Ex vivo modelling of paediatric brain tumours with hydrogel scaffolds

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Paediatric high-grade gliomas (pHGGs) are a heterogeneous group of tumours with a dismal outcome and are the leading cause of death in children with brain tumours.[1] The lack of suitable models to study glioma biology and test new drugs in a high-throughput manner is a significant obstacle to improving the treatment of these deadly tumours. Traditional brain tumour *in vitro* models, such as 2D or neurosphere models, fail to mimic the complex environment of a patient's tumour, while engraftment into mice is time-consuming and variable in success.[2] Addressing this gap, we have developed 3D-bioprinted tumouroids using tunable hydrogels, to mimic the extracellular matrix of pHGGs. By incorporating biomimetic peptides and proteins, our models aim to mimic the tumour's extracellular environment, offering an advanced in vitro platform for studying pHGGs.

To identify the extracellular genes associated with pHGGs, we interrogated bioinformatics data obtained from patients with the disease. Using this information, we identified hydrogel conditions that resemble the patient's tumour extracellular environment. We evaluated the viability and growth characteristics of patient-derived glioma cells using our 3D bioprinting technique, and identified various hydrogel conditions at which high viability and proliferation was achieved. Our findings suggest that incorporating extracellular components, such as collagen, fibronectin, and hyaluronic acid, into the hydrogel influences the growth and morphology of these bioprinted cells.

By integrating patient-derived tumour cells, our pHGG models have the potential to capture the heterogeneity and genomic diversity of tumours and more accurately reflect human tumour-like features. Our models mimic the tumour's extracellular matrix, enable 3D growth, and facilitate high-throughput analysis.

[1] Quinn T. Ostrom et al., "CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012–2016," *Neuro-Oncology* 21, no. Supplement_5 (2019), https://doi.org/10.1093/neuonc/noz150, https://dx.doi.org/10.1093/neuonc/noz150.

[2] F. Akter et al., "Pre-clinical tumor models of primary brain tumors: Challenges and opportunities," *Biochim Biophys Acta Rev Cancer* 1875, no. 1 (Jan 2021), https://doi.org/10.1016/j.bbcan.2020.188458.