

Supplemental Table 1. Detailed information about antibodies and reagents.

Name	Vendor	Catalog number	Application
Anti-Notch1/NICD	Cell Signaling Technology	3608	WB, IF
Anti-p-NF- κ B-p65(S536)	Cell Signaling Technology	3033	WB, ChIP
Anti- NF- κ B-p65	Cell Signaling Technology	8242	WB
Anti- NF- κ B-p65	Santa Cruz Biotechnology	sc-514451	IF
Anti- β -Tubulin	Cell Signaling Technology	2146	WB
Anti-ADAM17/TACE	Cell Signaling Technology	3976	WB
Anti-rabbit IgG (HRP-linked)	Cell Signaling Technology	7074	WB
Anti-mouse IgG (HRP-linked)	Cell Signaling Technology	7076	WB
Anti-Delta Antibody (G-1)	Santa Cruz Biotechnology	sc-377310	WB, IF, IHC
Anti-DLL1 (N-terminal)	Thermo Fisher Scientific	PA5-42902	WB
Anti-APE1	Thermo Fisher Scientific	PA5-80342	WB
Anti-APE1	Thermo Fisher Scientific	PA5-29157	IF, IHC
Anti- β -Actin	Sigma-Aldrich	A1978	WB
Goat anti-Mouse IgG (H+L), Alexa Fluor 568	Thermo Fisher Scientific	A-111031	IF
Goat anti-Rabbit IgG (H+L), Alexa Fluor 488	Thermo Fisher Scientific	A-11034	IF
Anti-p84	GeneTex	GTX70220	WB
E3330	Novus Biologicals	NBP1- 49581	In vitro treatment
APX2009	Sigma-Aldrich	SML1887	In vitro treatment
LipoJet™ In Vitro Transfection Kit	SignaGen Laboratories	SL100468	In vitro transfection
PolyJet™ In Vitro DNA Transfection Reagent	SignaGen Laboratories	SL100688	In vitro transfection

Supplemental Table 2. Sequences of quantitative RT-PCR primers.

Gene name	Sequence
NOTCH1	F: 5'-TCCACCAGTTTGAATGGTCA-3' R: 5'-AGCTCATCATCTGGGACAGG-3'
NOTCH2	F: 5'-ATGACTGCCCTAACCACAGG-3' R: 5'-TGCAGTCATCTCCACTCCAG-3'
NOTCH3	F: 5'-TCTTGCTGCTGGTCATTCTC-3' R: 5'-TGCCTCATCCTCTTCAGTTG-3'
NOTCH4	F: 5'-TGTGAACGTGATGTCAACGAG-3' R: 5'-ACAGTCTGGGCCTATGAAACC-3'
DLL1	F: 5'-CCAGGGTTGCACACTTTCTC-3' R: 5'-CTACTACGGAGAGGGCTGCT-3'
DLL3	F: 5'-CCTGCGCGCTGAATGTC-3' R: 5'-CATCGAAACCTGGAGAGAGG-3'
DLL4	F: 5'-GTGCAGGTGTAGCTTCGCT-3' R: 5'-AGGCCTGTTTTGTGACCAAG-3'
HES1	F: 5'-TGAAGAAAGATAGCTCGCGG-3' R: 5'-GGTACTTCCCCAGCACACTT-3'
HES5	F: 5'-CCGGTGGTGGAGAAGATG-3' R: 5'-TAGTCCTGGTGCAGGCTCTT-3'
HEY1	F: 5'-CGAAATCCCAAACCTCCGATA-3' R: 5'-TGGATCACCTGAAAATGCTG-3'
HEY2	F: 5'-GGCACTCTCGGAATCCTATG-3' R: 5'-TTTGAAGATGCTTCAGGCAA-3'
HEYL	F: 5'-ATCCCTCTGCGTTTCTTCCT-3' R: 5'-ATCGACGTGGGCCAAGA-3'
ADAM17	F: 5'-GTGGATGGTAAAAACGAAAGCG-3' R: 5'-GGCTAGAACCCTAGAGTCAGG-3'
HPRT	F: 5'-TCCAGCAGGTCAGCAAAGAA-3' R: 5'-TTGGAAAGGGTGTTCATTCCTCA-3'

Supplemental Table 3. Sequences of ChIP primers.

Name	Sequence	Location
DLL1prom-ChIP-A	F: 5'-TGAAGCCTCCATTTGCTCT-3' R: 5'-GGATCAACAGAGATGTCCACTT-3'	-1893bp to -1730bp
DLL1prom -ChIP-B	F: 5'-AGGAGCCGCAGAGTAGCAAT-3' R: 5'-AGGGCACCGTCAAGGTAGAA-3'	-1670bp to -1482bp
DLL1prom-ChIP-C	F: 5'-AGCCTCGCACAATAACAGG-3' R: 5'-GAGAACCTGGCCTTCAACTC-3'	-934bp to -741bp
DLL1prom-ChIP-D	F: 5'-ACCACGAGAGGACACCGAA-3' R: 5'-CAGAGCGAAGCGGCAGTT-3'	-685bp to -520bp
DLL1prom-ChIP-E	F: 5'-AACTTCCCGAAACTGCCGC-3' R: 5'-AGCAGGAGGACGAAGTTCG-3'	-551bp to -361bp
DLL1prom-ChIP-F	F: 5'-AACTTCGTCCTCCTGCTCG-3' R: 5'-ACAGACGCCAGAGACCCT-3'	-377bp to -206bp

Supplemental Table 4. Top 100 potential transcription factors regulating DLL1 predicted by GSEA

	ID	Description	pvalue	p.adjust	qvalue	Count
1	GCCATNTTG	GCCATNTTG	9.34E-62	3.94E-59	3.44E-60	433
2	TCANNTGAY	TCANNTGAY	1.25E-54	3.50E-52	3.06E-53	465
3	CATTGTYY_S	CATTGTYY_S	1.34E-49	2.26E-47	1.97E-48	363
4	RGAANNTTC	RGAANNTTC	2.99E-46	3.34E-44	2.92E-45	439
5	CCCNNGGGA	CCCNNGGGA	3.17E-46	3.34E-44	2.92E-45	323
6	ETS2_B	ETS2_B	1.03E-42	8.64E-41	7.56E-42	280
7	EGR_Q6	EGR_Q6	1.47E-42	1.13E-40	9.84E-42	279
8	USF_Q6	USF_Q6	3.98E-42	2.79E-40	2.44E-41	264
9	ZNF260_TAR	ZNF260_TAR	4.02E-41	2.60E-39	2.28E-40	469
10	E2F1_Q3_01	E2F1_Q3_01	6.42E-40	3.50E-38	3.06E-39	250
11	SP1_Q2_01	SP1_Q2_01	6.42E-40	3.50E-38	3.06E-39	250
12	PEA3_Q6	PEA3_Q6	6.64E-40	3.50E-38	3.06E-39	262
13	NRF2_01	NRF2_01	1.10E-39	5.43E-38	4.75E-39	271
14	E4F1_Q6	E4F1_Q6	1.71E-39	8.03E-38	7.02E-39	288
15	AP2_Q6	AP2_Q6	2.80E-39	1.24E-37	1.08E-38	258
16	TGANNYRGC	TGANNYRGC	5.34E-39	2.20E-37	1.92E-38	301
17	USF_Q6_01	USF_Q6_01	5.66E-39	2.20E-37	1.92E-38	244
18	MYCMAX_01	MYCMAX_01	5.74E-39	2.20E-37	1.92E-38	256
19	ETS1_B	ETS1_B	6.49E-39	2.38E-37	2.08E-38	266
20	E2F1_Q6_01	E2F1_Q6_01	8.14E-39	2.77E-37	2.42E-38	243
21	ELK1_02	ELK1_02	8.21E-39	2.77E-37	2.42E-38	255
22	ERR1_Q2	ERR1_Q2	9.27E-39	2.92E-37	2.55E-38	265
23	MAX_01	MAX_01	1.32E-38	3.98E-37	3.48E-38	264
24	AP1_C	AP1_C	1.52E-38	4.42E-37	3.86E-38	273
25	USF2_Q6	USF2_Q6	1.68E-38	4.73E-37	4.14E-38	253
26	CETS1P54_01	CETS1P54_01	1.89E-38	4.82E-37	4.21E-38	263
27	E12_Q6	E12_Q6	1.89E-38	4.82E-37	4.21E-38	263
28	GABP_B	GABP_B	1.89E-38	4.82E-37	4.21E-38	263
29	OLF1_01	OLF1_01	2.16E-38	5.36E-37	4.68E-38	272
30	MYCMAX_03	MYCMAX_03	2.69E-38	6.31E-37	5.51E-38	262
31	USF_01	USF_01	2.69E-38	6.31E-37	5.51E-38	262
32	USF_C	USF_C	2.81E-38	6.40E-37	5.59E-38	280
33	ETS_Q4	ETS_Q4	3.45E-38	7.51E-37	6.56E-38	251
34	SP1_01	SP1_01	3.47E-38	7.51E-37	6.56E-38	239
35	YY1_Q6	YY1_Q6	4.95E-38	1.02E-36	8.89E-38	250
36	TTCYNRGAA	TTCYNRGAA	5.32E-38	1.07E-36	9.33E-38	330
37	NRF1_Q6	NRF1_Q6	5.48E-38	1.08E-36	9.40E-38	260
38	CREB_Q4	CREB_Q4	6.22E-38	1.19E-36	1.04E-37	269
39	ZNF784_TAR	ZNF784_TAR	8.79E-38	1.59E-36	1.39E-37	378
40	AP1_Q4	AP1_Q4	8.84E-38	1.59E-36	1.39E-37	268
41	AP2_Q6_01	AP2_Q6_01	8.84E-38	1.59E-36	1.39E-37	268

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42	SP1_Q6	SP1_Q6	1.12E-37	1.91E-36	1.67E-37	258
43	ER_Q6_01	ER_Q6_01	1.13E-37	1.91E-36	1.67E-37	276
44	NMYC_01	NMYC_01	1.13E-37	1.91E-36	1.67E-37	276
45	SP1_Q6_01	SP1_Q6_01	1.45E-37	2.40E-36	2.10E-37	247
46	SP1_Q4_01	SP1_Q4_01	1.59E-37	2.58E-36	2.26E-37	257
47	CREB_Q2	CREB_Q2	1.79E-37	2.79E-36	2.44E-37	266
48	EGR1_01	EGR1_01	1.79E-37	2.79E-36	2.44E-37	266
49	WGGAAATGY	WGGAAATGY	2.39E-37	3.66E-36	3.20E-37	369
50	ATF_01	ATF_01	3.62E-37	5.35E-36	4.67E-37	264
51	HNF4_DR1_Q	HNF4_DR1_Q	3.62E-37	5.35E-36	4.67E-37	264
52	ELF5_TARGET	ELF5_TARGET	4.53E-37	6.58E-36	5.75E-37	417
53	ELK1_01	ELK1_01	6.49E-37	9.27E-36	8.10E-37	271
54	NGFIC_01	NGFIC_01	6.60E-37	9.27E-36	8.10E-37	253
55	AP1_Q4_01	AP1_Q4_01	1.04E-36	1.39E-35	1.22E-36	261
56	DR1_Q3	DR1_Q3	1.04E-36	1.39E-35	1.22E-36	261
57	PPAR_DR1_Q	PPAR_DR1_Q	1.04E-36	1.39E-35	1.22E-36	261
58	IK2_01	IK2_01	1.30E-36	1.72E-35	1.50E-36	269
59	TGACCTG_S	TGACCTG_S	1.34E-36	1.74E-35	1.52E-36	251
60	IK1_01	IK1_01	1.39E-36	1.77E-35	1.55E-36	277
61	GATAAGR_G	GATAAGR_G	1.54E-36	1.94E-35	1.70E-36	292
62	RFX7_TARGET	RFX7_TARGET	1.89E-36	2.34E-35	2.04E-36	463
63	TEL2_Q6	TEL2_Q6	2.56E-36	2.98E-35	2.61E-36	239
64	AML1_01	AML1_01	2.62E-36	2.98E-35	2.61E-36	267
65	AML1_Q6	AML1_Q6	2.62E-36	2.98E-35	2.61E-36	267
66	AP1_01	AP1_01	2.62E-36	2.98E-35	2.61E-36	267
67	ARNT_01	ARNT_01	2.62E-36	2.98E-35	2.61E-36	267
68	HNF4ALPHA	HNF4ALPHA	2.62E-36	2.98E-35	2.61E-36	267
69	ATF4_Q2	ATF4_Q2	4.24E-36	4.77E-35	4.17E-36	257
70	E2F_02	E2F_02	5.25E-36	5.53E-35	4.83E-36	237
71	E2F_Q4	E2F_Q4	5.25E-36	5.53E-35	4.83E-36	237
72	E2F1DP1_01	E2F1DP1_01	5.25E-36	5.53E-35	4.83E-36	237
73	E2F1DP2_01	E2F1DP2_01	5.25E-36	5.53E-35	4.83E-36	237
74	E2F4DP2_01	E2F4DP2_01	5.25E-36	5.53E-35	4.83E-36	237
75	ELF1_Q6	ELF1_Q6	5.55E-36	5.78E-35	5.05E-36	247
76	ER_Q6_02	ER_Q6_02	6.03E-36	6.20E-35	5.42E-36	256
77	PAX4_01	PAX4_01	7.44E-36	7.56E-35	6.61E-36	264
78	NFKB_Q6	NFKB_Q6	8.57E-36	8.60E-35	7.51E-36	255
79	CEBPB_01	CEBPB_01	1.05E-35	1.03E-34	9.00E-36	263
80	E2F_Q6	E2F_Q6	1.08E-35	1.03E-34	9.00E-36	235
81	E2F1_Q6	E2F1_Q6	1.08E-35	1.03E-34	9.00E-36	235
82	VDR_Q6	VDR_Q6	1.10E-35	1.04E-34	9.12E-36	271
83	E2F1_Q3	E2F1_Q3	1.13E-35	1.06E-34	9.24E-36	245
84	ER_Q6	ER_Q6	1.43E-35	1.32E-34	1.16E-35	278

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85	CEBPB_02	CEBPB_02	1.49E-35	1.35E-34	1.18E-35	262
86	ZIC1_01	ZIC1_01	1.49E-35	1.35E-34	1.18E-35	262
87	NFE2_01	NFE2_01	1.55E-35	1.39E-34	1.22E-35	270
88	ARNT_02	ARNT_02	1.73E-35	1.49E-34	1.30E-35	253
89	MTF1_Q4	MTF1_Q4	1.73E-35	1.49E-34	1.30E-35	253
90	PAX4_03	PAX4_03	1.73E-35	1.49E-34	1.30E-35	253
91	TFIIA_Q6	TFIIA_Q6	1.73E-35	1.49E-34	1.30E-35	253
92	AP4_01	AP4_01	2.11E-35	1.80E-34	1.57E-35	261
93	AP2_Q3	AP2_Q3	2.46E-35	2.05E-34	1.79E-35	252
94	ZIC3_01	ZIC3_01	2.46E-35	2.05E-34	1.79E-35	252
95	HNF4_01	HNF4_01	3.10E-35	2.56E-34	2.24E-35	268
96	NERF_Q2	NERF_Q2	3.49E-35	2.83E-34	2.47E-35	251
97	AREB6_03	AREB6_03	4.24E-35	3.40E-34	2.98E-35	259
98	E2F_Q6_01	E2F_Q6_01	6.65E-35	5.24E-34	4.58E-35	240
99	E2F4DP1_01	E2F4DP1_01	6.65E-35	5.24E-34	4.58E-35	240
100	AP2GAMMA	AP2GAMMA	7.05E-35	5.50E-34	4.81E-35	249

Supplemental Table 5. Key transcription factors regulating DLL1 predicted by TRRUST

Key TF	# of overlapped genes	P value	Q value	List of overlapped genes
ATF1	4	0.000537	0.0156	FLT1,ERBB2,CCNA1,NTS
SP1	17	0.00169	0.0245	LAMA1,F10,TNNI3,AGT,SCNN1B,HYAL1,FBLN1,CYP3A7,GPR39,SRY,CXCL14,KLF8,PLAT,IGF2,ERBB2,PADI3,F7
CREB1	6	0.00328	0.0277	NTS,PLAT,FLT1,CYP11A1,RP1,ERBB2
NR1H4	3	0.00382	0.0277	UGT2B4,SLCO1B3,DCN
TFCP2	2	0.00859	0.0373	SRY,A2M
SP3	6	0.00982	0.0373	FBLN1,LAMA1,PADI3,PLAT,ERBB2,CYP3A7
YBX1	3	0.0121	0.0373	ERBB2,MIA,AGT
MEF2A	2	0.0128	0.0373	SOST,TNNI3
PITX2	2	0.0128	0.0373	WNT5A,LEF1
SOX10	2	0.0128	0.0373	GJC2,MIA
JUND	3	0.017	0.0448	PLAT,ERBB2,NTS
NR5A1	2	0.0481	0.107	SRY,CYP11A1
SOX2	2	0.0481	0.107	NTRK3,SEMA6A
CREM	2	0.0605	0.125	PLAT,CCNA1
HNF1A	2	0.0649	0.125	SLCO1B3,GPR39
MYB	2	0.119	0.215	ERBB2,CCNA1
KLF4	2	0.135	0.23	LAMA1,ZNF750
VDR	2	0.146	0.235	CYP3A7,ERBB2
EGR1	3	0.168	0.257	FLT1,HYAL1,IGF2
CEBPA	2	0.197	0.286	VLDLR,IGF2
JUN	4	0.218	0.294	DCN,PLAT,NTS,CYP11A1
FOS	2	0.233	0.294	NTS,NTF3
WT1	2	0.233	0.294	IGF2,SRY
TFAP2A	2	0.316	0.382	CYP11A1,ERBB2
ESR1	2	0.346	0.401	CRHBP,FLT1
YY1	2	0.431	0.48	ERBB2,HBE1
TP53	3	0.492	0.528	GPNMB,FLT1,CCNA1
NFKB1	5	0.538	0.557	HYAL1,IL17C,AGT,CYP3A7,A2M
RELA	4	0.715	0.715	CYP3A7,HYAL1,IL17C,AGT

Supplemental Table 6. Summary of IHC scores of APE1 and DLL1 protein expression in human EAC tissue microarrays.

APE1	Index score		
	0-2	3-4	6-12
NE	5	0	0
EAC	25	11	26

DLL1	Index score		
	0-2	3-4	6-12
NE	5	0	0
EAC	32	16	14