

Supplementary Table S1. Gene list of DEGs common and specific to HPAIV and LPAIV

Type of DEGs	Number of DEGs	Gene name
HPAIV specific DEGs	504	CALM SLMAP DTD1 CARHSP1 CCDC25 HERC1 NR3C2 MTF2 C11H16ORF70 GSR PDCD6 VPS35 CNN2 GPC4 LMO7 UCKL1 UBE2G1 KMT2E NDUFV3 OGT PTEN SLTM EP300 GNAL SREK1IP1 GUCY1A3 ATXN7L1 LMAN2 SETD2 MATR3 KIF26A UBB TRIM33 PTPRS HMGB3 LEPREL4 PTPN1 CBFB MSRB3 EPN2 FHL3 NXN EIF5B NUP214 DDX28 MARCKS DPYSL2 ZYG11B ATP5D IRF2BP2 RPL36A LONP1 CSNK1E IKZF5 SASH1 ATP6V1B2 FAP TPP2 RTN4IP1 HTR2B GTF2H1 GJA1 MLLT1 HECTD1 ATP5L ACTR8 HERC2 TOMM6 AIDA CRY2 AHS1 DIP2C ACTL6A NME2 CAND1 MAP3K5 EIF4G3 MAP2K5 CNPY3 RPS20 PALLD MXRA8 CPEB2 HNRNPA2B1 CEP63 LOC395676 PAIP2 SQSTM1 PHF6 ATL2 MESDC1 FAM136A SEL1L3 DCAF6 HMOX2 YIPF4 UBL3 NFIB EIF3A KIAA0020 PTPRF NME7 BTG1 ABR CDK2AP1 PGRMC2 PFAH1B1 PSMC2 ZDHHC6 AL158801.1 AFAP1 MAPKAP1 SRSF10 ISM1 THOC2 UBA6 DCUN1D1 AKIRIN2 PURA MYO1C ZFC3H1 ARMC1 RPL15 LMOD3 CNKSR3 FAM46A PI4KA PTPN21 PDLIM4 LSM14A ABHD13 RPL12 CCPG1 SKIV2L2 ANKHD1 SMARCB1 TIPARP PREP YWHAQ BAZ2B HNRNPR MEIS2 MCU PPM1A MRPS11 PPP1R8 COPG1 IFT140 MAFK C12orf75 TAF12 PXDN MYH9 CLK2 PLEKHB2 RAB35 IARS HMG3 URI1 PLSR1 PIK3C3 SACMIL DNAJC2 C11H16ORF87 SYNCRIP MICAL2 DHRSX CCT8 RPS4X EIF3M PTPN5 PHF2 HPRT1 ASMTL DYNC1L2 ABL1 OPN5L1 PSMA7 ZMYND8 MT3 DLGAP4 APLP2 NDNL2 MSI2 BTBD11 KDM6A THBS2 C16orf72 NCAM1 USP33 MTDH SLC25A6 COA5 GBAS SEMA6D MTHFD1L PPP4R3A ATG4B NCL EIF4EBP1 LOC770490 WDR20 GSPT1 MOB1A HOXB6 SSR2 AEBP2 CNN3 DCUN1D3 UBE4B NUDT16L1 LSM8 PARL EVI5 RASD1 LOC100859798 LOC101750049 DCAF13 MED14 RPL9 MYL6 SPRY2 TARDBP SMC4 CARS STAU1 PRSS35 PHLDA2 PDE10A ZNF410 HIF1AN SHOC2 NSFL1C KIAA1468 CRMP1 JMJD1C RBPMS NAA16 RBM38 SRPX ODC1 ATP1A1 NAA30 RPL13 BAZ1A PIK3R3 ACVR2A NEK7 MECOM SCUBE1 MAP2K6 SGCD BRF1 ARID4A NAB1 RPL23 TAF3 YLPM1 MED31 OSBPL10 ITFG1 RPS2 PRPF4B SEZ6L CHMP6 UBQLN1 TXNDC11 SPCS3 VPS54 GGNBP2 TM9SF3 SEC11A NPTX2 YWHAH PITX1 VSTM4 ICA1 EIF1AY PPP6R3 VAPB MLL3 COPB1 CREBRF BOD1 PRELID1 CTBP2 FBLN1 MYOF RBMX ZCCHC2 LUC7L RAF1 MST4 KLHDC8B SULF1 SMARCA5 TCP1 PPA2 GUCD1 PREX2 ST3GAL3 RAB11A SGK1 EIF3D KIAA0930 PDGFB ME3 SNCAIP TPM2 PCNA NUDCD3 UNK PPP2CB NREP DOLPP1 SYDE2 EXO1 CCND2 SLIT3 DSE EPRS SPAG9 GATSL2 COX20 TM9SF4 ANKIB1 C1ORF35 PDPK1 DMD NDUFA12 MPP1 ISCU STARD3NL KLHL5 CTBP1 EPS15 C18ORF8 INTS10 TNK2 CCT5 IDH1 CAMKK2 USP25 PRKX DLG5 PGM5 CUX1 NF1 ARHGDIG DUSP1 SQLE HDAC1 SPRED1 FNDC3B ZMYM6NB NELFCD NAP1L4 MRPS22 ZHX1 RP11-371E8.4 HNRNPK SOX11 KDM2B ACTA1 SREK1 HEXB WDR83OS VOPPI ATP5C1 EBF1 ZNF644 RARS PSMC3 CTSK MMADHC STC2 PSMD2 COL6A1 TULP4 ATXN2 ZMPSTE24 IPO5 LOC101752174 NAA25 BCAS2 TOP2B BMP4 RPN2 STRN3 DVL1 ZNF821 ASB7 CSNK2A2 RNF11 MAP4K4 COL11A1 IL1RAP CDC5L GYG1 YPEL1 NR1D2 SPRED2 HES4 SLIT2 CDC20 KCTD3 RCN1 UTP14A MDH2 CTHRC1 SLC4A7 EEF1B2 PARVB SBNO1 SETBP1 CHN1 RBM25 OLA1 DNAJB14 FAM20C TP53BP1 S100A6 SEC24A TPR LOC101748094 MCMBP RBPMS2 SERBP1 OSBPL6 NAA15 STMN2 SEPT6 NF2 PLS3 LBH PPP2R3A LPHN2 DRG1 INHBB ARID1B SNAI2 DDX3X TTC27 HNRNPU RPL24 NKX2-1 RP5-864K19.6 IL8L2 FAM91A1 LPCAT1 SP4 HNRNPH3 EIF3H RPL14 TMEM208 LRPAP1 MAFF UBR4 FKBP1A KTN1 EHBPI KPNA1 TRIB2 GSTT1L PIAS1 FAF2 EVL ARGLU1 XPO7 GPR75 MAN1A2 SMIM11 SET domain containing 5 BEND5 WAPAL PSME4 BRD1 FBXO30 KARS GRIA2 LMTK2 HEATR1 SLC2A1 BTAF1 ATP5G1 NR2F2 SMURF2 UBE2QL1 TEAD4 HSP90AA1 TNRC6B HECW1 WFS1 DUSP8 ZNF622 PDE3B SLC35B4 RPS6KB1 CHTOP PGK1 NCKAP1 BTF3L4 KLF3 ARHGDIB
LPAIV specific DEGs	212	PHLDB1 SEC23A RPS11 MMP2 DPY30 ACSS3 APBB2 TAGLN TACC2 MMGT1 DIO3 WASL VAC14 MBNL2 ADD3 DCAF5 GFPT1 GRB10 ATP9B EEF2 EPHA3 WDR61 HMG5 TNC PAPOLA ZNF276 PCDH1 RAB40B TNS3 protein HEXIM1 ST7L SFXN1 CRYZL1 ITM2B FOXN3 ADCYAP1 SUMO2 RGS3 FRMD1 ITGAD FBXO22 CAPRIN1 ANKRD10 TDRD3 MDH1 MAML1 DPH3 NDRG1 PEX14 UBE2I CCNE1 CCNY RBPJ SIRT5 DAB2IP RP11-152F13.10 QDPR HSPD1 LEPRE1 STAG1 MXD4 CPSF6 CKB FDXACB1 TTC8 MAAA GNG5 PSMD6 SH3GLB1 RP11-234B24.6 COG1 CELF1 KATNA1 UBA52 APOO HECTD3 TMEM260 SDC2 MRPS31 ACP2 PRSS23 HACE1 ARIHI RPL27A IPO13 WISP1 OSR2 KLHL7 GNB4 LOC101748129 SNX3 CELF2 PIGF TMEM165 STOX2 MTA1 MSX2 PBX1 PBRM1 AAGAB ACO2 TAMM41 S100A10 LOC424199

Supplementary Table S1. Continued

Type of DEGs	Number of DEGs	Gene name
LPAIV specific DEGs	212	VAPA KLF6 NEK6 PCDHGC5 PRRX1 MRS2 DDX17 ZDHHC14 ASIC4 SRP68 PCDH9 P4HA1 SUFU CCNL2 PPP2R2D ZFAND5 RAPGEF2 RNH1 CSRP1 RPL7 LOC768760 LOC424167 PGAM1 KBTBD2 FYN SH3KBP1 DLD ITGB1 HBS1L KLF15 TAB2 WSB2 SNRPC RPL37A PITRM1 HS6ST2 TRAK1 BICD1 TMEM258 USP22 RPS26 STXBP5 FAM212B RNF149 HADHA NUA2 RAD51C EIF2S2 LOC396479 SLC6A13 LPCAT3 LINGO1 RPL23A SMARCA2 UST RBM15B ADD1 C16ORF45 PSMB3 UBE3A HDGF ARID4B PVRL3 RNF114 RSPO3 DDA1 C1ORF198 PMPA1 EIF4G2 OST4 EDEM2 DHX37 CYB5A PANK4 COMMD9 PPP1R26 GALNT1 GALNS GAS6 ETV1 EOGT BIRC2 TOMM7 EPHB2 DYNC112 ARFIP2 SESTD1 SRSF3 APRT LASP1 ACHE GSK3B AMOTL2 AMIGO2 PANK3 PPP4R1 PDCD10 MKRN2 DPYSL3 CREM ADAMTS7 DNAJC13 CPSF2 HMGB1 CNOT6L NAP1L1 CDYL USP38
Common in both HPAIV and LPAIV	227	ABCA3 RPS17 ATRX TKT PFKP COL3A1 RPL10A HERPUD2 WNK2 NUTF2 GTF2A1 KPNA4 TRIO RDH10 HIC2 P4HA2 IGF2BP3 ZEB1 RPLP0 SMAD2 ATP5A1 YEATS4 NRP1 NLRP3 DNAJA2 USP15 SLC31A1 ARHGAP21 INHBA ASCC3 BASP1 TMEM60 PDLIM7 WDR33 RPL29 MTA3 FOXK2 LRRC8C COL1A1 PDIA3 PPP3CA FAM98A YTHDF3 RPS15A MXI1 LRRC8D PAPP2 ZFP36L1 MAGI2 POLR2F FBXO11 MRPL39 RP11-101E3.5 MYCBP2 DCBLD1 USP7 SPPL3 RPLP1 EML4 ALCAM ATP6V0C RPS12 ATF2 HNRNPM RPL18A ELOVL6 METRNL HNRNPAB FBLN2 BCL9 SPTBN1 CAPRN2 HSF2 BAMB1 ABCC5 TUBA1C IQSEC1 MCHR2 TRIP12 PRKD3 CDH2 DIO2 TCF12 ITGB1BP3 CABIN1 SPTAN1 RPL32 HSP90B1 NFIL3 GLG1 RARB HTRA1 RNF111 RPSA ATP2C1 ESRRG ZEB2 XRN1 FN1 IRF2 PPP1R12A PPP2CA RPS21 CTDSPL USP9X MSMO1 PTPRO YWHAZ LMO4 HZGJ HUS1 YY1 TARS ENO1 CKS1B DDX1 TPT1 FTH1 SLC25A13 SVIL PRPSAP2 GINM1 AC113404.1 TNKS2 AKTIP TCF21 ZFYVE21 GSN HERC4 SLC38A1 ARPP19 RBM26 VLDLR COL5A2 RPS7 SET CANX DESI2 ZNF462 CDC42BPB RAB5A EIF4A2 ADM COL6A3 MYH10 LAP3 NOVA1 ZFH3 DNAJA1 ADCK3 SOCS5 NDUFA4 TALDO1 YBX3 PSMD7 SEPHS1 ADAM10 MAP4K3 CTNBN1 OXR1 ANK3 HK1 NCK2 RUNX1T1 CCND1 P4HB SEPT11 AFTPH CALD1 HTRA3 EIF3E RLIM SNRNP200 RPS25 ZNF207 COL5A1 AGAP1 C14ORF4 SEC61A2 FAM53A ACTN1 UBE2K COX7C XPOT DOCK7 DNER ETV6 CEBPB VPS13A PKDCCa HIAT1 PARD3 KDM3A LOC421049 RPS14 RPL30 CHPF2 PGD RPL38 MAP3K1 RPS16 AP2A2 WAC GNA13 COL1A2 DTNA ATF4 ORAOV1 TSPAN14 CTCF AMD1 RANBP9 USP8 CLTC ZNF521 CNOT2 COL8A1 CAMK2G PRICKLE2 APP COL12A1 ATP2B1 RBMS1 ZNRF1 MIR1600 BBX RPS15

Supplementary Table S2. Gene list of up and down regulated DEGs common and specific to HPAIV and LPAIV

HPAIV specific DEGs	Up	557	<p> ABCA3 CALM SLMAP HERC1 NR3C2 MTF2 ATRX C11H16ORF70 GSR TKT PFKP COL3A1 HERPUD2 VPS35 GPC4 LMO7 KMT2E UBE2G1 WNK2 OGT PTEN SLTM GTF2A1 KPNA4 GNAL EP300 GUCY1A3 TRIO LMAN2 ATXN7L1 RDH10 HIC2 SETD2 P4HA2 MATR3 IGF2BP3 ZEB1 KIF26A UBB TRIM33 PTPRS HMGB3 LEPREL4 PTPN1 SMAD2 ATP5A1 EPN2 NXN FHL3 EIF5B NUP214 MARCKS DPYSL2 ZYG11B IRF2BP2 CSNK1E LONP1 SASH1 IKZF5 ATP6V1B2 YEATS4 FAP NRP1 TPP2 RTN4IP1 HTR2B DNAJA2 USP15 GTF2H1 GJA1 MLLT1 HECTD1 SLC31A1 ARHGAP21 ACTR8 HERC2 CRY2 ASCC3 AHS1 BASP1 DIP2C ACTL6A CAND1 EIF4G3 MAP3K5 TMEM60 WDR33 CNPY3 PALLD MXRA8 CPEB2 HNRNPA2B1 LOC395676 PAIP2 MTA3 FOXK2 LRRC8C COL1A1 ATL2 PDIA3 SEL1L3 DCAF6 YIPF4 PPP3CA NFIB EIF3A KIAA0020 PTPRF FAM98A NME7 ABR BTG1 YTHDF3 PAFAH1B1 PGRMC2 PSMC2 AL158801.1 MXI1 AFAP1 LRRC8D ISM1 PAPD7 ZFP36L1 MAGI2 THOC2 UBA6 POLR2F DCUN1D1 AKIRIN2 FBXO11 MYO1C ZFC3H1 ARMC1 MRPL39 CNKSR3 FAM46A RP11-101E3.5 PI4KA PTPN21 LSM14A ABHD13 MYCBP2 CCPG1 DCBLD1 SKIV2L2 ANKHD1 SMARCB1 TIPARP PREP USP7 YWHAQ BAZ2B SPPL3 HNRNPR MEIS2 MCU PPM1A PPP1R8 COG1 EML4 ALCAM ATP6V0C PXDN MYH9 ATF2 RAB35 PLEKHB2 HNRNPM IARS PLSCR1 UR1 PIK3C3 ELOVL6 SACMIL METRNL HNRNPAB BCL9 FBLN2 DNAJC2 C11H16ORF87 SYNCRIP DHRSX MICAL2 CCT8 SPTBN1 CAPRIN2 HSF2 PTPN5 PHF2 BAMBI ABCC5 TUBA1C ASMTL DYNC1L12 ABL1 IQSEC1 OPN5L1 TRIP12 PSMA7 ZMYND8 DLGAP4 APLP2 PRKD3 MSI2 BTBD11 CDH2 C16orf72 THBS2 KDM6A NCAM1 USP33 DIO2 MTDH SLC25A6 GBAS SEMA6D TCF12 CABIN1 SPTAN1 PPP4R3A MTHFD1L ATG4B HSP90B1 NCL WDR20 GSPT1 MOB1A HOXB6 SSR2 NFIL3 AEBP2 CNN3 DCUN1D3 UBE4B GLG1 NUDT16L1 LSM8 EVI5 LOC100859798 RARB DCAF13 MED14 HTRA1 RNF111 MYL6 TARDBP SMC4 STAU1 CARS ATP2C1 PRSS35 ESRRG PDE10A ZNF410 ZEB2 SHOC2 HIF1AN NSFL1C XRN1 KIAA1468 FN1 CRMP1 JMJD1C IRF2 PPP1R12A NAA16 PPP2CA SRPX ODC1 ATP1A1 NAA30 CTDSPL USP9X BAZ1A PIK3R3 MSMO1 ACVR2A PTPRO YWHAZ MECOM LMO4 SCUBE1 MAP2K6 SGCD ARID4A HZGJ NAB1 HUS1 YY1 TARS ENO1 MED31 YLPM1 TAF3 OSBPL10 DDX1 ITFG1 PRPF4B UBQLN1 VPS54 GGNBP2 TM9SF3 SEC11A YWHAH VSTM4 PPP6R3 VAPB MLL3 COPB1 CREBRF SLC25A13 SVIL CTBP2 FBLN1 GINM1 PRPSAP2 MYOF RBMX AC113404.1 TNKS2 ZCCHC2 LUC7L RAF1 MST4 AKTIP SULF1 TCF21 ZFYVE21 GSN SMARCA5 TCP1 PPA2 HERC4 PREX2 SLC38A1 RBM26 VLDLR RAB11A COL5A2 EIF3D ME3 SNCAIP PCNA UNK DOLPP1 CANX CCND2 DESI2 SLIT3 DSE ZNF462 EPRS SPAG9 CDC42BPB COX20 TM9SF4 ANKIB1 PDPK1 RAB5A EIF4A2 DMD ADM ISCU COL6A3 MYH10 LAP3 EPS15 NOVA1 ZFH3 DNAJA1 ADCK3 SOCS5 INTS10 TNK2 CCT5 IDH1 USP25 PRKX DLG5 PGM5 TALDO1 CUX1 NF1 DUSP1 SQLE HDAC1 PSMD7 SEPHS1 FNDC3B ADAM10 NELFCD MAP4K3 CTNBN1 NAP1L4 MRPS22 ZHX1 OXR1 ANK3 HNRNPK HK1 KDM2B SREK1 HEXB NCK2 EBF1 ZNF644 RARS PSMC3 RUNX1T1 CCND1 CTSK P4HB SEPT11 MMADHC STC2 AFTPH CALD1 COL6A1 PSMD2 ATXN2 HTRA3 EIF3E IPO5 ZMPSTE24 RLIM SNRNP200 NAA25 LOC101752174 TOP2B RPN2 DVL1 STRN3 ZNF207 COL5A1 AGAP1 C14ORF4 MAP4K4 SEC61A2 COL11A1 FAM53A IL1RAP GYG1 CDC5L YPEL1 NR1D2 ACTN1 SPRED2 SLIT2 CDC20 RCN1 UBE2K XPOT MDH2 CTHRC1 SLC4A7 PARVB SBNO1 SETBP1 DOCK7 DNER RBM25 DNAJB14 FAM20C SEC24A TP53BP1 TPR CEBPB MCMBP VPS13A SERBP1 OSBPL6 HIAT1 PKDCCa NAA15 PARD3 KDM3A LOC421049 SEPT6 PLS3 LBH PPP2R3A LPHN2 CHPF2 ARID1B SNAI2 DDX3X TTC27 HNRNPU PGD NKX2-1 MAP3K1 AP2A2 FAM91A1 LPCAT1 SP4 WAC EIF3H HNRNPH3 COL1A2 GNA13 DTNA ATF4 LRPAP1 ORAOV1 TSPAN14 UBR4 CTCF KTN1 KPNA1 AMD1 TRIB2 RANBP9 USP8 FAF2 PIAS1 ARGLU1 CLTC ZNF521 XPO7 CNOT2 MAN1A2 SET domain containing 5 BEND5 COL8A1 CAMK2G WAPAL PSME4 FBXO30 BRD1 PRICKLE2 KARS GRIA2 APP ATP2B1 LMTK2 COL12A1 SLC2A1 HEATR1 BTAF1 RBMS1 NR2F2 SMURF2 UBE2QL1 TEAD4 MIR1600 BBX HSP90AA1 TNRC6B HECW1 WFS1 DUSP8 PDE3B ZNF622 CHTOP PGK1 NCKAP1 KLF3 </p>
	Down	174	<p> RPS17 DTD1 CCDC25 CARHSP1 RPL10A PDCD6 CNN2 UCKL1 NDUFV3 NUTF2 SREKIIP1 RPLP0 CFBF MSRB3 DDX28 ATP5D RPL36A NLRP3 ATP5L TOMM6 AIDA INHBA NME2 PDLIM7 MAP2K5 RPL29 RPS20 CEP63 SQSTM1 PHF6 MESDC1 FAM136A HMOX2 UBL3 CDK2AP1 ZDHHC6 RPS15A MAPKAP1 SRSF10 PURA LMOD3 RPL15 PDLIM4 RPL12 RPLP1 MRPS11 IFT140 MAFK RPS12 C12orf75 TAF12 CLK2 HMGN3 RPL18A RPS4X EIF3M HPRT1 MCHR2 MT3 NDNL2 COA5 ITGB1BP3 RPL32 LOC770490 EIF4EBP1 PARL RASD1 LOC101750049 RPL9 SPRY2 RPSA PHLDA2 RBPMS </p>

Supplementary Table S2. Continued

HPAIV specific DEGs	Down	174	RBM38 RPS21 RPL13 NEK7 BRF1 RPL23 CKS1B RPS2 SEZ6L CHMP6 TXNDC11 SPCS3 TPT1 NPTX2 FTH1 PITX1 ICA1 EIF1AY PRELID1 BOD1 KLHDC8B GUCD1 ARPP19 ST3GAL3 SGK1 KIAA0930 PDGFB RPS7 TPM2 SET NUDCD3 PPP2CB NREP SYDE2 EXO1 GATSL2 C1ORF35 NDUFA12 MPP1 STARD3NL KLHL5 CTBP1 C18ORF8 CAMKK2 NDUFA4 ARHGDIG YBX3 SPRED1 ZMYM6NB RP11-371E8.4 SOX11 ACTA1 WDR83OS VOPP1 ATP5C1 TULP4 BCAS2 RPS25 BMP4 ZNF821 ASB7 CSNK2A2 RNF11 HES4 KCTD3 COX7C UTP14A EEF1B2 CHN1 OLA1 ETV6 S100A6 LOC101748094 RBPMS2 STMN2 RPS14 NF2 RPL30 DRG1 INHBB RPL24 RPL38 RP5-864K19.6 RPS16 IL8L2 RPL14 TMEM208 MAFF FKBP1A EHBP1 GSTT1L EVL GPR75 SMIM11 ATP5G1 ZNRF1 SLC35B4 RPS6KB1 BTF3L4 RPS15 ARHGDIB
LPAIV specific DEGs	Up	351	HZGJ PHLDB1 SEC23A ZDHHC14 MMP2 ABCA3 HUS1 TARS YY1 ACSS3 ENO1 SRP68 P4HA1 APBB2 DDX1 ATRX TACC2 MGMT1 TKT DIO3 PFKP COL3A1 SUFU HERPUD2 WASL CCNL2 PPP2R2D WNK2 MBNL2 ADD3 ZFAND5 GFPT1 RAPGEF2 DCAF5 RNHI ATP9B GTF2A1 GRB10 KPNA4 EEF2 TRIO SLC25A13 EPHA3 WDR61 RDH10 HMGNS5 HIC2 SVIL P4HA2 GINMI PRPSAP2 AC113404.1 TNKS2 IGF2BP3 ZEB1 AKTIP KBTBD2 ZFYVE21 TCF21 GSN TNC SMAD2 ATP5A1 PAPOLA FYN HERC4 SH3KBP1 ZNF276 SLC38A1 DLD ITGB1 PCDHI RAB40B TNS3 RBM26 VLDLR HBS1L KLF15 TAB2 COL5A2 YEATS4 WSB2 NRP1 DNAJA2 USP15 protein HEXIM1 SLC31A1 ARHGAP21 ST7L SFXN1 CANX CRYZL1 ASCC3 DESI2 BASP1 ZNF462 ITM2B FOXN3 CDC42BPB TMEM60 PITRM1 HS6ST2 BICD1 TRAK1 WDR33 RAB5A EIF4A2 ADM COL6A3 USP22 MYH10 LAP3 MTA3 FOXK2 LRRC8C COL1A1 PDIA3 NOVA1 ZFH3 STXBP5 ADCK3 DNAJA1 SOCS5 RNF149 HADHA TALDO1 FBXO22 PPP3CA PSMD7 SEPHS1 CAPRIN1 ANKRD10 RAD51C EIF2S2 TDRD3 ADAM10 MAP4K3 CTNBN1 MDH1 OXR1 FAM98A ANK3 MAML1 DPH3 YTHDF3 NDRG1 PEX14 HK1 CCNE1 CCNY LPCAT3 MXI1 NCK2 RBPJ CCND1 SMARCA2 LRRC8D SIRT5 RUNX1T1 PAPD7 ZFP36L1 MAGI2 P4HB SEPT11 UST AFTPH CALD1 RBM15B ADD1 POLR2F DAB2IP FBXO11 HTRA3 EIF3E C16ORF45 RP11-152F13.10 PSMB3 RLIM QDPR MRPL39 UBE3A SNRNP200 HSPD1 ARID4B RP11-101E3.5 PVRL3 LEPRE1 RSPO3 STAG1 ZNF207 MYCBP2 COL5A1 DCBLD1 AGAP1 MXD4 C1ORF198 USP7 PMEPA1 C14ORF4 EIF4G2 SPPL3 CPSF6 SEC61A2 CKB FDXACB1 TTC8 FAM53A MMAA EDEM2 DHX37 ACTN1 EML4 ALCAM CYB5A ATP6V0C PSMD6 ATF2 UBE2K HNRNPM XPOT RP11-234B24.6 PANK4 COMMD9 COG1 ELOVL6 GALNT1 METRNL CELF1 GALNS DOCK7 HNRNPAB DNER BCL9 FBLN2 KATNA1 CEBPB CAPRIN2 SPTBN1 HSF2 GAS6 VPS13A HIAT1 PKDCCa APOO ETV1 BAMB1 PARD3 ABCC5 HECTD3 KDM3A TUBA1C LOC421049 TMEM260 IQSEC1 TRIP12 PRKD3 EPHB2 SDC2 DYNC1I2 CHPF2 CDH2 ACP2 DIO2 PGD SESTD1 PRSS23 TCF12 MAP3K1 HACE1 ARIH1 AP2A2 SPTAN1 CABIN1 SRSF3 HSP90B1 WAC APRT ACHE GSK3B COL1A2 GNA13 DTNA NFIL3 ATF4 ORAOV1 AMIGO2 GLG1 TSPAN14 CTCF PANK3 AMD1 RARB RANBP9 USP8 CLTC ZNF521 PPP4R1 HTRA1 IPO13 CNOT2 PDCD10 RNF111 WISP1 COL8A1 KLHL7 CAMK2G MKRN2 GNB4 ATP2C1 PRICKLE2 APP ATP2B1 COL12A1 ESRRG CELF2 ZEB2 PIGF TMEM165 RBMS1 STO2 DNAJC13 MTA1 XRN1 PBX1 FN1 CPSF2 IRF2 PBRM1 PPP1R12A MIR1600 BBX PPP2CA ACO2 TAMM41 CNOT6L HMGB1 CTDSPL USP9X NAP1L1 VAPA MSMO1 KLF6 NEK6 PTPRO YWHAZ PRRX1 LMO4 MRS2 USP38 CDYL DDX17
	Down	88	RPS11 RPS17 ASIC4 DPY30 PCDH9 CKS1B TAGLN RPL10A VAC14 TPT1 NUTF2 FTH1 CSRP1 RPL7 LOC768760 LOC424167 RPLP0 PGAM1 ARPP19 RPS7 SNRPC NLRP3 SET RPL37A INHBA ADCYAP1 PDLIM7 TMEM258 RPL29 SUMO2 RGS3 RPS26 FRMD1 FAM212B NDUFA4 ITGAD NUA2 YBX3 LOC396479 SLC6A13 UBE2I RPS15A LINGO1 RPL23A HDGF RPS25 RNF114 DDA1 RPLP1 OST4 GNG5 RPS12 COX7C SH3GLB1 RPL18A PPP1R26 ETV6 UBA52 EOGT BIRC2 RPS14 MCHR2 TOMM7 RPL30 ARFIP2 MRPS31 RPL38 ITGB1BP3 RPS16 RPL32 LASP1 AMOTL2 RPL27A OSR2 RPSA DPYSL3 LOC101748129 SNX3 CREM ADAMTS7 ZNRF1 MSX2 AAGAB RPS21 S100A10 LOC424199 PCDHGC5 RPS15

Supplementary Table S3. Gene list of down-regulated DEGs for both HPAIV and LPAIV

HPAIV only	140	BCAS2 BMP4 RPL23 DTD1 PDLIM4 ZNF821 CCDC25 CARHSP1 RPL12 ASB7 CSNK2A2 RPS2 RNF11 SEZ6L CHMP6 TXNDC11 PDCD6 SPCS3 CNN2 MRPS11 UCKL1 NPTX2 NDUFV3 IFT140 MAFK HES4 PITX1 EIF1AY C12orf75 ICA1 TAF12 CLK2 KCTD3 SREK1IP1 BOD1 PRELID1 UTP14A HMGN3 EEF1B2 KLHDC8B CHN1 OLA1 S100A6 CBF3 LOC101748094 MSRB3 RPS4X GUCD1 RBPMS2 EIF3M DDX28 STMN2 ATP5D HPRT1 ST3GAL3 RPL36A NF2 SGK1 KIAA0930 MT3 PDGFB DRG1 INHBB NDNL2 TPM2 ATP5L NUDCD3 COA5 RPL24 PPP2CB NREP RP5-864K19.6 SYDE2 TOMM6 AIDA EXO1 IL8L2 NME2 EIF4EBP1 LOC770490 GATSL2 RPL14 TMEM208 C1ORF35 MAFF MAP2K5 RPS20 NDUFA12 MPP1 STARD3NL FKBP1A EHBP1 PARL CEP63 KLHL5 RASD1 LOC101750049 SQSTM1 CTBP1 PHF6 GSTT1L EVL MESDC1 C18ORF8 GPR75 RPL9 FAM136A CAMKK2 SMIM11 SPRY2 ARHGDIG HMOX2 UBL3 SPRED1 PHLDA2 ZMYM6NB RP11-371E8.4 ATP5G1 CDK2AP1 SOX11 ZDHHC6 ACTA1 WDR83OS ATP5C1 VOPPI RBPMS MAPKAP1 RBM38 SRSF10 RPL13 SLC35B4 RPS6KB1 TULP4 PURA NEK7 LMOD3 RPL15 BTF3L4 BRF1 ARHGDIB
LPAIV only	53	HDGF RPS11 ASIC4 RNF114 DPY30 PCDH9 TAGLN DDA1 VAC14 OST4 GNG5 CSRP1 SH3GLB1 RPL7 LOC768760 PPP1R26 LOC424167 PGAM1 UBA52 EOGT BIRC2 TOMM7 SNRPC ARFIP2 MRPS31 RPL37A ADCYAP1 LASP1 AMOTL2 TMEM258 SUMO2 RGS3 RPS26 FRMD1 RPL27A FAM212B OSR2 NUA2 DPYSL3 SNX3 LOC101748129 LOC396479 CREM ADAMTS7 SLC6A13 UBE2I MSX2 LINGO1 RPL23A AAGAB S100A10 LOC424199 PCDHGC5
Common	34	RPS25 RPS17 CKS1B RPL10A RPLP1 TPT1 NUTF2 FTH1 RPS12 COX7C RPL18A RPLP0 ETV6 ARPP19 RPS14 MCHR2 RPL30 RPS7 NLRP3 SET RPL38 ITGB1BP3 RPS16 RPL32 INHBA PDLIM7 RPL29 RPSA NDUFA4 YBX3 ZNRF1 RPS15A RPS21 RPS15

Supplementary Table S4. Gene list of up-regulated DEGs for both HPAIV and LPAIV

HPAIV only	364	<p>CALM SLMAP HERC1 NR3C2 MTF2 C11H16ORF70 GSR VPS35 GPC4 LMO7 KMT2E UBE2G1 OGT PTEN SLTM GNAL EP300 GUCY1A3 LMAN2 ATXN7L1 SETD2 MATR3 KIF26A UBB TRIM33 PTPRS HMGB3 LEPREL4 PTPN1 EPN2 NXN FHL3 EIF5B NUP214 MARCKS DPYSL2 ZYG11B IRF2BP2 CSNK1E LONP1 SASH1 IKZF5 ATP6V1B2 FAP TPP2 RTN4IP1 HTR2B GTF2H1 GJA1 MLLT1 HECTD1 ACTR8 HERC2 CRY2 AHSA1 DIP2C ACTL6A CAND1 EIF4G3 MAP3K5 CNPY3 PALLD MXRA8 CPEB2 HNRNPA2B1 LOC395676 PAIP2 ATL2 SEL1L3 DCAF6 YIPF4 NFIB EIF3A KIAA0020 PTPRF NME7 ABR BTG1 PAFAH1B1 PGRMC2 PSMC2 AL158801.1 AFAP1 ISM1 THOC2 UBA6 DCUN1D1 AKIRIN2 MYO1C ZFC3H1 ARMC1 CNKSR3 FAM46A PI4KA PTPN21 LSM14A ABHD13 CCPG1 SKIV2L2 ANKHD1 SMARCB1 TIPARP PREP YWHAQ BAZ2B HNRNPR MEIS2 MCU PPM1A COPG1 PPP1R8 PXDN MYH9 RAB35 PLEKHB2 IARS PLSCR1 URI1 PIK3C3 SACM1L DNAJC2 C11H16ORF87 SYNCRIP MICAL2 DHRSX CCT8 PTPN5 PHF2 ASMTL DYNC1L12 ABL1 OPN5L1 ZMYND8 PSMA7 DLGAP4 APLP2 MSI2 BTBD11 KDM6A THBS2 C16orf72 NCAM1 USP33 MTDH SLC25A6 GBAS SEMA6D PPP4R3A MTHFD1L ATG4B NCL WDR20 MOB1A GSPT1 HOXB6 SSR2 AEBP2 CNN3 DCUN1D3 UBE4B NUDT16L1 LSM8 EVI5 LOC100859798 DCAF13 MED14 MYL6 TARDBP SMC4 STAU1 CARS PRSS35 PDE10A ZNF410 SHOC2 HIF1AN NSFL1C KIAA1468 CRMP1 MJMD1C NAA16 SRPX ODC1 ATP1A1 NAA30 BAZ1A PIK3R3 ACVR2A MECOM SCUBE1 MAP2K6 SGCD ARID4A NAB1 TAF3 YLPM1 MED31 OSBPL10 ITFG1 PRPF4B UBQLN1 VPS54 GGNBP2 TM9SF3 SEC11A YWHAH VSTM4 PPP6R3 VAPB MLL3 COPB1 CREBRF CTBP2 FBLN1 MYOF RBMX ZCCHC2 LUC7L RAF1 MST4 SULF1 SMARCA5 TCP1 PPA2 PREX2 RAB11A EIF3D ME3 SNCAIP PCNA UNK DOLPP1 SLIT3 CCND2 DSE EPRS SPAG9 COX20 TM9SF4 ANKIB1 PDPK1 DMD ISCU EPS15 INTS10 TNK2 CCT5 IDH1 USP25 PRKX DLG5 PGM5 CUX1 NF1 DUSP1 HDAC1 SQLE FNDC3B NELFCD NAP1L4 MRPS22 ZHX1 HNRNPK KDM2B SREK1 HEXB EBF1 ZNF644 RARS PSMC3 CTSK MMADHC STC2 PSMD2 COL6A1 ATXN2 IPO5 ZMPSTE24 LOC101752174 NAA25 TOP2B RPN2 STRN3 DVL1 MAP4K4 COL11A1 IL1RAP CDC5L GYG1 NR1D2 YPEL1 SPRED2 SLIT2 CDC20 RCN1 CTHRC1 MDH2 SLC4A7 PARVB SBNO1 SETBP1 RBM25 DNAJB14 FAM20C TP53BP1 SEC24A TPR MCMBP SERBP1 OSBPL6 NAA15 SEPT6 PLS3 LBH PPP2R3A LPHN2 ARID1B SNAI2 DDX3X TTC27 HNRNPU NKX2-1 FAM91A1 LPCAT1 SP4 EIF3H HNRNPH3 LRPAP1 UBR4 KTN1 KPNA1 TRIB2 FAF2 PIAS1 ARGLU1 XPO7 MAN1A2 SET domain containing 5 BEND5 WAPAL PSME4 FBXO30 BRD1 KARS GRIA2 LMTK2 HEATR1 SLC2A1 BTAF1 NR2F2 UBE2QL1 SMURF2 TEAD4 HSP90AA1 TNRC6B HECW1 DUSP8 WFS1 ZNF622 PDE3B CHTOP PGK1 NCKAP1 KLF3</p>
LPAIV only	158	<p>PHLDB1 SEC23A MMP2 ACSS3 APBB2 TACC2 MGMT1 DIO3 WASL MBNL2 ADD3 GFPT1 DCAF5 ATP9B GRB10 EEF2 EPHA3 WDR61 HMG5 TNC PAPOLA ZNF276 PCDH1 RAB40B TNS3 protein HEXIM1 ST7L SFXN1 CRYZL1 ITM2B FOXN3 FBXO22 CAPRIN1 ANKRD10 TDRD3 MDH1 MAML1 DPH3 NDRG1 PEX14 CCNE1 CCNY RBPJ SIRT5 DAB2IP RP11-152F13.10 QDPR HSPD1 LEPRE1 STAG1 MXD4 CPSF6 CKB FDXACB1 TTC8 MMAA PSMD6 RP11-234B24.6 COG1 CELF1 KATNA1 APOO HECTD3 TMEM260 SDC2 ACP2 PRSS23 HACE1 ARIH1 IPO13 WISPI KLHL7 GNB4 CELF2 PIGF TMEM165 STOX2 MTA1 PBX1 PBRM1 ACO2 TAMM41 VAPA KLF6 NEK6 PRRX1 MRS2 DDX17 ZDHHC14 SRP68 P4HA1 SUFU CCNL2 PPP2R2D ZFAND5 RAPGEF2 RNH1 KBTBD2 FYN SH3KBP1 DLD ITGB1 HBS1L KLF15 TAB2 WSB2 PITRM1 HS6ST2 BICD1 TRAK1 USP22 STXBP5 RNF149 HADHA RAD51C EIF2S2 LPCAT3 SMARCA2 UST RBM15B ADD1 C16ORF45 PSMB3 UBE3A ARID4B PVRL3 RSPO3 C10RF198 PMEPA1 EIF4G2 EDEM2 DHX37 CYB5A PANK4 COMMD9 GALNT1 GALNS GAS6 ETV1 EPHB2 DYNC1I2 SESTD1 SRSF3 APRT ACHE GSK3B AMIGO2 PANK3 PPP4R1 PDCD10 MKRN2 DNAJC13 CPSF2 CNOT6L HMGB1 NAP1L1 USP38 CDYL</p>
Common	193	<p>ABCA3 ATRX TKT PFKP COL3A1 HERPUD2 WNK2 GTF2A1 KPNA4 TRIO RDH10 HIC2 P4HA2 IGF2BP3 ZEB1 SMAD2 ATP5A1 YEATS4 NRP1 DNAJA2 USP15 SLC31A1 ARHGAP21 ASCC3 BASP1 TMEM60 WDR33 MTA3 FOXK2 LRRC8 COL1A1 PDIA3 PPP3CA FAM98A YTHDF3 MXI1 LRRC8D PAPD7 ZFP36L1 MAGI2 POLR2F FBXO11 MRPL39 RP11-101E3.5 MYCBP2 DCBLD1 USP7 SPPL3 EML4 ALCAM ATP6V0C ATF2 HNRNPM ELOVL6 METRNL HNRNPAB FBLN2 BCL9 CAPRIN2 SPTBN1 HSF2 BAMB1 ABCC5 TUBA1C IQSEC1 TRIP12 PRKD3 CDH2 DIO2 TCF12 CABIN1 SPTAN1 HSP90B1 NFIL3 GLG1 RARB HTRA1 RNF111 ATP2C1 ESRRG ZEB2 XRN1 FN1 IRF2 PPP1R12A PPP2CA CTDSPL USP9X MSMO1 PTPRO YWHAZ LMO4 HZGJ HUS1 YY1 TARS ENO1 DDX1 SLC25A13 SVIL GINM1 PRPSAP2 AC113404.1 TNKS2 AKTIP TCF21 ZFYVE21 GSN HERC4 SLC38A1 RBM26 VLDLR COL5A2 CANX DESI2 ZNF462 CDC42BPB RAB5A EIF4A2 ADM COL6A3 MYH10 LAP3 NOVA1 ZFH3 ADCK3 DNAJA1 SOCS5 TALDO1 PSMD7 SEPHS1 ADAM10 MAP4K3 CTNNB1 OXR1 ANK3 HK1 NCK2 RUNX1T1 CCND1 P4HB SEPT11 AFTPH CALD1 HTRA3 EIF3E RLIM SNRNP200 ZNF207 COL5A1 AGAP1 C14ORF4 SEC61A2 FAM53A ACTN1 UBE2K XPOT DOCK7 DNER CEBPB VPS13A PKDCCa HIAT1 PARD3 KDM3A LOC421049 CHPF2 PGD MAP3K1 AP2A2 WAC GNA13 COL1A2 DTNA ATF4 ORAOV1 TSPAN14 CTCF AMD1 RANBP9 USP8 CLTC ZNF521 CNOT2 COL8A1 CAMK2G PRICKLE2 APP COL12A1 ATP2B1 RBMS1 MIR1600 BBX</p>

