Supporting Information

Review of Integrin-targeting Biomaterials in Tissue Engineering

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Supplemental Table 1: Key integrins, ligands, and functions in osteogenic differentiation and bone remodeling.

Integrin	Ligand (Proteins and Peptides)	Cellular Function *
α1β1	Collagen I [11, 353], $Scl2_{GFPGER}$ [74], $Scl2_{GFPGEN}$ [74]	-Facilitates adhesion of hMSCs *in vitro* [11] -Increased hMSC osteogenic differentiation (osteogenic medium) [74] -Promoted cartilage production in mouse model [353]
α2β1	Collagen I [11], GFOGER** [73], P15 [354], DGEA [355], FNIII9-10 [25], $Scl2_{GFPGER}$ [74]	-Facilitates adhesion and survival of hMSCs, rOC *in vitro* [11, 89] and hMSCs in mouse models [66] -Activated focal adhesion kinase, osteoblast-specific promoters, and induced osteogenic differentiation (ALP and mineralization) in mPOB and hMSCs (osteogenic medium) [69, 71, 73, 74, 354-356] -Promoted bone formation in murine bone defect model [357]
α3β1	Collagen [14], Fibronectin [14, 16]	-Increased cell expression under conditions favoring osteoblastic phenotype [55] -rOBs showed decreased mineralization during nodule morphogenesis (w/ function-perturbing antibodies) [14] -Expressed on OBs actively synthesizing bone [55, 358]
α4β1	Fibronectin [18, 19]	-Increased homing and rolling of mMSCs to the bone marrow [60, 61] -Mediates initial attachment of MSCs to bone marrow or basement membrane (human and mouse) [61, 63]
α5β1	Fibronectin [25], cRRETAWA [294], GACRETAWACGA [359], FNIII7-10 [360]	-Facilities hMSC migration [62] -Increased proliferation in osteoblasts (rat and mouse) [14, 81]

		-Promotes osteogenic differentiation mMSC and hMSC (growth/osteogenic media) [25, 50, 51, 75-77, 294, 359-361] -Plays a role in mechanosensitive osteogenic differentiation in hMSCs in vitro [76, 77] -Regulates mechanotransduction in osteoblasts [82] -Promotes mineralization in osteoblasts (rat and mouse) [14, 71]
α9β1	ADAM8 (autocrine factor) [33], Osteopontin [32]	-Increases mobility of osteoclasts (human and rat) [33] -Regulator of osteoclastogenesis (increased bone volume in rats with double knockdown for integrin) [32, 33]
α11β1	Osteolectin (growth factor) [35], Collagen I [11]	-Promotes hMSCs survival (integrin knockdown had high levels of apoptosis) [11] -Promotes differentiation of osteoprogenitors to OBs (human and mouse) [35]
αvβ3	Vitronectin [38], Fibronectin [25], Bone Sialoprotein [39], RGD (cyclic and linear) [362]	-Increases mOC migration [85] -Inhibits proliferation and differentiation of hMSCs [25, 50] -Plays a role in mechanosensitive osteogenic differentiation in hMSCs in vitro [76, 77] -Involved in both phases of bone remodeling, formation and resorption [38, 85, 362, 363]

a) *Mesenchymal stem cell (MSC), osteoblast (OB), preosteoblasts (POB), osteoclast (OC), h- (human), r- (rat), and m- (murine); b) ** Synthetic collagen-mimetic motif that resides in sequence $GPOGCO(GPO)_2GFOGER(GPO)_5$

Supplementary Table 2: Key integrins, ligands, and mediated cellular functions in wound healing.

Integrin	Ligands	Cellular functions
α1β1	Collagen I, IV	-Upregulates dermal fibroblast proliferation [9] -Downregulates collagen synthesis and increase collagenase synthesis during ECM deposition [134] -Promotes collagen gel contraction by fibroblast [146, 147]
α2β1	Collagen I, GFOGER* [364], $Scl2_{GFPGER}$ [129], EF1(DYATLQLQEGRLHFMFDLG, Laminin)[130]	-Induces the MMP-1 production and promotes keratinocyte migration [105] -Promotes keratinocyte proliferation [117] -Mediates fibroblast proliferation [128-130] -Promotes the gel collagen matrix contraction [37, 148, 365]

α3β1	Laminin 332, entactin[13]	-Regulates keratinocyte polarization and processive migration [107] [17] -Induce basement membrane formation [366] -Enhances the deposition of entactin and fibronectin [13]
α4β1	EDA-fibronectin, ELIMIN1[20]	-Downregulates fibroblast and keratinocyte proliferation [20] -Mediates fiber assembly and fibronectin synthesis by fibroblast [138] -Enhances the fibronectin-matrix contraction by interacting with region V of fibronectin [143]
α5β1	Fibronectin, Gelatin [22-24]	-Enhances keratinocyte proliferation [115, 367] -Enhances fibroblast migration into blood clot [132] -Improves fibroblast proliferation [22-24] -Promotes fibronectin fibril deposition [136, 137, 368] -Mediates TGF-β1-induced myofibroblast differentiation [140] -Promotes fibronectin matrix contraction [141, 142]
α6β1	Laminin 111, CCN2[27], YIGSR(Laminin)[28]	-Mediates keratinocyte proliferation [28] -Regulates basement membrane formation and laminin synthesis [135] -Stimulates collagen synthesis [27]
α9β1	Fibronectin[30], tenascin-C[31], ELIMIN1 [20]	-Mediates keratinocyte and fibroblast proliferation [20, 30] -Regulates dermal fibroblasts migration [31]
α11β1	Collagen I	-Regulates fibroblast migration [133] -Mediates myofibroblast differentiation [133] -Participates in collagen remodeling [133]
α6β4	Laminin 332	-Promote keratinocyte migration [109] -Constitutes hemidesmosomes as an essential component [111]
αvβ3	Gelatin [22-24], Fibrinogen[37], tenascin-C[139], CCN1 [40, 43]	-Improves fibroblast proliferation [22-24, 40] -Induces MMP expression and collagen degradation [43] -Modulates the deposition of tenascin-C [139] -Mediates collagen gel contraction [37]
αvβ5	CCN1	-Enhances fibroblast migration [40]

a) * Synthetic collagen-mimetic motif that resides in sequence $GPOGCO(GPO)_2GFOGER(GPO)_5$ [364]

Supplementary Table 3: Key integrins, ligands, and functions in angiogenesis.

Integrin	Ligand	Function
α1β1	Collagen[8, 10], Laminin[10],	-Inhibits production of MMP 7 and 9 that produce angiostatin thus preventing reduced endothelial proliferation [195] -Support proliferation and migration of endothelial cells during VEGF induced angiogenesis[160, 181, 369]
α2β1	Collagen[10], Laminin [10],	-Support proliferation and migration of endothelial cells during VEGF induced angiogenesis[160, 181, 369] -Involved in morphogenesis and tube formation[166, 256, 370]
α3β1	laminin[10], collagen[10], fibronectin[15], Fn9∗10 sequence containing RGD[203]	-Organized and non-leaky networks [203] -Represses pathological angiogenesis [204] -Promotes endothelial cell motility and multicellular network formation [371]
α4β1	Fibronectin[15], VCAM[21], REDV[197, 198]	-Mediates endothelial cell-pericyte interaction for the survival of both cell types[21]
α5β1	Fibronectin and Fibrin [10], PHSRN[200, 372], Fn9∗10 sequence containing RGD[203]	- organized and non-leaky vascular networks [203] -Regulates tube diameter and the formation of multicellular networks [42, 202]
α6β1	Laminin [26] IKVAV[216, 217, 373]	-Supports migration of endothelial cells during VEGF induced angiogenesis [168] - capillary morphogenesis and tube formation [168, 214]
α6β4	Laminin [26]	-Downregulated during initial phases of angiogenesis to promote migration[180] -Adhesion of endothelial cells to the basement membrane promoting vessel integrity, maturation, and function [158, 180]
α9β1	VEGF-A[34]	-Directly binds VEGF-A promoting angiogenesis [34]
αVβ3	Vitronectin, fibronectin, fibrinogen, denatured collagen I and IV[10, 15, 374], Fn9(4G)10 containing RGD[203]	-Disorganized, dense and leaky vascular networks[203] -Aids in VEGFR2 phosphorylation during VEGF induced angiogenesis[159] -Promotes endothelial cell proliferation [210] -Substrate dependent vacuole and lumen formation[173] -Mediates MMP-2 localization of the cell surface [188, 207]
αVβ5	Vitronectin, fibronectin [15, 26],	-VEGF mediated angiogenesis [206] -Substrate dependent vacuole and lumen formation[173]