Supplemental material for

Epithelial to mesenchymal transition rewires the molecular path to PI3-Kinase-dependent proliferation

Megan B. Salt[1,2], Sourav Bandyopadhyay[1,3] and Frank McCormick[1]

Authors Affiliations: 1-Helen Diller Family Comprehensive Cancer Center; 2-Biomedical Sciences Graduate Program, University of California San Francisco, San Francisco, California; 3-California Institute for Quantitative Biosciences, San Francisco, California.

Supplemental Figure Legends

Table S1. EMT associated changes in gene expression. Significantly (A) up- and (B) down-regulated genes in comparing H358-TwistER cells to control H358-GFP expressing cells treated with 100nM 4OHT for 12 days. The four columns on the right are associated with significantly upregulated genes, while the four columns furthest left described significantly downregulated genes. The first column for the up- and downregulated genes shows the Probe ID associated with each gene from the Affymetric Human Gene 1.0 ST microarrays. The gene name are shown in the next column, followed by the $\log_2$(fold change) in expression for each gene after 4OHT treatment in the H358-TwistER cells. The final column shows the p-value for each gene adjusted for the false discovery rate.

Figure S1. Akt inhibition reduces serum-independent proliferation. (A) Proliferation of H358-TwistER cells with increasing concentrations (uM) of GSK-690693 (top) or MK-2206 (bottom). (B) Lysates from H358-TwistER cells treated for 48hrs in serum free media with indicated concentrations of GSK-690693 (top), or MK-2206 (bottom).

Figure S2. The effects of TGFβ1 are specific to epithelial cells and lead to reduced serum-independent proliferation. (A) Proliferation of untreated (top) or TGFβ1 pre-treated (bottom) H358 and H441 cells in the presence (10%) or absence (SS) of serum. (B) Lysates from indicated cell lines treated with 2ng/ml TGFβ1 for 14d.

Figure S3. siRNAs targeting ErbB3 and NRG1 are efficient and on target and knockdown of autocrine TGFα/EREG does not affect ErbB3-PI3K signaling. (A) Knockdown efficiencies at the protein level of indicated oligos 72hrs post-transfection. (B) Fold change in RNA level 48hrs post-transfection with indicated oligos. (C) Proliferation of H35-TwistER cells transfected with the indicated

siNRG1 oligos in the absence (-) or presence (+) of exogenous NRG1 ligand (100ng/ml). (D) Lysates from H358-TwistER cells (NT) collected 72hrs after transfection with indicated siRNA oligos, serum starved overnight. (E) qPCR quantification of fold change RNA level 72hrs post-transfection with indicated siRNAs. (F) Immunoprecipitation of ErbB3 and p85 from H358-TwistER lysates 72hrs after transfection with indicated oligos, serum starved overnight.

Figure S4. Proliferation of epithelial cells after knockdown of TGFα/EREG and ErbB3 in serum and in mesenchymal cells after EGFR expression in H358-TwistER cells. (A) Proliferation of H358-TwistER cells in the presence of indicated siRNA oligos and serum conditions. (B) Proliferation of H358-TwistER cells before EMT in the presence of 10% serum after transfection with indicated siRNAs. (C) Proliferation of H358-TwistER cells after 14d 4OHT pre-treatment, after transfection with indicated expression constructs.

Figure S5. ErbB3 and NRG1 promote Akt activity in H441 and H2122 cells and ErbB3 knockdown reduces serum-independent proliferation. (A) Lysates from H441 and H2122 cell lines collected 72hrs after transfection with indicated siRNAs, serum starved overnight. (B) Immunoprecipitation of p85 from H441 and H2122 lysates 72hrs after transfection with NRG1 targeting siRNA, serum starved overnight. (C) Proliferation of H441 and H2122 cells in the absence of serum after transfection with indicated siRNAs. SS: serum starved; IP: Immunoprecipitation; WCL: whole cell lysates.

Figure S6. GAB1 mediates growth factor stimulated signaling from EGFR to PI3K-Akt, and is required for proliferation in H358-TwistER cells after EMT. (A) Lysates from H358-GFP expressing control cells 72hrs after transfection with indicated siRNAs, serum starved overnight, and treated -/+ EGF for 10 minutes. (B) H358-TwistER cells pre- (NT) and post- (4OHT) EMT 72 hrs after transfection with control of GAB1 targeting siRNAs. Lysates collected from cells asynchronously growing in serum,

or starved overnight and treated 10min -/+ EGF as indicated. (C) Proliferation of H358-TwistER cells with and without 4OHT pre-treatment after transfection with indicated siRNAs in 10% serum.

Figure S7. KRas is required for proliferation before and after the induction of EMT. Proliferation of H358-TwistER cells (A) before and (B) after 4OHT induced EMT in the presence of indicated siRNAs. (C) Lysates from H358-TwistER cells 72hrs after transfection with indicated siRNAs, serum starved overnight. (D) Relative cell numbers of H358-TwistER with and without 4OHT pre-treatment after 72 hours growth in the presence of indicated doses of PD0325901(uM).

Figure S8. EMT alters sensitivity to inhibition of EGFR but does not affect sensitivity to PI3K inhibitors. (A) Relative cell number of H358-TwistER with and without 4OHT pre-treatment after 72 hours growth in the presence of indicated doses of Erlotinib (top) or BKM-120 (bottom). (B) Relative number of H441 cells with and without 2 weeks TGFβ1 pre-treatment (2ng/ml) after 72 hours treatment with Erlotinib (top) or BKM-120 (bottom). (C) Relative number of H358 and H441 cells after transfection with ErbB3 siRNAs followed by treatment the next day with indicated doses of Erlotinib for 72 hours. Sensitivity to Erlotinib and Lapatinib compared to EMT Score (see methods) across all cell lines in the CCLE (D) and NSCLC lines (E). Sensitivity to GDC-0941 across NSCLC cell lines (F). Drug sensitivities are based on AUC from dose-responses analysis in the Cancer Cell Line Encyclopedia, with AUC<1 (area under the curve) used to define drug sensitive lines. *** indicates p<0.0001, n.s.=not significant.

Supplemental Methods

Gene expression analysis

RNA was extracted from three biological replicates of each condition using Qiagen RNeasy mini kit according to manufacturer's instructions. Quality was analyzed on a 2100 BioAnalyzer (Agilent). GeneChip Human Gene 1.0 ST Arrays (Affymetrix) were used to quantitate gene expression in each sample. RNA preparation and data collection was performed at the Gladstone Institute Genomics Core Facility. Additional data analysis was performed by the Bioinformatics Core at the Helen Diller Family Comprehensive Cancer Center. Raw data and results can be found in the GEO database, accession number GSE52308.

Phospho-Receptor Tyrosine Kinase Arrays

Phospho-RTK arrays were purchased from R&D Systems. Equal quantities of protein lysates from cells with and without 4OHT pre-treatment, were collected in supplied lysis buffer supplemented with protease inhibitor cocktail (Roche) and incubated on membranes and analyzed according to manufacturer's protocol.

siRNA oligonucleotides

The following siRNA oligonucleotides were used for this study.

siRNA Name	Company	Catalogue Number	Target Sequence
Control	Qiagen	1027281	Proprietary
ErbB3 pool	Dharmacon	M-003127-03-0005	See below (pool of 08/22/23/24)
ErbB3 08	Dharmacon	D-003127-08	GCAGUGGAUUCGAGAAGUG
ErbB3 22	Dharmacon	D-003127-22	AGAUUGUGCUCACGGGACA
ErbB3 23	Dharmacon	D-003127-23	GUGGAUUCGAGAAGUGACA

ErbB3 24	Dharmacon	D-003127-24	GCGAUGCUGAGAACCAAUA
NRG1 pool	Dharmacon	M-004608-02-0005	See below (pool of 21/22/23/24)
NRG1 21	Dharmacon	D-004608-21	UUUCAAACCCCUCGAGAUA
NRG1 22	Dharmacon	D-004608-22	GGGGAGUGCUUCAUGGUGA
NRG1 23	Dharmacon	D-004608-23	UUGUAAAAUGUGCGGAGAA
NRG1 24	Dharmacon	D-004608-24	ACAUCCACCACUGGGACAA
TGFα pool	Dharmacon	M-019737-01-0005	Pool: CAGCAGUGGUGUCCCAUUU GCAUGUGUCUGCCAUUCUG GUACGUUGGUGCACGCUGU ACUGCUGCCAGGUCCGAAA
Ereg pool	Dharmacon	M-011268-01-0005	Pool: GCUCUGACAUGAAUGGCUA GUACAACUGUGAUUCCAUC GAAGUGGGUUAUACUGGUG GCUUUGACCGUGAUUCUUA
GAB1 pool	Dharmacon	M-003553-00-0005	Pool: AUACUUAGAUCUCGACUUA CAUCAAAGCUAGACACUAU GAUGCUGGAUUGACAUUUA GAGAGUGGAUUAUGUUGUU
ErbB2 14	Qiagen	S102223571	AACAAAGAAATCTTAGACGAA
ErbB2 15	Qiagen	S102223578	CACGTTTGAGTCCATGCCCAA
EGFR 10	Qiagen	S102660140	TACGAATATTAAACACTTCAA
EGFR 12	Qiagen	S102663983	CAGGAACTGGATATTCTGAAA
KRas 234	Mirimus	N/A	Proprietary
KRas 355	Mirimus	N/A	Proprietary

SYBR Green qPCR

RNA was isolated from cells using the RNEasy Mini kit (Qiagen). cDNA was synthesized from total RNA using SuperScript First-Strand Synthesis System for RT-PCR (Invitrogen). 10ng cDNA template was used in qPCR reaction along with 1X SYBR green master mix (Applied Biosystems), 0.2uM indicated forward and 0.2uM reverse primers. Data was collected on the Stratagene Mx 3000P machine and analyzed using $\Delta(\Delta ct)$ method to calculate fold change. Primers sequences are shown below.

The following qPCR primers were used for this study.

Primers Targets	Sequence
ErbB3 forward	GGTGATGGGGAACCTTGAGAT
ErbB3 reverse	CTGTCACTTCTCGAATCCACTG
NRG1 forward	GCCAGGAATCGGCTGCAGGT
NRG1 reverse	AGCCAGTGATGCTTTGTTAATGCGA
EGFR forward	AGGCACGAGTAACAAGCTCAC
EGFR reverse	ATGAGGACATAACCAGCCACC
EREG forward	ATACTGGTGTCCGATGTGAACA
EREG reverse	CCGACGACTGTGATAAGAAACA
TGFα forward	AGGTCCGAAAACACTGTGAGT
TGFα reverse	AGCAAGCGGTTCTTCCCTTC

Table S1. Up- and downregulated genes after EMT in H358-TwistER cells.

Probe Id	Gene	logFC	adj.P.Val		Probe Id	Gene	logFC	adj.P.Val
	Upregulated Genes					**Downregulated Genes**		
8175531	CDR1	4.63463	1.75E-05		7996837	CDH1	-4.88313	4.18E-06
8151768	RUNX1T1	4.31314	1.43E-06		8138466	MACC1	-4.43717	1.43E-06
8113709	LOX	3.84381	1.71E-06		8147697	GRHL2	-4.3459	3.88E-06
8056222	DPP4	3.76184	1.43E-06		8138381	AGR2	-4.25826	2.59E-05
7937772	IGF2	3.72641	1.71E-06		8041853	EPCAM	-4.10976	1.51E-06
8127563	COL12A1	3.71022	1.71E-06		8147351	RBM35A	-4.04475	2.84E-06
8172022	TMEM47	3.59735	9.59E-06		7906079	RAB25	-3.8594	7.30E-05
7922976	PTGS2	3.52396	1.71E-06		8091515	GPR87	-3.76871	1.71E-06
8171248	KAL1	3.51931	1.71E-06		7901175	TSPAN1	-3.68392	7.65E-05
8045688	TNFAIP6	3.3745	4.18E-06		8099467	FGFBP1	-3.45693	3.92E-05
8169115	NRK	3.32632	1.71E-06		8148040	MAL2	-3.40043	6.88E-06
8012906	NA	3.12006	0.001827		7988876	MYO5C	-3.33204	3.88E-06
8012896	PMP22	3.05346	0.000149		7934898	ANKRD22	-3.17542	1.10E-05
8139207	INHBA	3.01441	3.88E-06		8015349	KRT19	-3.07426	9.59E-06
8163908	GGTA1	2.92608	2.78E-05		8056184	ITGB6	-3.04222	2.84E-06
8111772	DAB2	2.86815	4.18E-06		7953291	CD9	-3.03772	1.10E-05
8081036	CADM2	2.85393	9.59E-06		8038683	KLK6	-2.96906	0.000383
7908204	HMCN1	2.8232	1.41E-05		8095728	EREG	-2.93825	4.18E-06
8148070	COL14A1	2.74084	1.57E-05		7980828	CCDC88C	-2.91812	0.000172
8102587	C4orf31	2.70024	5.34E-06		8126820	GPR110	-2.8445	3.16E-06
8092839	LRRC15	2.6855	2.14E-05		7980891	TC2N	-2.71335	2.78E-05
8110932	SEMA5A	2.6215	9.26E-06		8022711	DSC2	-2.65946	5.34E-06
8136200	CPA4	2.57226	8.67E-05		7951686	IL18	-2.61783	0.000139
7939056	BBOX1	2.5505	2.85E-05		7983157	TMEM62	-2.54362	9.59E-06
8077499	LOH3CR2A	2.52392	2.59E-05		8099850	TMEM156	-2.45245	0.000119
8145669	RBPMS	2.48779	9.59E-06		8096602	DAPP1	-2.38953	3.45E-05
8046922	COL3A1	2.42752	2.15E-05		8091799	C3orf57	-2.35357	7.12E-06
8059279	EPHA4	2.41061	1.10E-05		8054479	MALL	-2.35077	9.59E-06
8160260	BNC2	2.40748	1.78E-05		7908072	LAMC2	-2.32671	0.000624
8135734	C7orf58	2.3846	9.59E-06		7901765	HOOK1	-2.31318	4.52E-05
8103244	RNF175	2.3825	4.83E-05		8034084	AP1M2	-2.30972	0.004149
8168678	FAM133A	2.35913	0.000635		7952046	MPZL2	-2.26365	2.15E-05
7939184	TCP11L1	2.29015	4.14E-05		7996081	GPR56	-2.24638	0.000145
8113278	LIX1	2.26841	6.06E-05		8028311	SPINT2	-2.23516	0.000223
7902495	NEXN	2.23709	3.20E-05		7963421	KRT6A	-2.21261	0.000236
7988467	FBN1	2.21824	7.65E-05		8084766	TP63	-2.20458	0.000222
8089544	CCDC80	2.20817	9.59E-06		7961524	ERP27	-2.2026	3.25E-05

8009073	NA	2.18011	0.001209		7961182	KLRC2	-2.19814	0.00373
8161964	FRMD3	2.16029	0.000101		7960529	SCNN1A	-2.16876	0.000136
8097628	HHIP	2.15743	2.15E-05		8134351	PPP1R9A	-2.13242	2.04E-05
8057578	CALCRL	2.15144	0.000134		7973067	NP	-2.1055	0.00051
8077490	LMCD1	2.15143	4.21E-05		8078380	ZNF860	-2.09924	0.000604
8058765	FN1	2.11916	0.000633		7981427	CKB	-2.08755	0.000324
8176234	CLIC2	2.09084	0.001302		7920285	S100A2	-2.08706	2.29E-05
8008819	YPEL2	2.08173	2.57E-05		8021301	RAB27B	-2.05519	2.44E-05
8040103	ID2	2.07668	2.78E-05		8096130	CDS1	-2.02287	9.54E-05
8089112	FILIP1L	2.0756	4.21E-05		8058708	ABCA12	-2.01918	0.000103
8101260	ANTXR2	2.06234	2.29E-05		7939314	EHF	-1.97204	0.001052
8073015	KDELR3	2.05824	0.000155		8131550	SCIN	-1.95194	7.65E-05
8089464	LOC151760	2.05093	2.57E-05		8059350	AP1S3	-1.93254	0.001833
7971015	SMAD9	2.02881	0.000213		8051583	CYP1B1	-1.87405	7.88E-05
8033744	OR7E19P	2.02699	0.002679		8134030	STEAP1	-1.87038	0.001371
8111915	SEPP1	2.02485	0.000589		8056408	GALNT3	-1.86435	0.000136
8092169	TNFSF10	2.02382	0.00067		7918323	SORT1	-1.84935	5.71E-05
8081001	ROBO2	1.99813	8.10E-05		8020551	LAMA3	-1.83503	7.65E-05
8100541	IGFBP7	1.99772	4.66E-05		8083978	NAALADL2	-1.81231	0.000932
8104901	IL7R	1.9911	2.15E-05		8067955	CXADR	-1.78273	0.000164
7957570	PLXNC1	1.95451	3.92E-05		8099967	RBM47	-1.78141	8.10E-05
7910680	GPR137B	1.94739	7.65E-05		8096682	FLJ20184	-1.77976	0.001132
7999909	GPRC5B	1.91599	3.20E-05		7916584	TACSTD2	-1.7703	0.000321
8100393	KDR	1.9074	5.93E-05		7962197	NA	-1.75101	4.83E-05
8121916	RSPO3	1.90395	4.40E-05		7954729	FGD4	-1.72726	0.000363
8115543	EBF1	1.89742	4.23E-05		8041179	CLIP4	-1.70661	7.65E-05
8166243	REPS2	1.86915	7.65E-05		8012126	CLDN7	-1.68891	6.60E-05
8089015	PROS1	1.86587	0.000156		7939150	PRRG4	-1.68859	0.000201
8090193	HEG1	1.85875	8.80E-05		8027748	FXYD3	-1.68724	0.00043
8094789	LIMCH1	1.83663	6.30E-05		8099760	ARAP2	-1.67164	0.001466
7985317	KIAA1199	1.83025	0.000323		8127854	ME1	-1.65731	0.000294
7917532	GBP2	1.82337	0.00019		7965403	LUM	-1.65643	0.001043
8156060	TLE4	1.821	0.000106		7954899	CNTN1	-1.64958	0.000232
8096704	NPNT	1.82018	0.00029		8161945	RASEF	-1.64299	0.000663
7939173	DEPDC7	1.81104	8.10E-05		8151475	TPD52	-1.63113	0.001257
8121749	GJA1	1.80975	0.000316		7962212	PKP2	-1.62948	0.000213
7980680	FOXN3	1.79487	0.000142		8103951	ACSL1	-1.62487	0.001262
7950307	UCP2	1.78093	0.003198		8117630	ZNF165	-1.62002	0.000717
7917530	NA	1.77461	0.002269		7964927	TSPAN8	-1.61856	0.000868
8162183	LOC440173	1.77399	0.001344		8023267	MYO5B	-1.60747	0.000213
7918857	TSPAN2	1.75818	0.000327		8088247	ARHGEF3	-1.59573	0.001664

7951910	BACE1	1.75799	0.000427	7933855	RTKN2	-1.58539	0.000428
8082965	MRAS	1.72797	8.10E-05	7951246	MMP8	-1.57619	0.002642
8056890	CHN1	1.72743	0.000176	8095986	ANXA3	-1.57454	0.000308
8081235	COL8A1	1.72218	0.000751	8112274	ELOVL7	-1.5703	0.000964
8167815	MAGED2	1.70193	0.000324	7988414	GATM	-1.57015	0.000201
8029006	AXL	1.70191	0.000363	7956120	ERBB3	-1.56973	0.001538
8073775	FBLN1	1.69529	0.000324	8116780	DSP	-1.55659	0.000345
8102792	PCDH18	1.6933	0.000142	7954065	GPRC5A	-1.55468	0.003137
8021685	CCDC102B	1.69173	0.002038	7979524	TMEM30B	-1.53967	0.000779
8149877	PNMA2	1.68643	0.000142	8097801	FAM160A1	-1.53936	0.00225
7951077	SESN3	1.68364	9.16E-05	7944164	TMPRSS4	-1.53885	0.00242
8017850	WIPI1	1.62783	0.000816	8098177	KLHL2	-1.52628	0.00015
8157582	GSN	1.61354	0.000259	7957351	C12orf64	-1.52175	0.00231
8171624	GPR64	1.59595	0.000689	8155707	TJP2	-1.50907	0.000594
8097903	TLR2	1.59085	0.000364	8100026	ATP8A1	-1.50147	0.000221
8003667	SERPINF1	1.58775	0.000447	8121152	FUT9	-1.49428	0.001245
8102938	RNF150	1.57735	0.001371	7952036	MPZL3	-1.49391	0.000176
8143188	CREB3L2	1.57361	0.000348	8133360	CLDN4	-1.48928	0.001118
8115327	SPARC	1.56993	0.000223	8146500	LYN	-1.48085	0.000497
8155169	RECK	1.56784	0.001447	7924029	LAMB3	-1.47776	0.004332
8104663	CDH6	1.56602	0.000136	7986446	ALDH1A3	-1.45003	0.000387
8147469	PGCP	1.54561	0.000572	8157300	BSPRY	-1.44589	0.000378
8129254	MAN1A1	1.52491	0.000136	7920642	MUC1	-1.43903	0.000425
8043995	IL1R1	1.52392	0.000176	8147661	SPAG1	-1.43271	0.000608
7913655	ID3	1.51966	0.001371	8120783	MYO6	-1.42748	0.000221
8099721	KIAA0746	1.51613	0.000156	8092095	TNIK	-1.42269	0.000348
7922268	KIFAP3	1.5159	0.000232	8160151	ZDHHC21	-1.41346	0.006296
8141016	TFPI2	1.50683	0.000322	8096116	AGPAT9	-1.41305	0.000321
8148059	DEPDC6	1.50682	0.004706	7905406	CGN	-1.41107	0.000279
8097657	SMAD1	1.50566	0.000164	8129783	MAP7	-1.40628	0.000635
8147461	SDC2	1.50216	0.000117	8023855	CYB5A	-1.40583	0.001517
8169541	DOCK11	1.50098	0.000327	8092541	LIPH	-1.40161	0.000478
8131844	GPNMB	1.50076	0.000166	7967993	FGF9	-1.39218	0.000443
7964722	WIF1	1.50061	0.000333	8120833	SH3BGRL2	-1.36707	0.000555
8172043	SRPX	1.4968	0.003964	7947147	SVIP	-1.36397	0.00373
8142100	ATXN7L1	1.48984	0.000497	7954711	C12orf35	-1.35975	0.001073
7971150	LHFP	1.48298	0.000322	8078397	CMTM8	-1.35456	0.002532
8155734	C9orf61	1.48132	0.000267	8149762	TNFRSF10A	-1.33827	0.007364
8146967	CRISPLD1	1.46536	0.000232	7970441	GJB2	-1.31357	0.000605
8102482	SEC24D	1.46302	0.00023	7923958	C1orf116	-1.29486	0.003253
8127051	TRAM2	1.45591	0.00329	8152812	FAM84B	-1.28948	0.000816

7944554	TMEM136	1.45451	0.000417		8089467	ZBED2	-1.28568	0.000438
8156261	NA	1.45206	0.000387		8021584	SERPINB5	-1.27755	0.000649
8111387	ADAMTS12	1.44322	0.001876		8138613	OSBPL3	-1.27698	0.000323
8069676	ADAMTS1	1.44061	0.000213		8044605	LOC654433	-1.27593	0.00269
8094609	FAM114A1	1.4394	0.000609		8098379	WDR17	-1.27123	0.004084
7933821	RHOBTB1	1.43929	0.000348		8015412	JUP	-1.26472	0.007251
8078286	RARB	1.43556	0.000947		7899407	SMPDL3B	-1.25767	0.001809
8147065	RALYL	1.43411	0.000635		8046238	MYO3B	-1.25406	0.001943
8059376	SERPINE2	1.43183	0.000514		8105267	ITGA2	-1.24645	0.001481
8109333	GPX3	1.43099	0.00045		8166469	SAT1	-1.24615	0.00491
8059565	PID1	1.42579	0.000232		7965040	PHLDA1	-1.23195	0.000348
8174119	ZMAT1	1.42304	0.000556		8124331	HIST1H2AA	-1.23147	0.001401
7944970	NA	1.42111	0.000213		8098006	GLRB	-1.21753	0.00301
8075142	TTC28	1.4139	0.000232		8109001	SPINK5	-1.21411	0.001371
8175217	GPC4	1.41386	0.000458		8127193	BMP5	-1.20729	0.001458
7927631	DKK1	1.41375	0.000208		8016994	RNF43	-1.20483	0.000581
8164580	PTGES	1.41343	0.000319		8058498	FZD5	-1.2007	0.001183
8041447	CRIM1	1.4118	0.003383		8122336	C6orf115	-1.20057	0.004798
8155192	GLIPR2	1.41144	0.000417		8091600	PLCH1	-1.19919	0.001576
8127094	GSTA4	1.41	0.001102		8076757	CELSR1	-1.19829	0.005372
8063382	SNAI1	1.40651	0.000323		8124166	MBOAT1	-1.19797	0.000546
7950810	SYTL2	1.40493	0.000453		8155883	OSTF1	-1.19135	0.000549
8014316	CCL5	1.39992	0.001724		7942118	MYEOV	-1.18531	0.0038
8056877	CHRNA1	1.39685	0.000463		7932765	MPP7	-1.18453	0.000673
8009040	MRC2	1.39013	0.000464		8171725	MAP7D2	-1.18196	0.000853
8107563	PRR16	1.38798	0.000285		7936439	AFAP1L2	-1.17717	0.004875
8094936	LOC280665	1.38494	0.001051		8149534	ASAH1	-1.17704	0.000498
8055624	ZEB2	1.38448	0.000308		8159992	ERMP1	-1.1681	0.002179
8162533	PTCH1	1.3741	0.000573		7970954	DCLK1	-1.16502	0.009259
8115234	ANXA6	1.35551	0.000438		8121768	PKIB	-1.15902	0.004486
8091306	PLSCR4	1.3496	0.000278		7902290	CTH	-1.15736	0.001189
8107133	PAM	1.34818	0.000402		8129071	FRK	-1.15298	0.000628
7990632	SGK269	1.34352	0.000826		8169949	RP6-213H19.1	-1.14286	0.001118
7943369	TMEM133	1.34115	0.002506		8043522	PROM2	-1.14074	0.003374
8096032	PRDM8	1.33958	0.000511		8015016	TNS4	-1.13561	0.006065
8102678	TRPC3	1.33746	0.000581		8095819	FAM47E	-1.13236	0.001741
8053379	LOC129293	1.33552	0.000853		8047078	MFSD6	-1.13145	0.001044
8067985	NCAM2	1.33463	0.000853		8096301	SPP1	-1.12712	0.002238
7908161	C1orf21	1.33181	0.000816		8018082	SLC39A11	-1.1264	0.002494
7925531	AKT3	1.33021	0.000478		8021453	SEC11C	-1.12397	0.001431
8029950	EHD2	1.32914	0.000418		7978544	EGLN3	-1.11868	0.001022

8118890	SCUBE3	1.32501	0.001651		7991562	NA	-1.11345	0.009588
8112731	F2RL2	1.32282	0.000232		7899265	SFN	-1.10568	0.003404
8059345	SCG2	1.32192	0.002373		8150138	TEX15	-1.10486	0.004649
8097288	FAT4	1.31515	0.000361		8127158	GCLC	-1.09756	0.000852
8108370	EGR1	1.31059	0.000511		8052872	TGFA	-1.09733	0.002641
7983527	SEMA6D	1.30855	0.003989		7983512	SQRDL	-1.09134	0.008589
8057599	TFPI	1.30842	0.001848		7902850	GBP6	-1.08633	0.002415
8072735	APOL1	1.3051	0.001302		8122756	PLEKHG1	-1.08585	0.003787
8053484	ST3GAL5	1.29375	0.000635		8166202	GRPR	-1.08406	0.003057
7908388	RGS1	1.29184	0.000438		8166747	SYTL5	-1.0787	0.00178
8129497	EPB41L2	1.28276	0.000816		8009685	SLC9A3R1	-1.07055	0.002931
7961514	MGP	1.28009	0.00225		7957608	KRT19P2	-1.06837	0.004141
8101126	CXCL10	1.27564	0.001952		7901272	CYP4X1	-1.06681	0.00136
7961083	CLEC2B	1.27411	0.000556		8139021	KIAA0895	-1.06089	0.003725
8062312	MYL9	1.27312	0.00045		7993588	TMC7	-1.05966	0.001833
8158250	CERCAM	1.27236	0.004017		7930139	TRIM8	-1.05469	0.001647
7988563	SHC4	1.26397	0.000418		8083146	PLS1	-1.0514	0.002833
8169235	FRMPD3	1.25486	0.002439		7917954	FRRS1	-1.05138	0.000836
8023575	CCBE1	1.25422	0.001996		8080013	MAPKAPK3	-1.04848	0.003546
8052654	PELI1	1.25257	0.000816		8042211	B3GNT2	-1.04132	0.008448
8105061	NA	1.24114	0.00211		8047854	CCNYL1	-1.04039	0.00927
8057898	HECW2	1.23724	0.000324		8107005	CAST	-1.03637	0.000836
8060854	PLCB1	1.23533	0.000364		7915787	PIK3R3	-1.03627	0.000947
8095868	UNQ3028	1.23416	0.002276		8123884	C6orf52	-1.03043	0.005276
7952249	USP2	1.22729	0.001		8116835	GCNT2	-1.01971	0.001012
7942697	CAPN5	1.2271	0.000474		8117301	HIST1H2BA	-1.01583	0.005881
7902425	ST6GALNAC3	1.22367	0.000428		8130505	EZR	-1.01533	0.002234
8174228	TCEAL8	1.21915	0.000635		8127534	C6orf150	-1.01254	0.004721
8088602	MAGI1	1.21855	0.001821		8121015	C6orf165	-1.01122	0.005858
7964602	LRIG3	1.21453	0.000417		7993638	TMC5	-1.00889	0.003536
7943319	CNTN5	1.21453	0.000497		8090091	PTPLB	-1.00885	0.001546
7971905	PCDH20	1.21319	0.000924		8091411	TM4SF1	-1.00411	0.001875
8091243	PCOLCE2	1.21303	0.000345		7921882	OLFML2B	-1.00366	0.002924
7928944	PAPSS2	1.21285	0.000749		8041961	CHAC2	-1.00331	0.007659
8147000	ZFHX4	1.21165	0.000816		7989146	MNS1	-1.00035	0.005
7934906	ACTA2	1.21039	0.001741		8082673	ACPP	-0.99581	0.002323
7975932	TMEM63C	1.21014	0.002438		8084206	B3GNT5	-0.99555	0.002256
8057677	SLC40A1	1.20934	0.000678		7990054	UACA	-0.99395	0.001081
8175263	PLAC1	1.20837	0.000333		8021546	ZCCHC2	-0.9937	0.005958
8048026	CPS1	1.2057	0.001102		8163116	EPB41L4B	-0.99168	0.002296
7903162	TMEM56	1.20468	0.002231		7918157	VAV3	-0.99045	0.001741

7926545	PLXDC2	1.20425	0.000974		8032392	MKNK2	-0.98972	0.002494
7985016	SNX33	1.2038	0.003706		8174005	TRMT2B	-0.98913	0.002158
8069541	SAMSN1	1.20326	0.003282		8022728	DSC1	-0.98622	0.00229
8105220	ISL1	1.20249	0.000428		7980265	ACYP1	-0.98552	0.008724
7906954	PBX1	1.19781	0.001876		7944722	UBASH3B	-0.98095	0.006306
8157802	NA	1.19416	0.000752		7957417	TMTC2	-0.98023	0.002593
7965979	ALDH1L2	1.19354	0.000671		8166956	UTX	-0.97976	0.006114
8046333	CYBRD1	1.1933	0.000572		8102311	CASP6	-0.97709	0.003847
8015635	PTRF	1.19276	0.001458		8112998	LOC645261	-0.97335	0.0094
8123678	C6orf145	1.19271	0.005114		8098041	TMEM144	-0.9683	0.00884
7908125	RGL1	1.19264	0.004024		8166511	PDK3	-0.96778	0.00175
8095080	PDGFRA	1.18988	0.001191		7908351	PLA2G4A	-0.96552	0.007432
7988426	SLC30A4	1.18988	0.002227		8147516	MATN2	-0.96448	0.00599
8012464	LOC100128288	1.1887	0.004048		7938890	PRMT3	-0.9633	0.005446
8126760	RCAN2	1.18515	0.001555		8122202	MYB	-0.96207	0.009232
7974214	KLHDC1	1.18504	0.001191		7932453	NEBL	-0.95649	0.002113
8103389	CTSO	1.17778	0.001083		7941505	CST6	-0.95476	0.005958
8091715	LXN	1.17517	0.003374		7965964	SLC41A2	-0.95457	0.002164
8175666	GABRE	1.17413	0.000635		8065344	FOXA2	-0.948	0.005659
7937335	IFITM1	1.17334	0.00137		8027642	PDCD2L	-0.94591	0.00339
8161701	TMEM2	1.1711	0.001103		8081171	CRYBG3	-0.93749	0.006359
7987439	GPR176	1.1707	0.000939		8044919	RALB	-0.93627	0.005163
8080964	GLT8D4	1.16994	0.001087		7965390		-0.93507	0.00373
7943349	FLJ32810	1.16846	0.001		7962579	AMIGO2	-0.93278	0.002038
8081838	CDGAP	1.16699	0.00138		8060949	ANKRD5	-0.92867	0.00288
8151890	TP53INP1	1.16341	0.0019		7983890	GCOM1	-0.92464	0.005446
7933750	SLC16A9	1.16018	0.000521		8113691	DTWD2	-0.92004	0.006036
8105121	GHR	1.15777	0.000831		7961983	TM7SF3	-0.91577	0.00175
8041206	LBH	1.15713	0.000816		8063410	PARD6B	-0.91006	0.00373
7930454	PDCD4	1.15627	0.000939		7909285	PFKFB2	-0.90402	0.002865
8081081	EPHA3	1.15405	0.005955		8123562	GMDS	-0.89985	0.002055
7917052	SLC44A5	1.14978	0.002146		7943293	ENDOD1	-0.8997	0.001933
8108724	PCDHB10	1.14872	0.000954		8094778	UCHL1	-0.8978	0.005626
7910387	RHOU	1.14779	0.000816		8122807	AKAP12	-0.89682	0.002854
7989073	PRTG	1.14648	0.001478		8135514	IFRD1	-0.89304	0.008532
8099797	RELL1	1.14307	0.003423		7951545	EXPH5	-0.88884	0.002555
8138834	FKBP14	1.1423	0.009792		8107673	GRAMD3	-0.88865	0.002979
8056343	COBLL1	1.14132	0.005685		8150076	DUSP4	-0.88838	0.003312
8106516	JMY	1.13957	0.002852		8092726	CLDN1	-0.88343	0.002077
8098204	CPE	1.13475	0.000635		7950391	PGM2L1	-0.88021	0.005955
7951133	MAML2	1.13281	0.00081		8001830	CMTM4	-0.87822	0.004094

8128284	EPHA7	1.1296	0.002077		7961151	KLRK1	-0.87556	0.008173
8129562	CTGF	1.12798	0.000605		8068633	B3GALT5	-0.87538	0.002931
7980316	TGFB3	1.12606	0.000675		7899087	PDIK1L	-0.87454	0.003057
8097867	KIAA0922	1.12528	0.000942		8017150	TUBD1	-0.87072	0.009306
7905428	TUFT1	1.12504	0.006347		8069998	C21orf59	-0.87016	0.003134
8136347	CALD1	1.12496	0.001052		8162652	CTSL2	-0.86731	0.003721
8105411	IL31RA	1.11713	0.001073		7958174	TXNRD1	-0.86463	0.008757
8146115	C8orf4	1.11683	0.002184		8067233	PMEPA1	-0.86213	0.008321
7902541	IFI44L	1.11669	0.002641		8106784	RASA1	-0.86143	0.003721
8103544	SPOCK3	1.1138	0.005685		8008547	TOM1L1	-0.86088	0.002077
7912887	MFAP2	1.11312	0.001073		8138857	GGCT	-0.86077	0.004898
8151532	FABP4	1.11064	0.004888		7901804	INADL	-0.85906	0.003536
8099982	APBB2	1.10929	0.006608		7969171	DLEU1	-0.85794	0.006982
8103789	GPM6A	1.10631	0.004017		8028563	MRPS12	-0.85353	0.004706
8095303	LPHN3	1.10561	0.000725		8079153	ABHD5	-0.85244	0.004132
8133961	RUNDC3B	1.10166	0.001371		7909214	RASSF5	-0.84785	0.00337
8102532	PDE5A	1.10128	0.001044		8050160	MBOAT2	-0.84767	0.006798
7926916	ZEB1	1.1007	0.002307		8152845	FAM49B	-0.84055	0.007251
8084219	KLHL24	1.09901	0.001292		8081431	ALCAM	-0.83717	0.002924
7951565	ARHGAP20	1.09101	0.00096		7919326	ACP6	-0.83651	0.005678
8117045	RBM24	1.09095	0.001419		8043902	PDCL3	-0.83457	0.00591
7906919	RGS4	1.09081	0.003312		8141107	SLC25A13	-0.82825	0.005774
7984704	NEO1	1.08425	0.001262		8171392	ASB9	-0.82308	0.007251
8112107	PPAP2A	1.08285	0.000754		8089329	MYH15	-0.82299	0.003546
8020495	CABLES1	1.08179	0.002555		8103106	LRBA	-0.82117	0.003202
7902565	LPHN2	1.08099	0.000568		8049542	LRRFIP1	-0.81947	0.003384
8174092	ARMCX2	1.08006	0.001367		7920057	TDRKH	-0.81722	0.006965
8112971	HAPLN1	1.07828	0.001431		8171901	MAP3K7IP3	-0.81579	0.003987
7907213	SCYL1BP1	1.07649	0.001908		7921434	AIM2	-0.81519	0.006065
7970999	SPG20	1.07448	0.000893		8106193	UTP15	-0.8132	0.007326
7985248	KIAA1024	1.07325	0.004852		7899534	EPB41	-0.81224	0.008072
7984019	TLN2	1.07231	0.002055		8148270	NDUFB9	-0.80498	0.006591
8120613	RIMS1	1.07106	0.001555		7943413	BIRC3	-0.80423	0.009463
7956856	MSRB3	1.07073	0.006798		7898549	MRTO4	-0.80259	0.003919
7958346	C12orf23	1.07036	0.001888		8107520	TNFAIP8	-0.79939	0.007687
8151223	SLCO5A1	1.06632	0.002839		7934133	PPA1	-0.79707	0.008724
7930181	AS3MT	1.06484	0.006432		7985134	IDH3A	-0.79683	0.004252
8106393	F2R	1.06076	0.001052		8124527	HIST1H1B	-0.79646	0.005243
8142098	ATXN7L1	1.06028	0.002184		8113577	TRIM36	-0.79571	0.005958
8091260	SLC9A9	1.05963	0.002506		7957072	RAB3IP	-0.79465	0.005132
8098214	TLL1	1.05681	0.001128		8048898	SP140	-0.79229	0.006253

7936322	GPAM	1.04976	0.002037		8058670	IKZF2	-0.7889	0.00416
7934196	PSAP	1.04904	0.002596		8171006	BRCC3	-0.78863	0.005973
7964119	STAT2	1.04763	0.003186		8020468	RBBP8	-0.78714	0.00961
8085797	THRB	1.04757	0.006287		8157233	HSDL2	-0.7867	0.008412
7915444	LEPRE1	1.04739	0.00809		7958211	C12orf45	-0.78561	0.005276
8090690	CPNE4	1.04589	0.007251		7986350	ARRDC4	-0.78304	0.008506
8139212	GLI3	1.04171	0.003441		8097335	HSPA4L	-0.78041	0.004024
7934570	KCNMA1	1.04147	0.00288		7978174	CHMP4A	-0.77822	0.006741
7971690	NA	1.0382	0.007094		8164013	STRBP	-0.77291	0.004084
8021154	KIAA0427	1.03071	0.001952		8157828	ARPC5L	-0.766	0.006798
7918426	SLC16A4	1.03046	0.005586		8026047	JUNB	-0.76585	0.005685
7961120	CLEC7A	1.02987	0.002837		8042066	CCDC104	-0.76458	0.009821
8123651	TUBB2B	1.02412	0.00175		7989953	FLJ11506	-0.76441	0.008539
8078350	TGFBR2	1.02261	0.002234		8120335	FAM83B	-0.76344	0.007916
8027279	ZNF430	1.02224	0.003546		8147344	PPM2C	-0.76254	0.005586
8027285	ZNF714	1.02156	0.008721		8038993	ZNF28	-0.75767	0.008445
7917850	ARHGAP29	1.01767	0.003546		8123407	MLLT4	-0.75509	0.007251
8101657	NA	1.01764	0.008506		8132922	MRPS17	-0.75304	0.009161
8112803	LHFPL2	1.01249	0.009089		8163402	ROD1	-0.742	0.006653
8056376	SCN3A	1.00985	0.001805		8129974	FUCA2	-0.73957	0.00772
8173917	NAP1L3	1.00849	0.002356		7963333	KRT80	-0.73639	0.005893
8169995	FAM122C	1.0055	0.008757		8154151	PPAPDC2	-0.73408	0.007718
8096959	ANK2	1.00537	0.002877		8103769	HPGD	-0.7228	0.00952
8007323	CNTNAP1	1.00492	0.001103		8156321	SYK	-0.72133	0.007251
7997642	CRISPLD2	1.00346	0.001681		8175052	AIFM1	-0.71904	0.009161
7947199	LGR4	1.00104	0.004663		7949679	SPTBN2	-0.71118	0.009768
7907370	DNM3	0.999599	0.003231		8021169	LIPG	-0.7075	0.007678
8113761	ZNF608	0.998896	0.004072		8040655	SELI	-0.70351	0.008275
8047300	AOX1	0.997046	0.00136		7934367	ANXA7	-0.69448	0.007261
8122365	GPR126	0.996313	0.004084		8083630	GFM1	-0.693	0.007251
8089701	ZBTB20	0.993347	0.003772		8064904	FERMT1	-0.68397	0.008643
8049471	CXCR7	0.991584	0.007251		8049512	LRRFIP1	-0.67938	0.007433
8175574	SLITRK4	0.987388	0.003086					
8088634	NA	0.984343	0.009161					
8138647	C7orf31	0.982396	0.002736					
8168875	ARMCX3	0.981238	0.00175					
8135544	FOXP2	0.980416	0.001741					
8069269	COL6A1	0.98007	0.001183					
8152867	ASAP1	0.977961	0.002249					
8020141	APCDD1	0.977538	0.002854					
8161044	TPM2	0.977299	0.001913					

8104788	RAI14	0.977231	0.001431					
8018652	RNF157	0.977058	0.00178					
7978718	SEC23A	0.975574	0.00175					
8142554	AASS	0.974237	0.001643					
8142102	ATXN7L1	0.971482	0.001952					
8068238	IFNAR2	0.971331	0.005695					
8163257	LPAR1	0.970155	0.001731					
8113433	EFNA5	0.9689	0.003374					
7909529	RCOR3	0.964976	0.001741					
8142096	ATXN7L1	0.962836	0.00178					
7919669	MTMR11	0.962711	0.001344					
7946478	DENND5A	0.96268	0.006682					
8152355	GOLSYN	0.962349	0.006729					
8095854	11-Sep	0.958495	0.001654					
8127109	ICK	0.955404	0.001651					
8175256	MGC16121	0.953665	0.00339					
8111220	CDH18	0.951793	0.008006					
7935188	SORBS1	0.949925	0.002073					
8046726	SSFA2	0.949155	0.001245					
7917151	C1orf118	0.945583	0.003574					
8091537	IGSF10	0.944787	0.002637					
8102200	DKK2	0.942074	0.006874					
8096160	ARHGAP24	0.941734	0.003915					
8068280	IFNGR2	0.939175	0.001983					
8047069	INPP1	0.939074	0.00884					
7983867	CGNL1	0.936527	0.00491					
7917347	DDAH1	0.935062	0.002037					
8012918	CDRT4	0.934106	0.006762					
7974425	SAMD4A	0.933725	0.006216					
8114263	LECT2	0.929546	0.00491					
8081758	GRAMD1C	0.927725	0.006036					
8176163	GAB3	0.923358	0.004782					
8023497	ATP8B1	0.920158	0.006653					
7924465	HHIPL2	0.919412	0.002142					
7924071	KCNH1	0.918018	0.004706					
8078605	C3orf35	0.913386	0.002038					
8000574	NUPR1	0.91203	0.004084					
8077899	PPARG	0.906487	0.005808					
7917503	GBP3	0.905981	0.004803					
8160138	NFIB	0.905456	0.00301					
8175647	CD99L2	0.904239	0.004574					

8164269	ENG	0.902823	0.008589					
8105436	MAP3K1	0.90275	0.005163					
8001800	CDH11	0.900702	0.003805					
7907222	PRRX1	0.900522	0.007708					
7957140	LGR5	0.886672	0.006794					
8167763	TSPYL2	0.886622	0.004123					
8154059	SMARCA2	0.885715	0.002077					
8170239	NA	0.88566	0.009792					
8133860	GNAI1	0.885031	0.00558					
8097449	PCDH10	0.883696	0.002865					
7957298	NAV3	0.877755	0.006982					
7984112	RAB8B	0.876989	0.009161					
7935968	LDB1	0.875637	0.007463					
8068713	MX1	0.870726	0.00809					
8156199	DAPK1	0.868859	0.006296					
8105077	CARD6	0.863966	0.006448					
8078330	RBMS3	0.862431	0.006448					
8078187	PLCL2	0.861301	0.00954					
8138277	VWDE	0.857326	0.008004					
7927732	ARID5B	0.856913	0.005695					
8061305	NCRNA00153	0.849433	0.003551					
8168984	BHLHB9	0.848535	0.003538					
8008289	TMEM92	0.848279	0.003937					
8058091	SATB2	0.843138	0.005514					
7922130	DPT	0.842998	0.008006					
8059413	DOCK10	0.839158	0.002924					
8081590	PHLDB2	0.838696	0.002877					
7954481	SSPN	0.837577	0.006653					
8107100	RGMB	0.836798	0.006216					
8167887	MAGEH1	0.836627	0.005416					
7961798	SOX5	0.834989	0.008553					
8155754	MAMDC2	0.832763	0.008573					
7902687	CYR61	0.832359	0.006155					
8089759	TMEM39A	0.832296	0.003442					
7947624	PHF21A	0.831766	0.004866					
7921088	NES	0.831596	0.007061					
8047538	BMPR2	0.821181	0.007866					
8023727	DSEL	0.817354	0.008485					
7899851	ADC	0.816963	0.00461					
7950248	FCHSD2	0.814872	0.008178					
7954077	KIAA1467	0.813736	0.003237					

8113214	GLRX	0.80155	0.006036					
7906400	IFI16	0.80012	0.005964					
8083471	SGEF	0.799467	0.003714					
8140739	TP53TG1	0.793989	0.007379					
8151056	CYP7B1	0.791078	0.006982					
8157524	TLR4	0.79037	0.006798					
7985285	ARNT2	0.786287	0.003678					
7990657	TBC1D2B	0.784118	0.005626					
7962895	FKBP11	0.783285	0.006653					
7927784	MGC14425	0.782853	0.003772					
7947165	SLC5A12	0.782722	0.006359					
8169240	PRPS1	0.781517	0.004888					
7946401	ST5	0.778929	0.006741					
8122600	STXBP5	0.774656	0.009194					
8080781	PXK	0.774578	0.007806					
8154100	VLDLR	0.772864	0.008527					
7913582	ZNF436	0.765103	0.008178					
8094911	ATP10D	0.764741	0.007379					
8070182	RCAN1	0.76088	0.008209					
7939434	TTC17	0.760712	0.008004					
8127234	DST	0.753755	0.006653					
7917912	DPYD	0.747564	0.005493					
8091402	TM4SF18	0.746188	0.006359					
8004571	EFNB3	0.745742	0.005466					
8015590	STAT5B	0.745245	0.006347					
8052689	SPRED2	0.745092	0.007046					
8175369	MAP7D3	0.73884	0.006798					
8147837	ZFPM2	0.737449	0.009306					
7954293	PDE3A	0.735628	0.007031					
8058477	KLF7	0.733328	0.009161					
7905754	ATP8B2	0.732026	0.007251					
8112649	FAM169A	0.726654	0.006653					
8108753	PCDHB15	0.723274	0.009397					
8140620	PCLO	0.723	0.009287					
8163892	C9orf31	0.722064	0.006036					
8129573	MOXD1	0.721576	0.008553					
7980616	PTPN21	0.716431	0.008275					
8101376	SEC31A	0.71607	0.00809					
7984771	LOXL1	0.713133	0.008127					
7947425	CD59	0.708443	0.008559					
7978407	PRKD1	0.708069	0.006359					

7983132	LOC645106	0.700161	0.009592					
8154449	CNTLN	0.693362	0.00964					
8173428	NA	0.684125	0.00811					
8148553	LY6K	0.679264	0.007605					