Development of an instrumented physiological microdevice to study the impact of the vascular microarchitecture and tumoral context on the brain angiogenesis and blood-brain barrier

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The blood-brain barrier (BBB) strictly controls exchanges between the blood and the brain to block most external aggressions. However, the glioblastoma multiforme, the most common and aggressive primary brain cancer, modifies its microenvironment and the BBB with an uncertain evolution. Organs-on-chips are innovative biotechnological tools that artificially reproduce an organ, helping to understand many pathological mechanisms. Developing a BBB-on-chip (BBBoC) model is particularly pertinent to compare function in a healthy and tumoral context[1].

An initial BBBoC model was constructed with a straight hollow channel surrounded by a hydrogel matrix containing cancer cells and support cells: astrocytes and pericytes. This straight channel, seeded with endothelial cells, acts as an arteriole when perfused with nutritive medium mimicking blood flow. Complexifying channel design is necessary to bring the model closer to reality. Several sacrificial materials were compared to be used as templates for the new complex channel: carbohydrate glass, gelatin, or mixed waxes[2]. They were assessed in terms of synthesis, molding and demolding (in a PDMS mold obtained from 3D-printing), shape retaining, and triggered dissolution, considering constraints of cell preservation. Their biocompatibility was assessed on glioblastoma (U87-MG) and endothelial cells (HBEC-5i) dispersed in hydrogel (live-dead kit). Gelatin appeared as the optimal choice for the BBBoC model. Dissolution of gelatin template with an albumin solution makes way for a complexified network of about 100-200 µm diameter channels.

The next step will be to assess the organization of endothelial cells seeded in the channels, especially their tight junctions to recreate a functional endothelium by immunolabelling and biomolecular assays[3]. Using fluorescent dextran and nanoparticles will allow validation of BBBoC model integrity before adding cancer cells. In the longer term, it could be an innovative tool for disease modeling and drug assays.

References:

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