

# Interactive and anisometric colloidal building blocks for regenerative medicine and tissue engineering

Laura De Laporte

DWI Leibniz Institute for Interactive Materials  
Department of Macromolecular Materials for Medicine, RWTH Aachen University, Germany

We apply polymeric molecular and micron-scale building blocks to assemble into soft 3D biomaterials with anisotropic and dynamic properties. We focus on injectable materials that can be pipetted using automated systems, bioprinted or delivered *in vivo* in a low invasive manner. Spherical and rod-shaped microgels and fibers are produced by microfluidics, in-mold polymerization, and fiber spinning. To arrange the building blocks in a spatially controlled manner, self-assembly mechanisms and alignment by magnetic fields are employed. Reactive and/or bioactive spherical and rod-shaped microgels interlink and form macroporous constructs facilitating 3D cell growth and cell-cell interactions or cells are able to use microgels as bricks to build their own house. Chemically defined poly(ethylene glycol)-based microgels, produced via parallelized step-emulsification microfluidics, self-organize with induced pluripotent stem cells (iPSCs) into 3D constructs by robust cell-material interactions. The iPSCs expand and retain their pluripotency, after which they can be differentiated into the three germ layers, providing a suitable platform for organoid differentiation, which was exemplary demonstrated for cardiac organoids. This new organoid production technology enables iPSC expansion and differentiation in the same construct in a reproducible and scalable manner, compatible with high-throughput automation. On the other hand, magneto-responsive rod-shaped microgels form the core of the patented Anisogel technology, which offers a low-invasive therapy to regenerate sensitive tissues with an oriented architecture. It can be injected and structured *in situ* to guide cells in a linear manner. Finally, a thermoresponsive hydrogel system, encapsulated with plasmonic gold-nanorods, actuates by oscillating light and elucidates how rapid hydrogel beating affects cell migration, focal adhesions, extracellular matrix production, and nuclear translocation of mechanosensitive proteins, depending on the amplitude and frequency of actuation. The time spent in the *in vitro* gym seems to affect myoblast differentiation and fibrosis, while actuation seems to induce mesenchymal stem cell differentiation into bone cells.