

SUPPLEMENTAL MATERIAL

LEGENDS TO SUPPLEMENTARY FIGURES

Supplemental Fig. 1. Preparation of E13.5 and E14.5 palatal mesenchyme. *A-D*. Quantitative RT-PCR analysis of palatal epithelium (Ep) and mesenchyme (Mes) separated from E13.5 and E14.5 *Tgfb²^{fl/fl}* control (open columns) and *Tgfb²^{fl/fl};Wnt1-Cre* (closed columns) palates (see Materials and Methods). Keratin 14 (K14) served as an epithelial specific marker. **p*<0.05.

Supplemental Fig. 2. Protein expression of FGF9 and PITX2 in the palate of *Tgfb²^{fl/fl}* control and *Tgfb²^{fl/fl};Wnt1-Cre* mice. *A,B*. Immunohistochemical analysis of FGF9 (A) and PITX2 (B) in the palate of *Tgfb²^{fl/fl}* control and *Tgfb²^{fl/fl};Wnt1-Cre* mice at E13.5 and E14.5. Arrows indicate expression. Inserts (upper right) show low magnification of the craniofacial region. Insert in *B* (bottom left) shows high magnification of the dotted area.

Supplemental Fig. 3. Preparation of E14.5 palatal mesenchyme from *Tgfb²^{fl/fl}* control (open columns) and *Tgfb²^{fl/fl};Wnt1-Cre* (closed columns) mice. Quantitative RT-PCR analysis of Cytokeratin 14 (K14) in the separated epithelium (Ep) and mesenchyme (Mes) during the preparation of the palatal mesenchyme organ culture used in Fig. 2*B*. **p*<0.05.

Supplemental Fig. 4. Schematic diagram of TGFβ-mediated FGF9 signaling. TGFβ signaling contributes to mesenchymal cell proliferation via a *Fgf9-Pitx2* signaling pathway during palatal formation.

LEGENDS TO SUPPLEMENTARY TABLES

Supplemental Table 1. List of genes with cleft palate phenotype in mice.

Supplemental Table 2. Conserved SMAD recognition sequences in the *FGF9* gene.

^aThe binding site motif is underlined in all cases. It is placed on blue if the sequence is conserved in all eight species except dog and/or horse and in red if conserved in all eight species. These species include: human (Build 19), chimpanzee (Build 2.1.3), orangutan (Build 2.0.2), rhesus macaque (Build 1.0), mouse (Build 37), rat (Build 3.4), dog (Build 2) and horse (Build equCab2).

Supplemental Table 3. Conserved ATF2 recognition sequences in the *FGF9* gene.

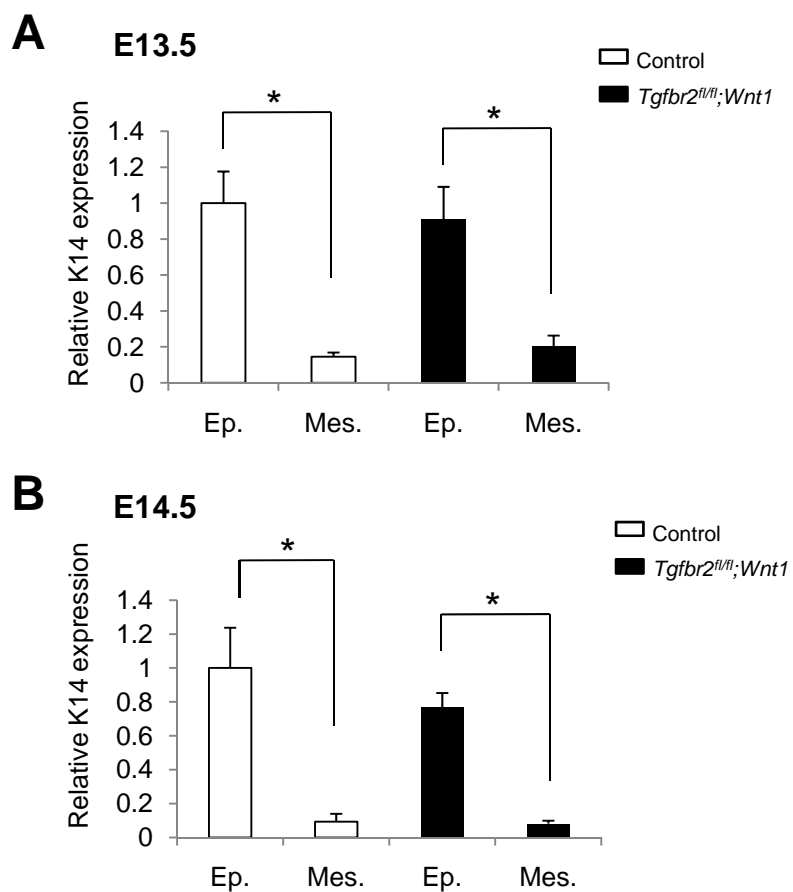
^aThe binding site motif is underlined and placed in red to indicate that it is conserved in all eight species: (human (Build 19), chimpanzee (Build 2.1.3), orangutan (Build 2.0.2), rhesus macaque (Build 1.0), mouse (Build 37), rat (Build 3.4), dog (Build 2) and horse (Build equCab2).

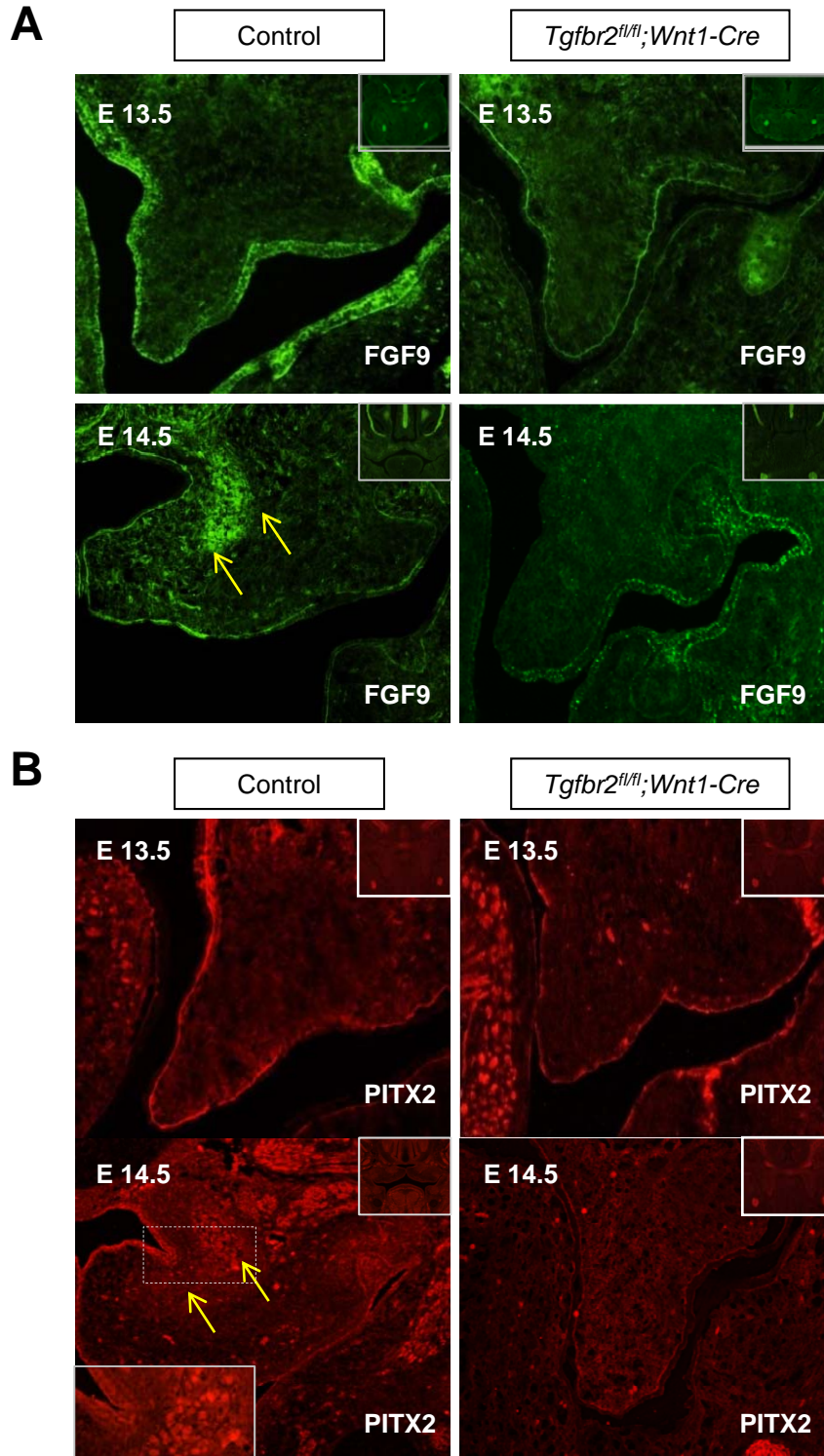
Supplemental Table 4. Conserved SMAD recognition sequences in the *PITX2* gene.

^aThe binding site motif is underlined in all cases. It is placed on blue if the sequence is conserved in all eight species except dog and/or horse and in red if conserved in all eight species. These include: human (Build 19), chimpanzee (Build 2.1.3), orangutan (Build 2.0.2), rhesus macaque (Build 1.0), mouse (Build 37), rat (Build 3.4), dog (Build 2) and horse (Build equCab2).

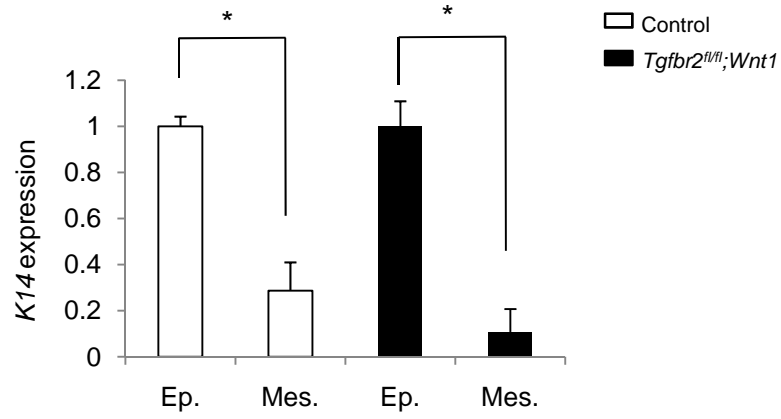
Supplemental Table 5. Conserved ATF2 recognition sequences in the *PITX2* gene

^aThe binding site motif is underlined and placed in red to indicate that it is conserved in all eight species: (human (Build 19), chimpanzee (Build 2.1.3), orangutan (Build 2.0.2), rhesus macaque (Build 1.0), mouse (Build 37), rat (Build 3.4), dog (Build 2) and horse (Build equCab2).

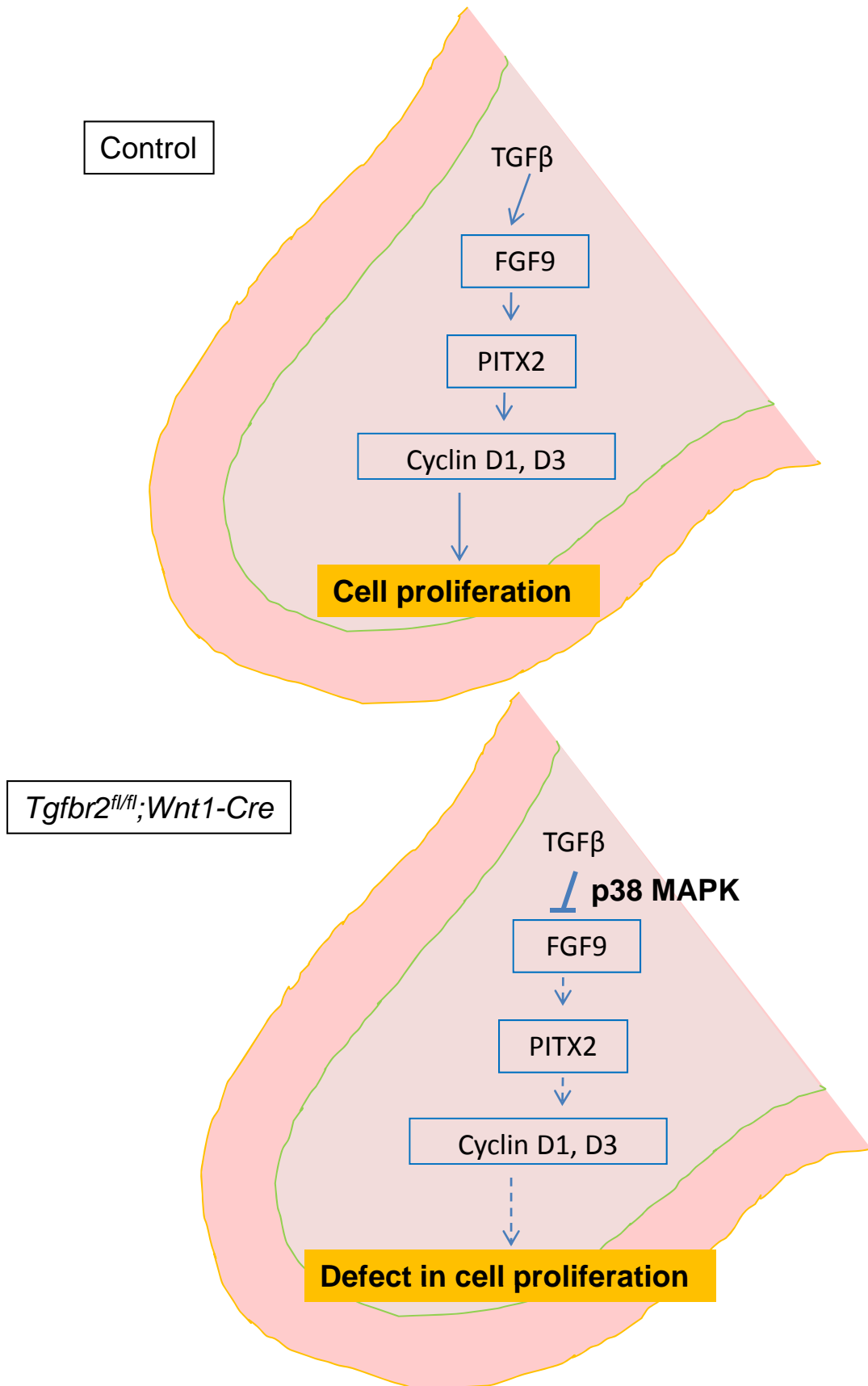




Supplemental Figure 3. Iwata *et al.*



Supplemental Figure 4. Iwata *et al.*



Supplemental Table 1.

Allele Symbol	Gene	Chromosome	Category
Abn	abnormal	UN	Spontaneous
Acan	aggrecan	7	Spontaneous
Acvr1	activin A receptor, type 1	2	Targeted (knock-out) Targeted (conditional)
Acvr2a	activin A receptor IIA	2	Targeted (knock-out)
Aecp	vitamin A enhanced cleft palate	17	QTL
Ahr	aryl-hydrocarbon receptor	12	Not applicable Targeted (reporter)
Akap8		17	Gene trapped
Alx1	ALX homeobox 1	10	Targeted (knock-out)
Alx4	aristaless-like homeobox 4	2	Targeted (knock-out)
Am	amputated	8	Radiation induced
Apaf1	apoptotic peptidase activating factor 1	10	Gene trapped
Arid5b	AT rich interactive domain 5B (Mrf1 like)	10	Gene trapped
Asph	aspartate beta-hydroxylase	4	Targeted (knock-out)
Axin1	axin 1	17	Targeted (knock-in)
Ay	nonagouti	2	Spontaneous
AY074887	cDNA sequence AY074887	9	Targeted (knock-out)
Barx1	BarH-like homeobox 1	13	Targeted (knock-out)
Bmi1	Bmi1 polycomb ring finger oncogene	2	Targeted (knock-out)
Bmp7	bone morphogenetic protein 7	2	Targeted (conditional) Targeted (knock-out)
Br	brachyrrhine	17	Targeted (knock-out)
Cacna1s	calcium channel, voltage-dependent, L type, alpha 1S subunit	1	Spontaneous
Cask	calcium/calmodulin-dependent serine protein kinase (MAGUK family)	X	Transgenic (random, gene disruption) Targeted (knock-out) Targeted (conditional)
Cdkn1a	cyclin-dependent kinase inhibitor 1A (p21)	17	Targeted (knock-out)
Cdkn1c	cyclin-dependent kinase inhibitor 1C (p57)	7	Targeted (knock-out)
Chd7	chromodomain helicase DNA binding protein 7	4	Chemically induced (ENU)
Chrd	chordin	16	Targeted (knock-out)
Chuk	conserved helix-loop-helix ubiquitous kinase	19	Targeted (knock-out)
Clf1	cleft lip 1	11	Spontaneous
Clf2	cleft lip 2	13	Spontaneous
Clptm1	cleft lip and palate associated transmembrane protein 1	7	Targeted (knock-out)
Col2a1	collagen, type II, alpha 1	15	Radiation induced Targeted (knock-in) Targeted (knock-out)
Col11a1	collagen, type XI, alpha 1	3	Spontaneous
Col11a2	collagen, type XI, alpha 2	17	Targeted (knock-out)
Col12a1	collagen, type XII, alpha 1	9	Targeted (knock-out)
Cp2	cleft palate 2	UN	Targeted (knock-out)
Crebbp	CREB binding protein	16	Targeted (knock-in)
Crk	v-crk sarcoma virus CT10 oncogene homolog (avian)	11	Targeted (knock-out)
Crn	cranioschisis	UN	Spontaneous
Csp1	cleft secondary palate 1	4	Chemically induced (ENU)
Csp2	cleft secondary palate 2	UN	Chemically induced (ENU)
Ctgf	connective tissue growth factor	10	Targeted (knock-out)
Ctnnbip1	catenin beta interacting protein 1	4	Targeted (knock-out)
Cycsp	curly tail and cleft secondary palate	3	Chemically induced (ENU)
Dhcr7	7-dehydrocholesterol reductase	7	Targeted (knock-out)
Dkk1	dickkopf homolog 1 (Xenopus laevis)	19	Targeted (knock-out)
Dlg1	discs, large homolog 1 (Drosophila)	16	Gene trapped Targeted (knock-out)
Dlx1	distal-less homeobox 1	2	Targeted (knock-out)
Dlx2	distal-less homeobox 2	2	Targeted (reporter) Targeted (knock-out)
Dlx1 & Dlx2		2 2	Targeted (Dlx1; knock-out) Targeted (Dlx2; knock-out)
Dlx5	distal-less homeobox 5	6	Targeted (reporter) Targeted (knock-out)

Supplemental Table 1. (Continued)

Allele Symbol	Gene	Chromosome	Category
Dph1	DPH1 homolog (<i>S. cerevisiae</i>)	11	Targeted (knock-out)
Dxcp1	dexamethasone induced cleft palate 1	17	QTL
Dxcp2	dexamethasone induced cleft palate 2	17	QTL
Dxcp3	dexamethasone induced cleft palate 3	17	Targeted (knock-out)
Edn1	endothelin 1	13	Targeted (knock-out)
Ednra	endothelin receptor type A	8	Targeted (knock-out)
Ednrb	endothelin receptor type B	14	Radiation induced
Efna5	ephrin A5	17	Targeted (knock-out)
Efnb1	ephrin B1	X	Targeted (knock-out) Targeted (conditional)
Egfr	epidermal growth factor receptor	11	Targeted (knock-out)
Eya1	eyes absent 1 homolog (<i>Drosophila</i>)	1	Targeted (knock-out)
Eya4	eyes absent 4 homolog (<i>Drosophila</i>)	10	Targeted (knock-out)
Far	first arch	2	Spontaneous
Fbxo11	F-box protein 11	17	Chemically induced (ENU)
Fgf9	fibroblast growth factor 9	14	Targeted (knock-out)
Fgf10	fibroblast growth factor 10	13	Targeted (knock-out)
Fgf18	fibroblast growth factor 18	11	Targeted (knock-out)
Fgfr1	fibroblast growth factor receptor 1	8	Targeted (knock-out) Targeted (conditional, Wnt1-Cre)
Fgfr2	fibroblast growth factor receptor 2	7	Targeted (knock-out) Targeted (knock-in) Targeted (reporter) Targeted (conditional, K14-Cre)
Figf	fidgetin	2	Spontaneous
Flna	filamin, alpha	X	Chemically induced (ENU)
Foxc2	forkhead box C2	8	Targeted (knock-out)
Foxd3	forkhead box D3	4	Targeted (conditional)
Foxe1	forkhead box E1 (thyroid transcription factor 2)	4	Targeted (knock-out)
Foxf2	forkhead box F2	13	Targeted (knock-out)
Fst	follistatin	13	Targeted (knock-out)
Gab1	growth factor receptor bound protein 2-associated protein 1	8	Targeted (reporter) Targeted (knock-in)
Gabbr3	gamma-aminobutyric acid (GABA-A) receptor, subunit beta 3	7	Targeted (knock-out) Targeted (conditional)
Gad1	glutamic acid decarboxylase 1	2	Targeted (knock-out) Targeted (reporter)
Gad2	glutamic acid decarboxylase 2	2	Targeted (knock-out)
Gbx2	gastrulation brain homeobox 2	1	Targeted (knock-out)
Glce	glucuronyl C5-epimerase	9	Targeted (knock-out)
Gli2	GLI-Kruppel family member GLI2	1	Targeted (knock-out)
Gli3	GLI-Kruppel family member GLI3	13	Spontaneous Targeted (other)
Grb2	growth factor receptor bound protein 2	11	Targeted (knock-in)
Gsk3b	glycogen synthase kinase 3 beta	16	Targeted (knock-out)
H19 & Igf2r	H19 fetal liver mRNA Insulin-like growth factor 2 receptor	7 17	Targeted (H19; knock-out) Targeted (Igf2r; knock-out)
Hand2	heart and neural crest derivatives expressed transcript 2	8	Targeted (conditional) Targeted (knock-out)
Hic1	hypermethylated in cancer 1	11	Targeted (knock-out)
Hoxa1	homeo box A1	6	Targeted (knock-out)
Hoxa2	homeo box A2	6	Targeted (knock-in) Targeted (knock-out)
Hpmd	hypoplastic mandible	UN	Chemically induced (ENU)
Hs2st1	heparan sulfate 2-O-sulfotransferase 1	3	Gene trapped
Hspg2	perlecan (heparan sulfate proteoglycan 2)	4	Targeted (knock-out)
Ift88	intraflagellar transport 88 homolog (<i>Chlamydomonas</i>)	14	Transgenic (random, gene disruption)
Igf2	insulin-like growth factor 2	7	Transgenic (random, gene disruption)

Supplemental Table 1. (Continued)

Allele Symbol	Gene	Chromosome	Category
Ilk	integrin linked kinase	7	Targeted (conditional)
Impad1	inositol monophosphatase domain containing 1	4	Targeted (knock-out)
Inhba	inhibin beta-A	13	Targeted (knock-out)
Inhbb	inhibin beta-B	1	Targeted (knock-out)
Inpp5e	inositol polyphosphate-5-phosphatase E	2	Targeted (knock-out)
Insig1 & Insig2	insulin induced gene, 1 and 2	5	Targeted (Insig1; knock-out)
		1	Targeted (Insig2; knock-out)
Irf6	interferon regulatory factor 6	1	Gene trapped Targeted (knock-in)
Itgav	integrin alpha V	2	Targeted (knock-out)
Itgb1	integrin beta 1 (fibronectin receptor beta)	8	Targeted (conditional) Targeted (knock-out)
Itgb8	integrin beta 8	12	Targeted (knock-out)
Jag2	jagged 2	12	Targeted (knock-out)
Jmjd6	jumonji domain containing 6	11	Targeted (knock-out)
Kcnj2	potassium inwardly-rectifying channel, subfamily J, member 2	11	Targeted (knock-out)
Krt5	keratin 5	15	Targeted (knock-out)
Lbr & Dhcr14	lamin B receptor	1	Targeted (Lbr; knock-out) Targeted (Dhcr14; knock-out)
Lgl	legless	12	Transgenic (random, gene disruption)
Lhx8	LIM homeobox protein 8	3	Targeted (knock-out) Targeted (reporter)
Lrp6	low density lipoprotein receptor-related protein 6	6	Targeted (knock-out)
Lse	low set ears	UN	Spontaneous
Luzp1	leucine zipper protein 1	4	Targeted (knock-out)
Mdm2 & Mdm4	transformed mouse 3T3 cell double minute, 2 and 4	10	Targeted (Mdm2; knock-out)
		1	Targeted (Mdm4; knock-out)
Meox2	mesenchyme homeobox 2	12	Targeted (knock-out)
Met	met proto-oncogene	6	Targeted (knock-out)
Mmp14	matrix metalloproteinase 14 (membrane-inserted)	14	Targeted (knock-out)
Mmp16	matrix metalloproteinase 16	4	Targeted (knock-out)
Mn1	meningioma 1	5	Targeted (knock-out)
Mnt	max binding protein	11	Targeted (knock-out)
Msc	musculin	1	Targeted (knock-out)
Msx1	homeobox, msh-like 1	5	Targeted (reporter) Targeted (conditional) Targeted (knock-out)
Msx2	homeobox, msh-like 2	13	Targeted (knock-out)
Myst3	MYST histone acetyltransferase (monocytic leukemia) 3	8	Targeted (knock-out)
Ncor2	nuclear receptor co-receptor 2	5	Targeted (knock-out)
Ndst1	N-deacetylase/N-sulfotransferase (heparan glucosaminyl) 1	18	Targeted (knock-out)
Oca2	oculocutaneous albinism II	7	Radiation induced
Oel	open eyelids with cleft palate	UN	Spontaneous
Ofd1	oral-facial-digital syndrome 1 gene homolog (human)	X	Targeted (conditional)
Osr2	odd-skipped related 2 (Drosophila)	15	Targeted (reporter)
Pad	paddle	UN	Spontaneous
Papss2	3'-phosphoadenosine 5'-phosphosulfate synthase 2	19	Spontaneous
Pax3	paired box gene 3	1	Targeted (conditional)
Pax9	paired box gene 9	12	Targeted (conditional) Targeted (reporter)
Pc	phocomelic	UN	Spontaneous
Pcgf2	polycomb group ring finger 2	11	Targeted (knock-out)
Pcp	polydactyly with cleft palate	UN	Spontaneous
Pdgfc	platelet-derived growth factor, C polypeptide	3	Targeted (knock-out) Targeted (reporter)
Pdgfra	platelet-derived growth factor receptor, alpha polypeptide	5	Targeted (knock-in) Targeted (knock-out) Targeted (conditional)
Pdgfrb	platelet-derived growth factor receptor, beta polypeptide	18	Targeted (conditional)

Supplemental Table 1. (Continued)

Allele Symbol	Gene	Chromosome	Category
Pds5a	PDS5, regulator of cohesion maintenance, homolog A (<i>S. cerevisiae</i>)	5	Targeted (knock-out)
Pds5b	PDS5, regulator of cohesion maintenance, homolog B (<i>S. cerevisiae</i>)	5	Targeted (knock-out)
Phc1	polyhomeotic-like 1 (<i>Drosophila</i>)	6	Targeted (knock-out)
Phc2	polyhomeotic-like 2 (<i>Drosophila</i>)	4	Targeted (knock-out)
Pitx1	paired-like homeodomain transcription factor 1	13	Targeted (knock-out)
Pitx2	paired-like homeodomain transcription factor 2	3	Targeted (knock-out) Targeted (reporter)
Pkdcc	protein kinase domain containing, cytoplasmic	17	Targeted (knock-out)
Plekha1	pleckstrin homology domain containing, family A (phosphoinositide binding specific) member 1	7	Gene trapped
Prdm16	PR domain containing 16	4	Targeted (knock-out)
Prrx1	paired related homeobox 1	1	Targeted (reporter) Targeted (knock-out)
Prrx2	paired related homeobox 2	2	Targeted (reporter) Targeted (knock-out)
Ptd	palate-tail-digits abnormality	X	Not applicable
Ptprf & Ptprs	protein tyrosine phosphatase, receptor type, F and S	4 17	Targeted (Ptprf; knock-in) Targeted (Ptprs; knock-out)
Pvrl1	poliovirus receptor-related 1	9	Targeted (knock-out)
Pygo2	pygopus 2	3	Targeted (knock-out)
Rad23b	RAD23b homolog (<i>S. cerevisiae</i>)	4	Targeted (knock-out)
Rax	retina and anterior neural fold homeobox	18	Targeted (knock-out)
Recql4	RecQ protein-like 4	15	Targeted (knock-out)
Rfng	RFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase	11	Targeted (knock-out)
Ror2	receptor tyrosine kinase-like orphan receptor 2	13	Targeted (reporter) Targeted (knock-out)
Rspo2	R-spondin 2 homolog (<i>Xenopus laevis</i>)	15	Transgenic (random, gene disruption) Targeted (reporter)
Runx2	runt related transcription factor 2	17	Targeted (reporter)
Ryk	receptor-like tyrosine kinase	9	Targeted (reporter)
Satb2	special AT-rich sequence binding protein 2	1	Targeted (knock-in) Targeted (knock-out)
Sc5d	sterol-C5-desaturase (fungal ERG3, delta-5-desaturase) homolog (<i>S. cerevisiae</i>)	9	Targeted (knock-out)
Sfn	stratifin	4	Radiation induced
Shh	sonic hedgehog	5	Targeted (knock-out) Targeted (conditional, K14-Cre)
Sho	shorthead	UN	Spontaneous
Shox2	short stature homeobox 2	3	Targeted (knock-out)
Sim2	single-minded homolog 2 (<i>Drosophila</i>)	16	Targeted (knock-out)
Six1	sine oculis-related homeobox 1 homolog (<i>Drosophila</i>)	12	Targeted (reporter)
Six3	sine oculis-related homeobox 3 homolog (<i>Drosophila</i>)	17	Targeted (knock-out)
Six4	sine oculis-related homeobox 4 homolog (<i>Drosophila</i>)	12	Targeted (reporter)
Slc32a1	solute carrier family 32 (GABA vesicular transporter)	2	Targeted (knock-out)
Sme	small ear	UN	Radiation induced
Snai1	snail homolog 1 (<i>Drosophila</i>)	2	Targeted (knock-out) Targeted (conditional)
Snai2	snail homolog 2 (<i>Drosophila</i>)	16	Targeted (knock-out)
Sos1	Son of sevenless homolog 1 (<i>Drosophila</i>)	17	Targeted (reporter)
Sox4	SRY (sex determining region Y)-box containing gene 4	13	Targeted (knock-in)
Sox5	SRY (sex determining region Y)-box containing gene 5	6	Targeted (reporter)
Sox9	SRY (sex determining region Y)-box containing gene 9	11	Targeted (knock-out) Targeted (reporter) Targeted (conditional)
Sox11	SRY-box containing gene 11	12	Targeted (reporter)
Spry2	sprouty homolog 2 (<i>Drosophila</i>)	14	Targeted (knock-out)
Srn	siren	UN	Spontaneous
Srt	shorty	17	Chemically induced (ENU)
Sumo1	SMT3 suppressor of mif two 3 homolog 1 (yeast)	1	Gene trapped

Supplemental Table 1. (Continued)

Allele Symbol	Gene	Chromosome	Category
Tbx1	T-box 1	16	Targeted (conditional) Targeted (knock-out) Targeted (reporter)
Tbx10	T-box 10	19	Spontaneous
Tbx22	T-box 22	X	Targeted (knock-out)
Tcf21	transcription factor 21	10	Targeted (reporter)
Tcfap2a	transcription factor AP-2, alpha	13	Targeted (reporter) Targeted (conditional)
Tcof1	Treacher Collins Franceschetti syndrome 1, homolog	18	Targeted (knock-out)
Tg(CAG-cre)1Nagy	transgene insertion 1, Andras Nagy	UN	Transgenic (Cre/Flp)
Tg (CMV-cre)1Cgn	transgene insertion 1, University of Cologne	UN	Transgenic (Cre/Flp)
Tg(COL2A1)1Prc	transgene insertion 1, Darwin J Prockop	UN	Transgenic (random, gene disruption)
Tg(Col2a1-cre)1Asz	transgene insertion 1, Attila Aszodi	UN	Transgenic (Cre/Flp)
Tg(KRT14-cre)1Amc	transgene insertion 1, Andrew P McMahon	UN	Transgenic (Cre/Flp)
Tg(Msx2-cre)5Rem	transgene insertion 5, Robert E Maxson	UN	Transgenic (Cre/Flp)
Tg(Myh6-Hoxb7)18Ssp	transgene insertion 18, S Steven Potter	UN	Transgenic (random, gene disruption)
Tg(Myh6-Ncor2)1Kjep	transgene insertion 1, Kristen Jepsen	UN	Transgenic (random, gene disruption)
Tg(Pgk1-cre)1Lni	transgene insertion 1, Peter Lonai	UN	Transgenic (Cre/Flp)
Tg(Prm-cre)58Og	transgene insertion 58, Stephen O'Gorman	UN	Transgenic (Cre/Flp)
Tg(Spry2)2Tpo	transgene insertion 2, Timothy P O'Brien	UN	Transgenic (random, gene disruption)
Tg(Spry2)69Tpo	transgene insertion 69, Timothy P O'Brien	UN	Transgenic (random, gene disruption)
Tg(Wnt1-cre)11Rth	transgene insertion 11, David H Rowitch	UN	Transgenic (Cre/Flp)
Tgfb2	transforming growth factor, beta 2	1	Targeted (knock-out)
Tgfb3	transforming growth factor, beta 3	12	Targeted (knock-in) Targeted (knock-out)
Tgfr1	transforming growth factor, beta receptor I	4	Targeted (Floxed/Frt, K14-Cre) Targeted (Floxed/Frt, Wnt1-Cre)
Tgfr2	transforming growth factor, beta receptor II	9	Targeted (Floxed/Frt, K14-Cre) Targeted (Floxed/Frt, Wnt1-Cre)
Trp63	transformation related protein 63	16	Targeted (knock-out)
Tshz1	teashirt zinc finger family member 1	18	Targeted (knock-out)
Tw	twirler	18	Spontaneous
Twist1	twist gene homolog 1 (Drosophila)	12	Chemically induced (ENU)
Ur	urogenital	UN	Spontaneous
Vax1	ventral anterior homeobox containing gene 1	19	Targeted (knock-out) Targeted (reporter)
Vax2	ventral anterior homeobox containing gene 2	6	Targeted (knock-out)
Vegfa	vascular endothelial growth factor A	17	Targeted (knock-out)
Whsc1	Wolf-Hirschhorn syndrome candidate 1 (human)	5	Targeted (knock-out)
Wnt9b	wingless-type MMTV integration site 9B	11	Targeted (knock-out)
Zeb1	zinc finger E-box binding homeobox 1	18	Targeted (reporter)

Supplemental Table 2. Conserved SMAD recognition sequences in the *FGF9* gene

Position relative to human transcription start site	Genomic context	Binding site sequence context ^a	Conservation of 4-bp site
-2014	Upstream	CCT <u>GTCT</u> CTC	All but horse, dog
-1723	Upstream	GCA <u>AGAC</u> GCA	All but dog
-1513	Upstream	TTC <u>GTCT</u> TCA	All but horse, dog
-1376	Upstream	TC <u>AGTCT</u> CTG	All but dog
-1317	Upstream	CAA <u>GTCT</u> CGG	All 8 species
-1270	Upstream	CTA <u>AGAC</u> AAT	All 8 species
-231	Upstream	TGA <u>GTCT</u> CGG	All but horse, dog
332	Exon 1	GAT <u>GTCT</u> GCA	All 8 species
527	Exon 1	TGA <u>AGAC</u> CCTT	All 8 species
625	Exon 1	CTT <u>AGAC</u> TAT	All 8 species
1615	Intron 1	AGG <u>GTCT</u> GAA	All 8 species
1946	Intron 1	TGC <u>AGAC</u> TCG	All but dog
2112	Intron 1	ACT <u>AGAC</u> TGT	All 8 species
3020	Intron 1	TGG <u>GTCT</u> GGC	All but horse, dog
4247	Intron 1	GCG <u>GTCT</u> CCC	All 8 species

^aThe binding site motif is underlined in all cases. It is placed on blue if the sequence is conserved in all eight species except dog and/or horse and in red if conserved in all eight species. These species include: human (Build 19), chimpanzee (Build 2.1.3), orangutan (Build 2.0.2), rhesus macaque (Build 1.0), mouse (Build 37), rat (Build 3.4), dog (Build 2) and horse (Build equCab2).

Supplemental Table 3. Conserved ATF2 recognition sequences in the *FGF9* gene

Position relative to human transcription start site	Genomic context	Binding site sequence context ^a	Conservation of 8-bp site
397	Exon 1	TTCT <u>TGACGTAG</u> CCC	All 8 species

^aThe binding site motif is underlined and placed in red to indicate that it is conserved in all eight species: (human (Build 19), chimpanzee (Build 2.1.3), orangutan (Build 2.0.2), rhesus macaque (Build 1.0), mouse (Build 37), rat (Build 3.4), dog (Build 2) and horse (Build equCab2)).

Supplemental Table 4. Conserved SMAD recognition sequences in the *PITX2* gene

Position relative to human transcription start site	Genomic context	Binding site sequence context ^a	Conservation of 4-bp site
717	Intron 1	GGA <u>GTCT</u> TCC	All but horse
4132	Exon 2	TCT <u>AGACT</u> CT	All 8 species
4658	Exon 2	TCT <u>GTCT</u> CCC	All but horse, dog
5113	Exon 2	GCG <u>AGAC</u> CGA	All 8 species
5317	Exon 2	CGG <u>AGAC</u> AGC	All 8 species
5387	Intron 2	CGA <u>GTCT</u> GGA	All but horse, dog
5519	Intron 2	CAC <u>AGAC</u> ACT	All but dog

^aThe binding site motif is underlined in all cases. It is placed on blue if the sequence is conserved in all eight species except dog and/or horse and in red if conserved in all eight species. These include: human (Build 19), chimpanzee (Build 2.1.3), orangutan (Build 2.0.2), rhesus macaque (Build 1.0), mouse (Build 37), rat (Build 3.4), dog (Build 2) and horse (Build equCab2).

Supplemental Table 5. Conserved ATF2 recognition sequences in the *PITX2* gene

Position relative to human transcription start site	Genomic context	Binding site sequence context ^a	Conservation of 4-bp site
5032	Exon 2	TGCT <u>AGACGTCA</u> CGT	All 8 species

^aThe binding site motif is underlined and placed in red to indicate that it is conserved in all eight species: (human (Build 19), chimpanzee (Build 2.1.3), orangutan (Build 2.0.2), rhesus macaque (Build 1.0), mouse (Build 37), rat (Build 3.4), dog (Build 2) and horse (Build equCab2)).