

Supplementary Table S9: Uniquely Genes Ontologies enriched in Mild / Moderate Severity group

Unique Gene Ontologies identified from comparison between control and Mld / Moderate genes (n = 328 genes)	PValue
Control+Mld	
regulation_of_mitrosome, polymerization , depolymerization	0.0407585636, SKA1, SKA2
negative_regulation_of_immune_response	0.05507554 COL3A1, LILRA1, FOPX2
negative regulation_of_inflammatory_response	0.063805817 RILP, LARA, ACOD1, RPTN, CTDSP2
chromosome_segregation	0.0675181 NCK2, BULB, SKA1, SKA2
cellular_localization, beta -tubulin_beta	0.06869731 ACCD1, IFITC, RPTN, CTDSP2
digestive tract_development	0.07037141 TBL1XR1, RPL22, RPL22L
cellular_response_to_hypoxia	0.0745511836 CANBL, BNIP3, SLC2A1
response_to_mechanical_stimulus	0.14187972 COL3A1, JUN, CNTR
positive_regulation_of_fibroblast_proliferation	0.14451935 JUN, CTDSP2, RPL22
negative_regulation_of_NF-kappaB_transcription_factor_activity	0.1458738136 CTDSP2, RPL22, FOPX2
cellular_response_to_cyclic_organic_compound	0.183634871 CCBNL, PAC1, RFLS
cell_matrix_adhesion	0.197770231 COL3A1, ITGAL, EPOR1
embryo_development	0.201945468 CSK, BCL2, EPIC
positive_regulation_of_cell_growth	0.243450043 RPL22, RPL22L, RPL22XL
hematopoietic_progenitor_cell_differentiation	0.275525283 RPS1, GRACH2, 4930A
positive_regulation_of_MAPK_cascade	0.295895927 PEJU, PLK1, PRMT6
response_to_hypoxia	0.327375049 PAK1, PRMT6, BNIP3, RPL22, RPL22L, RPL22XL
cellular_response_to_cell_migration	0.454889814 CISH, RIN1, KIF11
cytokine-mediated_signaling_pathway	0.535033048 AR13, U2F, CELSR3
clium_morphogenesis	0.72296497 LMA10, C1QB, MTERF1
RNA_splicing	

Supplementary Table S9: Unique Gene Ontologies enriched in Severe group

Same Gene Ontologies identified from comparison between control and Severe genes ($n = 38$ genes)	
	PValue
adipose_tissue_development	0.07322301_LRP5, SPCD, PPARD
positive_regulation_of_fat_cell_differentiation	0.1304735 LRP5, B2TB16, LRP5
learning_or_memory	0.13916196_BHBDH, LRP5
embryo_digital_morphogenesis	0.1467444 ZBTB16, LRP5, MAPK1
translational_heteromeric_RNA_polymerase_I	0.2345454 CTDSP1, ACAD5, ACADS
mitochondrion_organization	0.278792455 CXADR, CHCHD10, MAP2
endocytosis	0.415115207 MRC1, LPR5, LDLR, RIN2
anterior/posterior_pattern_specification	0.42292156_ZBTB16, LRP5, RIN2
cellular_protection	0.42320466_ZBTB16, LRP5
positive_regulation_of_angiogenesis	0.46153673_SPAK3, SPHK2, CAMP
peptidyl-serine_phosphorylation	0.510961619 RPS6KA2, STK38, MAPK
regulation_of_cell_shape	0.53462841 EP3S1, CDCA2C, RHOU
positive_regulation_of_ERK1_and_ERK2_cascade	0.6977454 JUN, EGR1, EPOR, HAVCR2

Supplementary Table S9: Unique Gene Ontologies enriched in Severe-specific genes

Mild/Serious	Untested Ontologies identified from comparison between Mild / Moderate and Severe genes ($n = 32$ genes)	PValue
covariant_chirality_modification		0.023964868 CBX8, TSP12, HIRA, PR
RNA_processing		0.021851869 DS52, TNSM4, ZBTB80
intracellular_transport		0.037958175 ACVR1, RPLP0, BCL11A
cellular_assembly_biosynthetic_process		0.040000000 RPLP0, ACVR1, RPLP0
negative_regulation_of_peptidase_activity		0.067215759 ITIH5, SERPINB10, PR
microtubule_cytoskeleton_organization		0.130622533 UXT, MAP3K1, MARK3, TSHZ4
cellular_calcium_content_homeostasis		0.145000000 PRPF8, RPLP0, FANCI, NUDT1
cellular_mitochondrial_ion_cycle		0.153000000 PRPF8, RPLP0, FANCI
cholesterol_metabolic_process		0.323965939 PMVK, LPR5, LDR
ubiquitin-dependent_protein_catabolic_process		0.326029192 USKAM, USP1, FKHD4, HOAC4D
protein_polyubiquitination		0.388911997 USKAM, USP1, FKHD4, HOAC4D

Supplementary Table S9: Common Gene Ontologies in Mild / Moderate and Severe groups

Supplementary Table S9: Common Gene Ontologies in Severe and Severe-specific Groups

Midwives Genes Ontologies identified from comparison between Severe ($n = 383$ genes) and Non-Severe ($n = 352$ genes)	MS_Pvalue
metabolism	0.323964939 PVALB, LDR
metabolic_process	0.388921197 LRSAM1, HKOAC, HDAC1
protein_polyubiquitination	0.136022531 MAP3K1, MARCKS, PRKDC
posttranslational_cytokinesis	0.000200000 RPL22, RPL23A
organization	0.145265183 SLC2AA1, SCY17CA, NUO1
cellular_ionomeric_homeostasis	0.023964686 CBR3, TSPYL19, HRA, PRKDC
covalent_chromatin_modification	0.323964928 FBXW7, USP9X, FBXO4
ubiquitin-dependent_protein_degradation	0.000179101 RPL22, RPL23A
protein_catabolic_process	0.139328424 PUK3, RCHH, RHOU
GI/S_transition_of_mitotic_kinetic_process	0.031295175 ACD, ORK3, RPMLAB, CC
intracellular_protein_transport	0.067215579 ERBB1IP1, SERPINB10, NGF
negative regulation_of_peptidase_activity	

Common Gene Ontologies identified from comparison between Mild / Moderate (n = 328 genes), Severe

	CM_value
Commensal	0.0010201781945, ARL1, CCM1
cell_cycle	0.0010529371445, BNP, TNF
cell_death_process	0.0002063764 CNBR, COKS, PSMC1
cell_division	0.010221031 ACAD, CPM, GPM
metabolic_process	0.0600447 JUN, PAK1, KLF5, GRM8
positive_regulation_of_cell_proliferation	0.0828938 HACDI, GRAP, OSK2, TSHZ3
fast_oxidative_phosphorylation	0.0828938 HACDI, GRAP, OSK2, TSHZ3
response_to_starch	0.138364571 GRPR8, CBL, HMMTR1
response_to_starch	0.244393702 PLCL1, PLAG1, RPS6KA4
positive_regulation_of_gene_expression	0.290519556 MPMP2, TUSC2, ZFP28, ZFP28L
inflammatory_response	0.357364774 GM4325, ZFP28, ZFP28L
regulation_of_transcription,_DNA-templated	0.357364774 GM4325, ZFP28, ZFP28L
immunological_process	0.400900139 CS4H, CX51, RBL2, PP
cell_proliferation	0.400900139 CS4H, CX51, RBL2, PP
intracellular_signal_transduction	0.454203799 PRMT6, BC13, FBXO35
cellular_response_to_DNA_damage_stimulus	0.549729739 PLCL1, TNFRSF18, IL2R
immune_response	0.578123039 NLRP3, NLRP3, NLRP3A
posterior_regulation_of_protein phosphorylation	0.608821363 C4HC4, C1QBP, OAS1A
protein_phosphorylation	0.608821363 C4HC4, C1QBP, OAS1A
innate_immune_response	0.615622922 JUN, TNFRSF18, ACOD1
response_to_lipopolysaccharide	0.621119318 TNFRSF18, BC13, FBXO35
regulation_of_apoptotic_process	0.672830611 ADGRG2, CPRE3, CLRS3
cell_surface_receptor_signaling_pathway	0.760001005 FOMES, HACDI, DACH1
multicellular_organism_development	

Supplementary Table S9. Total Gene Ontologies enriched in Mild / Moderate Group.

Gene ontologies were identified by DAVID pathway analyses of n = 328 unique genes in Mild / Moderate group compared with Control group.	PValue	Genes
Control vs Mild		
cell_cycle	2.70E-04	ZBTB49, ARL3, FOXM1, SKA1, SKA2, ING4, CCNB1, CDC45, PSRC1, NUF2, CKS2, NEK2, KCTD11, PIM3, SPDL1, BUB1, E2F7, LIN52
apoptotic_process	0.001039237	BEX3, DFFB, BNIP3, TNFRSF18, PDCD5, GOS2, FBXO10, GADD45G, ING4, PAK1, PLSCR1, MIEN1, C1QBP, PIM3, BUB1, PPARD
cell_division	0.002068768	CCNB1, CDC45, PSRC1, ARL3, NUF2, CKS2, NEK2, SPDL1, BUB1, SKA1, SPG20, SKA2
methylation	0.002088567	PRMT6, METTL25, CARMNT1, PRMT2, SMYD5, NOP2, HNMT, TRMT61A
phospholipid_biosynthetic_process	0.003425744	GPAM, CHPT1, LCLAT1, CRLS1, PPARD
regulation_of_microtubule_polymerization_or_depolymerization	0.004675858	STMN1, SKA1, SKA2
mitotic_metaphase_plate_congression	0.005377955	CCNB1, PSRC1, RRS1, SPDL1
negative_regulation_of_immune_response	0.005675584	COL3A1, IL2RA, FOXP3
negative_regulation_of_cell_proliferation	0.007552869	ING4, JUN, RPS6KA2, ZBTB49, ITGA1, PDCD5, FUZ, FOXP3, SOX4, IFIT3, E2F7
defense_response_to_virus	0.008492174	PLSCR1, EXOSC4, GPAM, BNIP3, IFIT3, OA51A, IFIT3
positive_regulation_of_apoptotic_process	0.009114764	ING4, PLSCR1, JUN, PRMT2, RPS6KA2, BNIP3, C1QBP, PDCD5, SOX4, GADD45G
DNA_replication	0.009682336	ING4, CDC45, ORC6, RFC4, MCMDC2, DT1
metabolic_process	0.010021031	ACAD8, PAK1, GPAM, NAT2, OXSM, EGOT, ACOD1, ACSBG1, ACSL3, UMP5, LCLAT1, ACAT2
response_to_virus	0.011865461	BCL3, STMN1, OA51A, FOXP3, IFIT3
cellular_process	0.026048354	JUN, PSRC1, PPARD
brain_development	0.026740033	EOMES, SPHK1, STMN1, CTNS, ACSL3, HNMT, EPOR
mitotic_nuclear_division	0.027390632	CCNB1, PSRC1, NUFP2, NEK2, SPDL1, BUB1, SKA1, SKA2
regulation_of_cell_cycle	0.030523021	JUN, PSMG2, E2F5, PRR11, GADD45G
response_to_radiation	0.039410461	COL3A1, JUN, KIT
rRNA_processing	0.040410438	EXOSC4, GM9493, NOP2, MTERF4, RRPP9
heart_development	0.047830088	COL3A1, CXADR, RPS6KA2, MTERF4, EPOR, SOX4, PPARD
positive_regulation_of_cell_proliferation	0.050600447	JUN, PAK1, KLF5, H1X, SPHK1, NOP2, KIT, FOXM1, EPOR, SOX4, PPARD
negative_regulation_of_inflammatory_response	0.063805817	ACOD1, FOXP3, PPARD
chromosome_segregation	0.06735181	NEK2, BUB1, SKA1, SKA2
cellular_response_to_interferon-beta	0.068967231	ACOD1, IFIT3, GM12185
digestive_tract_development	0.071930361	COL3A1, CCNB1, KIT
negative_regulation_of_apoptotic_process	0.076024403	JUN, MIEN1, BNIP3, TNFRSF18, SPHK1, BCL3, PIM3, PSMG2, TAF9B, IFIT3, PPARD
negative_regulation_of_protein_kinase_activity	0.078512511	PKB, CISH, RTN4R1L, GADD45G
fatty_acid_metabolic_process	0.08239829	HACD1, GPAM, OXSM, ACSBG1, ACSL3
positive_regulation_of_transcription_DNA-templated	0.083115457	EOMES, JUN, KLF5, PSRC1, PRMT2, BCL3, CKS2, FOXM1, FOXP3, SOX4, PPARD
cellular_response_to_hypoxia	0.094551368	CCNB1, BNIP3, SLC29A1, PPARD
actin_cytoskeleton_reorganization	0.103610151	PAK1, CXADR, KIT
lipid_metabolic_process	0.111665352	HACD1, GPAM, OXSM, ACSBG1, CHPT1, ACSL3, LCLAT1, CRLS1, PPARD
protein_autophosphorylation	0.126814458	PAK1, KIT, STK39, NEK2, PIM3
response_to_mechanical_stimulus	0.141879272	COL3A1, JUN, CCNB1
positive_regulation_of_fibroblast_proliferation	0.149129155	JUN, CCNB1, SPHK1
negative_regulation_of_NF-kappaB_transcription_factor_activity	0.152781901	PRMT2, ACOD1, FOXP3
fatty_acid_biosynthetic_process	0.182571082	HACD1, OXSM, ACSL3
cellular_response_to_organic_cyclic_compound	0.186354871	CCNB1, PAK1, KLF5
response_to_glucocorticoid	0.186354871	GPR83, ACSBG1, HNMT
actin_cytoskeleton_organization	0.187978658	PAK1, FMNL2, CDC42EP2, FHL3
cell-matrix_adhesion	0.197770231	COL3A1, ITGA1, EPDR1
embryo_development	0.201954568	CKS2, BUB1, EPOR
regulation_of_cell_proliferation	0.214444117	RNF126, TNFRSF18, KCTD11, FOXM1, PPARD
negative_regulation_of_transcription_from_RNA_polymerase_II_promoter	0.238027278	PRMT6, EOMES, JUN, KLF5, DACH1, C1QBP, FOXM1, TAF9B, FOXP3, E2F7, PPARD
positive_regulation_of_gene_expression	0.243397082	PLSCR1, PLAG1, RPS6KA2, PDCD5, KIT, FOXP3, PPARD
positive_regulation_of_cell_growth	0.244102541	EXOSC4, SPHK1, TAF9B
wound_healing	0.259674433	COL3A1, PAK1, PPARD
liver_development	0.263570388	JUN, H1X, FOXM1
negative_regulation_of_transcription_DNA-templated	0.264837728	PRMT6, ING4, JUN, DACH1, PRMT2, BASP1, BCL3, FOXM1, FOXP3
hematopoietic_progenitor_cell_differentiation	0.275258283	RSS1, GPATCH4, 4930430F08RIK
inflammatory_response	0.293095189	MMP25, TUSC2, TNFRSF18, SPHK1, KIT, ACOD1
positive_regulation_of_MAPK_cascade	0.298596927	PEL12, KIT, NENF
response_to_hypoxia	0.327175040	PAK1, PRMT2, BNIP3, SOX4
positive_regulation_of_transcription_from_RNA_polymerase_II_promoter	0.353729997	EOMES, JUN, PLAG1, ZBTB49, FOXM1, FOXP3, PLSCR1, KLF5, JPX, BCL3, TAF9B, SOX4, E2F7
regulation_of_transcription_DNA-templated	0.357634774	GM14326, ZFP825, PLAG1, ZBTB49, ZFP948, FOXM1, IKZF5, DACH1, H1X, C1QBP, TAF9B, E2F5, SOX4, E2F7, PRMT6, EOMES, JUN, ZFP994, MTERF4, FOXP3, KLF5, ZFP40, BCL3, TFEC, ZFP27, PPARD
positive_regulation_of_cell_migration	0.359402181	PAK1, MIEN1, SPHK1, KIT
immune_system_process	0.375487094	EOMES, CLEC4N, C1QBP, IL2RA, ACOD1, IFIT3
cellular_response_to_lipopopolysaccharide	0.376732741	PLSCR1, MRC1, ACOD1, PPARD
protein_phosphorylation	0.402257556	CCNB1, PAK1, RPS6KA2, KIT, STK39, NEK2, PIM3, BUB1
cell_proliferation	0.408828343	DACH1, CKS2, BUB1, PPARD
intracellular_signal_transduction	0.409061339	SRS1, CISH, RPS6KA2, GPR182, KIT, STK39
transcription_DNA-templated	0.422558050	PRMT6, EOMES, JUN, PLAG1, ZBTB49, FOXM1, FOXP3, IKZF5, KLF5, DACH1, H1X, C1QBP, TAF9B, E2F5, SOX4, E2F7, PPARD, LIN52
positive_regulation_of_neuron_projection_development	0.426707341	RANBP1, SPHK1, EPOR
adaptive_immune_response	0.430307702	EOMES, CLEC4N, C1QBP
cellular_response_to_DNA_damage_stimulus	0.452403799	PRMT6, BCL3, FBXO6, FOXM1, AP551, E2F7
small_GTPase-mediated_signal_transduction	0.452646087	ARHGAP31, RAB20, ARL3, RND1
cytokine-mediated_signaling_pathway	0.454888918	CISH, RTN4R1L, KIT
phosphorylation	0.464041547	PAK1, RPS6KA2, SPHK1, KIT, STK39, NEK2, PIM3, BUB1
negative_regulation_of_neuron_apoptotic_process	0.502623886	JUN, BHLH89, EPOR
cilium_morphogenesis	0.535033048	ARL3, FUZ, CELSR3
immune_response	0.542973399	PLSCR1, TNFRSF18, IL2RA, TNFSF13B
positive_regulation_of_protein_phosphorylation	0.577818217	PAK1, SPHK1, PEL12
protein_transport	0.593190633	RAB20, NXK1, ARL3, FUZ, PEX12, AP551, GPM6B
innate_immune_response	0.608824163	CLEC4N, C1QBP, OA51A, ACOD1, IFIT3
response_to_lipopopolysaccharide	0.615612922	JUN, TNFRSF18, ACOD1
protein_homooligomerization	0.615612922	TMEM120A, KCTD11, KCTD7
regulation_of_apoptotic_process	0.621113918	TNFRSF18, BCL3, FBXO10
DNA_repair	0.652572005	PRMT6, FBXO6, FOXM1, AP551
cell_surface_receptor_signaling_pathway	0.672820961	ADGRG3, GPR83, CELSR3
RNA_splicing	0.72296497	LSM10, C1QBP, MTERF4
multicellular_organism_development	0.760001005	EOMES, HACD1, DACH1, TNFRSF18, STMN1, KCTD11, FUZ, LCLAT1, CELSR3, GADD45G
negative_regulation_of_gene_expression	0.770148354	CCNB1, PLAG1, FOXP3
regulation_of_transcription_from_RNA_polymerase_II_promoter	0.790727682	EOMES, KLF5, CKS2, FOXP3
translation	0.796326874	GM9493, MTF1, MRPI43, WARS2

Supplementary Table S9. Total Gene Ontologies enriched in Severe Group.

Gene ontologies were identified by DAVID pathway analyses of n = 383 unique genes in Severe group compared with Control group.		
	PValue	Genes
ControlvSevere		
metabolic_process	2.37E-06	ACAD8, ARSA, FAHD1, CRTC1, OXSM, PGAM1, ACOD1, MCAT, LCLAT1, ACAT2, GALNS, ALDH3A1, GPAM, EOGT, ALPL, NEIL1, UMP5, DIP2C, ACADS, GLA, ENOPH1
phospholipid_biosynthetic_process	0.006923676	GPAM, PLD1, LCLAT1, CRLS1, PPARD
apoptotic_process	0.015388052	DFFB, PLK3, CSRNP2, TNFRSF18, PDCD5, NAI1, GOS2, GZMB, MFSD10, GADD45G, ING4, PLSCR1, EMC4, BMF, PPARD
DNA_replication	0.022123743	ING4, CDT1, CHAF1B, CDC45, MCMDC2, DTD1
cellular_process	0.037588764	JUN, PSCK3, PPARD
regulation_of_reactive_oxygen_species_metabolic_process	0.040518844	RIPK3, TUSC2, FOXM1
cellular_amino_acid_biosynthetic_process	0.040518842	PSAT1, ASL, ENOPH1
neuromuscular_process	0.04053213	POMK, IGHMBP2, SPG20
G1/S_transition_of_mitotic_cell_cycle	0.045367227	RANBP1, PLK3, RCC1, RHOU
positive_regulation_of_cell_proliferation	0.047508729	CBX8, JUN, SPHK1, NOP2, LRP5, FOXM1, EPOR, ALDH3A1, KLF5, HLX, MARK4, CAMP, PPARD
positive_regulation_of_telomerase_activity	0.049797998	PKIB, ACD, WRAP5
heart_development	0.051664945	NEKB, COL3A1, CXADR, RPS6KA2, MTERF4, EPOR, HOPX, PPARD
cellular_response_to_lipopolysaccharide	0.053025125	PLSCR1, TNIP3, MRC1, ACOD1, CAMP, PPARD, HAVCR2
response_to_radiation	0.056366214	PLK3, COL3A1, JUN
positive_regulation_of_telomere_maintenance_via_telomerase	0.063217432	PKIB, ACD, WRAP5
positive_regulation_of_apoptotic_process	0.06784274	ING4, PLSCR1, JUN, RPS6KA2, ZBTB16, PDCD5, CTLA4, BMF, GADD45G
mitotic_metaphase_plate_congression	0.070333091	PSRC1, KIFC5B, RRS1
adipose_tissue_development	0.070333091	LRP5, SPG20, PPARD
response_to glucocorticoid	0.071921398	ALDH3A1, ANXA3, ALPL, GPR83
lipid_metabolic_process	0.072617973	GPAM, PTGES2, OXSM, PMVK, PLD1, ACADS, LCLAT1, LDLR, MCAT, CRLS1, PPARD
inflammatory_response	0.07641609	MMP25, TUSC2, TNFRSF18, SPHK1, TB4R1, STAB1, ACOD1, TNFRSF4, HAVCR2
phosphorylation	0.096393027	NEKB, PLK3, RIPK3, SPHK1, CDC42BP, STK39, MAPK13, NAGK, GRK4, RPS6KA2, PMVK, POMK, MARK4
protein_tetramerization	0.097067974	SHMT1, ASL, SBF2
actin_cytoskeleton_organization	0.11024577	FMNL2, CD42EP2, FHL3, RHOU, PDLM4
positive_regulation_of_transcription_DNA-templated	0.122978897	EOMES, SERTAD3, JUN, KLF5, PSRC1, PTGES2, ZBTB16, BCL3, TADA3, LRP5, FOXM1, PPARD
liver_development	0.12306059	JUN, HLX, ASL, FOXM1
positive_regulation_of_fat_cell_differentiation	0.13044735	KLF5, ZBTB16, LRP5
learning_or_memory	0.139161393	BHLH89, POMK, DBI
fatty_acid_metabolic_process	0.141250509	GPAM, PTGES2, OXSM, ACADS, MCAT
actin_cytoskeleton_reorganization	0.143565029	EP58, CXADR, CDC42BP
brain_development	0.145415798	EOMES, SPHK1, STMN1, POMK, CTNS, EPOR
cellular_response_to_DNA_damage_stimulus	0.17329052	PLK3, CHAF1B, BCL3, EXOS, CTLA4, FBXO6, NEIL1, FOXM1, AP551
regulation_of_cell_cycle	0.174174359	JUN, PSMG2, PRR11, GADD45G
embryonic_digit_morphogenesis	0.207645744	ZBTB16, LRP5, FUZ
negative_regulation_of_cell_growth	0.216586548	SERTAD3, PSRC1, NAI1, PPARD
rRNA_processing	0.219937657	GM9493, NOP2, MTERF4, RRP9
negative_regulation_of_cell_proliferation	0.224585613	ING4, JUN, RPS6KA2, ZBTB49, ZBTB16, PDCD5, FUZ, CHERP
negative_regulation_of_transcription_from_RNA_polymerase_II_promoter	0.229900591	CBX8, EOMES, PLK3, JUN, ZBTB16, IGHMBP2, ZBTB42, FOXM1, HOPX, UXT, KLF5, DACH1, PPARD
defense_response_to_bacterium	0.230926304	ANXA3, BCL3, STAB1, MUC5B, CAMP
transcription_DNA-templated	0.232573012	CSRNP2, PRDM9, PLAG1, CRTC1, ZBTB49, IGHMBP2, DPY30, ZBTB42, FOXM1, HDAC6, UXT, HIRA, CHAF1B, SERTAD3, DACH1, HLX, POLR2J, CBX8, EOMES, JUN, HOPX, MAPK13, KLF5, MAFB, BCL3, TADA3, TFEC, ZFP27, PPARD
protein_heterotrimerization	0.245479557	CRTC1, SHMT1, ACADS
fatty_acid_biosynthetic_process	0.245479557	PTGES2, OXSM, MCAT
response_to_lipopolysaccharide	0.247136969	JUN, TNFRSF18, ACOD1, ALPL, TNFRSF4
covalent_chromatin_modification	0.257732979	ING4, CBX8, HIRA, PRDM9, DPY30, HDAC6
adaptive_immune_response	0.264327303	EOMES, CLEC4N, CTLA4, HAVCR2
cell_cycle	0.265031384	ING4, CDT1, PLK3, CHAF1B, CDC45, PSRC1, ZBTB49, RCC1, MARK4, FOXM1, MAPK13
immune_response	0.269263804	PLSCR1, TNFRSF18, CTLA4, OAS1C, TNFRSF4, TNFSF13B
mitochondrion_organization	0.278792455	CXADR, CHCHD10, MAPK13
response_to_virus	0.299305384	BCL3, STMN1, OAS1A
tRNA_processing	0.297800171	TSEN34, LAGE3, GTBP3
cholesterol_metabolic_process	0.316730229	PMVK, LRP5, LDLR
protein_phosphorylation	0.319177215	NEKB, PLK3, RIPK3, GRK4, RPS6KA2, CDC42BP, STK39, POMK, MARK4, MAPK13
regulation_of_transcription_DNA-templated	0.319543727	CSRNP2, PRDM9, PLAG1, CRTC1, ZBTB49, IGHMBP2, DPY30, ZBTB42, FOXM1, HDAC6, UXT, HIRA, CHAF1B, SERTAD3, DACH1, HLX, ZFP560, CBX8, EOMES, JUN, ZBTB16, MTERF4, ZFP619, HOPX, MAPK13, ZFP69, KLF5, MAFB, BCL3, TADA3, TFEC, ZFP27, PPARD
defense_response_to_Gram-positive_bacterium	0.3355424	PLD1, CAMP, HAVCR2
negative_regulation_of_protein_kinase_activity	0.344892868	PKIB, CISH, GADD45G
microtubule_cytoskeleton_organization	0.349552351	UXT, MARK4, TTL
defense_response_to_virus	0.362350864	PLSCR1, GPAM, OAS1A, OAS1C
cellular_calcium_ion_homeostasis	0.368073914	SLC24A1, NUCB2, CHERP
methylation	0.369297056	PRDM9, CARNMT1, SMYD5, NOP2
protein_polyubiquitination	0.381830236	LRSAM1, FBXO4, HDAC6
aging	0.383270539	ALDH3A1, COL3A1, JUN, FBXO4
DNA_repair	0.387818211	CHAF1B, EXOS, FBXO6, NEIL1, FOXM1, AP551
intracellular_signal_transduction	0.398763044	SPSP1, CISH, RPS6KA2, CDC42BP, GPR182, STK39, MAPK13
skeletal_system_development	0.399971014	ACD, COL3A1, ZBTB16
positive_regulation_of_gene_expression	0.404766943	PLSCR1, PLAG1, RPS6KA2, TADA3, PDCD5, LDLR, PPARD
endocytosis	0.411511207	MRC1, LRP5, LDLR, RIN2
anterior/posterior_pattern_specification	0.422291256	ZBTB16, LRP5, FUZ
defense_response	0.439838047	NGP, ACOD1, CAMP
negative_regulation_of_peptidase_activity	0.444179427	CSTB, NGP, STFA2
positive_regulation_of_angiogenesis	0.461356273	ANXA3, SPHK1, CAMP
protein_homoooligomerization	0.4646921439	RIPK3, TMEM120A, IGHMBP2, KCTD7
regulation_of_apoptotic_process	0.471482083	TNFRSF18, BCL3, LRP5, TNFRSF4
peptidyl-serine_phosphorylation	0.510966168	RPS6KA2, STK39, MAPK13
positive_regulation_of_transcription_from_RNA_polymerase_II_promoter	0.513940621	EOMES, CSRNP2, JUN, PRDM9, PLAG1, CRTC1, ZBTB49, LRP5, FOXM1, PLSCR1, KLF5, JPX, MAFB, BCL3
cell_division	0.528979235	CDC45, PSRC1, KIFC5B, RCC1, MARK4, SPG20
positive_regulation_of_neuron_projection_development	0.530739709	RANBP1, SPHK1, EPOR
regulation_of_cell_shape	0.534628941	EP58, CDC42EP2, RHOU

cell_surface_receptor_signaling_pathway	0.540840308 ADGRG3, ADGRF1, GPR83, CELSR3
immune_system_process	0.54612887 EOMES, CLEC4N, CTLA4, ACOD1, ECSIT, HAVCR2
regulation_of_cell_proliferation	0.559736606 RNF126, TNFRSF18, FOXM1, PPARD
intracellular_protein_transport	0.57439964 ACD, ARFIP1, SEC24D, HDAC6
regulation_of_transcription_from_RNA_polymerase_II_promoter	0.579084886 EOMES, KLF5, MAFB, TADA3, IGHMBP2, ECSIT
innate_immune_response	0.585786013 CLEC4N, OAS1A, ACOD1, ECSIT, CAMP, HAVCR2
translation	0.588007006 GM8210, GM9493, IGHMBP2, MRPL39, MTIF3, WARS2
ubiquitin-dependent_protein_catabolic_process	0.590423947 RANBP1, FBXO4, HDAC6
negative_regulation_of_neuron_apoptotic_process	0.611132364 JUN, BHLLH9, EPOR
negative_regulation_of_transcription_DNA-templated	0.616546879 ING4, JUN, DACH1, BASP1, ZBTB16, BCL3, FOXM1, TNFRSF4
protein_ubiquitination	0.685880539 FBXO40, CISH, PEL12, FBXO4, FBXL22
positive_regulation_of_protein_phosphorylation	0.68642477 SPHK1, PEU2, CAMP
mitotic_nuclear_division	0.693002853 PSRC1, TADA3, RCC1, MARK4
positive_regulation_of_ERK1_and_ERK2_cascade	0.6977464 JUN, EPOR, HAVCR2
negative_regulation_of_apoptotic_process	0.737463569 PLK3, JUN, TNFRSF18, SPHK1, BCL3, PSMG2, PPARD
multicellular_organism_development	0.774662388 EOMES, DACH1, OLFM3, TNFRSF18, STMN1, LRP5, FUZ, LCLAT1, TNFRSF4, HOPX, CELSR3, GADD45G
cell_proliferation	0.776590976 GM8210, DACH1, PPARD
small_GTPase-mediated_signal_transduction	0.808847745 RAB20, RHOU, RND1
negative_regulation_of_gene_expression	0.856909789 PLAG1, LDLR, HAVCR2
oxidation-reduction_process	0.869480562 ACAD8, ALDH3A1, AKR7A5, TMLHE, RETSAT, NDUFC2, ACADS
protein_transport	0.880486911 LRSAM1, RAB20, FUZ, PEX12, AP551, PEX26
response_to_drug	0.933877148 ALDH3A1, JUN, ABCB18
signal_transduction	0.934253352 ADGRG3, ADGRF1, GRK4, IMPA2, RGS1, GPR182, LTB4R1, GPR83, TAS2R135, RIN2, EPOR, CELSR3
transmembrane_transport	0.949498893 SCN4A, ABCB1B, MFSD10
cell_adhesion	0.95045278 PTRP3, CXADR, STAB1, CELSR3
transport	0.963954675 LRSAM1, NDUFC2, CTNS, DBI, FUZ, PEX12, ABCA13, MFSD10, PEX26, CACNB1, RAB20, CPTP, SCN4A, SLC29A1, LDLR, ABCB1B, AP551
proteolysis	0.98114848 MMP25, GCA, GZMB, OTUD3
cell_differentiation	0.99114339 EOMES, HIX, STMN1, PPARD, GADD45G
G-protein_coupled_receptor_signaling_pathway	0.999967465 ADGRG3, ADGRF1, RGS1, GPR182, LTB4R1, GPR83, TAS2R135, CELSR3

Supplementary Table S9. Total Gene Ontologies enriched in Severe-specific Group

Gene ontologies were identified by DAVID pathway analyses of n = 352 unique genes in Severe group compared with Mild / Moderate group

MeSHDescriptor	Value	Gene
toll-like_receptor_3_signaling_pathway	4.02E-04	ARSA, FAH01, CRTC1, GSTP1, PGAM1, MCAT, HK2, GALTNS, ALDH3A1, BDH1, ALPL, DNA2, NEIL1, DIP2C, ACADS, GLA, ENOPH1
protein_methionine_beta-elimination	0.00574847	COLECE12, CPTP1, HNRNCR2
regulation_of_transcription_DNA-templated	0.00620004	PTEN, PEX12
phosphorylation	0.01279323	INOB08, CRNP2, PRDM9, HDAC10, CRTC1, IGHMBP2, DPY30, ZBTB42, TTF2, HDAC6, UXT, PRPSKAA4, HIRA, 9130019Q028R0K, MNT, CHAF1B, SERTAD3, ALKBH4, TAF1C, ZFP560, NRBF2, DMAP1, DEDD, BCL9L, TSPYL2, CBX8, PIAS3, GM15446, SS18L1, ZBTB16, ZFP619, AXIN2, KLF4, POU2F2, HOPX, 2FP69, MAPK13, 2FP12, ERCC2, PIR, ZSCAN25
transcription_DNA-templated	0.01474709	NEIL2, PLX3, CRNP2, PRDM9, HDAC10, CRTC1, IGHMBP2, DPY30, ZBTB42, TTF2, HDAC6, UXT, HIRA, MNT, CHAF1B, SERTAD3, ALKBH4, TAF1C, NRBF2, DMAP1, POLR2J, DEDD, BCL9L, TSPYL2, CBX8, PIAS3, SS18L1, KLF4, POU2F2, HOPX, 2FP69, MAPK13, MAFB, TADA3, ERCC2, PIR, PPI, PRPF3, PRPF8, PRPF35, PRPF35B
covalent_chromatin_modification	0.02059401	INOB08, CRNP2, PRDM9, HDAC10, CRTC1, IGHMBP2, DPY30, ZBTB42, TTF2, HDAC6, UXT, HIRA, MNT, CHAF1B, SERTAD3, ALKBH4, TAF1C, NRBF2, DMAP1, POLR2J, DEDD, BCL9L, TSPYL2, CBX8, PIAS3, SS18L1, KLF4, POU2F2, HOPX, 2FP69, MAPK13, MAFB, TADA3, ERCC2, PIR, ZSCAN25
tRNA_processing	0.02395464	TSPYL2, CRNP2, PRDM9, HDAC10, CRTC1, IGHMBP2, DPY30, ZBTB42, LAGE3, CTBP3
intracellular_protein_transport	0.02518366	DUS2, TSEN34, ZBTB40S, LAGE3, CTBP3
cellular_amino_acid biosynthetic_process	0.03295818	ACD, GRK3, RPH3AL, COG7, RNDCC1, EVISL, SEC24D, HDAC6
positive regulation_of_telomerase_activity	0.04179136	PTST1, ASL, ENOPH1
histone_deacetylation	0.05134023	ACD, KLF4, WRAP53
DNA_repair	0.05468067	HDAC10, HDAC6, HOPX
negative regulation_of_peptidase_activity	0.05770222	INOB08, CHAF1B, ERCC2, RPS27L, EXO5, DNA2, DMAP1, NEIL1, FAAP100
bone_mineralization	0.06721558	THHS, SERPINB10, NGP, SPINT2, STFA2
mitochondrial_translation	0.07620147	ERCC2, AXIN2, GLA
telomere_maintenance	0.08001253	MRP525, MRP518A, QRSL1
cellular_response_to_DNA_damage_stimulus	0.08780668	ACD, FBXO4, DN2A
canonical_Wnt_signaling_pathway	0.10158417	INOB08, PLX3, CHAF1B, ERCC2, RPS27L, EXO5, CTLA4, DNA2, NEIL1, FAAP100
somatic_stem_cell_population_maintenance	0.11067924	ICLRS, LRP5, KLF4, BCL9L
histone_H3_acetyltransferase	0.12027643	LRP5, KLF4, BCL9L
lung_development	0.13232323	TPAF1, HOPX, MBP
microtubule_cytoskeleton_organization	0.12969078	ERBB1, ACE, HOPX
protein_phosphorylation	0.13063225	UXT, MAP1S, MARK4, TTL
cellular_calcium_ion_homeostasis	0.13424422	PRPSKAA4, NEIL2, PLX3, CRNP2, PRDM9, HDAC10, CRTC1, IGHMBP2, POMK, MARK4, PASK, MAPK13
transformation	0.14256188	SLC7A41, SLC7A4, NUCB2, CHERP
organ_regeneration	0.15540519	GMD20, NHPI2, IGHMBP2, MRPL39, RPS27L, MRP518A, MRPL36, QRS11, MTRF1L
cellular_response_to_hydrogen_peroxide	0.16582538	ACN, ANXA3, GSTP1
oxidation_reduction_process	0.17046055	CBX8, ARSA, HDAC6
G1_S_transition_of_mitotic_cell_cycle	0.17526092	ONXAD1, RETSAT, NDUF2C, HIGD1A, DHDOD, DUS2, ALDH3A1, AKR7A5, ALKBH4, BDH1, PIR, D2HGDH, ACADS
cholesterol_homeostasis	0.19393284	PLX3, RCL4, ROHU
apoptotic_processes	0.19867761	LRP5, SLC37A4, LDLR
negative regulation_of_ERK1_and_ERK2_cascade	0.20807038	PLX3, CRNP2, MAP15, FASTK, ERCC2, NAIF1, EMC4, G2MB, BMF, DEDD, MFSD10
positive regulation_of_transcription_DNA-templated	0.21290979	ERRR1, GSTP1, KLF4
regulation_of_protein_stability	0.22221737	TADAD3, QRS11, HDAC6
response_to_nutrient	0.24670748	ALDH3A1, ARSA, SLC37A4
lipid_metabolic_process	0.25188457	ALCB1, PLCB3, PTGES2, PMVK, PLD1, ACADS, LDLR, MCAT, PLBD2
response_to_glucocorticoid	0.25200001	ALCB1, PLCB3, PTGES2, PMVK, PLD1, ACADS, LDLR, MCAT, PLBD2
response_to_organic_cyclic_compound	0.28058911	ALDH3A1, PNTB, CLC37A4
autophagy	0.28326278	ARSA, USM1, NRBF2, VDR24
cellular_response_to_lipoopolysaccharide	0.29116806	CD86, TNIP3, GSTP1, CAMP, HAVCR2
steroid_metabolic_process	0.29992627	PMVK, CLC37A4, LDLR
ribosome_biosynthesis	0.32396654	NHPI2, MRPL36, ERA1L
cholesterol_metabolic_process	0.32396654	PMVK, LRP5, LDLR
ubiquitin-dependent_protein_catabolic_process	0.32602593	FBXW8, USP11, FBXO4, HDAC6
transmembrane_transport	0.33952195	ABCD4, SLC12A4, SCN4A, SLC37A4, SLC8B1, ABCB1B, MFSD10
defense_response_to_Gram-positive_bacterium	0.34304728	PLD1, CAMP, HAVCR2
negative regulation_of_transcription_from_RNA_polymerase	0.35828938	UXT, CBX8, PLX3, MNT, HDAC10, ZBTB16, IGHMBP2, ZBTB42, DMAP1, KLF4, HOPX, ZFP90
protein_polyubiquitination	0.3899212	USM1, FBXO4, HDAC6
aging	0.39391981	CBX8, ALDH3A1, ERCC2, FBXO4
nucleosome_assembly	0.39453067	PTSP12, TSPY13, CHAF1B
dephosphorylation	0.41733334	PTPNS, PTPR, ALPL
lipid_catabolic_process	0.41733334	PLC8, PLD1, PLB2
response_to_ethanol	0.45288985	ARSA, GSTP1, DMAP1
DNA_replication	0.47471361	ALCB1, PLCB3, CHAF1B, HDAC6
negative regulation_of_cell_growth	0.48718504	PTPNS, SFRP3, MAF1
glucose_homeostasis	0.52011294	RPH3AL, SLC37A4, SLC8B1
regulation_of_transmembrane_transport	0.52812307	CACNB1, CLIC5, SCNA4
transcription_from_RNA_polymerase_II_promoter	0.53995814	ERCC2, KLF4, POU2F1
sensory_perception_of_sound	0.53996814	CLIC5, TMIE, ESPN
protein_dephosphorylation	0.53996814	PTPNS, PTPR2RD3, PTPRO
adaptive immune_response	0.54387077	CD65, CTLA4, HAVCR2
cell_proliferation	0.54411361	GMD20, FBXW8, ERCC2, AXIN2
cell_cycle	0.55231066	PTSP12, CDT1, PLX3, CHAF1B, KHLH22, RCC1, MARK4, PDCD2L, MAPK13
negative regulation_of_cell_proliferation	0.56463611	PPPR23D, ZBTB16, FNTB, AXIN2, KLF4, CHERP
regulation_of_transcription_from_RNA_polymerase_II_promoter	0.59427377	MARF3, TADA3, IGHMBP2, NRBF2, KLF4, ECSIT
fatty_acid_metabolic_process	0.60666041	PTGES2, ACADS, MCAT
positive regulation_of_apoptotic_process	0.63953837	ACE, ZBTB16, CTLA4, BMF, DHDOD
response_to_drug	0.64875116	CBX8, ALDH3A1, RPH3AL, ABCB1B, DHDOD
chemical_synaptic_transmission	0.65958927	CACNB1, SLC12A4, PLCB3
inflammatory_response	0.66004747	PTPSKAA4, LTB4R1, STAB1, TNFRSF4, HAVCR2
negative regulation_of_gene_expression	0.67526697	ACE, KLF4, LDBP, HAVCR2
immune_response	0.68227159	CD65, CD40, CD44, D6G1C, TNFRSF4
positive regulation_of_protein_phosphorylation	0.69091511	AXIN2, CAMP
protein Ubiquitination	0.69865597	FBXW8, FBXO4, HDAC6, KHLH22, FBXL22
mitotic_cohetero_division	0.70409407	TADAD3, KHLH22, RCC1, MARK4
defense_response_to_bacterium	0.71488016	ANXA3, STAB1, CAMP
response_to_lipoopolysaccharide	0.73070878	ACE, ALPL, TNFRSF4
regulation_of_apoptotic_process	0.73581748	LRP5, TNFRSF4, DEDD
immune_system_process	0.73964125	CB65, GH, CTLA4, ECSIT, HAVCR2
Wnt_signaling_pathway	0.76931695	BCL3, LRP5, AXIN2
intracellular_signal_transduction	0.76963124	PTPSKAA4, PLCB3, CDC42BPG, DEF8, MAPK13
cell_surface_receptor_signaling_pathway	0.78250954	UPK1B, ADGRF1, TSPN3
mRNA_processing	0.79461681	TSEN34, PHE1, TFF2, CMTR1
positive regulation_of_cell_proliferation	0.83953178	CBX8, ALDH3A1, FNTB, LRP5, MARK4, CAMP
positive regulation_of_transcription_from_RNA_polymerase	0.84243454	PTPSKAA4, CLC5, CRNP2, MAFB, PRDM9, CRTC1, ERCC2, RPS27L, KLF4, POU2F2, BCL9L
heart_development	0.85762892	NEIL2, KDEL11, HOPX
cell_division	0.86938767	KIFC8, KHLH22, RCC1, MARK4
transport	0.87774731	ABCD4, CLIC5, SLC12A4, LRSAM1, COG1, SLC35C1, PDK1L1, NDUF2C, VPS37B, TRAM2, MFSD10, PEX26, CACNB1, RILPL2, CPTP, SCN4A, LDLR, ABCB1B
negative regulation_of_transcription_DNA-templated	0.88774731	ABCD4, CLIC5, SLC12A4, LRSAM1, COG1, SLC35C1, PDK1L1, NDUF2C, VPS37B, TRAM2, PEX26
protein_transport	0.89595794	NEIL2, TADA3, KHLH22, RCC1, LDBP
positive regulation_of_gene_expression	0.90291255	CTFL, FGFR, CAMP, HAVCR2
metabolic_enzyme_response	0.94826928	ACE, GCA, USP11, G2MB, PRSS22
proteinolytic_process	0.95429122	PTPNS, AMIGO3, STAB1, MILIN1
cell_adhesion	0.95916932	AMIGO3, MAP19, MARK4
nervous_system_development	0.9708523	AC, PRDM9, DEDD
spermatogenesis	0.99543161	PLX3, GSTP1, HIGD1A
negative regulation_of_apoptotic_process	0.99926083	GRK3, PLCB3, GNAT2, ADGRF1, GRK4, IMPA2, LTBR4R1

multicellular_organism_development	0.99944825 OLFM13, FNTB, LRPS, TNFRSF4, HOPX
G-protein_coupled_receptor_signaling_pathway	0.9999998 PLCB3, GNGT2, ADGRF1, LTB4R1
mitophagy_in_response_to_mitochondrial_depolarization	0.0295736 SERPINB10, CHAF1B, SLC35C1, SLC37A4, HDAC6, HK2
xenophagy	
positive_regulation_of_defense_response_to_virus_by_host	0.15173832 SERPINB10, CHAF1B, SLC35C1, SLC37A4
calcium_ion_transmembrane_transport	0.21358567 SERPINB10, CHAF1B, SLC35C1, SLC37A4
calcium_ion_transport	0.010793219 CACNB1, SLC24A1, PKD1L1, SLC8B1
ion_transport	0.088226645 CACNB1, CLIC5, SLC12A4, PKD1L1, SCN4A, SLC8B1