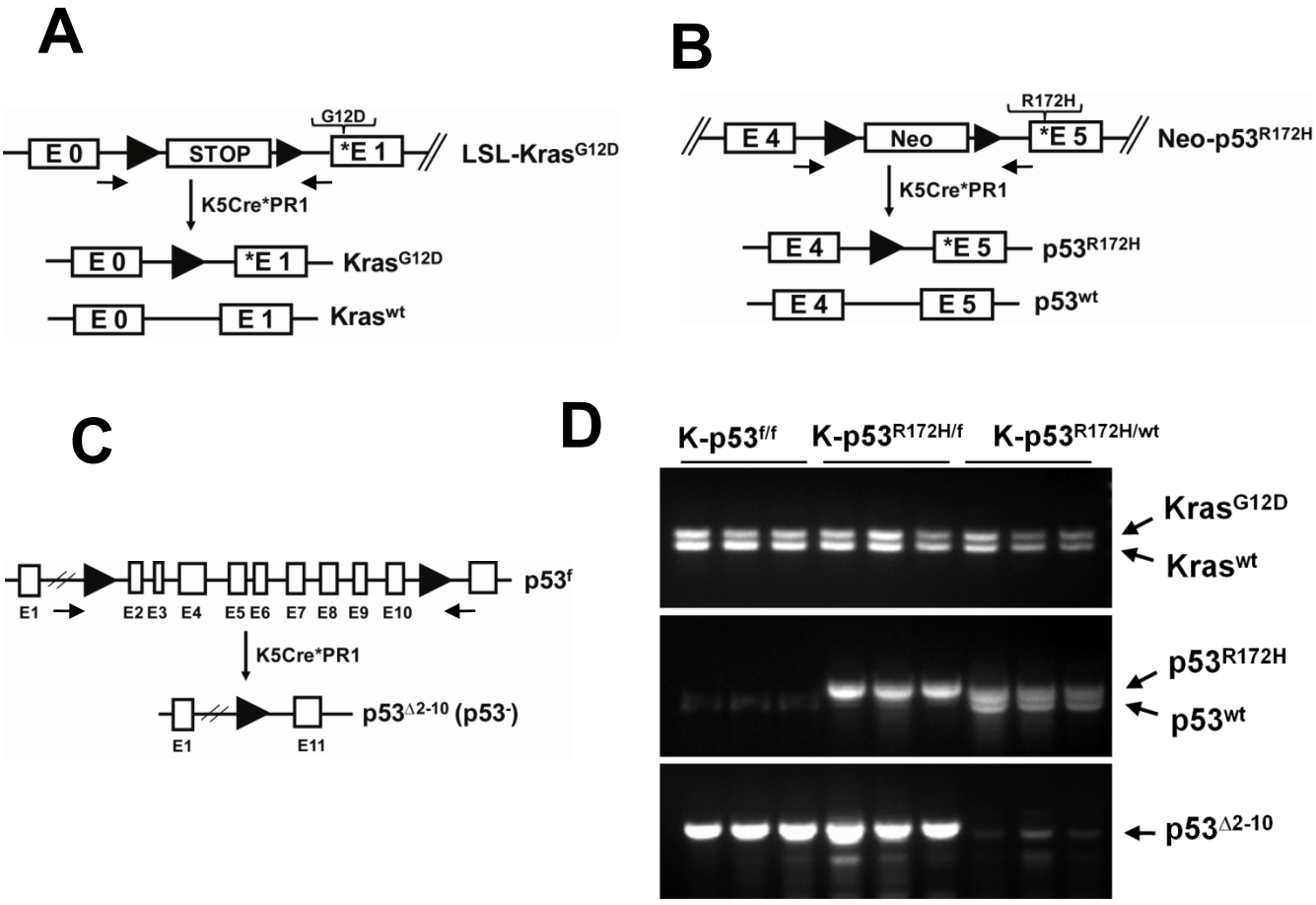
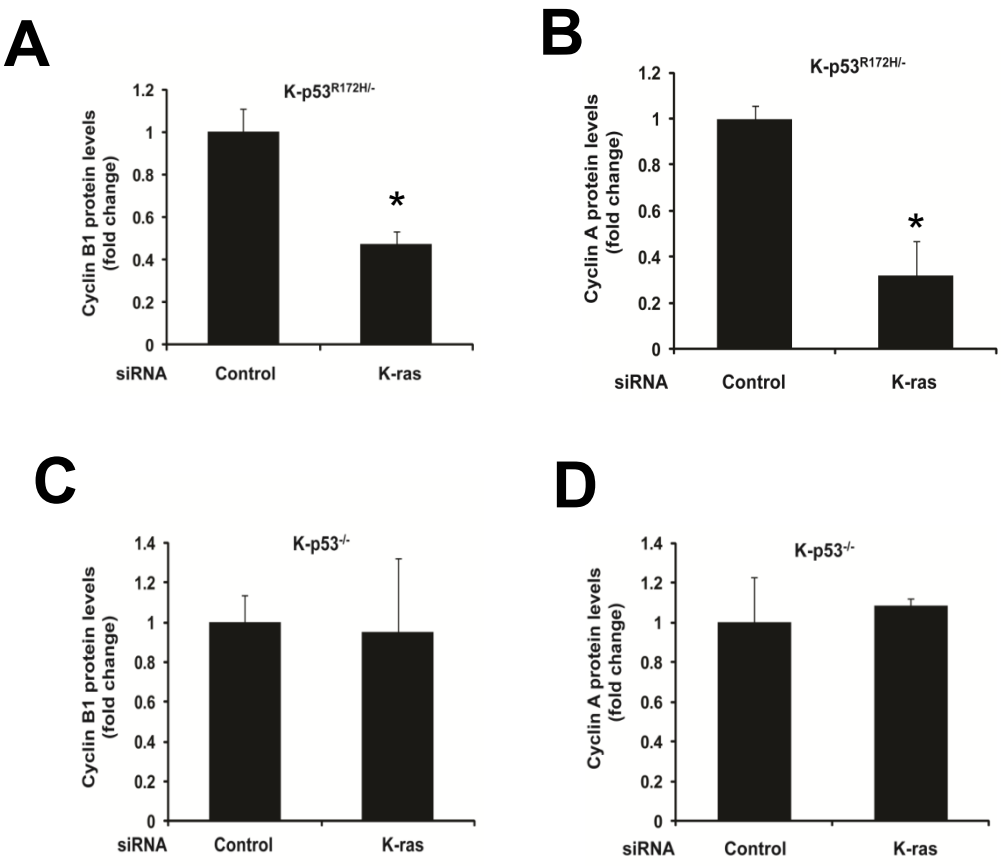
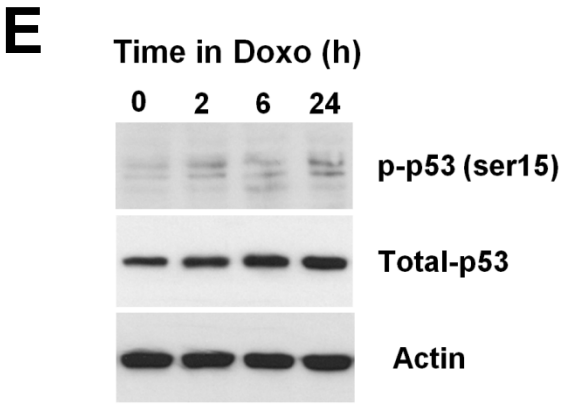
Supplementary Figure 1

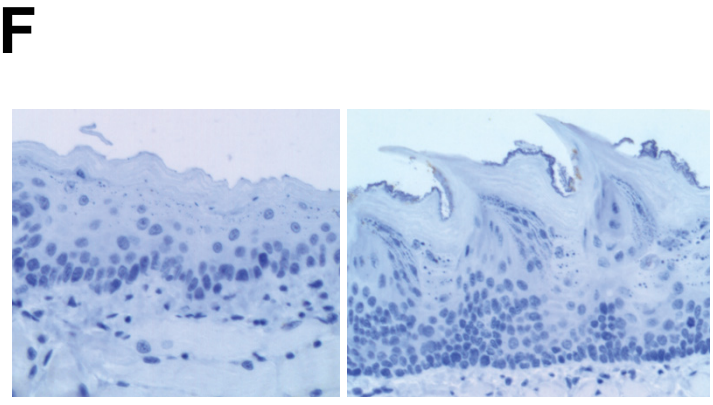


Supplementary Figure 1. Schematic representation of the conditional alleles and activation in tumors. (A) LSL-Ras^{G12D} allele. After Cre activation the STOP cassette is deleted and the K-ras^{G12D} mutation is expressed. **(B)** Neo-p53^{R172H} allele. Cre activation induces deletion of the Neo cassette and activation of the p53^{R172H} mutation. **(C)** Floxed p53 (p53^{f}) allele. After Cre activation Exons 2-10 of the p53 gene are deleted. Black triangles denote loxP sites. **(D)** Activation of conditional alleles in oral tumors that developed in mice with the indicated genotypes, using primers indicated by arrows in panels **A-C**, for each of the conditional alleles. Three tumors per genotype were analyzed.

Supplementary Figure 2







Supplementary Figure 2. (A) Cyclin B1 and **(B)** cyclin A levels in western blots shown in Figure 6F were quantified after normalization with β-actin. **(C)** Quantification of cyclin B1 and **(D)** cyclin A protein levels shown in Figure 6G after normalization with β-actin. Results in **A-D** were expressed as fold change relative to cells transfected with control siRNA. *p=0.01-0.05. **(E)** Phosphorylation of mutant p53 at serine 15 after incubating K-p53$^{R172H/-}$ cells in 200ng/ml Doxorubicin for the indicated times. **(F)** Immunohistochemistry for γH2AX in normal oral epithelium. Note the lack of DNA damage in epithelial cells.

Supplementary Table 1. Genes differentially expressed in K-p53$^{R172H/-}$ and K-p53$^{R172H/+}$ oral tumors compared to K-p53$^{-/-}$ tumors. Fold change is indicated

Gene sysmbol	Gene name	fold change (K-p53$^{R172H/-}$)	fold change (K-p53$^{R172H/+}$)
2310002L13Rik	RIKEN cDNA 2310002L13 gene	6.63	5.66
H19	H19 fetal liver mRNA	4.64	3.63
Chi3l3	chitinase 3-like 3	3.79	2.86
Dusp6	dual specificity phosphatase 6	3.53	3.47
Cxcl2	chemokine (C-X-C motif) ligand 2	3.19	3.62
Ifi205	interferon activated gene 205	3.13	2.15
Mm.209077.1		2.74	2.92
Dusp4	dual specificity phosphatase 4	2.65	2.59
Cxcl1	chemokine (C-X-C motif) ligand 1	2.54	2.31
Cyp1b1	cytochrome P450, family 1, subfamily b, polypeptide 1	2.49	2.14
D17H6S56E-5	DNA segment, Chr 17, human D6S56E 5	2.49	2.14
Mmp13	matrix metallopeptidase 13	2.46	3.64
Depdc1a	DEP domain containing 1a	2.43	2.28
Il1a	interleukin 1 alpha	2.41	2.03
Hp	haptoglobin	2.4	2.31
Il1rn	interleukin 1 receptor antagonist	2.36	2.12
1600029D21Rik	RIKEN cDNA 1600029D21 gene	2.35	1.9
Cpeb4	cytoplasmic polyadenylation element binding protein 4	2.29	2.33
Scd2	stearoyl-Coenzyme A desaturase 2	2.19	2.06
Hmmr	hyaluronan mediated motility receptor (RHAMM)	2.16	1.78
Uox	urate oxidase	2.13	1.8
D530037H12Rik	RIKEN cDNA D530037H12 gene	2.13	2.09
Cbr2	carbonyl reductase 2	2.11	1.97
Gda	guanine deaminase	2.11	1.82
Areg	amphiregulin	2.1	2.06
Slc4a7	solute carrier family 4, sodium bicarbonate cotransporter, member 7	2.07	2
Snapc1	small nuclear RNA activating complex, polypeptide 1	2.04	1.9
Nusap1	nucleolar and spindle associated protein 1	1.99	1.73
Ifitm1	interferon induced transmembrane protein 1	1.99	2.16
6430706D22Rik /// A730008H23Rik	RIKEN cDNA 6430706D22 gene /// RIKEN cDNA A730008H23 gene	1.98	2.02
C330027C09Rik	RIKEN cDNA C330027C09 gene	1.97	1.79

Ddx6	DEAD (Asp-Glu-Ala-Asp) box polypeptide 6	1.96	1.94
Kif11	kinesin family member 11	1.96	1.72
Malat1	metastasis associated lung adenocarcinoma transcript 1 (non-coding RNA)	1.96	1.66
Tgif1	TGFB-induced factor homeobox 1	1.95	2
Zwilch	Zwilch, kinetochore associated, homolog (Drosophila)	1.93	1.71
Adam8	a disintegrin and metallopeptidase domain 8	1.93	1.89
Aspm	asp (abnormal spindle)-like, microcephaly associated (Drosophila)	1.93	1.67
Mall	mal, T-cell differentiation protein-like	1.93	1.77
Kcne3	potassium voltage-gated channel, Isk-related subfamily, gene 3	1.92	2.05
Fam129a	family with sequence similarity 129, member A	1.92	1.84
Lin7c	lin-7 homolog C (C. elegans)	1.9	1.84
Bnc1	basonuclin 1	1.9	1.89
Cugbp1	CUG triplet repeat, RNA binding protein 1	1.88	1.74
Ccnb2	cyclin B2	1.88	1.65
Kif20b	kinesin family member 20B	1.88	1.7
Ccnb1	cyclin B1	1.87	1.67
Schip1	schwannomin interacting protein 1	1.87	1.71
Abcb10	ATP-binding cassette, sub-family B (MDR/TAP), member 10	1.84	2.02
Kif20a	kinesin family member 20A	1.84	1.74
Cep55	centrosomal protein 55	1.83	1.65
Ccr1	chemokine (C-C motif) receptor 1	1.81	2
Megf9	multiple EGF-like-domains 9	1.78	1.82
Tgm3	transglutaminase 3, E polypeptide	1.75	1.76
Anxa4	annexin A4	1.75	1.78
Tmem48	transmembrane protein 48	1.74	1.55
Ass1	argininosuccinate synthetase 1	1.73	1.7
Ugcg	UDP-glucose ceramide glucosyltransferase	1.73	1.71
6720463M24Rik	RIKEN cDNA 6720463M24 gene	1.73	1.63
Cdc27	cell division cycle 27 homolog (S. cerevisiae)	1.73	1.71
DXErtd223e	DNA segment, Chr X, ERATO Doi 223, expressed	1.72	1.68
Pthlh	parathyroid hormone-like peptide	1.72	1.81
Tspan7	tetraspanin 7	1.71	1.61
Net1	neuroepithelial cell transforming gene 1	1.71	1.6
Ero1l	ERO1-like (S. cerevisiae)	1.7	1.54
Kif2c	kinesin family member 2C /// similar to Kinesin-like protein KIF2C (Mitotic centromere-associated kinesin) (MCAK)	1.7	1.55

Pkn2	protein kinase N2	1.7	1.72
Mier1	mesoderm induction early response 1 homolog (Xenopus laevis	1.7	1.76
Mmp10	matrix metallopeptidase 10	1.69	1.82
Suz12	suppressor of zeste 12 homolog (Drosophila)	1.69	1.53
Sgol2	shugoshin-like 2 (S. pombe)	1.67	1.69
Ccna2	cyclin A2	1.66	1.5
Ect2	ect2 oncogene	1.66	1.53
Cenpa	centromere protein A	1.66	1.55
Yes1	Yamaguchi sarcoma viral (v-yes) oncogene homolog 1	1.65	1.58
D130067C23Rik /// Sp3	RIKEN cDNA D130067C23 gene /// trans-acting transcription factor 3	1.64	1.68
Mpp5	membrane protein, palmitoylated 5 (MAGUK p55 subfamily member 5)	1.64	1.52
Bzw1	basic leucine zipper and W2 domains 1	1.64	1.6
Etv3	ets variant gene 3	1.63	1.64
Papolg	poly(A) polymerase gamma	1.63	1.54
Terf1	telomeric repeat binding factor 1	1.62	1.76
Dsc2	desmocollin 2	1.62	1.61
LOC630729	similar to Glutathione reductase, mitochondrial precursor (GR) (GRase)	1.62	1.76
P2ry5	purinergic receptor P2Y, G-protein coupled, 5	1.62	1.56
Stom	stomatin	1.61	1.59
Cenpq	centromere protein Q	1.6	1.53
Bub1	budding uninhibited by benzimidazoles 1 homolog (S. cerevisiae)	1.6	1.49
Smek1	SMEK homolog 1, suppressor of mek1 (Dictyostelium)	1.6	1.58
2810417H13Rik	RIKEN cDNA 2810417H13 gene	1.59	1.49
Ppp1r12a	protein phosphatase 1, regulatory (inhibitor) subunit 12A	1.59	1.53
Birc5	baculoviral IAP repeat-containing 5	1.58	1.46
Klf6	Kruppel-like factor 6	1.57	1.47
E2f7	E2F transcription factor 7	1.57	1.64
Bcl10	B-cell leukemia/lymphoma 10	1.56	1.47
Zfp36l1	zinc finger protein 36, C3H type-like 1	1.56	1.56
Fcho2	FCH domain only 2	1.56	1.6
Cks1b	CDC28 protein kinase 1b	1.55	1.46
Spry2	sprouty homolog 2 (Drosophila)	1.54	1.75
Elavl1	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 1 (Hu antigen R)	1.53	1.5

Krt14	keratin 14	1.53	1.45
Hist1h3a /// Hist1h3b /// Hist1h3c /// Hist1h3d /// Hist1h3e /// Hist1h3f /// Hist1h3g /// Hist1h3h /// Hist1h3i /// Hist2h3b /// Hist2h3c1 /// Hist2h3c2	histone cluster 1, H3a /// histone cluster 1, H3b /// histone cluster 1, H3c /// histone cluster 1, H3d /// histone cluster 1, H3e /// histone cluster 1, H3f /// histone cluster 1, H3g /// histone cluster 1, H3h /// histone cluster 1, H3i /// histone cluster 2, H3b /// histone cluster 2, H3c1 /// histone cluster 2, H3c2	1.53	1.39
Snhg3	small nucleolar RNA host gene (non-protein coding) 3	1.53	1.56
Nup160	nucleoporin 160	1.52	1.47
1190005F20Rik	RIKEN cDNA 1190005F20 gene	1.51	1.44
Hif1a	hypoxia inducible factor 1, alpha subunit	1.51	1.47
Sc5d	sterol-C5-desaturase (fungal ERG3, delta-5-desaturase) homolog (S. cerevisae)	1.51	1.51
Hbs1l	Hbs1-like (S. cerevisiae)	1.51	1.44
Tprkb	Tp53rk binding protein	1.49	1.56
Sbno1	sno, strawberry notch homolog 1 (Drosophila)	1.49	1.48
Acsl3	acyl-CoA synthetase long-chain family member 3	1.49	1.42
Plk4	polo-like kinase 4 (Drosophila)	1.48	1.45
Marveld2	MARVEL (membrane-associating) domain containing 2	1.48	1.45
Smc2	structural maintenance of chromosomes 2	1.48	1.39
Nrip1	nuclear receptor interacting protein 1	1.46	1.45
Ptpn12	protein tyrosine phosphatase, non-receptor type 12	1.46	1.42
6430527G18Rik	RIKEN cDNA 6430527G18 gene	1.46	1.51
Mrpl3	mitochondrial ribosomal protein L3	1.45	1.42
BC018507	cDNA sequence BC018507	1.45	1.4
Mrpl50	mitochondrial ribosomal protein L50	1.45	1.5
Far1	fatty acyl CoA reductase 1	1.45	1.37
Cdc20	cell division cycle 20 homolog (S. cerevisiae)	1.45	1.39
Senp2	SUMO/sentrin specific peptidase 2	1.44	1.41
Prpf4b	PRP4 pre-mRNA processing factor 4 homolog B (yeast)	1.44	1.43
Fam110c	family with sequence similarity 110, member C	1.43	1.49
Exosc8	exosome component 8	1.41	1.35
Cep192	centrosomal protein 192	1.41	1.39

Ppp3cb	protein phosphatase 3, catalytic subunit, beta isoform	1.4	1.34
Ywhaq	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, theta polypeptide	1.39	1.33
A830080D01Rik	RIKEN cDNA A830080D01 gene	1.38	1.34
Tmpo	thymopoietin	1.34	1.32
Nup54	nucleoporin 54	1.32	1.32
Tm2d2	TM2 domain containing 2	-1.32	-1.38
Drap1	Dr1 associated protein 1 (negative cofactor 2 alpha)	-1.35	-1.36
Cbx2	chromobox homolog 2 (Drosophila Pc class)	-1.38	-1.36
Slc17a5	solute carrier family 17 (anion/sugar transporter), member 5	-1.38	-1.39
Sumf2	sulfatase modifying factor 2	-1.38	-1.38
Rbck1	RanBP-type and C3HC4-type zinc finger containing 1	-1.39	-1.4
Krt12	keratin 12	-1.41	-1.39
Prrc1	proline-rich coiled-coil 1	-1.42	-1.36
Plxna2	plexin A2	-1.42	-1.38
Klc3	kinesin light chain 3	-1.44	-1.32
Mmd	monocyte to macrophage differentiation-associated	-1.46	-1.45
Kcnq2	potassium voltage-gated channel, subfamily Q, member 2	-1.46	-1.43
Gfod1	glucose-fructose oxidoreductase domain containing 1	-1.46	-1.4
Ilkap	integrin-linked kinase-associated serine/threonine phosphatase 2C	-1.47	-1.42
Plxna1	plexin A1	-1.48	-1.44
Pmm1	phosphomannomutase 1	-1.49	-1.43
1700094D03Rik	RIKEN cDNA 1700094D03 gene	-1.49	-1.43
Bicd2	bicaudal D homolog 2 (Drosophila)	-1.5	-1.49
Lrrc7	Lrrc7 leucine rich repeat containing 7	-1.5	-1.44
Ccdc80	coiled-coil domain containing 80	-1.51	-1.45
Zfp365	zinc finger protein 365	-1.51	-1.5
4933433N18Rik	RIKEN cDNA 4933433N18 gene	-1.52	-1.47
6330564D18Rik	RIKEN cDNA 6330564D18 gene	-1.52	-1.41
Pde6g	phosphodiesterase 6G, cGMP-specific, rod, gamma	-1.53	-1.53
Pla2g4f	phospholipase A2, group IVF	-1.53	-1.44
Vamp2	vesicle-associated membrane protein 2	-1.55	-1.6
Sytl1	synaptotagmin-like 1	-1.55	-1.42

ORF61	open reading frame 61	-1.57	-1.45
Ankrd35	ankyrin repeat domain 35	-1.57	-1.49
Nodal	nodal	-1.58	-1.49
Frmpd1	FERM and PDZ domain containing 1	-1.58	-1.51
Mem1	maternal embryonic message 1	-1.59	-1.56
Jarid1c	jumonji, AT rich interactive domain 1C (Rbp2 like)	-1.6	-1.64
Dnahc2	dynein, axonemal, heavy chain 2	-1.6	-1.63
Fam18a	family with sequence similarity 18, member A	-1.61	-1.55
Armc8	armadillo repeat containing 8	-1.61	-1.51
A230106M20Rik	RIKEN cDNA A230106M20 gene	-1.61	-1.59
Wscd1	WSC domain containing 1	-1.62	-1.54
Gas7	growth arrest specific 7	-1.62	-1.53
Msx3	homeobox, msh-like 3	-1.63	-1.56
Ddx55	DEAD (Asp-Glu-Ala-Asp) box polypeptide 55, mRNA (cDNA clone MGC	-1.63	-1.52
Oprm1	opioid receptor, mu 1	-1.64	-1.62
Zfp703	zinc finger protein 703	-1.65	-1.69
Cpt1c	carnitine palmitoyltransferase 1c	-1.66	-1.59
Maf	avian musculoaponeurotic fibrosarcoma (v-maf) AS42 oncogene homolog	-1.66	-1.47
2010107G23Rik	RIKEN cDNA 2010107G23 gene	-1.67	-1.57
Mm.172135.1		-1.68	-1.58
Col16a1	collagen, type XVI, alpha 1	-1.69	-1.43
Efna3	ephrin A3	-1.72	-1.66
Pou3f1	POU domain, class 3, transcription factor 1	-1.77	-1.82
Col1a1	collagen, type I, alpha 1	-1.78	-1.6
Tia1	cytotoxic granule-associated RNA binding protein 1	-1.78	-1.75
Dcxr	dicarbonyl L-xylulose reductase	-1.81	-1.57
Dcdc2b	Doublecortin domain-containing protein 2	-1.81	-1.82
4930555F03Rik	RIKEN cDNA 4930555F03 gene	-1.84	-1.69
Lbh	limb-bud and heart	-1.87	-1.68
Slc26a2	solute carrier family 26 (sulfate transporter), member 2	-1.94	-1.96
Nlrp6	NLR family, pyrin domain containing 6	-1.94	-1.65
Vamp3	Vesicle-associated membrane protein 3 (Vamp3), mRNA	-1.96	-2.06
Per2	period homolog 2 (Drosophila)	-2.03	-2.07
Cpt1a	carnitine palmitoyltransferase 1a, liver	-2.06	-1.74
Adh7	alcohol dehydrogenase 7 (class IV), mu or sigma polypeptide	-2.11	-1.82

Lce1m	late cornified envelope 1M	-2.11	-2.2
C030009J22Rik	RIKEN cDNA C030009J22 gene	-2.14	-1.98
1700097N02Rik	RIKEN cDNA 1700097N02 gene	-2.33	-2.1
Bckdhb	branched chain ketoacid dehydrogenase E1, beta polypeptide	-2.55	-2.04
Dbp	D site albumin promoter binding protein	-2.6	-2.18
Cited4	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 4	-2.62	-2.03
Clec2g	C-type lectin domain family 2, member g	-3.45	-3.07
Erdr1	Erythroid differentiation regulator 1	-3.87	-2.88