.01E-03	2.08E-02	Histone H1, Perforin, Granzyme A
<b>Enrichment by Process Networks</b>					
Cell cycle_S phase	149	13	2.48E-09	2.95E-07	MCM4, Histone H4, MCM3, TOP2 alpha, TOP2, HP1, Cyclin A2, HP1 alpha, Cyclin A, Brca1, Histone H1, Cyclin E, CDC14a
Inflammation_NK cell cytotoxicity	164	10	5.55E-06	2.60E-04	PPP2R2B, IL-2R beta chain, Lck, KIR2DL3, Histone H1, KIR2DL4, ZAP70, CD94, Perforin, Granzyme A
Cell cycle_G2-M	206	11	6.55E-06	2.60E-04	PDGF receptor, TOP2 alpha, UBE2C, TOP2, Cyclin A2, Cyclin A, CDC20, PDGF-R-beta, Brca1, Histone H1, CDC14a
Cell cycle_Core	115	8	1.99E-05	5.93E-04	MCM4, MCM3, TOP2, HP1 alpha, Cyclin A, CDC20, Cyclin E, CDC14a
Cell cycle_G1-S	163	9	3.75E-05	8.93E-04	Axin, TYSY, UHRF1, Cyclin A2, Cyclin A, Brca1, Cyclin E, CDC14a, Axin1
Cell cycle_Mitosis	179	9	7.80E-05	1.55E-03	TTK, Tubulin beta, TOP2, HP1, HP1 alpha, Cyclin A, CDC20, Histone H1, HDAC6
Cytoskeleton_Spinidie microtubules	109	7	1.13E-04	1.93E-03	MKLP2, TTK, Tubulin beta, UBE2C, CDC20, CDC14a, Sororin
Immune response_TCR signaling	174	8	3.69E-04	5.49E-03	CD8 alpha, PI3K cat class IA, MADD, CD8, Lck, SKAP55, ZAP70, CD3 gamma
Cell cycle_Meiosis	106	6	7.06E-04	9.34E-03	PI3K cat class IA, Tubulin beta, PP2A regulatory, Cyclin A, CDC20, Brca1
Cell cycle_G1-S Growth factor regulation	195	8	7.88E-04	9.37E-03	PI3K cat class IA, PPP2R2B, Cyclin A2, PP2A regulatory, FGF9, Cyclin A, Cyclin E, PI3K cat class IA (p110-beta)
<b>Enrichment by GO Processes</b>					
phosphatidylinositol-mediated signaling	178	11	1.33E-08	1.79E-05	Histone H4, PI3K cat class IA, PDGF receptor, TOP2 alpha, TYSY, UBE2C, TOP2, FGF9, PDGF-R-beta, Lck, PI3K cat class IA (p110-beta)
cell surface receptor signaling pathway	3985	14	3.40E-08	2.28E-05	CD8 alpha, PI3K cat class IA, MADD, IL7RA, CD8, CBL-B, LAG3, Lck, KLR1, Galpha(q)-specific peptide GPCRs, CD3 gamma, CD94, DR3(TNFRSF12), Fc epsilon RI alpha
positive regulation of phosphoprotein phosphatase activity	14	4	1.32E-06	5.92E-04	PDGF receptor, PP2A regulatory, PDGF-R-beta, Galpha(q)-specific peptide GPCRs
mitotic cell cycle	852	14	3.21E-06	8.90E-04	MCM4, MCM3, TOP2 alpha, Tubulin beta, TYSY, CEP164, UBE2C, TOP2, Cyclin A2, PP2A regulatory, Cyclin A, CDC20, Cyclin E, Sororin
embryonic cleavage	16	4	3.32E-06	8.90E-04	PI3K cat class IA, TOP2 alpha, TOP2, PI3K cat class IA (p110-beta)
cell activation	269	6	5.34E-06	1.19E-03	CD8 alpha, PI3K cat class IA, CD8, CBL-B, ZAP70, CD3 gamma
transmembrane receptor protein tyrosine kinase signaling pathway	705	7	9.98E-06	1.70E-03	CD8 alpha, PI3K cat class IA, PDGF receptor, CD8, PDGF-R-beta, Galpha(q)-specific peptide GPCRs, PI3K cat class IA (p110-beta)
mast cell chemotaxis	7	3	1.01E-05	1.70E-03	PI3K cat class IA, CCR3, Galpha(q)-specific peptide GPCRs
Wnt receptor signaling pathway involved in somitogenesis	9	3	2.41E-05	2.31E-03	Axin, PP2A regulatory, Axin1
platelet aggregation	26	4	2.59E-05	2.31E-03	PI3K cat class IA, PDGF receptor, Tspan32, PI3K cat class IA (p110-beta)
<b>Cluster 8: Undefined (n=45)</b>					
<b>Enrichment by Pathway Maps</b>					
Glycolysis and gluconeogenesis p.3 / Human version	24	2	1.13E-03	4.23E-02	ENO, ENO2
Glycolysis and gluconeogenesis p.3	24	2	1.13E-03	4.23E-02	ENO, ENO2
Muscle contraction_Relaxin signaling pathway	48	2	4.48E-03	9.82E-02	MMP-9, p90Rsk
Cell adhesion_ECM remodeling	52	2	5.24E-03	9.82E-02	MMP-9, SERPINE2
Development_c-Kit ligand signaling pathway during hemopoiesis	61	2	7.15E-03	1.04E-01	MMP-9, p90Rsk
Glycolysis and gluconeogenesis (short map)	66	2	8.32E-03	1.04E-01	ENO, ENO2
Cytoskeleton remodeling_RalB regulation pathway	13	1	2.71E-02	1.42E-01	REF52
Protein folding_Membrane trafficking and signal transduction of G-alpha (i) heterotrimeric G-protein	19	1	3.94E-02	1.42E-01	G-protein gamma
Cell cycle_Chromosome condensation in prometaphase	21	1	4.34E-02	1.42E-01	Histone H1
Role of ZNF202 in regulation of expression of genes involved in atherosclerosis	21	1	4.34E-02	1.42E-01	LCAT
<b>Enrichment by Process Networks</b>					
Muscle contraction_Relaxin signaling	83	2	1.44E-02	4.12E-01	MMP-9, p90Rsk
Proteolysis_Connective tissue degradation	119	2	2.84E-02	4.12E-01	MMP-9, SERPINE2
Reproduction_FSH-beta signaling pathway	160	2	4.88E-02	4.12E-01	p90Rsk3(RPS6KA2), p90Rsk
Cell adhesion_Platelet-endothelium-leucocyte interactions	174	2	5.67E-02	4.12E-01	MMP-9, SERPINE2
Development_Neurogenesis in general	192	2	6.74E-02	4.12E-01	p90Rsk3(RPS6KA2), SERPINE2
Cell cycle_G2-M	206	2	7.63E-02	4.12E-01	Histone H1, p90Rsk
Development_EMT_Regulation of epithelial-to-mesenchymal transition	226	2	8.95E-02	4.12E-01	MMP-9, p90Rsk
Development_Blood vessel morphogenesis	228	2	9.09E-02	4.12E-01	PDE, Prokineticin 2
Neurophysiological process_Melatonin signaling	43	1	9.22E-02	4.12E-01	STS
Reproduction_Male sex differentiation	246	2	1.03E-01	4.12E-01	Histone H1, Prokineticin 2
<b>Enrichment by GO Processes</b>					
positive regulation of G-protein coupled receptor protein signaling pathway	28	3	9.77E-06	2.23E-03	PDE6 reg, PDE, PDE6H
cardiac muscle cell apoptotic process	16	3	9.77E-06	2.23E-03	G-protein gamma, p90Rsk3(RPS6KA2), p90Rsk
regulation of autophagy	85	3	1.68E-05	2.56E-03	ULK1, Uncharacterized protein C20orf117, SOGA1
positive regulation of epidermal growth factor receptor signaling pathway	36	3	2.30E-05	2.62E-03	PDE6 reg, PDE, PDE6H
oocyte maturation	24	3	3.48E-05	3.17E-03	p90Rsk3(RPS6KA2), PDE, p90Rsk
activation of MAPK activity	190	5	4.31E-05	3.28E-03	G-protein gamma, PDE6 reg, PDE, PDE6H, Prokineticin 2
regulation of protein processing	62	2	6.93E-05	4.52E-03	p90Rsk3(RPS6KA2), p90Rsk
mitotic metaphase	6	2	1.04E-04	5.92E-03	p90Rsk3(RPS6KA2), p90Rsk
nucleosome positioning	7	2	1.45E-04	7.35E-03	Histone H1.2, Histone H1
cellular response to carbohydrate stimulus	103	2	1.93E-04	8.81E-03	p90Rsk3(RPS6KA2), p90Rsk