Advances in vascularization of cardiac tissues and hearts-on-a-chip

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Zoom Platform

Abstract

Vascularization is critical for the survival of engineered tissues in vitro and in vivo. In vivo, angiogenesis involves endothelial cell proliferation and sprouting followed by connection of extended cellular processes and subsequent lumen propagation through vacuole fusion. This presentation will first cover the requirements for functional vascularization of tissue engineered constructs and hearts-on-a-chip, followed by overview of recent approaches to achieve this goal. We will first describe an approach that mimicked the angiogenesis process in engineering an organized capillary network anchored by an artery and a vein. The network was generated by inducing directed capillary sprouting from vascular explants on micropatterned substrates containing thymosin β4-hydrogel. The capillary outgrowths connected between the parent explants by day 21, a process that was accelerated to 14 d by application of soluble VEGF and hepatocyte growth factor. We will then move to microfabrication approaches, through a fabrication of a microfluidic scaffold (hereafter referred to as AngioChip) that supports the assembly of parenchymal cells on a mechanically tunable matrix surrounding a perfusable, branched, three-dimensional microchannel network coated with endothelial cells. The design of AngioChip decouples the material choices for the engineered vessel network and for cell seeding in the parenchyma, enabling extensive remodelling while maintaining an open-vessel lumen. The incorporation of nanopores and micro-holes in the vessel walls enhances permeability, and permits intercellular crosstalk and extravasation of monocytes and endothelial cells on biomolecular stimulation. We will also show that vascularized hepatic tissues and cardiac tissues engineered by using AngioChips process clinically relevant drugs delivered through the vasculature, and that millimetre-thick cardiac tissues can be engineered in a scalable manner. Moreover, we demonstrate that AngioChip cardiac tissues implanted with direct surgical anastomosis to the femoral vessels of rat hindlimbs establish immediate blood perfusion. Finally, we will discuss the incorporation of pluripotent stem cell derived macrophages as an approach to support engineered vasculature in the cardiac tissue over long term.