

Table S1 The specific information of all robust DEGs

Name	P value	fdr	logFC
REG1A	3.60E-08	0.000804685	7.067253816
KRT23	9.99E-08	0.001072913	6.955363898
DPEP1	1.96E-07	0.001095266	6.72476472
MMP7	1.44E-07	0.001072913	6.549577091
FOXQ1	4.00E-07	0.001788189	6.384793419
CLDN2	1.60E-06	0.003251253	5.857558238
MMP3	8.99E-07	0.002873875	5.654452334
CLDN1	1.16E-06	0.00321874	5.542775508
FABP6	5.76E-07	0.002145827	5.538320689
REG3A	1.44E-06	0.003227681	5.409012457
REG1B	1.30E-06	0.00321874	5.184640207
GRIN2D	7.74E-06	0.009616483	5.048970125
KLK8	2.91E-06	0.005431624	4.835866166
KRT6B	4.62E-06	0.007301772	4.756270403
PITX2	4.09E-06	0.007042714	4.705183898
INHBA	9.60E-06	0.011298531	4.595602263
CDH3	2.31E-05	0.021517874	4.473172533
SLC35D3	1.17E-05	0.013035898	4.47180081
SAA2	4.90E-06	0.007301772	4.465944253
KLK6	1.96E-05	0.0190481	4.448137186
CPNE7	5.47E-05	0.034969313	4.382447635
CKMT2	6.72E-06	0.008841017	4.364945696
MMP1	5.47E-06	0.007650096	4.331675048
C17orf96	4.66E-05	0.031819246	4.198304502
FAM3B	1.74E-05	0.017703071	4.173726857
SLC7A5	6.35E-05	0.037354327	4.163926198
SAA1	4.66E-05	0.031819246	3.999204346
H19	2.43E-05	0.021758684	3.99540576
CA9	1.54E-05	0.016366187	3.970272462
SNAR-A3	8.17E-05	0.040629641	3.720662917
TACSTD2	4.16E-05	0.031007197	3.679116364
SULT2B1	4.84E-05	0.031819246	3.677548617
TESC	3.46E-05	0.027617941	3.62325825
LY6G6D	7.95E-05	0.040629641	3.601946959
PPBP	2.56E-05	0.02200848	3.568882823
VSNL1	5.85E-05	0.035379561	3.548623247
ASCL2	6.55E-05	0.037561139	3.399986192
TRIB3	3.68E-05	0.028413707	3.379930813
MDF1	4.75E-05	0.031819246	3.358477233
TUBB3	3.17E-05	0.026230084	3.322225549
SRPX2	7.28E-05	0.039743591	3.228786088
HULC	0.000106197	0.049489994	3.155162765
CXCL2	8.99E-05	0.043732883	3.153721806
TNFRSF6B	6.86E-05	0.03835889	3.149277493
SPP1	5.85E-05	0.035379561	3.134587104
CXCL1	7.50E-05	0.03995538	3.098551712
TGFB1	0.000108819	0.049676986	3.04600235
COL1A1	8.06E-05	0.040629641	2.958479939
TNS4	9.60E-05	0.045703448	2.627302161
PLAC8	0.000184762	0.047505194	-2.680929554
STMN2	0.000172927	0.046604945	-2.731111464
LOC401022	0.000136798	0.040800513	-2.795494485
NR3C2	0.000141271	0.041040099	-2.800447818
IL1R2	0.000114159	0.036480333	-2.909253911
BCAS1	0.000119627	0.03716577	-2.913712432
CAPN13	0.000125223	0.038371352	-2.928341249
BTNL3	0.000148885	0.042157122	-2.934733402
TNFRSF17	0.000184762	0.047505194	-2.959291194
HOXB13	0.000116877	0.036822841	-2.984102
C11orf86	9.11E-05	0.032881046	-3.022635275
SPINK5	0.000107504	0.035891889	-3.036781464
AKR1B15	9.60E-05	0.033997944	-3.043733368
AKR1B10	9.73E-05	0.033997944	-3.088296286
TMEM236	0.000101049	0.034680029	-3.108926689
PADI2	8.40E-05	0.030816946	-3.124531267
CHST5	0.000110142	0.036231865	-3.127271725
ST6GALNAC6	0.000144293	0.041380528	-3.153655015
MT1G	0.00016634	0.045936589	-3.216222322
HS3ST6	0.000155121	0.043373642	-3.21895104
TRPM6	0.000171269	0.046604945	-3.236563862
LDHD	7.61E-05	0.029279322	-3.252022588
FCGBP	0.000139772	0.041040099	-3.25376384
MFSD4	5.85E-05	0.025667525	-3.261631342
PDE6A	7.18E-05	0.028587495	-3.275371138
FAM55D	0.000176269	0.046830566	-3.29641639
CR2	6.15E-05	0.026437687	-3.340510097
SLC28A2	5.47E-05	0.024978081	-3.351177076
KIF5C	5.66E-05	0.025322545	-3.4006025
SCGB2A1	0.000102324	0.034680029	-3.404421705
C4orf7	8.17E-05	0.030472231	-3.421311474
TEX11	0.000177952	0.046830566	-3.442335511
PCK1	4.00E-05	0.020792895	-3.541396683
ANO5	6.35E-05	0.026705278	-3.552878636
C2orf88	4.58E-05	0.023264745	-3.581756146
KRTAP13-1	2.69E-05	0.015793377	-3.62724934
LGALS2	4.92E-05	0.02336567	-3.683600924
GLDN	4.75E-05	0.02336567	-3.693286819
GREM2	7.28E-05	0.028587495	-3.707330371
VSIG2	2.37E-05	0.015145961	-3.781985895
SLC26A2	6.45E-05	0.026705278	-3.799521108
SPINK2	2.01E-05	0.014400181	-3.804981368
PKIB	2.75E-05	0.015793377	-3.805917067
BEST2	3.03E-05	0.01611286	-3.807699947
BMP3	7.72E-05	0.029279322	-3.817950304
CHP2	2.19E-05	0.014400181	-3.830129937
MT1M	0.000132397	0.040021603	-3.855859584
CD177	5.01E-05	0.02336567	-3.923270978
ITLN1	0.000112812	0.036480333	-3.938716882
SCNN1B	1.49E-05	0.011881877	-3.952652682
SI	7.18E-05	0.028587495	-3.953383453
PI16	0.000193456	0.049175198	-4.005962822
TTR	2.96E-05	0.01611286	-4.076434414
ADH1C	2.19E-05	0.014400181	-4.077470972
HEPACAM2	2.56E-05	0.015793377	-4.086945719
LOC646627	3.03E-05	0.01611286	-4.092311352
ADH1A	2.07E-05	0.014400181	-4.150075466
SPIB	4.84E-05	0.02336567	-4.242971012
CWH43	1.74E-05	0.012982252	-4.371309279
CA4	6.08E-06	0.007157462	-4.447447023
SLC26A3	7.05E-06	0.007868032	-4.4496308
DAO	9.21E-06	0.00894467	-4.486186892
CDKN2B-AS	5.77E-06	0.007157462	-4.672630413
SLC30A10	1.21E-05	0.010402446	-4.680812871
LOC389023	1.12E-05	0.010046036	-4.720048388
CLCA4	2.70E-06	0.005036732	-4.776568993
CCL23	3.36E-06	0.005784104	-4.805062895
OGN	1.59E-05	0.012236762	-4.836822995
ZG16	7.74E-06	0.007868032	-4.845514424
SCGN	5.18E-06	0.007157462	-4.899460196
C2orf40	9.60E-06	0.00894467	-4.939166165
CA2	1.93E-06	0.004681804	-4.962759686
MYOC	6.08E-06	0.007157462	-5.00701001
GCG	5.18E-06	0.007157462	-5.010953842
AQP8	1.30E-05	0.010758937	-5.032363824
BEST4	2.62E-05	0.015793377	-5.052843
MS4A12	1.60E-06	0.004681804	-5.061831438
CLCA1	7.39E-06	0.007868032	-5.272034511
GUCA2A	8.99E-07	0.004681804	-5.31427127
SLC4A4	1.76E-06	0.004681804	-5.326196622
CA7	3.84E-06	0.00613732	-5.531522238
GUCA2B	2.30E-06	0.004681804	-5.560135294
SST	2.30E-06	0.004681804	-5.638536208
CHGA	2.11E-06	0.004681804	-5.68823246
CLDN8	1.44E-06	0.004681804	-5.871240528
INSL5	6.75E-07	0.004681804	-6.414954285
TMIGD1	1.44E-07	0.00160937	-6.44848406
CA1	1.60E-08	0.000357638	-6.980474323

Table S2 GO enrichment analysis of robust DEGs

ONTOLOGY	ID	Description	Gene ratio	Bg ratio	P value	p.adjust	q value	Gene ID	Count
BP	GO:0015701	bicarbonate transport	8/120	42/18670	2.26E-10	4.05E-07	3.75E-07	CA1/SLC4A4/CA2/CA7/CA4/SLC26A3/CA9/SLC26A2	8
BP	GO:0006821	chloride transport	9/120	108/18670	3.17E-08	2.84E-05	2.63E-05	CA2/CLCA4/CA7/SLC26A3/CLCA1/BEST4/BEST2/ANO5/SLC26A2	9
BP	GO:0019730	antimicrobial humoral response	9/120	122/18670	9.18E-08	5.47E-05	5.07E-05	REG1A/REG1B/REG3A/CHGA/PPBP/SPINK5/ITLN1/CXCL1/CXCL2	9
BP	GO:0015698	inorganic anion transport	10/120	169/18670	1.39E-07	6.24E-05	5.78E-05	SLC4A4/CA2/CLCA4/CA7/SLC26A3/CLCA1/BEST4/BEST2/ANO5/SLC26A2	10
BP	GO:0061844	antimicrobial humoral immune response mediated by antimicrobial peptide	7/120	73/18670	4.36E-07	0.000156015	0.000144501	REG1A/REG1B/REG3A/PPBP/SPINK5/CXCL1/CXCL2	7
BP	GO:0042572	retinol metabolic process	5/120	41/18670	6.28E-06	0.001874325	0.001735997	ADH1A/ADH1C/TTR/AKR1B15/AKR1B10	5
BP	GO:1902476	chloride transmembrane transport	6/120	88/18670	2.19E-05	0.00560664	0.005192859	CLCA4/SLC26A3/CLCA1/BEST4/BEST2/SLC26A2	6
BP	GO:1990868	response to chemokine	6/120	97/18670	3.81E-05	0.00758666	0.007026751	REG1A/CCL23/PPBP/PADI2/CXCL1/CXCL2	6
BP	GO:1990869	cellular response to chemokine	6/120	97/18670	3.81E-05	0.00758666	0.007026751	REG1A/CCL23/PPBP/PADI2/CXCL1/CXCL2	6
BP	GO:0071241	cellular response to inorganic substance	8/120	215/18670	7.56E-05	0.013221823	0.012246028	DPEP1/MMP3/CLDN1/SLC30A10/CHP2/CPNE7/MT1M/MT1G	8
BP	GO:0098661	inorganic anion transmembrane transport	6/120	111/18670	8.13E-05	0.013221823	0.012246028	CLCA4/SLC26A3/CLCA1/BEST4/BEST2/SLC26A2	6
BP	GO:0006959	humoral immune response	10/120	356/18670	0.000101419	0.015128279	0.014011784	REG1A/REG1B/REG3A/CHGA/PPBP/CR2/SPINK5/ITLN1/CXCL1/CXCL2	10
BP	GO:1990266	neutrophil migration	6/120	118/18670	0.000114011	0.015698396	0.014539826	CCL23/PPBP/CD177/SAI1/CXCL1/CXCL2	6
BP	GO:0016999	antibiotic metabolic process	6/120	122/18670	0.000136973	0.017512945	0.016220457	DPEP1/MMP3/ADH1A/ADH1C/PCK1/AKR1B10	6
BP	GO:0034754	cellular hormone metabolic process	6/120	129/18670	0.000185856	0.021834692	0.020223252	ADH1A/ADH1C/TTR/AKR1B15/AKR1B10/SPP1	6
BP	GO:0008544	epidermis development	11/120	464/18670	0.000202022	0.021834692	0.020223252	KRT23/FOXQ1/REG3A/PITX2/KRT6B/INHBA/KRTAP131/CDH3/SULT2B1/SPINK5/HOXB13	11
BP	GO:0071248	cellular response to metal ion	7/120	188/18670	0.000214281	0.021834692	0.020223252	DPEP1/CLDN1/SLC30A10/CHP2/CPNE7/MT1M/MT1G	7
BP	GO:0034308	primary alcohol metabolic process	5/120	85/18670	0.000219567	0.021834692	0.020223252	ADH1A/ADH1C/TTR/AKR1B15/AKR1B10	5
BP	GO:0030574	collagen catabolic process	4/120	47/18670	0.000233841	0.022030308	0.020404431	MMP7/MMP3/MMP1/KLK6	4
BP	GO:0070098	chemokine-mediated signaling pathway	5/120	88/18670	0.000258251	0.023113498	0.02140768	CCL23/PPBP/PADI2/CXCL1/CXCL2	5
BP	GO:0097530	granulocyte migration	6/120	141/18670	0.000300792	0.025638924	0.023746725	CCL23/PPBP/CD177/SAI1/CXCL1/CXCL2	6
BP	GO:0050900	leukocyte migration	11/120	499/18670	0.000375622	0.029276683	0.027111601	CHGA/CCL23/MMP1/PPBP/CD177/PADI2/SAI1/SLC7A5/CXCL1/COL1A1/CXCL2	11
BP	GO:0043588	skin development	10/120	419/18670	0.000376181	0.029276683	0.027111601	KRT23/FOXQ1/CLDN1/REG3A/KRT6B/INHBA/KRTAP13-1/CDH3/SPINK5/COL1A1	10
BP	GO:0016338	calcium-independent cell-cell adhesion via plasma membrane cell-adhesion molecules	3/120	23/18670	0.00041749	0.030007083	0.027792505	CLDN1/CLDN2/CLDN8	3
BP	GO:0097529	myeloid leukocyte migration	7/120	210/18670	0.000419093	0.030007083	0.027792505	CHGA/CCL23/PPBP/CD177/SAI1/CXCL1/CXCL2	7
BP	GO:0001523	retinoid metabolic process	5/120	104/18670	0.000558758	0.037043618	0.034309731	ADH1A/ADH1C/TTR/AKR1B15/AKR1B10	5
BP	GO:0030593	neutrophil chemotaxis	5/120	104/18670	0.000558758	0.037043618	0.034309731	CCL23/PPBP/SAI1/CXCL1/CXCL2	5
BP	GO:0098656	anion transmembrane transport	8/120	291/18670	0.000588718	0.037635932	0.034858332	SLC4A4/CLCA4/SLC26A3/CLCA1/BEST4/BEST2/SLC26A2/SLC7A5	8
BP	GO:0030595	leukocyte chemotaxis	7/120	224/18670	0.000615612	0.037998147	0.035193815	CHGA/CCL23/PPBP/PADI2/SAI1/CXCL1/CXCL2	7
BP	GO:0016101	diterpenoid metabolic process	5/120	110/18670	0.000721278	0.043036266	0.039860111	ADH1A/ADH1C/TTR/AKR1B15/AKR1B10	5
BP	GO:0042445	hormone metabolic process	7/120	233/18670	0.000776471	0.043786311	0.040554802	ADH1A/ADH1C/TTR/KLK6/AKR1B15/AKR1B10/SPP1	7
BP	GO:0060326	cell chemotaxis	8/120	304/18670	0.000782772	0.043786311	0.040554802	CHGA/CCL23/SAI1/PPBP/PADI2/SAI1/CXCL1/CXCL2	8
BP	GO:0048545	response to steroid hormone	9/120	383/18670	0.000827663	0.044894456	0.041581164	CLDN1/CA2/SST/PCK1/PADI2/SCGB2A1/SPP1/COL1A1/NR3C2	9
BP	GO:0032963	collagen metabolic process	5/120	115/18670	0.000881756	0.046421855	0.042995837	MMP7/MMP3/MMP1/KLK6/COL1A1	5
CC	GO:0045177	apical part of cell	12/126	384/19717	6.64E-06	0.001089398	0.000922982	DPEP1/CLDN1/CA2/CLCA4/CA4/SLC26A3/AQP8/SCNN1B/SLC26A2/SI/SLC7A5/TRPM6	12
CC	GO:0016324	apical plasma membrane	10/126	318/19717	3.82E-05	0.003133227	0.002854595	DPEP1/CLDN1/CLCA4/CA4/SLC26A3/SCNN1B/SLC26A2/SI/SLC7A5/TRPM6	10
CC	GO:0042588	zymogen granule	3/126	14/19717	8.81E-05	0.004816077	0.004080373	REG1A/CLCA1/ZG16	3
CC	GO:0005902	microvillus	5/126	83/19717	0.00019182	0.007864638	0.006663237	DPEP1/CA2/CLCA1/CA9/SLC26A2	5
CC	GO:0031253	cell projection membrane	9/126	326/19717	0.000250332	0.007938419	0.006725747	REG1A/DPEP1/CA4/SLC26A3/CA9/SLC26A2/TESC/ITLN1/TRPM6	9
CC	GO:0031526	brush border membrane	4/126	53/19717	0.00036542	0.007938419	0.006725747	CA4/SLC26A3/ITLN1/TRPM6	4
CC	GO:0098858	actin-based cell projection	7/126	208/19717	0.000384553	0.007938419	0.006725747	DPEP1/CA2/CLCA1/CA9/TUBB3/SLC26A2/LY6G6D	7
CC	GO:0031528	microvillus membrane	3/126	23/19717	0.00041099	0.007938419	0.006725747	DPEP1/CA9/SLC26A2	3
CC	GO:0005903	brush border	5/126	99/19717	0.000435645	0.007938419	0.006725747	CA4/SLC26A3/SI/ITLN1/TRPM6	5
CC	GO:0042589	zymogen granule membrane	2/126	11/19717	0.002145814	0.03519135	0.029815521	CLCA1/ZG16	2
CC	GO:0016323	basolateral plasma membrane	6/126	217/19717	0.002732176	0.038048876	0.032236531	CLDN1/CLDN8/SLC4A4/CA2/CA9/TACSTD2	6
CC	GO:0098862	cluster of actin-based cell projections	5/126	150/19717	0.002784064	0.038048876	0.032236531	CA4/SLC26A3/SI/ITLN1/TRPM6	5
CC	GO:0031225	anchored component of membrane	5/126	170/19717	0.004744703	0.055636741	0.047137675	DPEP1/CA4/CD177/ITLN1/LY6G6D	5
CC	GO:0060205	cytoplasmic vesicle lumen	7/126	325/19717	0.004923828	0.055636741	0.047137675	GCG/ZG16/TTR/PPBP/PADI2/CXCL1/PLAC8	7
CC	GO:0031983	vesicle lumen	7/126	327/19717	0.005088726	0.055636741	0.047137675	GCG/ZG16/TTR/PPBP/PADI2/CXCL1/PLAC8	7
MF	GO:0048018	receptor ligand activity	18/117	482/17696	2.74E-09	4.10E-07	3.18E-07	REG1A/INSL5/GUCA2A/SST/CCL23/GCG/SAI1/INHBA/OGN/TTR/FAM3B/PPBP/GREM2/BMP3/SAI1/SPP1/CXCL1/CXCL2	18
MF	GO:0030546	signaling receptor activator activity	18/117	487/17696	3.23E-09	4.10E-07	3.18E-07	REG1A/INSL5/GUCA2A/SST/CCL23/GCG/SAI1/INHBA/OGN/TTR/FAM3B/PPBP/GREM2/BMP3/SAI1/SPP1/CXCL1/CXCL2	18
MF	GO:0004089	carbonate dehydratase activity	5/117	15/17696	3.30E-08	2.80E-06	2.17E-06	CA1/CA2/CA7/CA4/CA9	5
MF	GO:0070492	oligosaccharide binding	4/117	15/17696	2.34E-06	0.000148713	0.000115248	REG1A/REG1B/REG3A/ITLN1	4
MF	GO:0015108	chloride transmembrane transporter activity	7/117	100/17696	4.44E-06	0.000195	0.000151119	CLCA4/SLC26A3/CLCA1/BEST4/BEST2/ANO5/SLC26A2	7
MF	GO:0015103	inorganic anion transmembrane transporter activity	8/117	142/17696	4.61E-06	0.000195	0.000151119	SLC4A4/CLCA4/SLC26A3/CLCA1/BEST4/BEST2/ANO5/SLC26A2	8
MF	GO:0005125	cytokine activity	9/117	220/17696	1.56E-05	0.000564869	0.000437756	CCL23/INHBA/FAM3B/PPBP/GREM2/BMP3/SPP1/CXCL1/CXCL2	9
MF	GO:0016836	hydro-lyase activity	5/117	56/17696	3.38E-05	0.001074314	0.00083256	CA1/CA2/CA7/CA4/CA9	5
MF	GO:0005254	chloride channel activity	5/117	75/17696	0.000138359	0.003108513	0.002409001	CLCA4/CLCA1/BEST4/BEST2/ANO5	5
MF	GO:0016835	carbon-oxygen lyase activity	5/117	75/17696	0.000138359	0.003108513	0.002409001	CA1/CA2/CA7/CA4/CA9	5
MF	GO:0005229	intracellular calcium activated chloride channel activity	3/117	16/17696	0.000148141	0.003108513	0.002409001	CLCA4/CLCA1/ANO5	3
MF	GO:0061778	intracellular chloride channel activity	3/117	16/17696	0.000148141	0.003108513	0.002409001	CLCA4/CLCA1/ANO5	3
MF	GO:0005179	hormone activity	6/117	122/17696	0.000159097	0.003108513	0.002409001	INSL5/GUCA2A/SST/GCG/INHBA/TTR	6
MF	GO:0042834	peptidoglycan binding	3/117	17/17696	0.000179019	0.003247921	0.002517038	REG1A/REG1B/REG3A	3
MF	GO:0015106	bicarbonate transmembrane transporter activity	3/117	19/17696	0.000252653	0.004278256	0.003315515	SLC4A4/SLC26A3/SLC26A2	3
MF	GO:0008009	chemokine activity	4/117	49/17696	0.000305659	0.004619625	0.003580065	CCL23/PPBP/CXCL1/CXCL2	4
MF	GO:0005253	anion channel activity	5/117	89/17696	0.000309187	0.004619625	0.003580065	CLCA4/CLCA1/BEST4/BEST2/ANO5	5
MF	GO:0008509	anion transmembrane transporter activity	9/117	336/17696	0.000394355	0.005564781	0.004312533	SLC4A4/CLCA4/SLC26A3/CLCA1/BEST4/BEST2/ANO5/SLC26A2/SLC7A5	9
MF	GO:0001664	G protein-coupled receptor binding	8/117	280/17696	0.000547332	0.007316963	0.005670419	INSL5/CCL23/GCG/MYOC/PPBP/SAI1/CXCL1/CXCL2	8
MF	GO:0008083	growth factor activity	6/117	163/17696	0.000750509	0.009531459	0.007386585	REG1A/INHBA/OGN/PPBP/BMP3/CXCL1	6
MF	GO:0005539	glycosaminoglycan binding	7/117	229/17696	0.000824171	0.009986855	0.007725316	REG1A/MMP7/REG1B/REG3A/CCL23/GREM2/SAI1	7
MF	GO:0042379	chemokine receptor binding	4/117	66/17696	0.000953788	0.011011912	0.008533889	CCL23/PPBP/CXCL1/CXCL2	4
MF	GO:0016616	oxidoreductase activity, acting on the CH-OH group of donors, NAD or NADP as acceptor	5/117	119/17696	0.001162877	0.012842207	0.009952311	ADH1A/ADH1C/LDHD/AKR1B15/AKR1B10	5
MF	GO:0008237	metallopeptidase activity	6/117	181/17696	0.001290424	0.01365699	0.010583743	MMP7/DPEP1/MMP3/CLCA4/MMP1/CLCA1	6
MF	GO:0016829	lyase activity	6/117	187/17696	0.001524149	0.015485349	0.012000664	CA1/CA2/CA7/CA4/CA9/PCK1	6
MF	GO:0016614	oxidoreductase activity, acting on CH-OH group of donors	5/117	128/17696	0.001607255	0.015701644	0.012168286	ADH1A/ADH1C/LDHD/AKR1B15/AKR1B10	5
MF	GO:0018455	alcohol dehydrogenase [NAD(P)+] activity	2/117	10/17696	0.001883955	0.017090162	0.013244344	ADH1A/ADH1C	2
MF	GO:0019531	oxalate transmembrane transporter activity	2/117	10/17696	0.001883955	0.017090162	0.013244344	SLC26A3/SLC26A2	2
MF	GO:0030246	carbohydrate binding	7/117	271/17696	0.002167334	0.018982857	0.014711124	REG1A/REG1B/REG3A/ZG16/LGALS2/SI/ITLN1	7
MF	GO:0052650	NADP-retinol dehydrogenase activity	2/117	11/17696	0.002292675	0.019411312	0.015043163	AKR1B15/AKR1B10	2
MF	GO:0022839	ion gated channel activity	3/117	43/17696	0.00				

Table S3 KEGG pathway enrichment analysis of robust DEGs

ID	Description	Gene ratio	Bg ratio	P value	p.adjust	q value	Gene ID	Count
hsa00910	Nitrogen metabolism	5/59	17/8102	9.97E-08	1.16E-05	9.97E-06	CA1/CA2/CA7/CA4/CA9	5
hsa04964	Proximal tubule bicarbonate reclamation	4/59	23/8102	2.03E-05	0.001174916	0.001012859	SLC4A4/CA2/CA4/PCK1	4
hsa04060	Cytokine-cytokine receptor interaction	9/59	295/8102	0.000251876	0.00973919	0.008395854	CCL23/INHBA/PPBP/BMP3/IL1R2/TNFRSF6B/CXCL1/CXCL2/TNFRSF17	9
hsa00620	Pyruvate metabolism	4/59	47/8102	0.000358211	0.010388126	0.008955281	ADH1A/ADH1C/PCK1/LDHD	4
hsa04972	Pancreatic secretion	5/59	102/8102	0.000837155	0.016559945	0.014275815	SLC4A4/CA2/CLCA4/SLC26A3/CLCA1	5
hsa04978	Mineral absorption	4/59	59/8102	0.000856549	0.016559945	0.014275815	SLC26A3/MT1M/MT1G/TRPM6	4

Table S4 GO enrichment analysis of hub genes

ONTOLOGY	ID	Description	Gene ratio	Bg ratio	P value	p.adjust	q value	Gene ID	Count
BP	GO:0050900	leukocyte migration	7/23	499/18670	1.58E-06	0.000867623	0.000552656	CHGA/MMP1/PPBP/SA1/CXCL1/COL1A1/CXCL2	7
BP	GO:0097529	myeloid leukocyte migration	5/23	210/18670	4.90E-06	0.000867623	0.000552656	CHGA/PPBP/SA1/CXCL1/CXCL2	5
BP	GO:0051591	response to cAMP	4/23	97/18670	5.62E-06	0.000867623	0.000552656	SLC26A3/AQP8/PCK1/COL1A1	4
BP	GO:0030595	leukocyte chemotaxis	5/23	224/18670	6.71E-06	0.000867623	0.000552656	CHGA/PPBP/SA1/CXCL1/CXCL2	5
BP	GO:0030593	neutrophil chemotaxis	4/23	104/18670	7.42E-06	0.000867623	0.000552656	PPBP/SA1/CXCL1/CXCL2	4
BP	GO:1990266	neutrophil migration	4/23	118/18670	1.22E-05	0.001054195	0.000671498	PPBP/SA1/CXCL1/CXCL2	4
BP	GO:0019730	antimicrobial humoral response	4/23	122/18670	1.40E-05	0.001054195	0.000671498	CHGA/PPBP/CXCL1/CXCL2	4
BP	GO:0071621	granulocyte chemotaxis	4/23	123/18670	1.44E-05	0.001054195	0.000671498	PPBP/SA1/CXCL1/CXCL2	4
BP	GO:0046683	response to organophosphorus	4/23	134/18670	2.02E-05	0.001312959	0.000836325	SLC26A3/AQP8/PCK1/COL1A1	4
BP	GO:0007586	digestion	4/23	139/18670	2.33E-05	0.001312959	0.000836325	GUCA2A/SST/GUCA2B/SI	4
BP	GO:0097530	granulocyte migration	4/23	141/18670	2.47E-05	0.001312959	0.000836325	PPBP/SA1/CXCL1/CXCL2	4
BP	GO:0060326	cell chemotaxis	5/23	304/18670	2.93E-05	0.001379569	0.000878754	CHGA/PPBP/SA1/CXCL1/CXCL2	5
BP	GO:0014074	response to purine-containing compound	4/23	149/18670	3.07E-05	0.001379569	0.000878754	SLC26A3/AQP8/PCK1/COL1A1	4
BP	GO:0071320	cellular response to cAMP	3/23	53/18670	3.67E-05	0.001535611	0.000978149	SLC26A3/AQP8/PCK1	3
BP	GO:0015698	inorganic anion transport	4/23	169/18670	5.02E-05	0.00195619	0.001246048	SLC4A4/CLCA4/SLC26A3/CLCA1	4
BP	GO:0031284	positive regulation of guanylate cyclase activity	2/23	10/18670	6.49E-05	0.002374256	0.001512346	GUCA2A/GUCA2B	2
BP	GO:0030198	extracellular matrix organization	5/23	368/18670	7.27E-05	0.002393714	0.001524741	MMP1/TTR/SPP1/TGFBI/COL1A1	5
BP	GO:0043062	extracellular structure organization	5/23	369/18670	7.37E-05	0.002393714	0.001524741	MMP1/TTR/SPP1/TGFBI/COL1A1	5
BP	GO:0031282	regulation of guanylate cyclase activity	2/23	12/18670	9.51E-05	0.002808445	0.001788915	GUCA2A/GUCA2B	2
BP	GO:0061844	antimicrobial humoral immune response mediated by antimicrobial peptide	3/23	73/18670	9.60E-05	0.002808445	0.001788915	PPBP/CXCL1/CXCL2	3
BP	GO:0070098	chemokine-mediated signaling pathway	3/23	88/18670	0.000167377	0.004450694	0.00283499	PPBP/CXCL1/CXCL2	3
BP	GO:1902476	chloride transmembrane transport	3/23	88/18670	0.000167377	0.004450694	0.00283499	CLCA4/SLC26A3/CLCA1	3
BP	GO:1990868	response to chemokine	3/23	97/18670	0.000223266	0.0054421	0.003466493	PPBP/CXCL1/CXCL2	3
BP	GO:1990869	cellular response to chemokine	3/23	97/18670	0.000223266	0.0054421	0.003466493	PPBP/CXCL1/CXCL2	3
BP	GO:0006821	chloride transport	3/23	108/18670	0.000306431	0.006609567	0.004210143	CLCA4/SLC26A3/CLCA1	3
BP	GO:0031281	positive regulation of cyclase activity	2/23	22/18670	0.000330357	0.006609567	0.004210143	GUCA2A/GUCA2B	2
BP	GO:0098661	inorganic anion transmembrane transport	3/23	111/18670	0.000332136	0.006609567	0.004210143	CLCA4/SLC26A3/CLCA1	3
BP	GO:0043200	response to amino acid	3/23	113/18670	0.000350022	0.006609567	0.004210143	SST/PCK1/COL1A1	3
BP	GO:0010447	response to acidic pH	2/23	23/18670	0.000361549	0.006609567	0.004210143	SST/PCK1	2
BP	GO:0030810	positive regulation of nucleotide biosynthetic process	2/23	23/18670	0.000361549	0.006609567	0.004210143	GUCA2A/GUCA2B	2
BP	GO:0051349	positive regulation of lyase activity	2/23	23/18670	0.000361549	0.006609567	0.004210143	GUCA2A/GUCA2B	2
BP	GO:1900373	positive regulation of purine nucleotide biosynthetic process	2/23	23/18670	0.000361549	0.006609567	0.004210143	GUCA2A/GUCA2B	2
BP	GO:0098656	anion transmembrane transport	4/23	291/18670	0.000405183	0.007182789	0.004575272	SLC4A4/CLCA4/SLC26A3/CLCA1	4
BP	GO:0071377	cellular response to glucagon stimulus	2/23	26/18670	0.000463397	0.007973163	0.005078722	PCK1/GCG	2
BP	GO:0009914	hormone transport	4/23	317/18670	0.000559542	0.009352338	0.005957225	CHGA/TTR/SPP1/GCG	4
BP	GO:0032496	response to lipopolysaccharide	4/23	330/18670	0.000650676	0.01057348	0.006735064	PPBP/PCK1/CXCL1/CXCL2	4
BP	GO:002237	response to molecule of bacterial origin	4/23	343/18670	0.000751923	0.011888518	0.007572713	PPBP/PCK1/CXCL1/CXCL2	4
BP	GO:0006959	humoral immune response	4/23	356/18670	0.000863899	0.013299493	0.008471472	CHGA/PPBP/CXCL1/CXCL2	4
BP	GO:0033762	response to glucagon	2/23	36/18670	0.000891575	0.013373619	0.008518688	PCK1/GCG	2
BP	GO:0009268	response to pH	2/23	40/18670	0.001100553	0.015703012	0.010002459	SST/PCK1	2
BP	GO:1900371	regulation of purine nucleotide biosynthetic process	2/23	40/18670	0.001100553	0.015703012	0.010002459	GUCA2A/GUCA2B	2
BP	GO:0048545	response to steroid hormone	4/23	383/18670	0.001133428	0.015728687	0.010018813	SST/SPP1/PCK1/COL1A1	4
BP	GO:0030808	regulation of nucleotide biosynthetic process	2/23	41/18670	0.001156126	0.015728687	0.010018813	GUCA2A/GUCA2B	2
BP	GO:0015701	bicarbonate transport	2/23	42/18670	0.001213024	0.0161277	0.010272975	SLC4A4/SLC26A3	2
BP	GO:0031279	regulation of cyclase activity	2/23	43/18670	0.001271243	0.016526165	0.010526788	GUCA2A/GUCA2B	2
BP	GO:0045981	positive regulation of nucleotide metabolic process	2/23	46/18670	0.001453805	0.017718246	0.011286116	GUCA2A/GUCA2B	2
BP	GO:0051339	regulation of lyase activity	2/23	46/18670	0.001453805	0.017718246	0.011286116	GUCA2A/GUCA2B	2
BP	GO:1900544	positive regulation of purine nucleotide metabolic process	2/23	46/18670	0.001453805	0.017718246	0.011286116	GUCA2A/GUCA2B	2
BP	GO:0043434	response to peptide hormone	4/23	436/18670	0.001826249	0.021803172	0.01388812	SLC30A10/PCK1/COL1A1/GCG	4
BP	GO:0071222	cellular response to lipopolysaccharide	3/23	205/18670	0.001964707	0.022987067	0.014642234	PPBP/CXCL1/CXCL2	3
BP	GO:0019935	cyclic-nucleotide-mediated signaling	3/23	212/18670	0.002161811	0.024320372	0.015491519	CHGA/GUCA2B/GCG	3
BP	GO:0071219	cellular response to molecule of bacterial origin	3/23	212/18670	0.002161811	0.024320372	0.015491519	PPBP/CXCL1/CXCL2	3
BP	GO:0007584	response to nutrient	3/23	219/18670	0.002370845	0.026168759	0.016668899	SST/SPP1/COL1A1	3
BP	GO:0007588	excretion	2/23	63/18670	0.002708599	0.029343156	0.018690917	GUCA2B/SLC26A3	2
BP	GO:0071216	cellular response to biotic stimulus	3/23	236/18670	0.002929681	0.031143503	0.019837697	PPBP/CXCL1/CXCL2	3
BP	GO:0031667	response to nutrient levels	4/23	499/18670	0.002981258	0.031143503	0.019837697	SST/SPP1/PCK1/COL1A1	4
BP	GO:0071300	cellular response to retinoic acid	2/23	69/18670	0.003239085	0.03324324	0.021175181	PCK1/COL1A1	2
BP	GO:0046883	regulation of hormone secretion	3/23	262/18670	0.003930896	0.039647826	0.025254756	CHGA/SPP1/GCG	3
BP	GO:0051453	regulation of intracellular pH	2/23	84/18670	0.004759422	0.047190879	0.030059507	SLC4A4/SLC26A3	2
CC	GO:0034774	secretory granule lumen	4/24	321/19717	0.000566363	0.011535838	0.00745622	TTR/PPBP/CXCL1/GCG	4
CC	GO:0060205	cytoplasmic vesicle lumen	4/24	325/19717	0.000593329	0.011535838	0.00745622	TTR/PPBP/CXCL1/GCG	4
CC	GO:0031983	vesicle lumen	4/24	327/19717	0.000607149	0.011535838	0.00745622	TTR/PPBP/CXCL1/GCG	4
CC	GO:0045177	apical part of cell	4/24	384/19717	0.001105281	0.01575026	0.010180223	CLCA4/SLC26A3/AQP8/SI	4
CC	GO:1904724	tertiary granule lumen	2/24	55/19717	0.002027219	0.023110296	0.014937403	PPBP/CXCL1	2
CC	GO:0005788	endoplasmic reticulum lumen	3/24	309/19717	0.00604535	0.046625468	0.030136498	SPP1/COL1A1/GCG	3
CC	GO:0005903	brush border	2/24	99/19717	0.00640979	0.046625468	0.030136498	SLC26A3/SI	2
CC	GO:0016324	apical plasma membrane	3/24	318/19717	0.006543925	0.046625468	0.030136498	CLCA4/SLC26A3/SI	3
MF	GO:0048018	receptor ligand activity	9/22	482/17696	2.78E-09	1.38E-07	6.89E-08	GUCA2A/SST/TTR/PPBP/SA1/SPP1/CXCL1/GCG/CXCL2	9
MF	GO:0030546	signaling receptor activator activity	9/22	487/17696	3.04E-09	1.38E-07	6.89E-08	GUCA2A/SST/TTR/PPBP/SA1/SPP1/CXCL1/GCG/CXCL2	9
MF	GO:0005179	hormone activity	4/22	122/17696	1.43E-05	0.000433406	0.000215575	GUCA2A/SST/TTR/GCG	4
MF	GO:0001664	G protein-coupled receptor binding	5/22	280/17696	2.02E-05	0.000449057	0.00022336	PPBP/SA1/CXCL1/GCG/CXCL2	5
MF	GO:0015103	inorganic anion transmembrane transporter activity	4/22	142/17696	2.60E-05	0.000449057	0.00022336	SLC4A4/CLCA4/SLC26A3/CLCA1	4
MF	GO:0008009	chemokine activity	3/22	49/17696	2.96E-05	0.000449057	0.00022336	PPBP/CXCL1/CXCL2	3
MF	GO:0042379	chemokine receptor binding	3/22	66/17696	7.25E-05	0.000942998	0.000469044	PPBP/CXCL1/CXCL2	3
MF	GO:0005125	cytokine activity	4/22	220/17696	0.000142613	0.001594252	0.000792977	PPBP/SPP1/CXCL1/CXCL2	4
MF	GO:0005229	intracellular calcium activated chloride channel activity	2/22	16/17696	0.000175193	0.001594252	0.000792977	CLCA4/CLCA1	2
MF	GO:0061778	intracellular chloride channel activity	2/22	16/17696	0.000175193	0.001594252	0.000792977	CLCA4/CLCA1	2
MF	GO:0015106	bicarbonate transmembrane transporter activity	2/22	19/17696	0.000249086	0.00189131	0.000940733	SLC4A4/SLC26A3	2
MF	GO:0015108	chloride transmembrane transporter activity	3/22	100/17696	0.000249404	0.00189131	0.000940733	CLCA4/SLC26A3/CLCA1	3
MF	GO:0008509	anion transmembrane transporter activity	4/22	336/17696	0.00071252	0.00498764	0.002480839	SLC4A4/CLCA4/SLC26A3/CLCA1	4
MF	GO:0022839	ion gated channel activity	2/22	4					

Table S5 KEGG pathway enrichment analysis of hub genes

ID	Description	Gene ratio	Bg ratio	P value	p.adjust	q value	Gene ID	Count
hsa04972	Pancreatic secretion	4/16	102/8104	3.83E-05	0.002031543	0.001291149	SLC4A4/CLCA4/SLC26A3/CLCA1	4
hsa05323	Rheumatoid arthritis	3/16	93/8104	0.000735285	0.008501102	0.005402885	MMP1/CXCL1/CXCL2	3
hsa04657	IL-17 signaling pathway	3/16	94/8104	0.000758609	0.008501102	0.005402885	MMP1/CXCL1/CXCL2	3
hsa04964	Proximal tubule bicarbonate reclamation	2/16	23/8104	0.000902567	0.008501102	0.005402885	SLC4A4/PCK1	2
hsa04061	Viral protein interaction with cytokine and cytokine receptor	3/16	100/8104	0.000908527	0.008501102	0.005402885	PPBP/CXCL1/CXCL2	3
hsa05146	Amoebiasis	3/16	102/8104	0.000962389	0.008501102	0.005402885	CXCL1/COL1A1/CXCL2	3

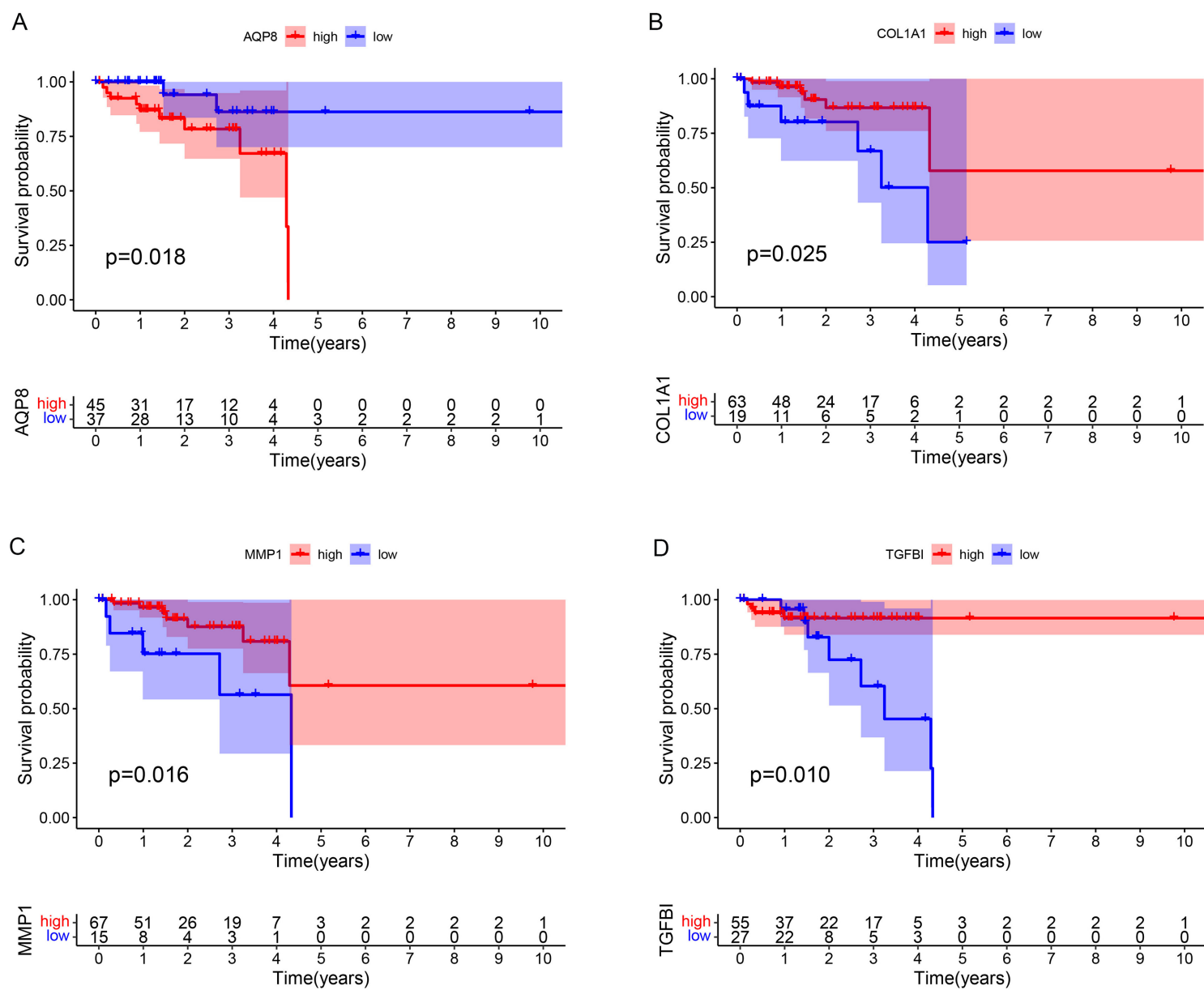


Figure S1 Survival analysis of the 24 hub genes. Gene changes of AQP8 (A), COL1A1 (B), MMP1 (C), and TGFBI (D) were significantly correlated with the overall survival of patients with rectal cancer ($P < 0.05$).

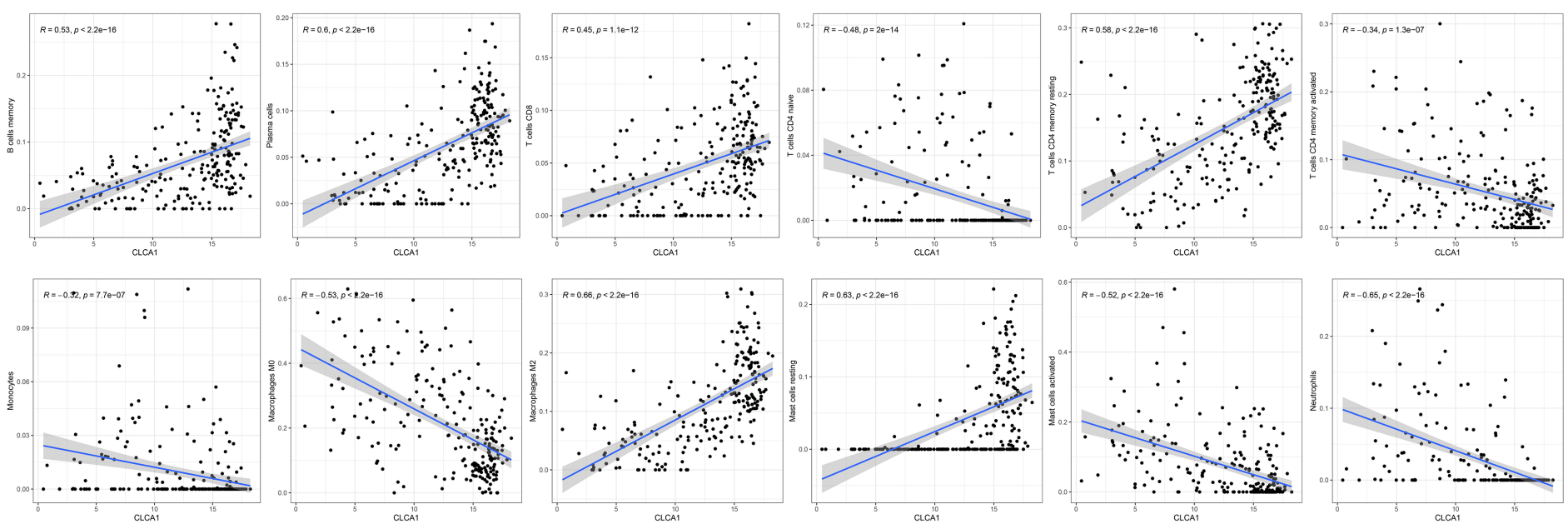


Figure S2 Relationship between the prognostic gene CLCA1 and immune cell infiltration.