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3D-bioprinting by design: A Dynamic Model of the Blood-Brain Barrier and Glioblastoma

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Introduction: The blood-brain barrier (BBB) severely restricts the passage of drugs into the brain, posing a significant challenge in treating central nervous system disorders such as glioblastoma (GBM). Therefore, there is an urgent need for advanced in vitro models that accurately characterize both BBB permeability and GBM behavior [1]. The evolution from two-dimensional (2D) to three-dimensional (3D) models, especially those incorporating dynamic conditions, is critical to enhancing our understanding and predictive capabilities regarding BBB permeability and GBM treatment [2,3]. In this study, we used 3D printing technology to develop a 3D model of the BBB and GBM microenvironment.

Materials and methods: The model is designed to replicate the complex architecture and dynamic conditions of the BBB and tumor tissue. It features a cylindrical structure with a core composed of a gelatin methacrylate (GelMA)-alginate bioink containing U87 glioblastoma (GBM) cells, microglia (HCM3), and astrocytes. Surrounding this core, a GelMA-fibrinogen bioink incorporating human brain microvascular endothelial cells (HBMECs) forms the perimeter.

Results: A risk-based analysis, using an Ishikawa diagram and a risk estimation matrix, identified potential sources of variability in the model. Principal component analysis assessed the impact of process variables, including nozzle type, pressure, temperature, and crosslinking, on critical quality attributes (CQAs). These CQAs encompassed printability, structural integrity, stiffness, porosity, and cell viability, with cell viability being the primary focus.

Conclusion: 3D bioprinting holds great potential for creating physiologically relevant and reproducible models that enhance our understanding of GBM biology. It may also act as a dependable platform for evaluating the effectiveness of drugs and nanoparticles, thus promoting personalized therapies.

References:

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