Supplementary Table 1
MicroRNAs involved in cartilage-protective mechanisms

MicroRNA	Tissue	Target Gene	Role of microRNA	Reference
miR-140	Articular cartilage	ADAMTS-5, IGFBP-5	Cartilage development and homeostasis	[1-3]
miR-30a	Articular cartilage	ADAMTS-5	Cartilage homeostasis	[4]
miR-9	Articular cartilage	NF-Kb MMP-13	Chondrocyte proliferation, anti-apoptosis Increases Type II Collagen	[5] [6]
miR-502-5p	Articular cartilage	TRAF2	Anti-apoptotic, anti-catabolic, anti-inflammatory	[7]
miR-145	Articular cartilage	TNFRSF11B	Regulates chondrocyte proliferation and fibrosis	[8]
miR-146a	Articular cartilage	TRAF6	Chondrocyte proliferation, anti-apoptosis. Inhibits NF-κB pathway	[9]
miR-26a-5p **miR26a, miR-26b**	Articular cartilage Articular cartilage	iNOS KPNA3	Cartilage homeostasis Promotes NF-κB p65 translocation	[10] [11]
miR-105	Articular cartilage	Runx2	Inhibits Runx2 activation and ADAMTS expression	[12]
miR-320a	Articular cartilage	BMI-1, RUNX2 MMP-13	Chondrocyte viability Chondrogenesis	[13] [14]
miR-411	Articular cartilage	MMP-13	Regulates catabolic signaling pathways in chondrocytes	[15]
miR-221-3p	Articular cartilage	SDF1	Prevents ECM degradation	[16]

miR-222	Articular cartilage	HDAC-4	Controls cartilage degradation via HDAC-mediated regulation of MMPs.	[17]
miR-27a	Synovium	FSTL1	Prevents synovial fibroblast migration and invasion	[18]
miR-27b	Articular cartilage Articular cartilage	MMP-13 Leptin	Anti-catabolic Inhibits NF-κB signaling	[19] [20]
miR-33	Articular cartilage	CCL2	Regulates monocyte chemotaxis	[21]
miR-130a	Articular cartilage	TNF-α (indirect)	Anti-inflammatory	[22]
miR-193b	Articular cartilage	TGFB2, TGFB3 MMP-19	Inhibits early chondrogenesis, regulates inflammation by repressing TNF-α expression	[23, 24]
miR-602 & miR-608	Articular cartilage	SHH	Regulates chondrocyte development and hypertrophic differentiation	[25]
miR-148a	Articular cartilage	Col10A1, MMP13, ADAMTS-5	Promotes hyaline cartilage production	[26]
miR-127-5p	Articular cartilage	MMP-13	Anti-catabolic	[27]
miR-488	Articular cartilage	ZIP-8	Chondrocyte differentiation and cartilage development	[28]
miR-558	Articular cartilage	COX-2	Anti-catabolic	[29]
miR-149	Articular cartilage	TNF-α	Anti-inflammatory	[30]
miR-125b	Articular cartilage	ADAMTS-4	Prevents aggrecan loss	[31]

miR-15a	Articular cartilage	ADAMTS-5	Pro-anabolic	[32]
miR-92a-3p	Articular cartilage	ADAMTS-4, ADAMTS-5	Anti-catabolic	[33]
		HDAC2	Increases collagen deposition	[34]
miR-19a	Articular cartilage	SOX9	Promotes chondrocyte viability and migration through NF-κB pathway	[35]
miR-199a-3p	Articular cartilage	COX-2	Anti-catabolic	[36]
miR-370	Articular cartilage	SHMT-2	Regulates apoptosis	[37]
miR-373	Articular cartilage	MECP-2	Regulates apoptosis	[37, 38]
		P2X7R	Anti-inflammatory	
miR-146 (late-stage OA)	Articular cartilage	IRAK-1, TRAF6, BCL2	Mediates NF-κB signaling Promotes autophagy by inhibiting Bcl-2	[39, 40]
miR-142-3p	Articular cartilage	HMGB1	Anti-apoptotic, anti-inflammatory	[41]
miR-210	Articular cartilage	DR6, HIF-3α	Inhibits NF-κB pathway, anti-apoptotic, promotes chondrocyte proliferation and ECM deposition	[42, 43]
miR-365	Articular cartilage	HIF-2α	Prevents IL-1β-mediated ECM loss	[44]
miR-24	Articular cartilage	$P16^{INK4A}$	Regulates chondrocyte senescence	[45]
miR-17-5p	Articular cartilage	p62/SQSTM1	Induces autophagy	[46]
miR-155	Synovium	MMP-3, MMP-1	Suppresses proliferation and invasion of synovial fibroblasts, anti-inflammatory	[47]

miR-98	Articular cartilage	Not identified	Anti-apoptotic	[48]
miR-188-5p	Synovium	DNMT	Regulates canonical Wnt pathway, decreases synovial fibroblast proliferation	[49]
miR-152	Synovium	DNMT	Regulates canonical Wnt pathway, decreases synovial fibroblast proliferation	[50]
miR-451	Synovium	P38-MAPK	Reduces synovial fibroblast proliferation and cytokine expression	[51]
miR-29a	Synovium	VEGF	Protects against excessive synovial remodeling	[52]

Supplementary Table 2
MiRNAs involved in cartilage-destructive mechanisms

MicroRNA	Tissue	Target Gene	Role of microRNA	Reference
miR-381	Articular cartilage	MMP-13, HDAC4 IκBα	Chondrocyte hypertrophy and cartilage degeneration	[53, 54] [55]
miR-23a-3p	Articular cartilage	SMAD3	Inhibits ECM synthesis	[56]
miR-216b	Articular cartilage	SMAD3	Inhibits chondrocyte proliferation	[57]
miR-302b	Articular cartilage	SMAD3, NOTCH2	Promotes inflammation	[58]
miR-138-5p	Articular cartilage	FOXC1	Promotes cartilage degradation	[59]
miR-139	Articular cartilage	EIF4G2, MCPIP	Inhibits chondrocyte proliferation and migration, induces apoptosis (in association with miR-9)	[60, 61]
miR-365	Articular cartilage	HDAC4	Mediates mechanical stress, pro-inflammatory	[62]
miR-101	Articular cartilage	SOX9	Cartilage degradation	[63, 64]
miR-145	Articular cartilage	SOX9, SMAD3	Cartilage degradation	[65, 66]
miR-15a-5p	Articular cartilage	VEGFA	Apoptosis, matrix degradation	[67]

miR-16-5p	Articular cartilage	SMAD3	Cartilage degradation	[68]
miR-181	Articular cartilage	PTEN, GPD1L	Inhibits chondrocyte proliferation and promotes apoptosis	[69, 70]
miR-181b	Articular cartilage	Not identified	Negatively regulates chondrocyte differentiation/cartilage development	[71]
miR-21	Articular cartilage	GDF-5	Negatively regulates chondrogenesis	[72]
miR-146a	Articular cartilage	SMAD4	Activator in early OA	[73]
miR-98	Articular cartilage	BCL-2	Promotes chondrocyte apoptosis	[74]
miR-9	Articular cartilage	MCPIP-1, PRTG, SIRT1	Enhances IL-6 expression, negatively regulates chondrocyte survival/proliferation Mediates cell death induced by H_2O_2	[75, 76] [77]
miR-34a	Articular cartilage	SIRT1	Apoptosis Expression increases in chondrocytes exposed to H_2O_2	[78, 79] [80]
miR-4262	Articular cartilage	SIRT1	Decreases cell viability, autophagy and matrix synthesis through PI3K/AKT/mTOR pathway	[81]
miR-449a	Articular cartilage	SIRT1	Cartilage degradation	[82]
miR-223	Articular cartilage	PEX-16	Peroxisomal dysfunction (OA in patients with type 2 diabetes mellitus)	[83]

miR-155	Articular cartilage	Autophagy-related genes (ATG3, GABARAPL1, ATG5, ATG2B, LAMP2, FOXO3)	Autophagy inhibition	[84]
miR-30b	Articular cartilage	BECN1, ATG5	Autophagy inhibition, pro-apoptotic, ECM degradation	[85]
miR-483-5p	Articular cartilage	Matn3, Timp2	Stimulates chondrocyte hypertrophy, ECM degradation and cartilage angiogenesis	[86]
miR-181a-5p	Facet cartilage	ZNF440	Pro-inflammatory, pro-catabolic, cell death	[87]
miR-4454	Facet cartilage	ZNF440	Pro-inflammatory, pro-catabolic, cell death	[87]
miR-221	Synovium	Not identified	Pro-inflammatory, promotes cell migration and invasion	[88]
miR-18a	Synovium	TNFAIP3	Induces NF-κB signaling, ECM degradation, pro-inflammatory	[89, 90]
miR-19b	Synovium	Not identified	Induces NF-κB signaling	[91, 92]
miR-203	Synovium	Not identified	Increased MMP-1 and IL-6 via NF-κB pathway	[93]
miR-125b-5p	Synovium	SYVN1	Promotes apoptosis	[94]

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