A hydrogel to enable the 3D self-organization of a brain micro-vasculature

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Homogenized oxygenation and nutrients transport within thick or large engineered tissues is a major challenge. Works on hydrogels supporting the establishment of a 3D vascular network is thus of technical interest for the tissue engineering field, and of scientific interest for the study of such vascularization. Here the objective was to develop a microenvironment reproducing the cerebral micro-vascularization, and its very selective filter function as blood-brain-barrier (BBB).
Previous work based on cell coating with collagen and layer by layer deposition lead to promising self-organization of endothelial cells as a capillary network supported by fibroblasts. However, simply translating this method to brain cells was not successful. A new hydrogel mixing microfibrillar collagen and fibrin had to be developed (1) to act as an extracellular matrix inducing the organization of the three cell types of the human BBB: brain endothelial cells (HBEC), astrocytes (HA) and pericytes (HP). While the collagen microfibrils seemed to support the cell migration, the polymerization of fibrin - caused by the action of thrombin on fibrinogen - helped the gelation and the angiogenesis. After 1 week of incubation, the endothelial tubulars showed lumens of 8-10 µm diameter corresponding to human cerebral capillaries' dimensions. Validation of the BBB function relied on the comparison of the expression of the main tight junction proteins, carriers and transporters between this 3D engineered tissue and a 2D conventional coculture.
Using a fluidic device, the engineered vascular tissue was exposed to a shear stress with nutritive medium flowing through the hydrogel (pressure of 10 kPa) (2). The capillaries organized perpendicularly to the flux. The resulting interstitial flow lead to a better definition of the network, and higher expression of some key BBB proteins. A BBB-on-chip is currently being developed to perfuse those capillaries and mimick the blood flow.

Références :
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Mots-Clés : Blood-brain barrier, extracellular matrix, sel-organization, capillaries, alternative model

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