Development of vascularized tumor-on-chips: toward a physiological microsystem modeling the glioblastoma and blood-brain barrier.

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The blood-brain barrier (BBB) limits the transport of drugs and nanocarriers, and hampers the development of innovative therapeutic solutions against neurological disorders. The typical survival after diagnosis of the most common and aggressive brain tumor, the glioblastoma multiforme (GBM), is of 12 to 18 months only. Preclinical screening of drug candidates relies on too simplistic conventional *in vitro* models, and animal experimentation with ethical and interspecies differences issues that lead to poor translational results in clinical assays. Tissue engineering and physiological microsystems as organ-on-chips promise alternative models that consider the different human cell types involved, their 3D organization in an extracellular matrix, and the mechanical constraints of the blood flow.

Firstly, a self-organized 3D model of BBB micro-vasculature was optimized in a fibrine and collagen type I hydrogel. Human brain microvascular endothelial cells arranged into capillaries, supported by pericytes, and astrocytes, and expressed specific tight-junction proteins membrane transporters and carriers (*1*–*3*). A second phase of the project has started, with the design of microchip prototypes as a scaffold for the hydrogel enabling nutritive medium to be flown into a central venule. Assays with GBM cells (U87-MG) are carried out aiming at understanding the impact of cell-cell communication on the stability of the extracellular matrix and the on BBB. One of the goals of this project is to question the possible EPR (enhanced permeability and retention) effect in the glioblastoma.

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