

Active node	Activated node	Reference	System
Sox9	Sox9	[6;40]	Chick chondrocytes
bFGF	NF- κ B	[59]	Human chondrocytes
BMP	Ihh	[18;49;57;91;92]	Chicken/mice embryo (fetal growth plate)
BMP	Col-X	[1;91]	ATDC5 (mouse chondrogenic cell line)/ chicken chondrocytes (in vivo)
BMP	BMPR	[92]	Canonical
BMP	FGFR1	[92]	Mouse chondrocytes
BMP	STAT1	[92]	Mouse chondrocytes
BMP	GATA4	[58;65]	Mouse cardiomyocytes (P19CL6)
BMP2-4-7	Runx2	[72]	Human C2C12, (mouse premyoblasts), C3H10T1/2 (mouse mesenchymal) human bone marrow derived cells, RoS 17.2.8 (rat osteosarcoma)
BMP6	Col-X, AP	[19;72]	Chick sternal cephalic chondrocytes
BMP pathway	R-smad	[1;18]	Canonical
BMPR	p38 kinase	[64;75;91]	Mouse embryonic fibroblasts (MEF)
cAMP	PKA	[49]	Canonical
CCND1	Runx2	[95]	Rat chondroprogenitor (RCJ3.1C5.18), C3H10T1/2
ERK 1/2	R-smad	[37;71]	Mouse lung, C2C12, MEFs
ERK1/2	Runx2	[9;28;89]	Human MSC, MC3T3 preosteoblasts (mouse)
FGF	Ras	[17]	Canonical
FGF	ERK	[48;91;92]	Chick embryo, mouse chondrocytes
bFGF	BMP7	[38;56]	Mouse limb bud
FGF18	FGFR3	[22;46;49;62]	Mice growth plate in vivo
FGF18	Ihh	[18;46]	Mice growth plate in vivo
FGFR1	NF- κ B	[73]	C2C12, T1/2, MC615 (chondrogenic mouse limb)
FGFR3	STAT1	[18;63;69]	Rat chondrosarcoma, murine primary chondrocytes
FGFs	Wnts	[18;80]	Mouse and chick limb buds
GATA4	MEF2C	[12]	Mouse anterior heart field in vivo
Gli	BMP2-7	[13]	HaCaT (Human adult)

			low Calcium Temperature keratinocytes)
Gli	TGF β 1	[13]	"
Gli	BMP6	[13]	"
Gli	BMP2	[63;78]	Mouse and human BMP2 promoter
Gli2	Wnt11, Ptch1	[41;45]	HaCat, MEFs
Gli2	MMP13	[13]	HaCaT
Gli2	PTHrP	[55;76]	Breast cancer, fetal mouse growth plate
Gli2	BMP4-7	[30]	Mouse and human promoter, osteoblastic Hos and renal COS-7 cells (human osteosarcoma and simian)
Gli2	FGFR1	[36]	Fetal growth plate
Gli2,3	Gli1	[41]	HaCaT (canonical?)
Gli3	PTHrP	[36;49]	Fetal growth plate
GSK3 β	Gli	[27]	Drosophila, canonical
GSK3 β	Gli2,3	[24]	Canonical
HDAC4	MEF2C	[35]	Mouse and chick limb bud cells
Ihh	PTHrP	[18;57;83]	Mouse fetal growth plate
Ihh	PPR	[50]	Mouse fetal growth plate (indirect)
Ihh	Ptch1, Gli1	[24]	canonical
Ihh	Wnt3a	[52]	Mouse limb explants, primary chondrocytes
Ihh pathway	Gli3	[1;18;49;51;88]	Canonical
MEF2C	Runx2	[5;49;54]	Mouse fetal growth plate
MEF2C	Col-X	[35;54]	Mouse and chick limb bud cells
MEF2C	Smaddlx5	[74;84]	Mouse branchial arch (enhancer element)
NF- κ B	Smad7	[7;11;53]	Mv1Lu, COS (simian), and NIH-3T3 (murine fibroblast cell lines)
NF- κ B	BMP2	[14;78;87]	MTC-23 (mouse chondrogenic cell line), mouse fetal growth plate
NF- κ B	Sox9	[34;73]	C2C12, C3H10T1/2, MC615
NF- κ B	MMP13	[59]	Human articular chondrocytes
Nkx3.2	Runx2	[18;49;67;90]	C3H10T1/2, murine (rib) chondrocytes, chick embryo explant
Noggin	BMP	[1;91]	canonical
p38 kinase	Sox9	[64]	MEFs
PKA	Sox9	[23;39;40]	Chicken primary chondrocytes, COS-7, RCS (rat

			chondrosarcoma)
PKA	Gli2,3	[24;85]	canonical
PKA	Col-X	[68]	Human and primary bovine chondrocytes
PKA	HDAC4	[35]	Mouse and chick limb bud cells
PKA	CCND1	[95]	Mouse fetal growth plate, COS, C3H10T1/2, RCJ3.1C5.18
PKA	Runx2	[43]	Chick sternal chondrocytes
PThrP	cAMP	[23]	canonical
PThrP	Nkx3.2	[49;67]	Chick embryo explant
R-smad	Dsh	[47]	C57BL/6 and ST2 mice primary bone marrow stromal cells
R-smad (BMP2)	PPR	[79]	C2C12 OB differentiation
Runx2	Col-X	[1;49]	Chick chondrocytes, functional sites in mice and chick promoter
Runx2	Ihh	[9;21;49;66;93]	Mouse fetal growth plate (+ promoter), MDA-MB-231 breast cancer cell line
FGFR1, FGF2-8	Runx2	[72;98]	MC3T3-E1 mouse calvarial cells, C3H10T1/2, in vivo
Runx2	FGF18	[28]	Mouse fetal growth plate
Runx2	MMP13	[21]	Mouse fetal growth plate
Runx2	MEF2C	[21]	Mouse fetal growth plate
Runx2-Smad complex		[9;26]	HeLa & mouse embryo
R-smad	Runx2	[61]	C2C12
Smad1	Col-X	[35]	Mouse and chick limb bud cells
Smad2,3	Col-II	[15]	Human MSCs and SW1353 (human chondrosarcoma)
Smad3	HDAC4	[28;29]	NIH3T3 (MEFs), ROS17/2.8, primary calvarial mouse osteoblasts
Smad3	Runx2	[3;11;72]	MC3T3-E1, ROS17/2.8, primary calvarial mouse osteoblasts
Smad3 β-catenin Lef/Tcf complex	Gli2	[10]	HaCaT, HepG2 (human)
Smad4	Smadcomplex	[1;18]	canonical
Smad7	R-smad	[1;18]	canonical
Smadcomplex	Runx2	[77;96]	C2C12
Smadcomplex	Smaddlx5	[33;44]	C2C12

Smad11x5	Runx2	[44]	C2C12
Sox9	Col-II	[16;18]	Human MSCs, chondrocytes, SW1353 (canonical)
Sox9	Nkx3.2	[90]	C3H10T1/2, murine (fetal) chondrocytes,
Sox9	β -catenin	[20;81]	Mouse limb bud cells, murine primary chondrocytes , L cells (fibroblasts), CHO (chinese hamster ovary), HEK293 (Human embryonic kidney), COS1
Sox9	CCND1	[25;32]	Mouse fetal growth plate, SW1353 (human)
Sox9	Runx2	[97]	Mouse fetal growth plate, ROS17/2.8, COS7, human CMD1 cartilage (indirect)
STAT1	CKI	[92]	Mouse fetal growth plate
STAT1	Smad7	[11;82]	U4A cells (human fibrosarcoma), human monocytic leukaemia U937 cells, epidermoid carcinoma A431 cells
STAT1	Ihh	[70]	Mouse fetal growth plate
STAT1	PPR	[38;60]	Mouse fetal growth plate (indirect)
TGF β	Sox9	[8;91]	Chick embryos
TGF β	Ras	[11]	Canonical
TGF β	Smad3	[2;28]	Canonical
TGF β	CCND1	[4;42]	HCS-2/8, human chondrocyte-like cell line
TGF β 1	Smad11x5	[44]	MC3T3-E1, ROS 17/2.8, and ST2 (mouse bone marrow osteogenic cells), ATDC5, C2C12 cells, C3H10T1/2, 3T3-L1 (adipogenic)
Wnt pathway	β -catenin	[49]	canonical
Wnt pathway	FGFs	[18;31]	Chick embryo
Wnt3a	Ras	[94]	Canonical (NIH3T3, L cells)
β -catenin	FGF8	[86]	Mouse <i>in vivo</i> (facial), chick limb bud

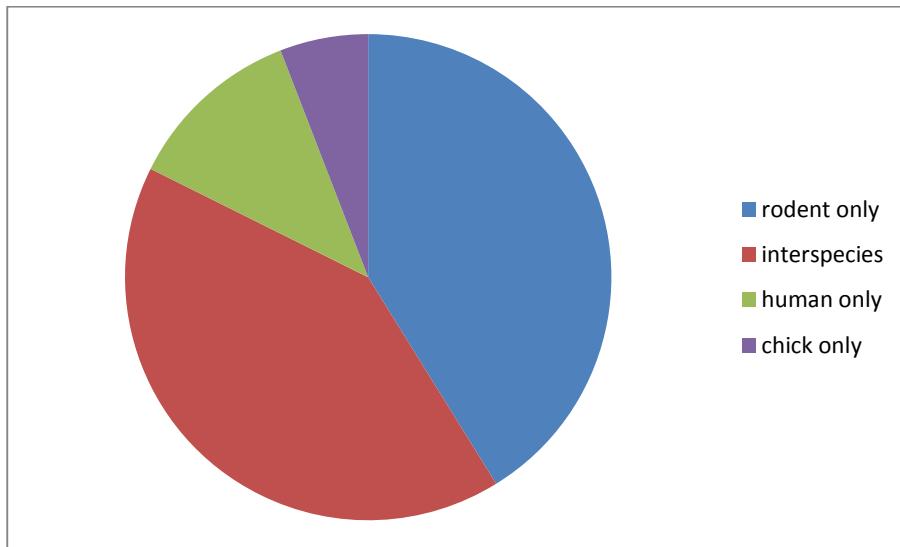


Figure 1: Overview of the sources of interactions by species. 82 % of the interactions were verified for mice.

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