Understanding how complex intrinsic and external cues are integrated to regulate cell behavior is crucial to the success of cell-based therapies in the treatment of human disease. Systematic and quantitative investigation of these microenvironment signals was first enabled by precise cell positioning using 2-D micropatterning tools [1]. However, cellular signaling is often altered in adherent tissue culture where structural cues are lacking (including tumor, stem, and differentiated cells), in contrast to 3-D culture systems that more closely resemble in vivo cell behavior [2]. Our goal was to develop new micropatterning tools capable of micron-scale cell patterning and organization within a 3-D hydrogel with tissue-like properties. We developed a technique for the rapid formation of reproducible, high-resolution, 3-D cellular structures within a photo-crosslinkable hydrogel using dielectrophoretic forces (Figure 1) [3]. We demonstrate parallel formation of ~20,000 cell clusters of precise size and shape within a 1 x 2 cm² slab of tissue (Figure 2a), with high cell viability and differentiated cell function maintained over 2 weeks in culture. By modulating cell-cell interactions in clusters of various size (independent of hydrogel geometry, chemistry, or volumetric seeding density; Figure 2b), we present the first evidence that 3-D microscale tissue organization regulates chondrocyte behavior (Figure 2c) [3]. This dielectrophoretic cell patterning (DCP) technology enables further investigation of the role of tissue architecture in many other multicellular processes from embryogenesis to regeneration to tumorigenesis.

REFERENCES