Hematopoietic stem cells (HSCs) are a well-characterized system in terms of isolation, surface makers, and functionality markers. HSCs are an invaluable tool for development of microenvironment mimetic biomaterials, and development of an HSC synthetic niche will provide insight applicable to many stem cell cultures. Heterotypic cultures of murine HSCs and mesenchymal stromal cells (MSCs) were maintained over a 7-day period in a series of gelatin-based hydrogels that were characterized in terms of mechanics (Young’s/Shear modulus) and biotransport (diffusion, mesh). The HSC population was best maintained in a high-stiffness gel (E≈25kPa), in a heterotypic culture of 1:1 HSCs:MSCs. Biomarkers (DNA/Ki-67) show that quiescence within the culture platform is increased/comparable to freshly isolated HSCs.

Figure 1. A. Overview of experiment B. Material characterization C. HSC population change over 7-day culture D. Scores plot of reduced PLS model, showing clustering based on seeding density.

Due to low cell density, the MSCs and HSCs interacted primarily through indirect effects of secreted factors. Microarrays were used to quantitatively analyze 200 cytokines from the cultured media, and the resulting large data set was reduced using a Partial Least Squares filtering technique. This identified 29 cytokines that were essential in capturing the HSC lineage response. Specifically of interest is the potentially inhibiting role of MIP-2 which was shown to be the most important cytokine within the model. Evidence of remodeling of the hydrogel by MSCs has also implicated remodeling as a factor in HSC fate decision, and future work will be aimed at synergistically coupling MSC-mediate remodeling and soluble factors.