Rapid 3D Bioprinting of Gelatin Hydrogels via Click Chemistry
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Recently, Click chemistry reactions (CCR) have emerged as an attractive method in 3D bioprinting; in contrast to chain-growth polymerization as used by methacrylated gelatin (GelMA), CCR uses lower radical concentrations, is oxygen insensitive, and has higher homogeneity in the microstructure. We aimed to produce an entirely natural biopolymer system, maximizing the natural motifs, and therefore better recapitulating the in vivo tissue microenvironment.

In this work, we have synthesized both norbornene-functionalized and thiol-functionalized gelatin (GelNB and GelSH, respectively), showcasing the ability to photopattern an entirely natural polymer scaffold. Using a microscale continuous optical printing (µCOP) method, a faster alternative to two-photon printing, we printed various molar ratios of GelNB and GelSH to form hydrogels with different mechanical properties. These gels were analyzed for compression, strain and swelling. We also characterized the porous structures of the gels under scanning electron microscopy, observing homogeneity and distinct changes in crosslinking density for each solution. After confirming the printability of the solutions, we investigated post-patterning of the gels. Growth factors are present in the tissue microenvironment, thus incorporating them into our system would add an extra level of functionality. To this end, we used click chemistry once again; we photopatterned an ovalbumin protein onto the hydrogel, anchoring it to the free norbornene groups. We successfully printed the protein in distinct shapes and various concentrations, tempered by the exposure time, demonstrating the great flexibility of the material system.

To evaluate its efficacy as a biomaterial, we then evaluated the cell compatibility for both seeded and encapsulated cells. Using live/dead assays and CellTiter Glo, we found high viability and activity for HUVECs, HEPG2, and iPSC-cardiomyocytes.

Figure 1. A schematic of the work. GelNB and GelSH are 3D printed to form a hydrogel that is cell compatible. Protein can be post-patterned onto the gel in specific designs.