

Table S1. Genes that are dispensable for mouse tooth development. Published information indicate that although these genes are expressed during mouse molar development, their null mutations have no detectable effects on the tooth phenotype. Only genes having read counts greater than zero in our RNAseq data were included.

Mouse Ensembl ID	Gene name	Mouse Ensembl ID	Gene name	Mouse Ensembl ID	Gene name
00000019256	<i>Ahr</i>	00000005320	<i>Fgfr4</i>	00000029838	<i>Ptn</i>
00000022636	<i>Alcam</i>	00000027004	<i>Frzb</i>	00000068748	<i>Ptprz1</i>
00000004655	<i>Aqp1</i>	00000030795	<i>Fus</i>	00000004768	<i>Rab23</i>
00000028435	<i>Aqp3</i>	00000022297	<i>Fzd6</i>	00000042453	<i>Reln</i>
00000024411	<i>Aqp4</i>	00000025407	<i>Gli1</i>	00000030110	<i>Ret</i>
00000044217	<i>Aqp5</i>	00000034220	<i>Gpc1</i>	00000025158	<i>Rfng</i>
00000032204	<i>Aqp9</i>	00000029510	<i>Gpc2</i>	00000070691	<i>Runx3</i>
00000000142	<i>Axin2</i>	00000048001	<i>Hes5</i>	00000039656	<i>Rxb</i>
00000004892	<i>Bcan</i>	00000064325	<i>Hhip</i>	00000015843	<i>Rxrg</i>
00000074483	<i>Bglap</i>	00000078735	<i>Il11ra</i>	00000020592	<i>Sdc1</i>
00000029335	<i>Bmp3</i>	00000026638	<i>Irf6</i>	00000025743	<i>Sdc3</i>
00000032179	<i>Bmp5</i>	00000001504	<i>Irx2</i>	00000017009	<i>Sdc4</i>
00000039004	<i>Bmp6</i>	00000031734	<i>Irx3</i>	00000057969	<i>Sema3b</i>
00000025217	<i>Btrc</i>	00000021604	<i>Irx4</i>	00000034684	<i>Sema3f</i>
00000061048	<i>Cdh3</i>	00000031738	<i>Irx6</i>	00000027996	<i>Sfrp2</i>
00000023067	<i>Cdkn1a</i>	00000022817	<i>Itgb5</i>	00000025020	<i>Slit1</i>
00000044303	<i>Cdkn2a</i>	00000019899	<i>Lama2</i>	00000056427	<i>Slit3</i>
00000022037	<i>Clu</i>	00000019846	<i>Lama4</i>	00000045871	<i>Slitrk6</i>
00000001506	<i>Col1a1</i>	00000029570	<i>Lfng</i>	00000025323	<i>Sp4</i>
00000031502	<i>Col4a1</i>	00000023845	<i>Lnpep</i>	00000056222	<i>Spock1</i>
00000032911	<i>Cspg4</i>	00000036295	<i>Lrr3</i>	00000029304	<i>Spp1</i>
00000032482	<i>Cspg5</i>	00000027239	<i>Mdk</i>	00000061762	<i>Tac1</i>
00000062432	<i>Cyp26c1</i>	00000018169	<i>Mfng</i>	00000032011	<i>Thy1</i>
00000028519	<i>Dab1</i>	00000027820	<i>Mme</i>	00000001131	<i>Timp1</i>
00000019929	<i>Dcn</i>	00000050578	<i>Mmp13</i>	00000017466	<i>Timp2</i>
00000026131	<i>Dst</i>	00000043613	<i>Mmp3</i>	00000030516	<i>Tjp1</i>
00000028017	<i>Egf</i>	00000017737	<i>Mmp9</i>	00000034917	<i>Tjp3</i>
00000038418	<i>Egr1</i>	00000019982	<i>Myb</i>	00000025215	<i>Tlx1</i>
00000028289	<i>Epha7</i>	00000005125	<i>Ndrp1</i>	00000028364	<i>Tnc</i>
00000006369	<i>Fbln1</i>	00000048616	<i>Nog</i>	00000060548	<i>Tnfrsf19</i>
00000064080	<i>Fbln2</i>	00000038146	<i>Notch3</i>	00000026875	<i>Traf1</i>
00000036585	<i>Fgf1</i>	00000025969	<i>Nrp2</i>	00000022996	<i>Wnt10b</i>
00000037225	<i>Fgf2</i>	00000032855	<i>Pkd1</i>		
00000027208	<i>Fgf7</i>	00000028681	<i>Ptch2</i>		

Table S2. Descriptive statistics of the different gene categories. Developmental-process category is based on Gene ontology 00332502 criteria and Other-category includes all the remaining protein coding genes.

Embryonic Day/Platform	Gene category	<i>n</i>	Median	Mean	Range	SD
Microarray						
E13	Progression	15	7.867	8.094	6.73–9.71	0.7874
	Shape	28	7.347	7.087	4.3–9.14	1.2489
	Double	10	7.419	7.360	4.84–8.87	1.0816
	Tissue	27	6.359	6.231	3.7–10.61	1.7706
	Dispensable	98	6.599	6.501	3.56–9.78	1.4400
	Dev. process	3983	6.100	6.063	1.45–10.43	1.4678
	Other	14825	5.616	5.601	1.45–12.02	1.5698
E14	Progression	15	8.029	8.087	7.11–9.81	0.7486
	Shape	28	7.592	7.389	4.63–9.71	1.1242
	Double	10	7.143	7.035	5.12–8.06	0.8071
	Tissue	27	6.343	6.315	3.81–10.24	1.7134
	Dispensable	98	6.798	6.606	3.75–9.29	1.3600
	Dev. process	3983	6.109	6.067	1.47–10.71	1.4597
	Other	14825	5.604	5.577	1.53–11.72	1.5629
RNAseq						
E13	Progression	15	12.125	11.665	7.07–14.26	1.6394
	Shape	28	9.695	9.522	3.82–13.19	2.4430
	Double	10	10.752	10.391	5.17–12.83	2.0987
	Tissue	27	9.463	7.619	-2.25–12.41	4.8379
	Dispensable	100	9.031	8.556	-2.35–13.31	3.5693
	Dev. process	4106	8.658	7.331	-2.36–13.47	4.2027
	Other	16165	7.033	5.571	-2.36–13.87	4.6101
E14	Progression	15	12.150	12.022	9.78–14.32	1.1495
	Shape	28	10.133	10.053	4.92–13.01	1.9134
	Double	10	10.949	10.647	6.67–12.86	1.7265
	Tissue	27	9.691	7.735	-2.25–12.47	4.8651
	Dispensable	100	9.541	8.861	-2.35–13.74	3.5664
	Dev. process	4106	8.708	7.383	-2.36–13.55	4.2174
	Other	16165	7.062	5.591	-2.36–14.06	4.6204
E16	Progression	15	12.147	12.134	10.1–14.27	1.0235
	Shape	28	10.310	10.239	4.17–12.92	1.8993
	Double	10	11.351	10.733	8.1–12.73	1.4792
	Tissue	27	9.917	7.842	-2.25–12.25	4.9495
	Dispensable	100	9.562	9.015	-2.35–14.4	3.5389
	Dev. process	4106	8.772	7.419	-2.36–13.63	4.1998
	Other	16165	7.193	5.634	-2.36–13.9	4.6119

Table S3. Permutation tests for microarray, RNAseq and scRNAseq expression levels of progression, shape, and double categories compared to tissue, dispensable, developmental process, and other-gene categories. These are permutation tests of differences between group medians (p -values of one-tailed significance levels obtained using 10 000 permutations).

Embryonic Day/Platform	Gene category	Tissue	Dispensable	Developmental process	Other
Microarray					
E13	Progression	0.0098	0.0426	0.0003	0.0000
	Shape	0.0689	0.0901	0.0010	0.0000
	Double	0.0978	0.1945	0.0322	0.0039
E14	Progression	0.0028	0.0466	0.0000	0.0000
	Shape	0.0027	0.0345	0.0001	0.0000
	Double	0.1743	0.5010	0.1072	0.0132
RNAseq					
E13	Progression	0.0379	0.0059	0.0370	0.0565
	Shape	0.8391	0.5138	0.2468	0.1082
	Double	0.3008	0.2425	0.1637	0.1533
E14	Progression	0.0199	0.0299	0.0339	0.0608
	Shape	0.6456	0.4646	0.1211	0.0759
	Double	0.3229	0.2751	0.1425	0.1416
E16	Progression	0.0240	0.0302	0.0312	0.0649
	Shape	0.5935	0.3100	0.0886	0.0770
	Double	0.3436	0.1464	0.1040	0.1349
scRNAseq					
E14	Progression	0.0146	0.0071	0.0310	0.0295
	Shape	0.9968	0.9087	0.7788	0.1357
	Double	0.1233	0.0683	0.1262	0.0939

Table S4. Pathway genes used to compare expression levels. Genes marked to belong into more than one pathway were tabulated only once in the calculations. The FGF pathway includes also EGF pathway genes. LG = ligand, RC = receptor, IC = intracellular cofactor, TF = transcription factor.

Ensembl ID	Gene name	Pathway	Type	Ensembl ID	Gene name	Pathway	Type
00000026836	<i>Acvr1</i>	TGFB	RC	00000024913	<i>Lrp5</i>	Wnt	IC
00000026834	<i>Acvr1c</i>	TGFB	RC	00000030201	<i>Lrp6</i>	Wnt	IC
00000052155	<i>Acvr2a</i>	TGFB	RC	00000050567	<i>Maml1</i>	Notch	TF
00000061393	<i>Acvr2b</i>	TGFB	RC	00000031925	<i>Maml2</i>	Notch	TF
00000054693	<i>Adam10</i>	Notch	IC	00000061143	<i>Maml3</i>	Notch	TF
00000052593	<i>Adam17</i>	Notch	IC	00000004936	<i>Map2k1</i>	FGF	IC
00000001729	<i>Akt1</i>	FGF/TGFB	IC	00000035027	<i>Map2k2</i>	FGF	IC
00000004056	<i>Akt2</i>	FGF/TGFB	IC	00000018932	<i>Map2k3</i>	TGFB	IC
00000035262	<i>Amh</i>	TGFB	LG	00000033352	<i>Map2k4</i>	TGFB	IC
00000005871	<i>Apc</i>	Wnt	IC	00000020623	<i>Map2k6</i>	TGFB	IC
00000020135	<i>Apc2</i>	Wnt	IC	00000028284	<i>Map3k7</i>	EDA /TGFB	IC
00000015750	<i>Aph1a</i>	Notch	IC	00000063358	<i>Mapk1</i>	FGF/TGFB	IC
00000001127	<i>Araf</i>	FGF/TGFB	IC	00000053436	<i>Mapk14</i>	TGFB	IC
00000022911	<i>Arl13b</i>	Hh	IC	00000063065	<i>Mapk3</i>	FGF/TGFB	IC
00000018909	<i>Arrb1</i>	Hh	IC	00000021936	<i>Mapk8</i>	TGFB	IC
00000060216	<i>Arrb2</i>	Hh	IC	00000020366	<i>Mapk9</i>	TGFB	IC
00000024182	<i>Axin1</i>	Wnt	IC	00000018169	<i>Mfng</i>	Notch	IC
00000000142	<i>Axin2</i>	Wnt	IC	00000024294	<i>Mib1</i>	Notch	IC
00000030046	<i>Bmp10</i>	TGFB	LG	00000029060	<i>Mib2</i>	Notch	IC
00000023279	<i>Bmp15</i>	TGFB	LG	00000034121	<i>Mks1</i>	Hh	IC
00000027358	<i>Bmp2</i>	TGFB	LG	00000028991	<i>Mtor</i>	FGF	IC
00000029335	<i>Bmp3</i>	TGFB	LG	00000018501	<i>Ncor1</i>	Notch	IC
00000021835	<i>Bmp4</i>	TGFB	LG	00000029478	<i>Ncor2</i>	Notch	IC
00000032179	<i>Bmp5</i>	TGFB	LG	00000003458	<i>Ncstn</i>	Notch	IC

Ensembl ID	Gene name	Pathway	Type	Ensembl ID	Gene name	Pathway	Type
00000039004	<i>Bmp6</i>	TGFB	LG	00000006435	<i>Neur1a</i>	Notch	IC
00000008999	<i>Bmp7</i>	TGFB	LG	00000034413	<i>Neur1b</i>	Notch	IC
00000032726	<i>Bmp8a</i>	TGFB	LG	00000028163	<i>Nfkb1</i>	EDA/FGF/TGFB	TF
00000002384	<i>Bmp8b</i>	TGFB	LG	00000025225	<i>Nfkb2</i>	EDA/FGF/TGFB	TF
00000021796	<i>Bmpr1a</i>	TGFB	RC	00000021025	<i>Nfkbia</i>	EDA	TF
00000052430	<i>Bmpr1b</i>	TGFB	RC	00000031661	<i>Nkd1</i>	Wnt	IC
00000067336	<i>Bmpr2</i>	TGFB	RC	00000021567	<i>Nkd2</i>	Wnt	IC
00000022687	<i>Boc</i>	Hh	RC	00000037171	<i>Nodal</i>	TGFB	LG
00000002413	<i>Braf</i>	FGF/TGFB	IC	00000026923	<i>Notch1</i>	Notch	RC
00000025217	<i>Btrc</i>	Hh	IC	00000027878	<i>Notch2</i>	Notch	RC
00000038119	<i>Cdon</i>	Hh	RC	00000038146	<i>Notch3</i>	Notch	RC
00000025199	<i>Chuk</i>	EDA	IC	00000015468	<i>Notch4</i>	Notch	RC
00000024576	<i>Csnk1a1</i>	Hh/Wnt	IC	00000027852	<i>Nras</i>	FGF/TGFB	IC
00000025162	<i>Csnk1d</i>	Wnt	IC	00000021224	<i>Numb</i>	Notch	IC
00000022433	<i>Csnk1e</i>	Wnt	IC	00000063160	<i>Numbl</i>	Notch	IC
00000032384	<i>Csnk1g1</i>	Hh/Wnt	IC	00000040586	<i>Ofd1</i>	Hh	IC
00000003345	<i>Csnk1g2</i>	Hh/Wnt	IC	00000029231	<i>Pdgfra</i>	FGF	RC
00000073563	<i>Csnk1g3</i>	Hh/Wnt	IC	00000027665	<i>Pik3ca</i>	FGF/TGFB	IC
00000006932	<i>Ctnnb1</i>	Wnt	IC	00000031834	<i>Pik3r2</i>	FGF/TGFB	IC
00000023000	<i>Dhh</i>	Hh	LG	00000016933	<i>Plcg1</i>	FGF	IC
00000024868	<i>Dkk1</i>	Wnt	IC	00000031169	<i>Porcn</i>	Wnt	IC
00000028031	<i>Dkk2</i>	Wnt	IC	00000005469	<i>Prkaca</i>	Hh	IC
00000030772	<i>Dkk3</i>	Wnt	IC	00000050965	<i>Prkca</i>	FGF	IC
00000031535	<i>Dkk4</i>	Wnt	IC	00000019969	<i>Psen1</i>	Notch	IC
00000014773	<i>Dll1</i>	Notch	LG	00000010609	<i>Psen2</i>	Notch	IC
00000003436	<i>Dll3</i>	Notch	LG	00000021466	<i>Ptch1</i>	Hh	RC
00000027314	<i>Dll4</i>	Notch	LG	00000028681	<i>Ptch2</i>	Hh	RC
00000029603	<i>Dtx1</i>	Notch	IC	00000013663	<i>Pten</i>	FGF	IC
00000029071	<i>Dvl1</i>	Wnt	IC	00000000441	<i>Raf1</i>	FGF/TGFB	IC
00000020888	<i>Dvl2</i>	Wnt	IC	00000039191	<i>Rbpj</i>	Notch	TF
00000003233	<i>Dvl3</i>	Wnt	IC	00000024927	<i>Rela</i>	EDA	TF
00000047193	<i>Dync2h1</i>	Hh	IC	00000002983	<i>Relb</i>	EDA	TF
00000059327	<i>Eda</i>	EDA	LG	00000025158	<i>Rfng</i>	Notch	IC
00000034457	<i>Eda2r</i>	EDA	RC	00000007815	<i>Rhoa</i>	TGFB	IC
00000003227	<i>Edar</i>	EDA	RC	00000034177	<i>Rnf43</i>	Wnt	IC
00000095105	<i>Edaradd</i>	EDA	IC	00000024290	<i>Rock1</i>	TGFB	IC
00000028017	<i>Egf</i>	FGF	LG	00000057132	<i>Rpgrip1</i>	Hh	IC
00000020122	<i>Egfr</i>	FGF	RC	00000031309	<i>Rps6ka3</i>	FGF	IC
00000029122	<i>Evc</i>	Hh	IC	00000031548	<i>Sfrp1</i>	Wnt	IC
00000028086	<i>Fbxw7</i>	Notch	IC	00000027996	<i>Sfrp2</i>	Wnt	IC
00000036585	<i>Fgf1</i>	FGF	LG	00000021319	<i>Sfrp4</i>	Wnt	IC
00000021732	<i>Fgf10</i>	FGF	LG	00000018822	<i>Sfrp5</i>	Wnt	IC
00000042826	<i>Fgf11</i>	FGF	LG	00000042626	<i>Shc1</i>	FGF	IC
00000022523	<i>Fgf12</i>	FGF	LG	00000020312	<i>Shc2</i>	FGF	IC
00000031137	<i>Fgf13</i>	FGF	LG	00000002633	<i>Shh</i>	Hh	LG
00000025551	<i>Fgf14</i>	FGF	LG	00000029050	<i>Ski</i>	Hh	IC
00000031230	<i>Fgf16</i>	FGF	LG	00000031681	<i>Smad1</i>	TGFB	TF
00000037225	<i>Fgf2</i>	FGF	LG	00000024563	<i>Smad2</i>	TGFB	TF
00000031603	<i>Fgf20</i>	FGF	LG	00000032402	<i>Smad3</i>	TGFB	TF
00000020327	<i>Fgf22</i>	FGF	LG	00000024515	<i>Smad4</i>	TGFB	TF
00000031074	<i>Fgf3</i>	FGF	LG	00000021540	<i>Smad5</i>	TGFB	TF
00000050917	<i>Fgf4</i>	FGF	LG	00000027796	<i>Smad9</i>	TGFB	TF
00000029337	<i>Fgf5</i>	FGF	LG	00000001761	<i>Smo</i>	Hh	RC
00000000183	<i>Fgf6</i>	FGF	LG	00000038037	<i>Socs1</i>	FGF	IC
00000027208	<i>Fgf7</i>	FGF	LG	00000020027	<i>Socs2</i>	FGF	IC
00000021974	<i>Fgf9</i>	FGF	LG	00000053113	<i>Socs3</i>	FGF	IC
00000031565	<i>Fgfr1</i>	FGF	RC	00000024241	<i>Sos1</i>	FGF	IC
00000030849	<i>Fgfr2</i>	FGF	RC	00000034801	<i>Sos2</i>	FGF	IC
00000054252	<i>Fgfr3</i>	FGF	RC	00000036169	<i>Sostdc1</i>	TGFB/Wnt	LG
00000005320	<i>Fgfr4</i>	FGF	RC	00000022114	<i>Spry2</i>	FGF	IC
00000020170	<i>Frs2</i>	FGF	IC	00000024427	<i>Spry4</i>	FGF	IC
00000021765	<i>Fst</i>	TGFB	LG	00000026104	<i>Stat1</i>	FGF	TF
00000011658	<i>Fuz</i>	Hh	IC	00000040033	<i>Stat2</i>	FGF	TF
00000044674	<i>Fzd1</i>	Wnt	RC	00000004040	<i>Stat3</i>	FGF	TF
00000081683	<i>Fzd10</i>	Wnt	RC	00000062939	<i>Stat4</i>	FGF	TF
00000050288	<i>Fzd2</i>	Wnt	RC	00000004043	<i>Stat5a</i>	FGF	TF
00000007989	<i>Fzd3</i>	Wnt	RC	00000020919	<i>Stat5b</i>	FGF	TF
00000049791	<i>Fzd4</i>	Wnt	RC	00000002147	<i>Stat6</i>	FGF	TF

Ensembl ID	Gene name	Pathway	Type	Ensembl ID	Gene name	Pathway	Type
00000045005	<i>Fzd5</i>	Wnt	RC	00000028718	<i>Stil</i>	Hh	IC
00000022297	<i>Fzd6</i>	Wnt	RC	00000025231	<i>Sufu</i>	Hh	IC
00000041075	<i>Fzd7</i>	Wnt	RC	00000034601	<i>Ta3</i>	Hh	IC
00000036904	<i>Fzd8</i>	Wnt	RC	00000015755	<i>Tab2</i>	EDA	IC
00000049551	<i>Fzd9</i>	Wnt	RC	00000000782	<i>Tcf7</i>	Wnt	TF
00000031714	<i>Gab1</i>	FGF	IC	00000055799	<i>Tcf7l1</i>	Wnt	TF
00000052957	<i>Gas1</i>	Hh	IC	00000024985	<i>Tcf7l2</i>	Wnt	TF
00000109523	<i>Gdf1</i>	TGFB	LG	00000038593	<i>Tctn1</i>	Hh	IC
00000025352	<i>Gdf11</i>	TGFB	LG	00000002603	<i>Tgfb1</i>	TGFB	LG
00000025407	<i>Gli1</i>	Hh	TF	00000039239	<i>Tgfb2</i>	TGFB	LG
00000048402	<i>Gli2</i>	Hh	TF	00000021253	<i>Tgfb3</i>	TGFB	LG
00000021318	<i>Gli3</i>	Hh	TF	00000007613	<i>Tgfb1</i>	TGFB	RC
00000059923	<i>Grb2</i>	FGF	IC	00000032440	<i>Tgfb2</i>	TGFB	RC
00000050069	<i>Grem2</i>	TGFB	LG	00000029287	<i>Tgfb3</i>	TGFB	RC
00000024858	<i>Grk2</i>	Hh	IC	00000008305	<i>Tle1</i>	Wnt	TF
00000057177	<i>Gsk3a</i>	Wnt	IC	00000032280	<i>Tle3</i>	Wnt	TF
00000022812	<i>Gsk3b</i>	Hh/Wnt	IC	00000026875	<i>Traf1</i>	EDA	IC
00000022528	<i>Hes1</i>	Notch	TF	00000026942	<i>Traf2</i>	EDA	IC
00000025499	<i>Hras</i>	FGF/TGFB	IC	00000021277	<i>Traf3</i>	EDA	IC
00000038564	<i>lft172</i>	Hh	IC	00000017386	<i>Traf4</i>	EDA /TGFB	IC
00000017858	<i>lft52</i>	Hh	IC	00000027164	<i>Traf6</i>	EDA/TGFB	IC
00000032965	<i>lft57</i>	Hh	IC	00000028173	<i>Wls</i>	Wnt	TF
00000040040	<i>lft88</i>	Hh	IC	00000022997	<i>Wnt1</i>	Wnt	LG
00000006538	<i>lhh</i>	Hh	LG	00000026167	<i>Wnt10a</i>	Wnt	LG
00000031537	<i>lkbkb</i>	EDA	IC	00000022996	<i>Wnt10b</i>	Wnt	LG
00000004221	<i>lkbkg</i>	EDA	IC	00000015957	<i>Wnt11</i>	Wnt	LG
00000041324	<i>Inhba</i>	TGFB	LG	00000029671	<i>Wnt16</i>	Wnt	LG
00000037035	<i>Inhbb</i>	TGFB	LG	00000010797	<i>Wnt2</i>	Wnt	LG
00000060798	<i>Intu</i>	Hh	IC	00000027840	<i>Wnt2b</i>	Wnt	LG
00000027598	<i>Itch</i>	Notch	IC	00000000125	<i>Wnt3</i>	Wnt	LG
00000027276	<i>Jag1</i>	Notch	LG	00000009900	<i>Wnt3a</i>	Wnt	LG
00000002799	<i>Jag2</i>	Notch	LG	00000036856	<i>Wnt4</i>	Wnt	LG
00000028530	<i>Jak1</i>	FGF	IC	00000021994	<i>Wnt5a</i>	Wnt	LG
00000024789	<i>Jak2</i>	FGF	IC	00000030170	<i>Wnt5b</i>	Wnt	LG
00000031805	<i>Jak3</i>	FGF	IC	00000033227	<i>Wnt6</i>	Wnt	LG
00000052684	<i>Jun</i>	TGFB	TF	00000030093	<i>Wnt7a</i>	Wnt	LG
00000046731	<i>Kctd11</i>	Hh	IC	00000022382	<i>Wnt7b</i>	Wnt	LG
00000018395	<i>Kif3a</i>	Hh	IC	00000012282	<i>Wnt8a</i>	Wnt	LG
00000050382	<i>Kif7</i>	Hh	IC	00000036961	<i>Wnt8b</i>	Wnt	LG
00000030265	<i>Kras</i>	FGF/TGFB	IC	00000000126	<i>Wnt9a</i>	Wnt	LG
00000027985	<i>Lef1</i>	Wnt	TF	00000018486	<i>Wnt9b</i>	Wnt	LG
00000029570	<i>Lfng</i>	Notch	IC	00000041961	<i>Znrf3</i>	Wnt	LG
00000027253	<i>Lrp4</i>	Wnt	RC				

Table S5. Descriptive statistics of the number of cells in which different gene types are expressed. The number of analyzed cells was 30930.

Type	<i>n</i>	Median	Mean	Range	SD
Progression and shape category genes					
Ligand	13	4585.0	7765.77	386–25360	7440.31
Receptor	7	13879.0	12897.14	607–23912	8261.00
Transcription factor	11	14165.0	13215.91	531–24359	8816.32
Intracellular	12	14522.0	15296.67	4247–30260	8741.45
Progression and shape category pathway genes					
Ligand	65	2308.0	4020.12	2–25360	5211.06
Receptor	38	8071.5	9437.92	101–27666	7831.50
Transcription factor	34	12832.0	12492.38	290–28213	8142.03
Intracellular	129	11919.0	12944.92	474–30770	8014.32

Appendix S1. Developmental keystone genes of mouse tooth development. Classification of genes whose null mutations affect the phenotype of the mouse first lower molar. The classification of each gene is usually based on multiple sources, with key references listed. Haplosufficiency is marked for progression and shape categories.

Gene name	Mouse Ensembl ID (ENSMUSG)	Category	Haplo-sufficient	Type of molecule	Mutant tooth phenotype	Ref.
<i>Acvr2a</i>	00000052155	progression	Yes	receptor	Bud stage arrest, partial penetrance	1
<i>Bmp4</i>	00000021835	progression	Yes?	signal	Wnt1 cKO: Bud or cap stage arrest	2 3
<i>Bmpr1a</i>	00000021796	progression	Yes	receptor	K14 cKO: Bud stage arrest	4
<i>Ctnna1</i>	00000037815	progression	Yes?	intracellular	K14 cKO: Cap stage arrest	5
<i>Ctnnb1</i>	00000006932	progression	Yes?	intracellular	K14 cKO: Early bud stage arrest	6
<i>Dicer1</i>	00000041415	progression	Yes?	intracellular	Wnt1 cKO: Arrest at cap stage or absence	7 8
<i>Fgfr2</i>	00000030849	progression	Yes	receptor	Bud stage arrest	9
<i>Inhba</i>	00000041324	progression	Yes?	signal	Bud stage arrest	10 11
<i>Lef1</i>	00000027985	progression	Yes	transcription factor	Late bud stage arrest	12 13
<i>Msx1</i>	00000048450	progression	Yes?	transcription factor	Bud stage arrest	14
<i>Pax9</i>	00000001497	progression	Yes	transcription factor	Bud stage arrest	15
<i>Pitx2</i>	00000028023	progression	Yes	transcription factor	Bud stage arrest	16 17
<i>Runx2</i>	00000039153	progression	Yes	transcription factor	Late bud stage arrest, extra budding	18 19
<i>Shh</i>	00000002633	progression	Yes	signal	K14 cKO: Cap stage arrest	20
<i>Trp63</i>	00000022510	progression	Yes?	transcription factor	Dental placode stage arrest	21 22
<i>Apc</i>	00000005871	shape	Yes	intracellular	K14 cKO: Deformed supernumerary teeth	23
<i>Barx1</i>	00000021381	shape	Yes	transcription factor	Slightly smaller molars	24
<i>Bcl11b</i>	00000048251	shape	Yes?	transcription factor	Blunted cusps and reduced stellate reticuli	25 26
<i>Bmp2</i>	00000027358	shape	Yes	signal	Osx cKO: Brittle and slightly misshaped, third molars missing	27 28
<i>Bmp7</i>	00000008999	shape	Yes	signal	Abnormal cusp patterning	29 30
<i>Chuk</i>	00000025199	shape	Yes	intracellular	Flattened cusps, no third molars	31
<i>Eda</i>	00000059327	shape	Yes	signal	Reduced number and size of cusps of the first and second molars	32 33 34
<i>Edar</i>	00000003227	shape	Yes	receptor	Reduced teeth	33 35
<i>Edaradd</i>	00000095105	shape	Yes	intracellular	Severe agenesis, cone/peg shaped teeth	36 37
<i>Evc</i>	00000029122	shape	Yes	intracellular	Conical molars, size reduction of the first molar and an enamel defect	38
<i>Fgf10</i>	00000021732	shape	Yes	signal	Smaller molars and/or different shape	39 40
<i>Fgf20</i>	00000031603	shape	Yes	signal	Smaller molars with mildly altered cusp pattern	41
<i>Fgf3</i>	00000031074	shape	Yes	signal	Change of cusp pattern	42
<i>Foxi3</i>	00000055874	shape	Yes	transcription factor	K14 cKO: Misshaped teeth	43
<i>Fst</i>	00000021765	shape	Yes?	signal	Non-polarized cusps with multiple shallow foldings	44 45
<i>Gas1</i>	00000052957	shape	Yes?	intracellular	Supernumerary teeth, molars slightly misshaped	46
<i>Jag2</i>	00000002799	shape	Yes	signal	Increase of cusp number	47
<i>Lrp4</i>	00000027253	shape	Yes?	receptor	Deformed supernumerary teeth	48 49
<i>Msx2</i>	00000021469	shape	Yes	transcription factor	Msx2 null: Misshaped teeth, enamel hypoplasia	50
<i>Pdgfra</i>	00000029231	shape	Yes?	receptor	Slight change in cusp pattern	51
<i>Rps6ka3</i>	00000031309	shape	Yes	intracellular	Small change in tooth shape, often additional molars	52
<i>Smo</i>	00000001761	shape	Yes	receptor	K14 cKO: Cusp pattern changed, molars fused and reduced	53
<i>Sostdc1</i>	00000036169	shape	Yes	signal	Change in cusp pattern,	54

Gene name	Mouse Ensembl ID (ENSMUSG)	Category	Haplo-sufficient	Type of molecule	Mutant tooth phenotype	Ref.
					supernumerary teeth	
<i>Sp6</i>	00000038560	shape	Yes?	transcription factor	Supernumerary teeth, reduction of cusp number	55
<i>Spry2</i>	00000022114	shape	Yes?	intracellular	Slight change in cusp pattern, supernumerary teeth	56
<i>Spry4</i>	00000024427	shape	Yes?	intracellular	Slight change in cusp pattern, supernumerary teeth	56
<i>Wnt10a</i>	00000026167	shape	Yes?	signal	Abnormal cusp patterning, smaller and supernumerary teeth	57
<i>Yap1</i>	00000053110	shape	Yes?	intracellular	K14 cKO: Smaller and abnormal tooth, fewer and flattened cusps	58
<i>Alpl</i>	00000028766	tissue		other	Dentinogenesis imperfecta	59
<i>Ambn</i>	00000029288	tissue		other	Severe enamel hypoplasia, odontogenic tumors	60
<i>Amelx</i>	00000031354	tissue		other	Enamel hypoplasia	61
<i>Amtn</i>	00000029282	tissue		other	Amelogenesis imperfecta	62
<i>Bmi1</i>	00000026739	tissue		transcription factor	Amylogenesis imperfecta	63
<i>Dmp1</i>	00000029307	tissue		other	Dentinogenesis imperfecta	64 65 66
<i>Dspp</i>	00000053268	tissue		other	Dentinogenesis imperfecta	67 68
<i>Enam</i>	00000029286	tissue		other	No enamel	69
<i>Evc2</i>	00000050248	tissue		intracellular	Amelogenesis imperfecta	70
<i>Fam20a</i>	00000020614	tissue		other	Severe amelogenesis imperfecta	71
<i>Fam20c</i>	00000025854	tissue		other	Severe amelogenesis imperfecta	71
<i>Fgfr1</i>	00000031565	tissue		receptor	K14 cKO: Amelogenesis imperfecta	72
<i>Gdnf</i>	00000022144	tissue		signal	Amelogenesis imperfecta, dentinogenesis imperfecta	73
<i>Grem2</i>	00000050069	tissue		signal	Enamel hypoplasia, dentine hypoplasia	74
<i>Klk4</i>	00000006948	tissue		other	Amelogenesis imperfecta	75
<i>Lama3</i>	00000024421	tissue		other	Enamel hypoplasia	76
<i>Mmp14</i>	00000000957	tissue		other	Amelogenesis imperfecta	77 78
<i>Mmp20</i>	00000018620	tissue		other	Amelogenesis imperfecta, enamel hypoplasia	79
<i>Mtor</i>	00000028991	tissue		intracellular	Osx1 cKO: Dentine hypoplasia	80
<i>Nectin1</i>	00000032012	tissue		other	Amelogenesis imperfecta	81 81
<i>Perp</i>	00000019851	tissue		other	Amelogenesis imperfecta	82
<i>Pkd2</i>	00000034462	tissue		other	Wnt1 cKO: Abnormal pulp cavities, fractured roots	83
<i>Postn</i>	00000027750	tissue		other	Amelogenesis imperfect and abnormal periodontal ligament	84 85
<i>Slc13a5</i>	00000020805	tissue		other	Enamel hypoplasia	86
<i>Slc39a13</i>	00000002105	tissue		other	Dentine hypoplasia	87
<i>Sp3</i>	00000027109	tissue		transcription factor	Enamel hypoplasia, dentinogenesis imperfecta	88
<i>Spp12a</i>	00000027366	tissue		other	Enamel hypoplasia	89
<i>Acvr2b</i>	00000061393	double		receptor	Double KO (ACVR2A+/-, ACVR2B-/-): Bud stage arrest	11
<i>Dlx1</i>	00000041911	double		transcription factor	Double KO: Placode stage arrest	90
<i>Dlx2</i>	00000023391	double		transcription factor	Double KO: Placode stage arrest	90
<i>Dlx3</i>	00000001510	double		transcription factor	Double KO: Misshaped teeth	91
<i>Dlx4</i>	00000020871	double		transcription factor	Double KO: Misshaped teeth	91
<i>Dlx5</i>	00000029755	double		transcription factor	Double KO: Misshaped teeth	92
<i>Dlx6</i>	00000029754	double		transcription factor	Double KO: Misshaped teeth	92
<i>Gli2</i>	00000048402	double		transcription factor	Double KO: Initiation stage arrest	93
<i>Gli3</i>	00000021318	double		transcription factor	Double KO: Initiation stage arrest	93

Gene name	Mouse Ensembl ID (ENSMUSG)	Category	Haplo-sufficient	Type of molecule	Mutant tooth phenotype	Ref.
<i>Lhx6</i>	00000026890	double		transcription factor	Double KO: Initiation stage arrest	94
<i>Lhx8</i>	00000096225	double		transcription factor	Double KO: Initiation stage arrest	94
<i>Csf1</i>	00000014599	no eruption		signal	No eruption of molars	95
<i>Fos</i>	00000021250	no eruption		transcription factor	No eruption of molars	96
<i>Ostm1</i>	00000038280	no eruption		other	No eruption of molars	97
<i>Pthlh</i>	00000048776	no eruption		signal	No eruption of molars	98
<i>Tcirg1</i>	00000001750	no eruption		other	No eruption of molars	99
<i>Traf6</i>	00000027164	no eruption		intracellular	No eruption of molars	100 101 102

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