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Optimizing Matrix Stiffness for Enhanced Differentiation of Neural Progenitor Cells in Tissue Engineering

Abstract: Matrix stiffness plays a crucial role in the differentiation of neural progenitor cells (NPCs), significantly impacting their morphology, function, and development. Matrix stiffness refers to the rigidity of the extracellular matrix (ECM) that surrounds cells, providing structural support and biochemical and biomechanical cues. Through mechanotransduction, cells convert mechanical signals from the ECM into biochemical signals, affecting gene expression and cellular function. For NPCs, which can differentiate into various neural lineages, ECM stiffness can direct their fate. Softer matrices, resembling the natural stiffness of brain tissue, promote neuronal differentiation, leading to neurons with extended neurites and functional properties like synapse formation and electrical activity. Understanding matrix stiffness's impact on NPC differentiation is crucial for neural tissue engineering and regenerative medicine. Designing scaffolds with appropriate stiffness can enhance neuronal differentiation and integration, offering potential treatments for neurodegenerative diseases and spinal cord injuries. To investigate this, we synthesized GelMA with varying methacrylation degrees and loaded NPCs onto these hydrogels. We also evaluated the matrix stiffness by exposing GelMA hydrogel to various dosages of UV light. Two models were designed: (i) a cell-free (low stiffness) and cell-laden (high stiffness) reciprocating layer, and (ii) a construct with increasing stiffness throughout. These models were used to study the role of matrix stiffness on NPC cellular responses. In conclusion, our findings underscore the critical importance of optimizing matrix stiffness for effective neuronal tissue engineering applications.

Keywords: Tissue engineering, stimulus-assisted bioprinting, Magnetic field, Skeletal muscle regeneration

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