Vascularization continues to represent a major challenge in the successful implementation of regenerative strategies. Current approaches for inducing vascularization in vivo include pre-forming a vasculature ex vivo, and the use of a variety of strategies to stimulate vascularization in situ. Vessel network assembly within 3D tissues can be induced in-vitro by means of co-culturing of endothelial cells, fibroblasts and cells specific to the tissue of interest. This approach supports formation of endothelial vessels and promotes endothelial and tissue-specific cell interactions. In addition, we have shown that in vitro pre-vascularization of engineered tissue can promote its survival and vascularization upon implantation and that implanted vascular networks, can anastomose with host vasculature and form functional blood vessels in vivo. Sufficient vascularization in engineered tissues can be achieved through coordinated application of improved biomaterial systems with proper cell types. We have shown that vessel network maturity levels and morphology are highly regulated by matrix composition and analyzed the vasculogenic dynamics within the constructs. In addition, we have recently shown that adipose-derived endothelial cells and mesenchymal stem cells enhance vascular network formation on 3D constructs in vitro and can contribute to in vivo vascularization of tissue-engineered flaps. We also explored the effect of mechanical forces on vessels organization and demonstrated that morphogenesis of 3D vascular networks is regulated by tensile forces. Revealing the cues controlling vascular network properties and morphology can enhance in-vitro tissue vascularization and improve graft and flap integration prospects.

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