

File S2: Supplementary results

Table S1: List of up and down regulated DEGs and key genes (KGs) marked by bold. adj.P.Value < 0.01 and |logFC| > 1.0 threshold have been considered to extracted the differential expressed genes.

Up regulated DEGs	Down regulated DEGs
<i>MATN3, PIGZ, PDE4DIP, SLCO2A1, SGK1, CLN8, ABLIM2, SEMA3C, YPEL4, C8orf58, SEMA3A, FBXO15, NR2F1, CASP4, KDM7A, HIC2, POLR3E, CCDC74B, C12orf76, CFAP206, CASP5, CDADC1, RELB, C5orf45, OSR2, FBXO16, MESP1, TMEM222, CLDN1, CDK6, TBX6, PCDH9, MYO15B, TCTN1, ZC3H10, GLIPR1L2, BCL11A, CREB5, NOC2L, RGPDI, CYB5R1, CECR5-AS1, NT5E, CITED4, C14orf37, EVL, LYRM9, LINC01016, JHDM1D-AS1, ANGPT1, LOC101929147.</i>	<i>MARCO, CDCA5, HRASLS2, CTSO, AQP3, FMOD, SORCS2, TRAPPC13, FAM105A, NEURL1, AKRIC3, RFC3, SLIT2, GSE1, HSH2D, TLE2, ANKRD1, CDCA3, CAPG, RASSF2, TP53INP1, CSTA, MPP1, RARRES3, AQP1, TSPAN2, IFI6, CALHM2, LPAR5, GJB2, NQO1, EPB41L5, GINS1, EGR1, KIAA0408, PLS3, HOPX, APOL3, PLXNA2, PCDH7, C4BPB, ST6GALNAC5, ZNF385B, SPEG, NUP62CL, PLCH1, DTX3L, IFIT3, AHRR, SESN3, GIMAP2, MELTF, KDELC2, BST2, TIMP3, CDH24, PRUNE2, HPN, METTL7A, JADE2, CARD6, EP400, TDRD10, PODNLI, IFI44L, CCNA1, DHRS2, FAXDC2, DGKH, FOLR1, NEMPI, SPRED1, LDHD, STAT1, OAS1, RACGAP1P, IRF9, HES1, PARP9, IFITM1, CITED1, SLC6A12, B3GNT3, NOSTRIN, TDO2, PLAT, TAGLN, FOXN3, CA2, PSMD9, FNI, SAMD9, COCH, EPB41LI, TRIM14, PML, AKRIC1, BHLHE40, IFI27, TRIP13, PLEKHS1, CENPJ, RNF39, RSAD2, PDE4A, GLS2, DDX60, OAS3, OAS2, REC8, TPP1, PMEPA1, ADCY7, CEP128, UNC13A, SECTM1, GLDN, LINC00933, SLC20A2, TRANK1, HPGD, ACTR3C, ATF6B, CENPN, COQ2, RAB3B, LINC01224, KNDC1, LNX2, PABPC4L, SLC16A7, C2, FAM101A, DNAH2, MBD3, SHISA2, TDRD12, ZMAT1.</i>
Bold indicates key genes (KGs).	

Table S2: list of 13 identified key genes (kg) with gene name, logFC, p-value, and adjusted p-value.

Gene.symbol	Gene name	logFC	P.Value	adj.P.Val
AKRIC1	aldo-keto reductase family 1 member C1	-2.908633	4.16E-10	4.28E-06
FNI	fibronectin 1	-2.480665	1.71E-06	0.001001
OAS3	2'-5'-oligoadenylate synthetase 3	-2.355372	1.62E-08	4.75E-05
IRF9	interferon regulatory factor 9	-2.331889	8.43E-09	3.15E-05
HPGD	hydroxyprostaglandin dehydrogenase 15-(NAD)	-1.956437	2.15E-09	1.36E-05
OAS1	2'-5'-oligoadenylate synthetase 1	-1.76677	7.49E-05	0.007712
SLCO2A1	solute carrier organic anion transporter family member 2A1	1.72759	5.94E-05	0.006722
ATF6B	activating transcription factor 6 beta	-1.68305	0.000115	0.009925
NT5E	5'-nucleotidase ecto	1.670646	8.56E-06	0.002494
BCL11A	B-cell CLL/Lymphoma 11A	1.636371	1.30E-05	0.003059
NQO1	NAD(P)H quinone dehydrogenase 1	-1.577233	5.89E-05	0.006702
ANGPT1	angiopoietin 1	1.55281	2.12E-07	0.000277
TP53INP1	tumor protein p53 inducible nuclear protein 1	-1.517725	6.24E-07	0.000562

S3 Table Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis of the differentially expressed genes (DEGs).

Terms/Functions	Count	PValue	Genes
GO functional analysis			
Down regulated DEGs			
GO Terms of Biological Process (BP)			
GO:0060337~type I interferon signaling pathway	12	8.41E-13	<i>BST2, EGR1, IFITM1, IFI27, RSAD2, OAS1, STAT1, OAS2, OAS3, IFI6, IRF9, IFIT3</i>
GO:0051607~defense response to virus	12	2.72E-08	<i>BST2, IFITM1, RSAD2, OAS1, STAT1, OAS2, OAS3, DDX60, IFI44L, IRF9, PML, IFIT3</i>
GO:0009615~response to virus	8	1.38E-05	<i>BST2, IFITM1, RSAD2, OAS1, OAS2, OAS3, DDX60, IFIT3</i>
GO:0060333~interferon-gamma-mediated signaling pathway	6	1.53E-04	<i>OAS1, STAT1, OAS2, OAS3, IRF9, PML, ATF6B</i>
GO:0045071~negative regulation of viral genome replication	5	1.86E-04	<i>BST2, IFITM1, RSAD2, OAS1, OAS3</i>
GO:0006302~double-strand break repair	5	0.00127	<i>DTX3L, CDCA5, TRIP13, PARP9, REC8</i>
GO:0035456~response to interferon-beta	3	0.00176	<i>BST2, IFITM1, STAT1</i>
GO:0034097~response to cytokine	4	0.0061	<i>CITED1, IFI27, STAT1, PML</i>
GO:0007141~male meiosis I	3	0.00719	<i>CCNA1, TRIP13, REC8</i>
GO:0034341~response to interferon-gamma	3	0.01261	<i>BST2, IFITM1, CITED1</i>
GO:0060700~regulation of ribonuclease activity	2	0.01424	<i>OAS1, OAS3</i>
GO:0007584~response to nutrient	4	0.01597	<i>NQO1, STAT1, AKR1C3, C2</i>
GO:0003340~negative regulation of mesenchymal to epithelial transition involved in metanephros morphogenesis	2	0.02129	<i>CITED1, STAT1</i>
GO:0003091~renal water homeostasis	3	0.02184	<i>ADCY7, AQP3, AQP1</i>
GO:0008285~negative regulation of cell proliferation	8	0.02361	<i>IFITM1, RARRES3, TP53INP1, NEURL1, SPEG, DHRS2, PML, IFIT3</i>
GO:0032355~response to estradiol	4	0.02744	<i>MBD3, NQO1, GJB2, IFI27</i>
GO:0015670~carbon dioxide transport	2	0.02828	<i>CA2, AQP1</i>
GO:0071395~cellular response to jasmonic acid stimulus	2	0.02828	<i>AKR1C1, AKR1C3</i>
GO:0046683~response to organophosphorus	2	0.02828	<i>RFC3, AKR1C1</i>
GO:0030336~negative regulation of cell migration	4	0.03063	<i>BST2, IFITM1, TP53INP1, SLIT2</i>
GO:0051902~negative regulation of mitochondrial depolarization	2	0.03523	<i>HSH2D, IFI6</i>
GO:0071504~cellular response to heparin	2	0.03523	<i>EGR1, SLIT2</i>
GO:0010756~positive regulation of plasminogen activation	2	0.03523	<i>HPN, MELTF</i>
GO:0061626~pharyngeal arch artery morphogenesis	2	0.04897	<i>HES1, FOLR1</i>
GO:0044598~doxorubicin metabolic process	2	0.05577	<i>AKR1C1, AKR1C3</i>

GO:0044597~daunorubicin metabolic process	2	0.05577	<i>AKR1C1, AKR1C3</i>
GO:0048146~positive regulation of fibroblast proliferation	3	0.05697	<i>FNI, PML, AQP1</i>
GO:1901796~regulation of signal transduction by p53 class mediator	4	0.05928	<i>MBD3, RFC3, TP53INP1, PML</i>
GO:0055114~oxidation-reduction process	9	0.06191	<i>NQO1, HPGD, SESN3, TDO2, FAXDC2, AKR1C1, LDHD, AKR1C3, DHRS2</i>
GO:0042448~progesterone metabolic process	2	0.06252	<i>AKR1C1, AKR1C3</i>
GO:0035457~cellular response to interferon-alpha	2	0.06252	<i>OAS1, IFIT3</i>
GO:0042981~regulation of apoptotic process	5	0.06656	<i>EGR1, STAT1, GLS2, TP53INP1, CARD6</i>
GO:0035455~response to interferon-alpha	2	0.06923	<i>BST2, IFITM1</i>
GO:0035385~Roundabout signaling pathway	2	0.08249	<i>SLIT2, FMOD</i>
GO:0042574~retinal metabolic process	2	0.08249	<i>AKR1C1, AKR1C3</i>
GO:0048846~axon extension involved in axon guidance	2	0.08249	<i>SLIT2, FMOD</i>
GO:0043517~positive regulation of DNA damage response, signal transduction by p53 class mediator	2	0.08249	<i>SPRED1, ANKRD1</i>
GO:0006164~purine nucleotide biosynthetic process	2	0.08249	<i>OAS1, OAS2</i>
GO:0032868~response to insulin	3	0.08297	<i>EGR1, CITED1, SESN3</i>
GO:0045087~innate immune response	7	0.08806	<i>BST2, MARCO, TRIM14, C4BPB, DDX60, PML, C2</i>
GO:0006693~prostaglandin metabolic process	2	0.08905	<i>HPGD, AKR1C3</i>
GO:0009992~cellular water homeostasis	2	0.08905	<i>AQP3, AQP1</i>
GO:0015793~glycerol transport	2	0.08905	<i>AQP3, AQP1</i>
GO:0030855~epithelial cell differentiation	3	0.08941	<i>TAGLN, AKR1C1, TPP1</i>
GO:0071361~cellular response to ethanol	2	0.09557	<i>TP53INP1, ADCY7</i>
GO:0007064~mitotic sister chromatid cohesion	2	0.09557	<i>CDCA5, REC8</i>

GO Terms of Cellular Component (CC)

GO:0005737~cytoplasm	57	4.91E-05	<i>RAB3B, CITED1, GIMAP2, PLAT, AQP3, IFI44L, IFIT3, AQP1, CEP128, PSMD9, SPRED1, PODNLI, RASSF2, SESN3, CA2, ANKRD1, PLS3, UNC13A, DTX3L, HRASLS2, PARP9, OAS1, OAS2, OAS3, AHRR, TRIM14, IRF9, DGKH, CSTA, TAGLN, DNAH2, SAMD9, HPGD, CDCA5, PRUNE2, CAPG, DDX60, EPB41L5, EPB41L1, TP53INP1, RNF39, HES1, SLIT2, METTL7A, APOL3, GINS1, MBD3, EGR1, NQO1, STAT1, AKR1C3, DHRS2, HOPX, PML, BST2, GJB2, PLCH1</i>
GO:0005578~proteinaceous extracellular matrix	7	0.009721	<i>PODNLI, FNI, TIMP3, SLIT2, FMOD, GLDN, COCH</i>
GO:0005911~cell-cell junction	5	0.029262	<i>CDCA3, EPB41L1, HPN, CDH24,</i>

			<i>AQP3</i>
GO:0016323~basolateral plasma membrane	5	0.033759	HPGD , CA2, <i>AQP3</i> , <i>FOLR1</i> , <i>AQP1</i> <i>CSTA</i> , <i>TLE2</i> , FNI , <i>SECTM1</i> , <i>PLAT</i> , <i>C4BPB</i> , <i>GLDN</i> , <i>C2</i> , <i>CTSO</i> , <i>CA2</i> , OAS3 , <i>TIMP3</i> , <i>SLIT2</i> , <i>MELTF</i> , <i>FMOD</i>
GO:0005615~extracellular space	16	0.037725	<i>CSTA</i> , FNI , <i>TIMP3</i> , <i>PLAT</i> , <i>FMOD</i> , <i>COCH</i>
GO:0031012~extracellular matrix	6	0.050375	<i>MPP1</i> , <i>SLC20A2</i> , <i>PCDH7</i> , <i>HPN</i> , <i>SLC6A12</i> , <i>AQP3</i> , <i>AQP1</i> , <i>BST2</i> , <i>MARCO</i> , <i>CALHM2</i> , <i>PLXNA2</i> , <i>B3GNT3</i> , <i>SLC16A7</i> , <i>TSPAN2</i> , <i>MELTF</i> , <i>FOLR1</i>
GO:0005887~integral component of plasma membrane	16	0.053921	<i>RAB3B</i> , <i>CSTA</i> , <i>SLC20A2</i> , HPGD , <i>HPN</i> , <i>SECTM1</i> , <i>PLAT</i> , <i>CAPG</i> , <i>JADE2</i> , <i>COCH</i> , <i>C2</i> , <i>AQP1</i> , <i>ACTR3C</i> , <i>CA2</i> , <i>TIMP3</i> , <i>SLIT2</i> , <i>METTL7A</i> , NQO1 , AKRIC1 , <i>AKRIC3</i> , FNI , <i>DHRS2</i> , <i>BST2</i> , <i>TPPI</i> , <i>MELTF</i> , <i>FOLR1</i>
GO:0070062~extracellular exosome	27	0.05531	<i>RSAD2</i> , <i>GIMAP2</i> , <i>METTL7A</i> <i>RAB3B</i> , <i>CDCA3</i> , <i>CITED1</i> , HPGD , <i>CDCA5</i> , <i>IFIT3</i> , <i>PSMD9</i> , <i>SPRED1</i> , <i>TDO2</i> , <i>EPB41L1</i> , <i>CA2</i> , TP53INP1 , <i>ANKRD1</i> , <i>PDE4A</i> , NQO1 , <i>DTX3L</i> , <i>STAT1</i> , AKRIC1 , <i>AKRIC3</i> , <i>PARP9</i> , <i>PML</i> , <i>CCNA1</i> , <i>HSH2D</i> , OAS1 , <i>OAS2</i> , OAS3 , <i>CENPJ</i> , <i>CENPN</i> , <i>PLCH1</i> , IRF9
GO:0005811~lipid particle	3	0.07331	<i>CA2</i> , <i>PLAT</i> , <i>AQP1</i>
GO:0005829~cytosol	30	0.07858	
GO:0045177~apical part of cell	3	0.091261	
GO Terms of Molecular Function (MF)			
GO:0001730~2'-5'-oligoadenylate synthetase activity	3	3.28E-04	OAS1 , <i>OAS2</i> , OAS3
GO:0003725~double-stranded RNA binding	4	0.010666	OAS1 , <i>OAS2</i> , OAS3 , <i>DDX60</i>
GO:0016779~nucleotidyltransferase activity	3	0.017174	OAS1 , <i>OAS2</i> , OAS3
GO:0004871~signal transducer activity	6	0.01849	<i>BST2</i> , <i>UNC13A</i> , <i>STAT1</i> , <i>SECTM1</i> , <i>PLCH1</i> , <i>APOL3</i>
GO:0047086~ketosteroid monooxygenase activity	2	0.022227	AKRIC1 , <i>AKRIC3</i>
GO:0047718~indanol dehydrogenase activity	2	0.022227	AKRIC1 , <i>AKRIC3</i>
GO:0018636~phenanthrene 9,10-monooxygenase activity	2	0.029526	AKRIC1 , <i>AKRIC3</i>
GO:0047115~trans-1,2-dihydrobenzene-1,2-diol dehydrogenase activity	2	0.029526	AKRIC1 , <i>AKRIC3</i>
GO:0004032~alditol:NADP+ 1-oxidoreductase activity	2	0.051101	AKRIC1 , <i>AKRIC3</i>
GO:0016655~oxidoreductase activity, acting on NAD(P)H, quinone or similar compound as acceptor	2	0.058187	AKRIC1 , <i>AKRIC3</i>
GO:0016491~oxidoreductase activity	5	0.062918	HPGD , <i>SESN3</i> , AKRIC1 , <i>AKRIC3</i> , <i>DHRS2</i>
GO:0048495~Roundabout binding	2	0.06522	<i>SLIT2</i> , <i>FMOD</i>
GO:0001191~transcriptional repressor	2	0.086008	<i>BHLHE40</i> , <i>AHRR</i>

activity, RNA polymerase II transcription factor binding			
GO:0015254~glycerol channel activity	2	0.086008	<i>AQP3, AQP1</i>
Up regulated DEGs			
GO Terms of BP			
GO:0010977~negative regulation of neuron projection development	4	1.04E-04	<i>BCL11A, SEMA3A, NR2F1, TBX6</i>
GO:0060666~dichotomous subdivision of terminal units involved in salivary gland branching	2	0.01038	<i>SEMA3C, SEMA3A</i>
GO:0045944~positive regulation of transcription from RNA polymerase II promoter	7	0.014821	<i>OSR2, MESP1, BCL11A, CITED4, NR2F1, TBX6, RELB, SLCO2A1</i>
GO:0000122~negative regulation of transcription from RNA polymerase II promoter	6	0.015973	<i>OSR2, BCL11A, NR2F1, TBX6, NOC2L, RELB, NT5E</i>
GO:0006351~transcription, DNA-templated	10	0.016336	<i>HIC2, ABLIM2, BCL11A, POLR3E, CITED4, NR2F1, TBX6, NOC2L, NT5E, KDM7A, RELB, ANGPT1</i>
GO:0006915~apoptotic process	5	0.029434	<i>CASP5, SEMA3A, CASP4, NOC2L, SGK1, ANGPT1,</i>
GO:0010633~negative regulation of epithelial cell migration	2	0.030825	<i>SEMA3A, EVL</i>
GO:0023019~signal transduction involved in regulation of gene expression	2	0.038888	<i>MESP1, TBX6</i>
GO:0007411~axon guidance	3	0.043237	<i>SEMA3C, SEMA3A, EVL</i>
GO:0048843~negative regulation of axon extension involved in axon guidance	2	0.052842	<i>SEMA3C, SEMA3A</i>
GO:0071526~semaphorin-plexin signaling pathway	2	0.066599	<i>SEMA3C, SEMA3A</i>
GO:0050919~negative chemotaxis	2	0.068548	<i>SEMA3C, SEMA3A</i>
GO:0042981~regulation of apoptotic process	3	0.072523	<i>CASP5, CASP4, SGK1</i>
GO:0001755~neural crest cell migration	2	0.089732	<i>SEMA3C, SEMA3A</i>
GO:0045893~positive regulation of transcription, DNA-templated	4	0.091214	<i>OSR2, MESP1, KDM7A, CREB5</i>
GO Terms of CC			
GO:0072557~IPAF inflammasome complex	2	0.010928	<i>CASP5, CASP4</i>
GO:0097169~AIM2 inflammasome complex	2	0.013099	<i>CASP5, CASP4</i>
GO:0072559~NLRP3 inflammasome complex	2	0.017428	<i>CASP5, FNI</i>
GO Terms of MF			
GO:0097153~cysteine-type endopeptidase activity involved in apoptotic process	2	0.02663	<i>CASP5, FNI</i>
GO:0038191~neuropilin binding	2	0.030665	<i>SEMA3C, SEMA3A</i>
GO:0030215~semaphorin receptor binding	2	0.046645	<i>SEMA3C, SEMA3A</i>
GO:0045499~chemorepellent activity	2	0.054538	<i>SEMA3C, SEMA3A</i>
KEGG enrichment analysis			
Down regulated DEGs			
hsa05164:Influenza A	7	0.002058	<i>RSAD2, OAS1, STAT1, OAS2, OAS3, PML, IRF9</i>
hsa05168:Herpes simplex infection	6	0.012895	<i>OAS1, STAT1, OAS2, OAS3, PML,</i>

			<i>ATF6B, IRF9</i>
hsa04964:Proximal tubule bicarbonate reclamation	3	0.013288	<i>CA2, GLS2, AQP1</i>
hsa05162:Measles	5	0.018835	<i>OAS1, STAT1, OAS2, OAS3, IRF9</i>
hsa05160:Hepatitis C	5	0.018835	<i>OAS1, STAT1, OAS2, OAS3, IRF9</i>
hsa00130:Ubiquinone and other terpenoid-quinone biosynthesis	2	0.081617	<i>NQO1, COQ2</i>
hsa04610:Complement and coagulation cascades	3	0.098614	<i>PLAT, C4BPB, C2</i>
hsa04976:Bile secretion	3	0.098614	<i>CA2, ADCY7, AQP1</i>
Up regulated DEGs			
hsa04360:Axon guidance	3	0.026619	<i>ABLIM2, SEMA3C, SEMA3A</i>
hsa04151:PI3K-Akt signaling pathway	4	0.030138	<i>CDK6, ANGPT1, SGK1, SLCO2A1, CREB5, BCL11A</i>

***Note:** Bold indicates key genes (KGs)