

Supplementary Table

Table S1: Downstream effectors of YAP/TAZ and their roles in skeletal related signaling pathways.			
Downstream factors/effectors	Altered pathways	Research subjects (cell lines/clinical samples/animal models)	Key references
TEAD, Runx2	Hippo-dependent signaling, osteogenesis, stem cell homeostasis	MSCs, HBM-MSCs	[16,17]
CGRP	YAP/TAZ-mediated osteogenesis, cell	BMSCs	[18]

	migration		
F-actin, AMOT130	Mechanical signal transduction, nuclear localization of YAP/TAZ	HBM-MSCs	[23]
OTM - F-actin, AMOT	Inhibition of Hippo signaling, YAP/TAZ activation	Periodontal tissues	[24]
TAZ-Runx2 complex	Osteogenic differentiation, inhibition of adipogenesis	Human ADSCs, <i>in vivo</i> β -TCP model	[27,29]
TAZ Activator	Phosphorylation of TAZ,	ADSCs <i>in vivo</i> ,	[29]

(TM-25659)	osteocalcin promoter activation	β -TCP loaded ADSCs	
RhoA	ECM stiffness, cytoskeletal tension, osteogenesis	ADSCs, HBM-MSCs	[30,31]
CAV1	ECM stiffness, YAP response through actin	Fibroblast (MEF)	[32]
Integrins	ECM mechanosensing, activation of YAP/TAZ	Osteoblasts, MLO-Y4 cells	[35,37,38]
Src Kinase, p130Cas	JNK phosphorylation, YAP/TAZ activation	Osteoblasts	[37]

TNF- α , NF- κ B	Osteoclast function inhibition, osteolytic disease prevention	Osteoclasts	[42]
CGRP, OSM, STAT3	YAP/TAZ-mediated osteogenesis, inflammation	Bone tissue macrophages, M2 macrophages	[46,47]
BMP2	Osteogenic differentiation promotion	MSCs, Macrophages	[48]
VEGF	Actin cytoskeleton, YAP translocation	BMSCs, EPCs	[49,50]
MBP2a	Osteoblast differentiation	Mesenchymal Cells,	[52]

	inhibition	Bone Progenitor Cells	
SOX9	Inhibition of chondrocyte differentiation and proliferation	Chondrocytes	[55,60]
SR3335, antagonist	ROR α Counteracted TNF- α -induced apoptosis, inhibited YAP phosphorylation	NPCs	[59]
Lat B	Disrupted actin filaments, altered YAP	NPCs	[60]

	activity		
Chsy3, Yap1 Activation	Enhanced ECM anabolic gene expression, suppressed catabolic genes	NPCs	[63]
Irisin, LATS/YAP/CTGF signaling	Promoted NPC anabolism and delayed intervertebral disc degeneration	NPCs	[64]
TAZ, Runx2	Mediated Wnt and BMP signaling in osteoblast	Osteoblasts	[67]

	differentiation		
Exosomal miR-1263, YAP Activation	Counteracted apoptosis in osteoporosis BMSCs	Osteoporosis BMSCs	[71]
TGF- β /BMP/Smad Pathway	YAP as a coactivator, promoted HO progression	HO Models	[72]
DDR2, YAP/TAZ	Modulated focal adhesion and ECM-MLin receptor interactions impacted HO development	HO Models	[74]

<p>RhoA, YAP1, ACVR1</p> <p>Mutant</p>	<p>Enhanced BMP</p> <p>signaling, increased</p> <p>sensitivity to mechanical</p> <p>forces, promoted HO</p>	<p>FOP Models</p>	<p>[75]</p>
<p>TEAD: TEA domain transcription factor, Runx2: Runt-related transcription factor 2, HBM-MSCs: Human bone marrow mesenchymal stem cells, CGRP: Calcitonin gene-related peptide, BMSCs: Bone marrow stem cells, AMOT130: Angiomotin 130 kDa, ADSCs: Adipose-derived stem cells, TM-25659: TAZ Activator (compound), RhoA: Ras homolog family member A, CAV1: Caveolin-1, MEF: Mouse embryonic fibroblasts, ECM: Extracellular matrix, MLO-Y4: Mouse lineage osteoblast-like 4 Cells, Src Kinase: Proto-oncogene tyrosine-protein kinase Src, p130Cas: Cas family adapter protein, TNF-α: Tumor necrosis factor alpha, NF-κB: Nuclear factor kappa B, OSM: Oncostatin M, STAT3: Signal transducer and activator of transcription 3, BMP2: Bone morphogenetic protein 2, VEGF: Vascular endothelial growth</p>			

factor, MBP2a: Myelin basic protein 2a, SOX9: SRY-box transcription factor 9, SR3335: Reverse agonist of ROR α , Lat B: Latrunculin B, Actin Polymerization Inhibitor, Chsy3: Chondroitin sulfate synthase 3, Yap1: Yes-associated protein 1, LATS: Large tumor suppressor kinase, CTGF: Connective tissue growth factor, PI3K: Phosphoinositide 3-kinase, AKT: Protein kinase B, FOP: Fibrodysplasia ossificans progressive, HO: Heterotopic ossification, DDR2: Discoidin domain receptor 2, ACVR1: Activin A receptor type 1, EPCs: Endothelial progenitor cells, NPCs: Nucleus pulposus cells