

Factor	Factor Full	Producing Cell	Target Cell	Function	Reference
Arg1	arginase 1	macrophages	fibroblasts, endothelial cells	Metabolizes L-arginine to produce polyamines and proline; Promotes collagen synthesis and cell proliferation	(Daley et al., 2010; Gordon and Martinez, 2010)
BMP	bone morphogenetic protein	hypertrophic chondrocytes, endothelial cells	mesenchymal lineage cells	Stimulates differentiation to chondrocyte or osteoblast lineage; Cartilage calcificator	(Tsuji et al., 2006, 2008, 2010; Yu et al., 2010)
FGF	fibroblast growth factor	inflammatory cells, mesenchymal lineage cells	mesenchymal lineage cells	Increases MSC number and migration, induces angiogenesis	(Hurley et al., 2016)
GDF5	growth differentiation factor-5	chondrocytes, perichondrium	chondrocytes, perichondrium	Impairs cartilaginous matrix deposition, reduced callus size, decreased biomechanics during fracture repair	(Coleman et al., 2011)
IGF	insulin growth factor	mesenchymal stem cells, proliferating chondrocytes, hypertrophic chondrocytes	osteoblast, chondrocytes, endothelial cells	Involved in osteoblast differentiation and coordinates chondrocyte, osteoclast and endothelial response during fracture repair	(Wildemann et al., 2003a)
IHH	indian hedgehog	prehypertrophic chondrocytes	chondrocytes, osteoblasts	Regulates chondrogenesis and osteoblastogenesis; Differential expression patterns in stabilized versus non-stabilized fracture	(Le et al., 2001)
IL1	interleukin-1	CAM	inflammatory cells, mesenchymal lineage cells	Pro-inflammatory cytokine; Increases Cox2 production and prostaglandin; promotes proliferation of osteoblasts and MSCs; inhibits differentiator	(Lange et al., 2010)
IL10	interleukin-10	AMM	osteoclasts, osteoblasts	Anti-inflammatory cytokine; chondrocyte proliferation/differentiation	(Jung et al., 2013)
IL20	interleukin-20	inflammatory cell, epithelial cells, endothelial cells	osteoclasts, osteoblasts	Anti-inflammatory cytokine; inhibits osteoblastogenesis; promotes osteoclastogenesis	(Hsu et al., 2016)
IL4/13	interleukin-4/13	mesenchymal stem cells	osteoblasts	Anti-inflammatory cytokine; maintenance of cortical bone mass	(Silfverswärd et al., 2008)
IL6	interleukin-6	CAM, mesenchymal lineage cells	Other inflammatory cells, mesenchymal lineage cells	Pro-inflammatory cytokine; Results in delays in callus mineralization, maturation, and conversion to bone	(Yang et al., 2007)
MCP1 (CCL2)	monocyte chemoattractant protein-1 (chemokine ligand-2)	platelets	monocytes	Promotes neutrophil recruitment; Disruption leads to a reduction in mesenchymal cell infiltrator	(Xing et al., 2010)
MIF	migration inhibitory factor	lymphocytes, other inflammatory cells	monocytes	Pro-inflammatory cytokine; disruption results in decreased callus strength and osteogenesis; regulates osteoclast migration	(Kobayashi et al., 2011)
MMP13	matrix metalloproteinase-13	hypertrophic chondrocytes	cartilage matrix	Endopeptidase which remodeling of extracellular matrix; Disruption delays callus resorptior	(Behonick et al., 2007)
MMP9	matrix metalloproteinase-9	endothelial cells	cartilage matrix	Degrades the cartilage matrix of hypertrophic chondrocytes; Regulates callus angiogenesis; disruption impairs ossification	(Colnot et al., 2003; Wang et al., 2013a)
PDGF	platelet derived growth factor	platelets, other inflammatory cells, hypertrophic chondrocytes	mesenchymal lineage cells, endothelial progenitor cells	Drives chemotaxis and proliferation of osteoblasts, Stimulates VEGF expression in endothelial cells	(Caplan and Correa, 2011; Fiedler et al., 2002)
PG	Prostaglandin (Produced by COX1/2)	macrophages and AMM	mesenchymal lineage cells	Stimulates bone formation; Inhibition of COX1/2 (NSAIDs) delays healing	(Zhang et al., 2002)
PIGF	placental growth factor	hypertrophic chondrocytes	endothelial progenitor cells	Enhances vascular invasion	(Maes et al., 2006)
PTHrP	Parathyroid hormone-related peptide	mesenchymal stem cells, perichondrial cells, chondrocytes	chondrocytes	Stimulates chondrocyte proliferation; Disruption leads to impaired endochondral bone repair due to small cartilage callus	(Okazaki et al., 2003; Wang et al., 2013b)
RANKL	Receptor activator of nuclear factor kappa-B ligand	hypertrophic chondrocytes, mesenchymal lineage cells	osteoclasts precursors	Regulates osteoclast differentiation; Disruption can increase bone strength	(Dougall et al., 1999)
SDF1	stem cell derived factor	inflammatory cells	mesenchymal stem cells, endothelial progenitor cells	Binds to CXCR4 to promote mesenchymal stem cell chemotaxis	(Kitaori et al., 2009)
TGFb	transforming growth factor b	AMM, mesenchymal lineage cells	chondrocytes	Stimulates matrix protein synthesis; Drives increased chondrogenesis and chondrocyte proliferation	(Wildemann et al., 2003b)
TNF	tumor necrosis factor	CAM		Enhances neutrophil recruitment and production of CCL2; Positively influences early and late healing	(Chan et al., 2015; Lam et al., 2000)
TSP	Thrombospondin	mesenchymal stem cells	endothelial cells	Regulates vascularization; Disruption can promote ischemic healing	(Miedel et al., 2013; Taylor et al., 2009)
VEGF	vascular endothelial growth factor	inflammatory cells, mesenchymal lineage cells	endothelial cells	Promotes blood vessel formation and osteoblastogenesis; Disruption impairs callus formation	(Gerber et al., 1999; Street et al., 2002; Zelzer et al., 2002)
Wnt	Wnt	osteoblasts, chondrocytes, progenitor cells	osteoblasts, chondrocytes, progenitors cells	Secreted glycoprotein which inhibits the degradation of β -catenin; Upregulated during fracture repair; Disruption impairs fracture healing	(Day et al., 2005; Secreto et al., 2009; Zhong et al., 2006)