FROM DEVELOPMENTAL BIOLOGY TO TISSUE-ENGINEERING: PRINTING BLOOD VESSELS

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ABSTRACT

Cardiovascular disease is a leading cause of death and often requires vascular reconstruction. However, the use of synthetic materials and scaffold-based approaches has shown several limitations for small-diameter blood vessel tissue-engineering, evidenced by the fact that they can elicit adverse host responses and interfere with, rather than guide, direct cell-cell interaction as well as assembly and alignment of cell-produced extracellular matrix. Understanding the physical principles of biological self-assembly is thus essential for developing efficient strategies to build living tissues and organs. Here we exploit well-established liquid-like developmental processes (such as tissue fusion, envelopment or cell-sorting phenomena) to engineer scaffold-free, multilayered, small-diameter blood vessels. In particular, we show that apparent surface tensions of the three major vascular cell types (endothelial cells, smooth muscle cells and fibroblasts), determined through the exact solution of Laplace equation, guide their segregation in a multilayered fashion *in vitro*. Moreover, we introduce a novel rapid-prototyping technology (bioprinting) that allows for directing the self-assembly of the vascular cell types into custom-shaped tubular tissue structures, from single vascular tubes to complex hierarchical macrovascular trees. In addition to its potential for fulfilling the crucial need for small diameter vascular grafts and providing new strategies for vascularization of tissues for transplantation, this physically based approach provides a new insight into cell-patterning and structure formation and questions the paradigm of scaffold-based tissue-engineering.