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Consumption and Diffusion Based Model of Tissue Organoid Development

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Abstract : In vitro organoid cultivation requires the simultaneous provision of necessary vascularization and nutrients perfusion of cells during organoid development. However, many aspects of this problem are still unsolved. The functionality of vascular network intergrowth is limited during early stages of organoid development since a function of the vascular network initiated on final stages of in vitro organoid cultivation. Therefore, a microchannel network should be created in early stages of organoid cultivation in hydrogel matrix aimed to conduct and maintain minimally required the level of nutrients perfusion for all cells in the expanding organoid. The network configuration should be designed properly in order to exclude hypoxic and necrotic zones in expanding organoid at all stages of its cultivation. In vitro vascularization is currently the main issue within the field of tissue engineering. As perfusion and oxygen transport have direct effects on cell viability and differentiation, researchers are currently limited only to tissues of few millimeters in thickness. These limitations are imposed by mass transfer and are defined by the balance between the metabolic demand of the cellular components in the system and the size of the scaffold. Current approaches include growth factor delivery, channeled scaffolds, perfusion bioreactors, microfluidics, cell co-cultures, cell functionalization, modular assembly, and in vivo systems. These approaches may improve cell viability or generate capillary-like structures within a tissue construct. Thus, there is a fundamental disconnect between defining the metabolic needs of tissue through quantitative measurements of oxygen and nutrient diffusion and the potential ease of integration into host vasculature for future in vivo implantation. A model is proposed for growth prognosis of the organoid perfusion based on joint simulations of general nutrient diffusion, nutrient diffusion to the hydrogel matrix through the contact surfaces and microchannels walls, nutrient consumption by the cells of expanding organoid, including biomatrix contraction during tissue development, which is associated with changed consumption rate of growing organoid cells. The model allows computing effective microchannel network design giving minimally required the level of nutrients concentration in all parts of growing organoid. It can be used for preliminary planning of microchannel network design and simulations of nutrients supply rate depending on the stage of organoid development.

Keywords : 3D model, consumption model, diffusion, spheroid, tissue organoid
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