Cell Mechanostimulation Study Using Advanced Microrobots Prepared via Stop-Flow Lithography Process

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Key words: cell encapsulation, stop-flow lithography, microactuators, mechanostimulation

The encapsulation of tissue cells within a three-dimensional (3D) hydrogel structure presents a valuable alternative to traditional two-dimensional (2D) cultivation methods, such as those utilized in Petri dishes or culture flasks. This 3D setup more accurately replicates the function of the extracellular matrix and resembles the tissues found in live organisms. In tendon, ligament, and muscle tissues, the mechanical properties also play a crucial role, significantly influencing cell physiology. Both excessive and insufficient tension can lead to pathological cell behavior. The impact of mechanostimulation remains largely uncharted, and suitable hydrogels containing encapsulated cells can serve as a tool for establishing a controlled biomechanical environment, relevant for research into regenerative medicine and disease models.

This work describes hydrogel microrobots capable of exerting force on encapsulated cells from the anterior cruciate ligament (ACL) to stimulate the production of cytokines—critical signaling and regulatory molecules. The encapsulation of ACL cells within hydrogels and the fabrication of microrobots for cell manipulation utilize the stop-flow lithography (SFL) technique, which involves a microfluidic chip, a photomask, and UV radiation. The microrobot is designed in the shape of a closed horseshoe, consisting of three components made from distinct materials: a rigid polyethylene glycol diacrylate (PEGDA) hydrogel, a thermoresponsive poly N-isopropylacrylamide (pNIPAM) hydrogel embedded with gold nanoparticles, and a septum composed of a biocompatible hydrogel containing encapsulated cells. In this study, four different methacrylated hydrogels were evaluated and compared for ACL cells encapsulation: methacrylated hyaluronic acid (HAMA), methacrylated collagen (ColMA), methacrylated human platelet lysate (hPLMA), and hydroxyethyl methacrylate-modified dextran (DexHEMA).