ACCSCIENCE PUBLISHING

Gene & Protein in Disease

ORIGINAL RESEARCH ARTICLE

Deciphering novel molecular gene expression signatures and pathways in cystic fibrosis through integrative bioinformatics strategies

Supplementary File

Table S1. Upregulated genes from GSE70442 dataset

Serial no.	ID	*P*-value	logFC	Gene symbol	Gene title
1	226636_at	0.00235	3.11	*PLD1*	phospholipase D1
2	1554479_a_at	0.00235	3.41	*CARD8*	caspase recruitment domain family member 8
3	225989_at	0.00238	4.07	*HERC4*	HECT and RLD domain containing E3 ubiquitin protein ligase 4
4	222016_s_at	0.00243	2.73	*ZSCAN31*	zinc finger and SCAN domain containing 31
5	235046_at	0.00262	2.78	*INPP4B*	inositol polyphosphate-4-phosphatase type II B
6	212565_at	0.00262	2.94	*STK38L*	serine/threonine kinase 38 like
7	220770_s_at	0.00262	3.44	*ZBED8*	zinc finger BED-type containing 8
8	226041_at	0.00272	2.58	*NAPEPLD*	N-acyl phosphatidylethanolamine phospholipase D
9	226230_at	0.00279	3.82	*PPP4R3B*	protein phosphatase 4 regulatory subunit 3B
10	229615_at	0.00279	2.98	*SLX4IP*	SLX4 interacting protein
11	208925_at	0.00279	2.47	*CLDND1*	claudin domain containing 1
12	222691_at	0.00279	2.88	*SLC35B3*	solute carrier family 35 member B3
13	65438_at	0.00279	2.71	*TLDC1*	TBC/LysM-associated domain containing 1
14	213269_at	0.00279	3.85	*ZNF248*	zinc finger protein 248
15	228268_at	0.00283	3.34	*FMO2*	flavin containing monooxygenase 2
16	229362_at	0.00287	3.17	*PUS10*	pseudouridylate synthase 10
17	222566_at	0.00297	2.49	*KMT5B*	lysine methyltransferase 5B
18	242093_at	0.00297	3.20	*SYTL5*	synaptotagmin like 5
19	233759_s_at	0.00321	2.36	*PPP4R3B*	protein phosphatase 4 regulatory subunit 3B
20	229285_at	0.00322	2.77	*RNASEL*	ribonuclease L
21	219383_at	0.00322	2.74	*PRR5L*	proline rich 5 like
22	208393_s_at	0.00322	2.49	*RAD50*	RAD50 double strand break repair protein
23	223351_at	0.00322	2.05	*C17orf80*	chromosome 17 open reading frame 80
24	228190_at	0.00322	2.85	*ATG4C*	autophagy related 4C cysteine peptidase
25	232382_s_at	0.00325	2.43	*PCMTD1*	protein-L-isoaspartate (D-aspartate) O-methyltransferase domain containing 1
26	221081_s_at	0.00325	2.38	*DENND2D*	DENN domain containing 2D
27	227025_at	0.00325	2.50	*PPHLN1*	periphilin 1
28	208055_s_at	0.00325	3.31	*HERC4*	HECT and RLD domain containing E3 ubiquitin protein ligase 4
29	203404_at	0.00325	2.22	*ARMCX2*	armadillo repeat containing, X-linked 2
30	202951_at	0.00325	2.27	*STK38*	serine/threonine kinase 38
31	205803_s_at	0.00325	2.68	*TRPC1*	transient receptor potential cation channel subfamily C member 1

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Table S1. ***(Continued)***

Serial no.	ID	*P*-value	logFC	Gene symbol	Gene title
32	215174_at	0.00325	4.23	*FMO6P*	flavin containing monooxygenase 6 pseudogene
33	212899_at	0.00325	2.15	*CDK19*	cyclin dependent kinase 19
34	203956_at	0.00325	2.30	*MORC2*	MORC family CW-type zinc finger 2
35	177_at	0.00333	2.59	*PLD1*	phospholipase D1
36	223404_s_at	0.00333	3.03	*TRMT1L*	tRNA methyltransferase 1 like
37	235953_at	0.00338	2.67	*ZNF610*	zinc finger protein 610
38	201362_at	0.00338	2.26	*IVNS1ABP*	influenza virus NS1A binding protein
39	209348_s_at	0.00338	2.88	*MAF*	MAF bZIP transcription factor
40	225988_at	0.00338	2.99	*HERC4*	HECT and RLD domain containing E3 ubiquitin protein ligase 4
41	1554480_a_at	0.00338	2.12	*ARMC10*	armadillo repeat containing 10
42	221895_at	0.00338	3.37	*MOSPD2*	motile sperm domain containing 2
43	1558794_at	0.00338	3.10	*NUTM2A-AS1*	NUTM2A antisense RNA 1
44	228280_at	0.00338	3.01	*ZC3HAV1L*	zinc finger CCCH-type containing, antiviral 1 like
45	228771_at	0.00338	2.90	*GRK3*	G protein-coupled receptor kinase 3
46	220992_s_at	0.00338	3.72	*TRMT1L*	tRNA methyltransferase 1 like
47	203518_at	0.00338	2.65	*LYST*	lysosomal trafficking regulator
48	226628_at	0.00359	2.39	*THOC2*	THO complex 2
49	209497_s_at	0.00368	2.39	*RBM4B*	RNA binding motif protein 4B
50	230561_s_at	0.00370	2.76	*KANSL1L*	KAT8 regulatory NSL complex subunit 1 like
51	228920_at	0.00370	1.89	*ZNF260*	zinc finger protein 260
52	231919_at	0.00370	2.99	*DBT*	dihydrolipoamide branched chain transacylase E2
53	209778_at	0.00370	1.98	*TRIP11*	thyroid hormone receptor interactor 11
54	207583_at	0.00370	2.80	*ABCD2*	ATP binding cassette subfamily D member 2
55	1556180_at	0.00370	1.96	*LINC00847*	long intergenic non-protein coding RNA 847
56	230192_at	0.00370	2.54	*TRIM13*	tripartite motif containing 13
57	202451_at	0.00370	2.99	*GTF2H1*	general transcription factor IIH subunit 1
58	230226_s_at	0.00372	2.47	*KDM5A*	lysine demethylase 5A
59	225594_at	0.00372	2.35	*CREBZF*	CREB/ATF bZIP transcription factor
60	230098_at	0.00372	2.21	*PHF20L1*	PHD finger protein 20-like 1
61	238149_at	0.00386	1.92	*ZNF818P*	zinc finger protein 818, pseudogene
62	1552585_s_at	0.00386	2.62	*GTF2A1L*	general transcription factor IIA subunit 1 like
63	227839_at	0.00386	3.26	*MBD5*	methyl-CpG binding domain protein 5
64	231828_at	0.00399	2.28	*PSMD5-AS1*	PSMD5 antisense RNA 1 (head to head)
65	236694_at	0.00399	3.46	*TXLNGY*	taxilin gamma pseudogene, Y-linked
66	204362_at	0.00406	2.22	*SKAP2*	src kinase associated phosphoprotein 2
67	235215_at	0.00406	2.36	*ERCC4*	ERCC excision repair 4, endonuclease catalytic subunit
68	1553992_s_at	0.00406	2.05	*NBR2*	neighbor of BRCA1 gene 2 (non-protein coding)
69	225332_at	0.00406	1.80	*OIP5-AS1*	OIP5 antisense RNA 1
70	223165_s_at	0.00406	2.01	*IP6K2*	inositol hexakisphosphate kinase 2
71	225040_s_at	0.00406	2.53	*RPE*	ribulose-5-phosphate-3-epimerase
72	208719_s_at	0.00406	3.62	*DDX17*	DEAD-box helicase 17
73	214739_at	0.00406	2.05	*LRCH3*	leucine rich repeats and calponin homology domain containing 3

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Table S1. ***(Continued)***

Serial no.	ID	*P*-value	logFC	Gene symbol	Gene title
74	225728_at	0.00408	2.03	*SORBS2*	sorbin and SH3 domain containing 2
75	235347_at	0.00414	1.92	*LRCH3*	leucine rich repeats and calponin homology domain containing 3
76	204225_at	0.00417	1.88	*HDAC4*	histone deacetylase 4
77	204950_at	0.00425	2.19	*CARD8*	caspase recruitment domain family member 8
78	219185_at	0.00425	2.52	*SIRT5*	sirtuin 5
79	232318_s_at	0.00425	4.55	*LINC00284*	long intergenic non-protein coding RNA 284
80	201363_s_at	0.00429	2.18	*IVNS1ABP*	influenza virus NS1A binding protein
81	227703_s_at	0.00429	2.05	*SYTL4*	synaptotagmin like 4
82	218889_at	0.00429	2.08	*NOC3L*	NOC3 like DNA replication regulator
83	216863_s_at	0.00429	1.98	*MORC2*	MORC family CW-type zinc finger 2
84	228223_at	0.00429	2.36	*ZSWIM3*	zinc finger SWIM-type containing 3
85	212215_at	0.00436	2.56	*PREPL*	prolyl endopeptidase-like
86	233750_s_at	0.00461	2.15	*TRMT1L*	tRNA methyltransferase 1 like
87	230557_at	0.00461	2.70	*XRRA1*	X-ray radiation resistance associated 1
88	225639_at	0.00461	1.97	*SKAP2*	src kinase associated phosphoprotein 2
89	1553269_at	0.0047	2.62	*ZNF718*	zinc finger protein 718
90	213573_at	0.00472	2.38	*KPNB1*	karyopherin subunit beta 1
91	228141_at	0.00473	2.11	*GPX8*	glutathione peroxidase 8 (putative)
92	206976_s_at	0.00473	1.83	*HSPH 1*	heat shock protein family H (Hsp110) member 1
93	239043_at	0.00473	2.73	*ZNF404*	zinc finger protein 404
94	209296_at	0.00473	2.24	*PPM1B*	protein phosphatase, Mg2+/Mn2+dependent 1B
95	212914_at	0.00475	2.05	*CBX7*	chromobox 7
96	205203_at	0.00475	2.00	*PLD1*	phospholipase D1
97	228865_at	0.00482	1.87	*C1orf116*	chromosome 1 open reading frame 116
98	226853_at	0.00482	2.01	*BMP2K*	BMP2 inducible kinase
99	225171_at	0.00490	2.03	*ARHGAP18*	Rho GTPase activating protein 18
100	225017_at	0.00495	2.00	*CCDC14*	coiled-coil domain containing 14
101	223384_s_at	0.00495	1.97	*TRIM4*	tripartite motif containing 4
102	228095_at	0.00495	2.09	*PHF14*	PHD finger protein 14
103	205371_s_at	0.00495	2.63	*DBT*	dihydrolipoamide branched chain transacylase E2
104	228150_at	0.00495	2.09	*SEC16B*	SEC16 homolog B, endoplasmic reticulum export factor

Table S2. Downregulated genes from GSE70442 dataset

Serial no.	ID	*P*-value	logFC	Gene symbol	Gene title
1	222045_s_at	0.00235	−3.22	*PCIF1*	PDX1 C-terminal inhibiting factor 1
2	1554026_a_at	0.00235	−4.04	*MYO10*	myosin X
3	230134_s_at	0.00235	−4.77	*RC3H2*	ring finger and CCCH-type domains 2
4	227757_at	0.00235	−4.00	*CUL4A*	cullin 4A
5	230133_at	0.00235	−4.18	*RC3H2*	ring finger and CCCH-type domains 2
6	1556911_at	0.00262	−2.76	*ALMS1-IT1*	ALMS1 intronic transcript 1
7	227910_at	0.00262	−4.38	*XPNPEP3*	X-prolyl aminopeptidase 3
8	1554415_at	0.00262	−2.61	*TAF5L*	TATA-box binding protein associated factor 5 like

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Table S2. ***(Continued)***

Serial no.	ID	*P*-value	logFC	Gene symbol	Gene title
9	239615_at	0.00262	−2.96	*SLC22A5*	solute carrier family 22 member 5
10	216049_at	0.00272	−3.39	*RHOBTB3*	Rho related BTB domain containing 3
11	204823_at	0.00272	−3.83	*NAV3*	neuron navigator 3
12	240570_at	0.00279	−3.00	*PATJ*	PATJ, crumbs cell polarity complex component
13	223584_s_at	0.00279	−2.46	*KBTBD2*	kelch repeat and BTB domain containing 2
14	241396_at	0.00279	−2.78	*NEDD4L*	neural precursor cell expressed, developmentally down-regulated 4-like, E3 ubiquitin protein ligase
15	211030_s_at	0.00283	−5.08	*SLC6A6*	solute carrier family 6 member 6
16	89948_at	0.00283	−2.53	*PCIF1*	PDX1 C-terminal inhibiting factor 1
17	1569136_at	0.00283	−4.59	*MGAT4A*	mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isozyme A
18	238509_at	0.00283	−2.92	*CUL1*	cullin 1
19	237408_at	0.00283	−2.78	*DCUN1D1*	defective in cullin neddylation 1 domain containing 1
20	1554794_a_at	0.00285	−2.42	*UBE3C*	ubiquitin protein ligase E3C
21	1554057_at	0.00297	−2.67	*ASH1L-AS1*	ASH1L antisense RNA 1
22	211998_at	0.00319	−2.65	*MIR4738*	microRNA 4738///H3 histone, family 3B///H3 histone, family 3A
23	210842_at	0.00321	−5.80	*NRP2*	neuropilin 2
24	1567224_at	0.00322	−4.39	*HMGA2*	high mobility group AT-hook 2
25	226750_at	0.00322	−2.38	*LARP1B*	La ribonucleoprotein domain family member 1B
26	210665_at	0.00324	−2.41	*TFPI*	tissue factor pathway inhibitor
27	225657_at	0.00324	−2.02	*NCBP2-AS2*	NCBP2 antisense RNA 2 (head to head)
28	214230_at	0.00324	−3.85	*CDC42*	cell division cycle 42
29	208776_at	0.00325	−2.27	*PSMD11*	proteasome 26S subunit, non-ATPase 11
30	220953_s_at	0.00325	−2.07	*MTMR12*	myotubularin related protein 12
31	227993_at	0.00325	−2.26	*METAP2*	methionyl aminopeptidase 2
32	1554906_a_at	0.00325	−3.35	*MPHOSPH 6*	M-phase phosphoprotein 6
33	219094_at	0.00325	−2.84	*ARMC8*	armadillo repeat containing 8
34	210200_at	0.00326	−2.45	*WWP2*	WW domain containing E3 ubiquitin protein ligase 2
35	1554522_at	0.00333	−3.09	*CNNM2*	cyclin and CBS domain divalent metal cation transport mediator 2
36	1554878_a_at	0.00333	−3.00	*ABCD3*	ATP binding cassette subfamily D member 3
37	223520_s_at	0.00333	−2.52	*KIF13A*	kinesin family member 13A
38	228544_s_at	0.00338	−2.00	*PET117*	PET117 homolog///lysine acetyltransferase 14
39	214704_at	0.00338	−2.72	*TCF25*	transcription factor 25
40	242218_at	0.00338	−2.59	*PPARD*	peroxisome proliferator activated receptor delta
41	234993_at	0.00338	−3.32	*ABHD13*	abhydrolase domain containing 13
42	1553133_at	0.00338	−2.77	*C9orf72*	chromosome 9 open reading frame 72
43	244137_at	0.00338	−4.04	*AREL1*	apoptosis resistant E3 ubiquitin protein ligase 1
44	235353_at	0.00338	−2.02	*SEL1L3*	SEL1L family member 3
45	240834_at	0.00338	−2.57	*OTULIN*	OTU deubiquitinase with linear linkage specificity
46	227932_at	0.00345	−2.04	*ARIH2*	ariadne RBR E3 ubiquitin protein ligase 2
47	220011_at	0.00349	−2.02	*AUNIP*	aurora kinase A and ninein interacting protein
48	1563842_at	0.00361	−1.81	*PIGG*	phosphatidylinositol glycan anchor biosynthesis class G
49	223598_at	0.00361	−2.16	*RAD23B*	RAD23 homolog B, nucleotide excision repair protein

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Table S2. ***(Continued)***

Serial no.	ID	*P*-value	logFC	Gene symbol	Gene title
50	1554291_at	0.00361	−2.88	*UHRF1BP1L*	UHRF1 binding protein 1 like
51	228381_at	0.00361	−2.35	*ATF7IP2*	activating transcription factor 7 interacting protein 2
52	241239_at	0.00361	−4.21	*EPN2-IT1*	EPN2 intronic transcript 1///epsin 2
53	240227_at	0.00368	−5.48	*MIER1*	MIER1 transcriptional regulator
54	214541_s_at	0.00368	−3.25	*QKI*	QKI, KH domain containing RNA binding
55	223946_at	0.00370	−1.86	*MED23*	mediator complex subunit 23
56	227650_at	0.00370	−2.35	*HSPA14*	heat shock protein family A (Hsp70) member 14
57	222309_at	0.00370	−3.37	*C6orf62*	chromosome 6 open reading frame 62
58	229892_at	0.00370	−1.99	*EP400NL*	EP400 N-terminal like
59	210567_s_at	0.00370	−2.85	*SKP2*	S-phase kinase-associated protein 2, E3 ubiquitin protein ligase
60	1554114_s_at	0.00370	−2.47	*SSH2*	slingshot protein phosphatase 2
61	1568733_at	0.00370	−2.93	*C10orf76*	chromosome 10 open reading frame 76
62	1569864_at	0.00370	−2.47	*SERAC1*	serine active site containing 1
63	1556361_s_at	0.00370	−2.99	*ANKRD13C*	ankyrin repeat domain 13C
64	229879_at	0.00370	−2.26	*ASPH*	aspartate beta-hydroxylase
65	231062_at	0.00372	−2.07	*DOCK9-AS2*	DOCK9 antisense RNA 2 (head to head)
66	211032_at	0.00372	−3.31	*COBLL1*	cordon-bleu WH2 repeat protein like 1
67	206919_at	0.00372	−3.15	*ELK4*	ELK4, ETS transcription factor
68	231423_s_at	0.00386	−2.49	*ANKRD16*	ankyrin repeat domain 16
69	229822_at	0.00386	−3.17	*PARVB*	parvin beta
70	229587_at	0.00386	−1.96	*UBA2*	Ubiquitin-like modifier activating enzyme 2
71	1559716_at	0.00394	−1.95	*INO80C*	INO80 complex subunit C
72	223780_s_at	0.00395	−1.94	*MED13*	mediator complex subunit 13
73	223800_s_at	0.00399	−2.54	*LIMS4*	LIM zinc finger domain containing 4///LIM zinc finger domain containing 3
74	207356_at	0.00399	−2.70	*DEFB4B*	defensin beta 4B///defensin beta 4A
75	216180_s_at	0.00406	−2.78	*SYNJ2*	synaptojanin 2
76	236198_at	0.00406	−2.48	*LINC01215*	long intergenic non-protein coding RNA 1215
77	229428_at	0.00406	−2.17	*TIMM23B*	translocase of inner mitochondrial membrane 23 homolog B
78	1554119_at	0.00406	−2.00	*USB1*	U6 snRNA biogenesis phosphodiesterase 1
79	228543_at	0.00406	−1.82	*PET117*	PET117 homolog
80	230652_at	0.00406	−3.01	*ARAF*	A-Raf proto-oncogene, serine/threonine kinase
81	224454_at	0.00406	−3.56	*ETNK1*	ethanolamine kinase 1
82	1554053_at	0.00406	−2.47	*SPTLC1*	serine palmitoyltransferase long chain base subunit 1
83	215617_at	0.00414	−2.28	*SPATS2L*	spermatogenesis associated serine rich 2 like
84	219212_at	0.00417	−1.81	*HSPA14*	heat shock protein family A (Hsp70) member 14
85	1555912_at	0.00426	−3.75	*ST7-AS1*	ST7 antisense RNA 1
86	241027_at	0.00426	−2.66	*OPA1*	OPA1, mitochondrial dynamin-like GTPase
87	1555476_at	0.00429	−2.39	*IREB2*	iron responsive element binding protein 2
88	217262_s_at	0.00429	−3.01	*CELSR1*	cadherin EGF LAG seven-pass G-type receptor 1
89	225072_at	0.00430	−2.41	*ZCCHC3*	zinc finger CCHC-type containing 3
90	214950_at	0.00430	−2.94	*IL9R*	interleukin 9 receptor

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Table S2. ***(Continued)***

Serial no.	ID	*P*-value	logFC	Gene symbol	Gene title
91	235289_at	0.00430	−2.21	*EIF5A2*	eukaryotic translation initiation factor 5A2
92	1554036_at	0.00446	−4.32	*ZBTB24*	zinc finger and BTB domain containing 24
93	1556321_a_at	0.00461	−2.91	*MESDC1*	mesoderm development candidate 1
94	238660_at	0.00461	−2.28	*WDFY3*	WD repeat and FYVE domain containing 3
95	227936_at	0.00470	−2.28	*TMEM68*	transmembrane protein 68
96	214962_s_at	0.00473	−2.42	*NUP160*	nucleoporin 160
97	242939_at	0.00475	−2.80	*TFDP1*	transcription factor Dp-1
98	1562259_at	0.00475	−2.08	*TEX9*	testis expressed 9
99	231863_at	0.00475	−2.35	*ING3*	inhibitor of growth family member 3
100	218219_s_at	0.00475	−1.91	*LANCL2*	LanC like 2
101	206596_s_at	0.00475	−3.29	*NRL*	neural retina leucine zipper
102	203036_s_at	0.00475	−2.15	*MTSS1*	metastasis suppressor 1
103	227110_at	0.00482	−2.16	*HNRNPC*	heterogeneous nuclear ribonucleoprotein C (C1/C2)
104	1555279_at	0.00495	−1.97	*ARMC8*	armadillo repeat containing 8
105	223296_at	0.00495	−2.12	*SLC25A33*	solute carrier family 25 member 33
106	1556063_s_at	0.00495	−2.28	*RPP30*	ribonuclease P/MRP subunit p30
107	212246_at	0.00496	−2.03	*MCFD2*	multiple coagulation factor deficiency 2

Table S3. Top 10 GO terms identified from functional analyses of upregulated genes

Category	Term	Gene count	Overlapped gene	*P*-value
GO_MF	Protein kinase activity	6	*CDK19, RNASEL, BMP2K, STK38L, GRK3, GTF2H1*	0.02062117
GO_MF	N-acyl phosphatidylethanolamine-specific phospholipase D activity	2	*PLD1, NAPEPLD*	0.02172936
GO_MF	N, N-dimethylaniline monooxygenase activity	2	*FMO2, FMO6P*	0.02601901
GO_CC	Nucleoplasm	20	*PPP4R3B, CARD8, PPHLN1, ZNF260, ZBED8, IVNS1ABP, SKAP2, CBX7, RAD50, GTF2H1, HDAC4, HSPH 1, DDX17, SYTL4, BMP2K, KDM5A, THOC2, KPNB1, ERCC4, IP6K2*	0.02684999
GO_MF	Single-stranded DNA endo deoxyribonuclease activity	2	*ERCC4, RAD50*	0.03029009
GO_MF	Zinc ion binding	11	*TRIM4, RBM4B, HDAC4, NAPEPLD, PHF14, TRIM13, SIRT5, KDM5A, KPNB1, ZSWIM3, MORC2*	0.03084729
GO_BP	Transcription, DNA-templated	15	*MAF, ZNF818P, CREBZF, PPHLN1, ZNF610, ZNF260, CBX7, GTF2H1, ZNF718, HDAC4, DDX17, ZSCAN31, ZNF248, ZNF404, KMT5B*	0.04039687
GO_MF	Syntaxin binding	3	*SYTL4, SYTL5, TXLNGY*	0.04491529
GO_CC	Cytoplasm	31	*STK38, TRIM13, ARHGAP18, DENND2D, SKAP2, IVNS1ABP, CBX7, TRIM4, HSPH 1, KDM5A, KPNB1, STK38L, PPP4R3B, MAF, CARD8, PPHLN1, ZNF260, HERC4, GTF2A1L, ZBED8, XRRA1, MORC2, HDAC4, C1ORF116, NAPEPLD, ATG4C, LYST, SYTL4, PCMTD1, LRCH3, INPP4B*	0.04614667
GO_BP	Protein phosphorylation	6	*CDK19, RNASEL, STK38, BMP2K, STK38L, GRK3*	0.04823305

Table S4. Top 10 GO terms identified from functional analyses of downregulated genes

Category	Term	Gene count	Overlapped gene	*P*-value
GO_BP	Protein ubiquitination involved in ubiquitin-dependent protein catabolic process	7	*ARIH2, AREL1, CUL4A, WWP2, UBE3C, NEDD4L, CUL1*	7.22E-05
GO_MF	Ubiquitin-protein transferase activity	9	*KBTBD2, ARIH2, AREL1, WWP2, SKP2, RC3H2, UBE3C, NEDD4L, CUL1*	1.50E-04
GO_BP	Protein polyubiquitination	7	*ARIH2, PSMD11, SKP2, RC3H2, UBE3C, NEDD4L, CUL1*	1.98E-04
GO_CC	Nucleoplasm	25	*C9ORF72, RAD23B, ING3, PPARD, MED23, ELK4, MIER1, RPP30, RC3H2, ETNK1, HNRNPC, NEDD4L, CUL1, TFDP1, OPA1, PCIF1, SKP2, SEL1L3, MED13, CELSR1, HMGA2, CUL4A, PSMD11, UBA2, MPHOSPH 6*	0.0013417
GO_MF	Ubiquitin protein ligase activity	6	*CDC42, ARIH2, CUL4A, WWP2, SKP2, CUL1*	0.0018374
GO_BP	Proteasome-mediated ubiquitin-dependent protein catabolic process	6	*RAD23B, CUL4A, PSMD11, WWP2, NEDD4L, CUL1*	0.0024004
GO_MF	Protein binding	53	*C9ORF72, MTSS1, PPARD, MED23, AUNIP, KIF13A, CDC42, TAF5L, MIER1, WWP2, RPP30, SYNJ2, QKI, SLC22A5, ASPH, CUL1, SPTLC1, OPA1, SKP2, PATJ, HMGA2, ZBTB24, MTMR12, DCUN1D1, NRL, EIF5A2, PARVB, RAD23B, NUP160, LARP1B, UBE3C, ARIH2, ELK4, LANCL2, ABCD3, ETNK1, HNRNPC, NEDD4L, TCF25, RHOBTB3, TFDP1, WDFY3, OTULIN, IREB2, C10ORF76, MYO10, ARMC8, CUL4A, PSMD11, UBA2, ARAF, HSPA14, MPHOSPH 6*	0.0090551
GO_BP	Ubiquitin-dependent protein catabolic process	5	*ARIH2, CUL4A, PSMD11, SKP2, CUL1*	0.0097749
GO_CC	Intercellular bridge	3	*USB1, C9ORF72, PCIF1*	0.0175211
GO_BP	Protein ubiquitination	6	*CDC42, KBTBD2, ARIH2, WWP2, NEDD4L, CUL1*	0.0245197

Table S5. KEGG pathway analysis for up and downregulated genes

DEGs category	Term	Gene count	Overlapped gene	*P*-value
Upregulated	Glutamatergic synapse	3	*TRPC1, PLD1, GRK3*	0.0156
	Basal transcription factors	2	*GTF2H1, GTF2A1L*	0.0184
	Nucleotide excision repair	2	*GTF2H1, ERCC4*	0.02
Downregulated	Ubiquitin mediated proteolysis	8	*CUL4A, WWP2, UBA2, SKP2, UBE3C, NEDD4L, CUL1, HERC3*	3.98E-05
	Nucleotide excision repair	2	*CUL4A, RAD23B*	0.0221
	Cell cycle	3	*CUL1, SKP2, TFDP1*	0.0225
	Acute myeloid leukemia	2	*PPARD, ARAF*	0.0414
	Staphylococcus aureus infection	2	*DEFB4B, DEFB4A*	0.0437
	Renal cell carcinoma	2	*ARAF, CDC42*	0.0448