SUPPLEMENTARY MATERIALS

MicroRNAs: Modulators of Cell Identity, and their Applications in Tissue Engineering

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Supplementary Table S1. A comprehensive list of the main microRNAs involved with the regulation of organ and tissue genesis and development in mammals.

microRNA	Validated Target(s)	Processes Regulated	Organism	Ref.
let-7e	Predicted targets only	Nephrogenesis (expression of early nephrogenic markers during embryoid bodies differentiation)	Mice	[1]
let-7f	TIMP-1	Osteogenesis (mesenchymal stem cell growth and osteogenic differentiation)	Human	[2]
miR-1	Hand2	Cardiogenesis (cardiomyocytes differentiation and ventricular cardiomyocyte proliferation)	Mice	[3]
	HDAC4	Skeletal muscle myogenesis (myogenic differentiation)	*Xenopus sp.* and mice	[4]
	Klf4	Smooth muscle myogenesis (myogenic differentiation of embryonic stem cells)	Mice	[5]
	kayak	Cardiogenesis (modulation of cardiac cell progenitors polarity)	*Drosophila sp.* and mice	[6]
	FZD7; FRS2	Cardiogenesis (cardiomyocyte differentiation of embryonic stem cell derived-multipotent cardiovascular progenitors)	Human	[7]
miR-7		Pancreatic function (potential role in the modulation of endocrine cell differentiation and/or function)	Human	[8]
	Pax6	Pancreatic development (modulation of endocrine cell differentiation)	Mice	[9]
miR-7a	Barx1	Stomach organogenesis (modulation of gastric epithelial differentiation)	Mice	[10]
miR-9*	Baf53a	Neurogenesis (dendritic development)	Mice	[11]
miR-10a	HOXA1	Megakaryocytopoiesis (megakaryocytic differentiation)	Human	[12]
	HDAC4	Smooth muscle myogenesis (myogenic differentiation of embryonic stem cells)	Mice	[13]
miR-15a	Dlk1	Cell proliferation (balance between cell density and cell growth in preadipocytes)	Mice	[14]
miR-17	Mapk14; Stat3	Pulmonary morphogenesis (modulation of embryonic epithelial branching)	Mice	[15]
	Predicted targets only	Osteogenesis (osteogenic differentiation of adipose-derived stem cells)	Human	[16]
miR-18b	FOXN1	Epithelial lineage development (epithelial lineage differentiation in embryonic stem cells and embryonal carcinoma pluripotent cells)	Human	[17]
miR-20a	Mapk14; Stat3	Pulmonary morphogenesis (modulation of embryonic epithelial branching)	Mice	[15]
	Predicted targets only	Osteogenesis (osteogenic differentiation of adipose-derived stem cells)	Human	[16]

(Table S1) contd….

microRNA	Validated Target(s)	Processes Regulated	Organism	Ref.
miR-20b	Predicted targets only	Osteogenesis (osteogenic differentiation of adipose-derived stem cells)	Human	[16]
miR-21	Predicted target only	Adipogenesis (adipocyte differentiation)	Mice	[18]
miR-22	HDAC6	Osteogenesis (osteogenic differentiation of mesenchymal stem cells)	Human	[19]
miR-23b	PKA	Chondrogenesis (chondrogenic differentiation of mesenchymal stem cells)	Human	[20]
miR-24	P16^{INK4a}	Inhibits chrondrogenesis in humans and mice	Human and mice	[21]
miR-26a	SMAD1	Osteogenesis (osteogenic differentiation of human adipose tissue-derived stem cells)	Human	[22]
	SMAD1; SMAD4	Vascular smooth muscle myogenesis and plasticity (modulation of smooth muscle cells proliferation, differentiation, migration, and apoptosis)	Human and mice	[23]
	TETs; TGD	Pancreatic development (pancreatic cell differentiation)	Mice	[24]
miR-27	Pax3	Skeletal muscle myogenesis (skeletal muscle stem cells differentiation)	Mice	[25]
miR-27a	GCA	Osteogenesis (osteogenic differentiation of mesenchymal stem cells)	Human	[26]
	sFRP1	Promotes osteoblastic differentiation in humans	Human	[27]
	Runx1	Hematopoiesis (megakaryocytic differentiation)	Human and mice	[28]
	PPARγ	Adipogenesis (adipogenic differentiation of preadipocytes)	Mice	[29]
miR-27b	PPARγ	Adipogenesis (adipogenic differentiation of multipotent adipose-derived stem cells)	Human	[30]
miR-29a	Osteonectin	Osteogenesis (osteoblastic differentiation)	Mice	[31]
miR-29b	HDAC4; TGFβ3; Acvr2a; Ctnnbip1; Dusp2	Osteogenesis (down-regulation of inhibitors of osteoblast differentiation)	Rat and mice	[32]
miR-29c	Osteonectin	Osteogenesis (osteoblastic differentiation)	Mice	[31]
miR-30a/c	Snail1	Chondrogenesis (tracheal chondrocytes differentiation)	Mice	[33]
miR-31	Predicted targets only	Adipogenesis (adipogenic differentiation of adipose-derived stem cells)	Rat	[34]
	Krt16; Krt17; Dlx3; Fgf10	Skin and appendages morphogenesis (anagen progression and hair shaft formation in the hair follicle)	Mice	[35]
	OSTERIX (SP7)	Osteogenesis (osteogenic differentiation of mesenchymal stem cells)	Human	[36]
	Predicted targets only	Osteogenesis (osteogenic differentiation of adipose-derived stem cells)	Human	[16]
miR-34 family	Cdk4; cyclin D1	Epithelial formation (keratinocytes proliferation)	Mice	[37]
miR-92a	Predicted targets only	Chondrogenesis (cartilage formation and chondrogenic differentiation of adipose-derived stem cells)	Human	[38]
miR-100	BMPR2	Osteogenesis (osteogenic differentiation of mesenchymal stem cells)	Human	[39]
miR-106	Predicted targets only	Osteogenesis (osteogenic differentiation of adipose-derived stem cells)	Human	[16]
miR-106b	Mapk14; Stat3	Pulmonary morphogenesis (modulation of embryonic epithelial branching)	Mice	[15]
miR-124	lamininγ1; integrinβ1	Neurogenesis (basal laminae integrity)	Human, mice and chicken	[40]
	Socs5	Promotes differentiation of CD4+ T cells	Human and mice	[41]
	Baf53a	Neurogenesis (dendritic development)	Mice	[11]

(Table S1) contd.…

microRNA	Validated Target(s)	Processes Regulated	Organism	Ref.
	Dlx2; Sox9; Jag1	Neurogenesis (neuronal differentiation in the brain subventricular zone)	Mice	[42, 43]
	NFATc1	Osteoclastogenesis (osteoclast differentiation of bone marrow macrophages)	Mice	[44]
	Sox9	Gonadal development (modulation of ovarian development and sex determination)	Mice	[45]
miR-124a	Foxa2	Pancreatic development (modulation of signaling in beta-cells)	Rat and mice	[46]
	Lhx2	Neurogenesis (prevention of retinal cones apoptosis and development of hippocampal neurons axons)	Mice	[47]
miR-125a/b	Predicted targets only	Osteogenesis (osteogenic differentiation of adipose-derived stem cells)	Mice	[16]
miR-125b	Snail1	Chondrogenesis (tracheal chondrocytes differentiation)	Mice	[33]
	Osx (predicted)	Inhibits osteogenic differentiation	Human	[48]
	Cbfβ	Inhibits osteoblastic differentiation	Mice	[49]
miR-126	SPRED1; VCAM1; PIK3R2	Angiogenesis (vascular formation and blood vessels integrity; modulation of leuko-cyte adherence to endothelial cells, and potential role in vascular inflammation)	Mice, human and zebrafish	[50, 51]
miR-127		Pulmonary development (fetal lung branching morphogenesis)	Rat	[52]
miR-130a	MAFB	Hematopoiesis (megakaryocytic differentiation, platelet physiology)	Human	[12]
	GAX; HOXA5	Angiogenesis (modulation of angiogenesis in vascular endothelial cells)	Human	[53]
	Hoxa5	Pulmonary development (modulation of airway and vascular morphogenesis)	Mice	[54]
miR-132	p250GAP	Neurogenesis and neuroplasticity (neuronal morphogenesis; dendritic spine formation in hippocampal neurons)	Rat	[55, 56]
		Neuroplasticity (ocular dominance plasticity; dendritic spines maturation)	Mice	[57, 58]
miR-133	SRF	Skeletal muscle myogenesis (myoblast proliferation)	Mice and *Xenopus sp.*	[4]
	Sp1	Vascular muscle development and integrity (vascular smooth muscle cell phenotypic switch and vascular remodeling)	Rat	[59]
miR-133a	SRF; cyclin D2	Cardiogenesis (cardiomyocyte proliferation; suppression of smooth muscle genes)	Mice	[60]
miR-136		Chondrogenesis (cartilage formation and chondrogenic differentiation of adipose-derived stem cells)	Human	[38]
miR-137	CDC42	Regulates differentiation adipose tissue-derived mesenchymal stem cells	Human	[61]
miR-138	APT1	Neurogenesis and neuroplasticity (dendritic spine morphogenesis)	Rat, mice and human	[62]
	EID-1	Adipogenesis (adipocyte differentiation of mesenchymal stem cells)	Human	[63]
	FAK	Osteogenesis (osteogenic differentiation of mesenchymal stem cells)	Human	[64]
miR-140	Predicted targets only	Chondrogenesis (chondrogenic differentiation of mesenchymal stem cells; cartilage homeostasis)	Human	[65]
	Dnpep	Chondrogenesis (endochondral bone development)	Mice	[66]
	RALA	Chondrogenesis (chondrogenic differentiation of mesenchymal stem cells)	Human	[67]
miR-140-3p miR-140-5p		Gonadal development (modulation of Leydig cell numbers in developing testis)	Mice	[68]
miR-143	Predicted targets only	Adipogenesis (adipocyte differentiation of preadipocytes)	Human	[69]

(Table S1) contd….

microRNA	Validated Target(s)	Processes Regulated	Organism	Ref.
miR-143 miR-145	Elk-1; Kfl4; Myocd	Smooth muscle myogenesis (smooth muscle differentiation and proliferation)	Mice	[70]
miR-145	Sox9	Chondrogenesis (chondrogenic differentiation of mesenchymal stem cells)	Mice	[71]
miR-146a	CXCR4	Hematopoiesis (megakaryocytic proliferation, differentiation and maturation)	Human	[72]
miR-148a	Rock1	Skeletal muscle myogenesis (myogenic differentiation of C2C12 myoblasts)	Mice	[73]
miR-148b	Predicted targets only	Osteogenesis (osteogenic differentiation of mesenchymal stem cells)	Human	[26]
miR-150	c-Myb	Hematopoiesis (modulation of megakaryocytes progenitor cell growth and differentiation)	Human and mice	[74, 75]
miR-153 miR-181a/a* miR-324-3p/5p		Induce neuronal differentiation of humans	Human	[76]
miR-181		Hematopoiesis and immune response (B-lymphoid lineage differentiation)	Mice	[77]
	Hox-A11	Skeletal muscle myogenesis (myoblast differentiation)	Mice	[78]
	NLK	Hematopoiesis and immune response (NK cells development)	Human	[79]
miR-181b	Six2	Nephrogenesis (modulation of metanephric mesenchymal cells proliferation)	Mice	[80]
miR-193a	Predicted targets only	Osteogenesis (osteogenic differentiation of adipose-derived stem cells)	Human	[16]
miR-193b	Predicted targets only	Chondrogenesis (cartilage formation and chondrogenic differentiation of adipose-derived stem cells)	Human	[38]
miR-196a	HOXC8	Osteogenesis (osteogenic differentiation and proliferation of mesenchymal stem cells)	Human	[81]
miR-199a-3p miR-199b-3p	Predicted targets only	Chondrogenesis (cartilage formation and chondrogenic differentiation of adipose-derived stem cells)	Human	[38]
miR-199a-5p	VEGF	Cell proliferation and differentiation (fine-tuning of human adipose tissue-derived stem cells multipotency)	Human	[82]
	c-Kit	Promotes erythroid differentiation	Human	[83]
miR-202-3p miR-202-5p		Gonadal development (modulation of testis development and sex determination)	Mice	[84]
miR-203	P63 (ΔNp63α)	Epithelial lineage development (epithelial differentiation and stratification, and keratinocyte differentiation)	Human and mice	[85, 86]
	Barx1	Stomach organogenesis (modulation of gastric epithelial differentiation)	Mice	[10]
		Skin and appendages morphogenesis (sebaceous lipogenesis)	Human	[87]
miR-204 miR-211	Runx2	Osteogenesis/adipogenesis (modulation of alternative fates of mesenchymal progenitor cells)	Human and mice	[88]
miR-206	Fstl1; Utrn	Skeletal muscle myogenesis (myoblast differentiation)	Mice	[89]
	Pola1; Bind1; Cx43; Mmd	Skeletal muscle myogenesis (myoblast differentiation)	Mice	[90]
	Cx43	Skeletal muscle myogenesis (regulation of muscular gap junctions)	Mice and human	[91]
	Cx43	Osteogenesis (modulation of osteoblast differentiation)	Mice	[92]

(Table S1) contd….

microRNA	Validated Target(s)	Processes Regulated	Organism	Ref.
miR-210	Predicted targets only	Chondrogenesis (cartilage formation and chondrogenic differentiation of adipose-derived stem cells)	Human	[38]
	Hif1a	Inhibits differentiation of immune system cells	Human	[93]
miR-214	Ezh2	Skeletal muscle myogenesis (myogenic differentiation of embryonic stem cells)	Mice	[94]
miR-218	RUNX2	Osteogenesis (osteogenic induction and differentiation of dental stem cells)	Human	[95]
	SFRP2; DKK2	Osteogenesis (osteogenic differentiation of adipose tissue-derived stem cells)	Human	[96]
miR-219	PDGFRα; Sox6; FoxJ3; ZFP238	Neurogenesis (oligodendrocyte differentiation and myelination)	Mice	[97]
miR-221	Kit	Hematopoiesis and erythropoiesis (erythroid differentiation of cord blood hematopoietic progenitor cells)	Human	[98]
	p27	Skeletal muscle myogenesis (myoblast differentiation and assembly of sarcomeres in myotubes)	Mice	[99]
	Predicted targets only	Osteogenesis (osteogenic differentiation)	Human	[100]
	Hoxb5	Pulmonary development (modulation of airway and vascular morphogenesis)	Mice	[54]
miR-222	Kit	Hematopoiesis and erythropoiesis (erythroid differentiation of cord blood hematopoietic progenitor cells)	Human	[98]
		Articular cartilage homeostasis (potential regulator of the cartilage mechanotransduction pathway)	Bovine	[101]
	p27	Skeletal muscle myogenesis (myoblast differentiation and assembly of sarcomeres in myotubes)	Mice	[99]
miR-223	NFI-A	Hematopoiesis (granulocytic differentiation of progenitor cells)	Human	[102]
	Mef2c	Hematopoiesis (granulocytic differentiation of progenitor cells and modulation of inflammatory response via neutrophil sensitivity)	Mice	[103]
	LMO2	Hematopoiesis and erythropoiesis (erythroid differentiation of cord blood hematopoietic progenitor cells)	Human	[104]
miR-224	Egr2; ACSL4	Adipogenesis (adipocyte differentiation of 3T3-L1 cells)	Mice	[105]
miR-320c		Chondrogenesis (cartilage formation and chondrogenic differentiation of adipose-derived stem cells)	Human	[38]
miR-326	Predicted targets only	Adipogenesis (adipogenic differentiation of adipose-derived stem cells)	Rat	[34]
miR-329	CD146	Angiogenesis (modulation of endothelial cell migration and tube formation)	Mice and human	[106]
miR-375		Pancreatic development (modulation of pancreatic islet morphology and development)	Human	[107, 108]
	HuD	Neurogenesis and neuronal plasticity (modulation of dendrite formation)	Rat, mice and human	[109]
miR-379-410 cluster	N-cadherin	Promotes neural stem cell differentiation in mice	Mice	[110]
miR-381	Predicted targets only	Chondrogenesis (cartilage formation and chondrogenic differentiation of adipose-derived stem cells)	Human	[38]
miR-432	NES, RCOR1/COREST, MECP2	Neurogenesis (enhances the formation of neurites)	Human	[111]
miR-455-3p	Predicted targets only	Chondrogenesis (cartilage formation and chondrogenic differentiation of adipose-derived stem cells)	Human	[38]

(Table S1) contd….

microRNA	Validated Target(s)	Processes Regulated	Organism	Ref.
miR-489	GCA	Osteogenesis (osteogenic differentiation of mesenchymal stem cells)	Human	[26]
miR-495	Sox9	Inhibition of chondrogenic differentiation of mesenchymal stem cells	Human	[112]
	Dnmt3a	Inhibition of mesendoderm differentiation	Mice	[113]
miR-499	Predicted targets only	Cardiogenesis (cardiac differentiation of embryonic stem cells)	Human	[114]
miR-518b	FOXN1	Epithelial lineage development (epithelial lineage differentiation in embryonic stem cells and embryonal carcinoma pluripotent cells)	Human	[17]
miR-574-3p	RXRα	Chondrogenesis (chondrogenic differentiation of mesenchymal stem cells)	Human	[115]
		Skin and appendages morphogenesis (sebaceous lipogenesis)	Human	[87]
miR-675		Chondrogenesis (chondrogenic differentiation and cartilage matrix production)	Human	[116]
miR-2861	HDAC5	Osteogenesis (osteoblast differentiation)	Mice	[117]
miR-3960	Hoxa2	Osteogenesis (osteoblast differentiation)	Mice	[118]
miR-4448 miR-4708 miR-4773	Prediction of SMAD1 and SMAD4	Inhibits osteoblast differentiation	Human	[119]

TABLE S1 REFERENCES

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