

SYNTHETIC BUILDING BLOCKS FOR HIERARCHICAL TISSUE ENGINEERING

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We focus on designing biomaterial systems for hierarchical tissue engineering. Polymeric molecular and nano-to micron-scale building blocks are assembled into soft 3D biomimetic constructs, which allow studying and controlling cell/material interactions that are difficult or impossible to investigate with current material systems.[1] These biomaterial platforms can then be applied to build *ex vivo* tissue models for drug testing or investigating pathologies, to grow tissue or organs *ex vivo* for transplantation *in vivo*, or for *in vivo* tissue regenerative therapies. The hybrid artificial biomaterial matrices consist of a polymeric crosslinked network and colloids to create macroscopic structures with new properties. Microgels and fibers are produced by adapted technologies based on fiber spinning, microfluidics, and in-mold polymerization. To arrange the building blocks in a spatially controlled manner, we rely on self-assembly mechanisms and assembly by external fields (e.g., magnetic). A better understanding of cellular processes in contact with synthetic biomaterials will supply information about the parameters, which are most important to make viable and functional regenerative materials for clinical use in a modular manner. The different methods are applied to embed and grow cells in micro-containers to form mini-tissues for transplantation or load specific biological molecules to control temporal release [2], and produce structural magnetic elements that can be aligned for cell guidance. Due to their size, the micro-objects can be injected, with or without a surrounding hydrogel. Their internal structure and degradation properties enable temporal control of tissue formation. To obtain anisotropic matrices after injection, rod-shaped elements are rendered magneto-responsive by the incorporation of superparamagnetic iron oxide nanoparticles. Due to their anisometric shape, the elements align parallel to a low external mTesla magnetic field, after which a surrounding hydrogel can crosslink to fix their unidirectional orientation after removal of the magnetic field. Fibroblasts and nerve cells sense the mechanical anisotropy, induced by a minimal amount of oriented structures, resulting in directed cell growth inside 3D hydrogels.[3] Modification of the guiding elements with adhesive peptides enhances the overall cell alignment, reduces ECM production, and increases nuclear shuttling of mechanosensitive proteins, such as YAP/TAZ.[4] Neurons inside the Anisogel show spontaneous electrical activity proving neuronal functionality and importantly, electrical signals propagate along the anisotropy axis of the material.[5] The developed hybrid hydrogel can be applied as a low invasive, injectable material to repair complex, sensitive tissues, such as the spinal cord.

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