New Horizons in Granular Hydrogel Scaffolds for Tissue Engineering

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Hydrogels, one of the main pillars of regenerative medicine, are crosslinked hydrophilic polymer networks containing a high water content that mimic the biological and physicochemical properties of extracellular matrices (ECMs). Conventional (bulk) hydrogels are fabricated via physical and/or chemical crosslinking of polymers or nanoparticles. These hydrogels are typically nanoporous with limited transport of oxygen, nutrients, and cellular byproducts. To overcome these limitations, granular hydrogel scaffolds (GHS), made up of hydrogel microparticles (microgels) have recently been developed as an emerging platform for biomedical applications. Using microgels as building blocks for scaffold fabrication provides cell-scale void spaces (microporosity), enhancing degradation-independent cell infiltration and proliferation. Tailoring the micro-architecture of GHS may enable fundamental studies on orthogonal cell responses to local stiffness and spatial confinement. Accordingly, compositional and architectural engineering of GHS can accelerate and guide in situ tissue regeneration. We have developed the first protein-based GHS using gelatin methacryloyl (GelMA) microgel building blocks. Our group has been engineering GelMA GHS as a platform for variety of applications, including accelerated vascularization, wound healing, brain regeneration after stroke, tumor cancer mimicking on-chip platforms, and 3D extrusion-based bioprinting.