Development of a complex vascular microarchitecture in a physiological microdevice to study the impact of a tumoral context on the brain angiogenesis and blood-brain barrier

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The blood-brain-barrier blocks the passage of many exogenous molecules into the brain, reducing treatment options for brain pathologies. In the case of multiform glioblastoma, the most frequent brain tumor, the evolution of the BBB remains uncertain. Developing a BBB-on-chip (BBBoC) model is particularly pertinent to compare its function in a healthy and tumoral context.

The BBB consists of a complex vascular network. The former BBBoC model was constructed with a single straight central channel seeded with endothelial cells and surrounded by a hydrogel matrix which may contains tumor and support cells. The complexification of the channel design brings the model closer to reality. Several biocompatible sacrificial materials were tested and compared: carbohydrate glass[1], gelatin[2], or a mixture of waxes[3]. They were assessed in terms of ease and rapidity of synthesis, molding and demolding (in a PDMS template obtained from 3D printing), shape conservation, and triggered dissolution, taking into account the constraints of cell preservation. Around those sacrificial materials, the hydrogel is cast. After gelation of the matrix, a buffered solution dissolves the material (different temperatures and protocols were tested), making way for a more complex network of about 100-200 µm diameter channels. The biocompatibility of the materials and the dissolution processes were assessed on glioblastoma cells (U87-MG) dispersed in the hydrogel (live-dead kit).

The next step will be to check the viability of endothelial cells seeded in the channels, and of the support cells (astrocytes and pericytes) seeded within the hydrogel. The perfusion of this vascular network, with a biological fluid, will reproduce the blood flow to study the angiogenesis phenomenon and the obtention of the blood-brain barrier functions with or without cancer cells in the matrix.

References:

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