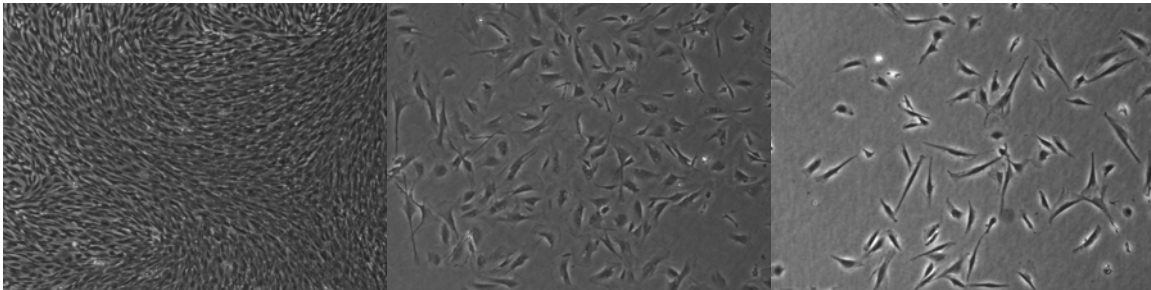
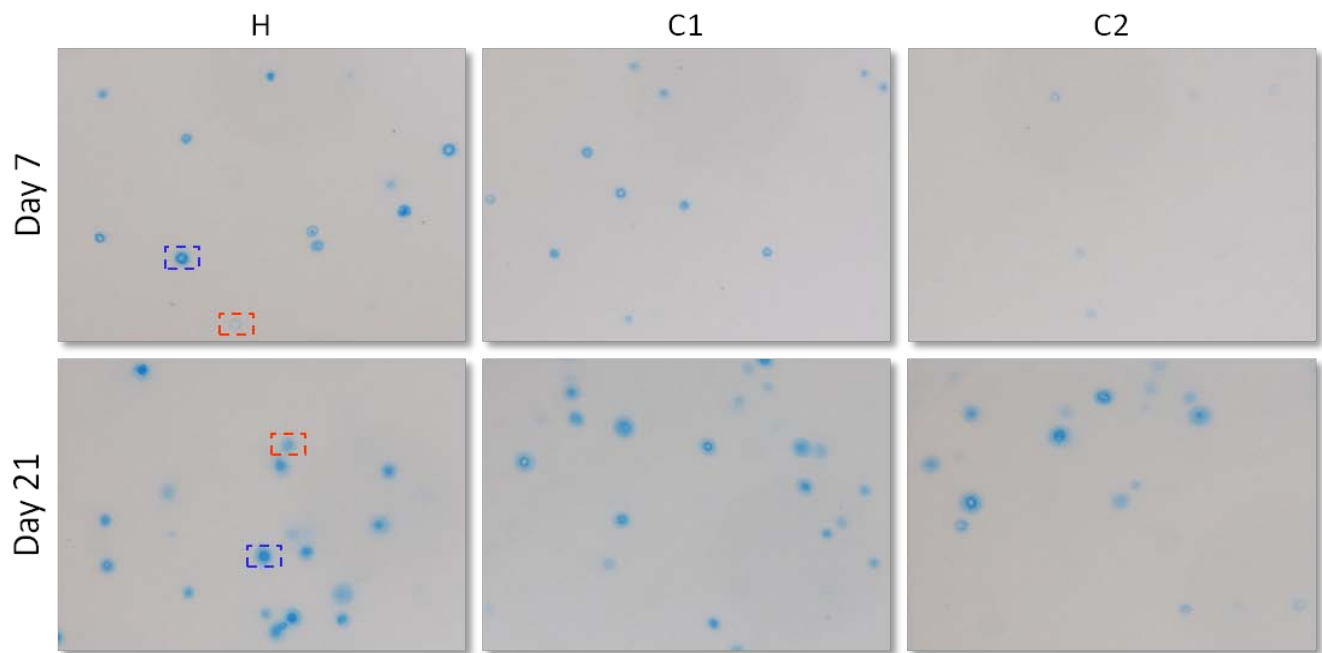


## **Analysis of Micromechanical Heterogeneity and Mechano-Sensitivity of Mesenchymal Stem Cells**

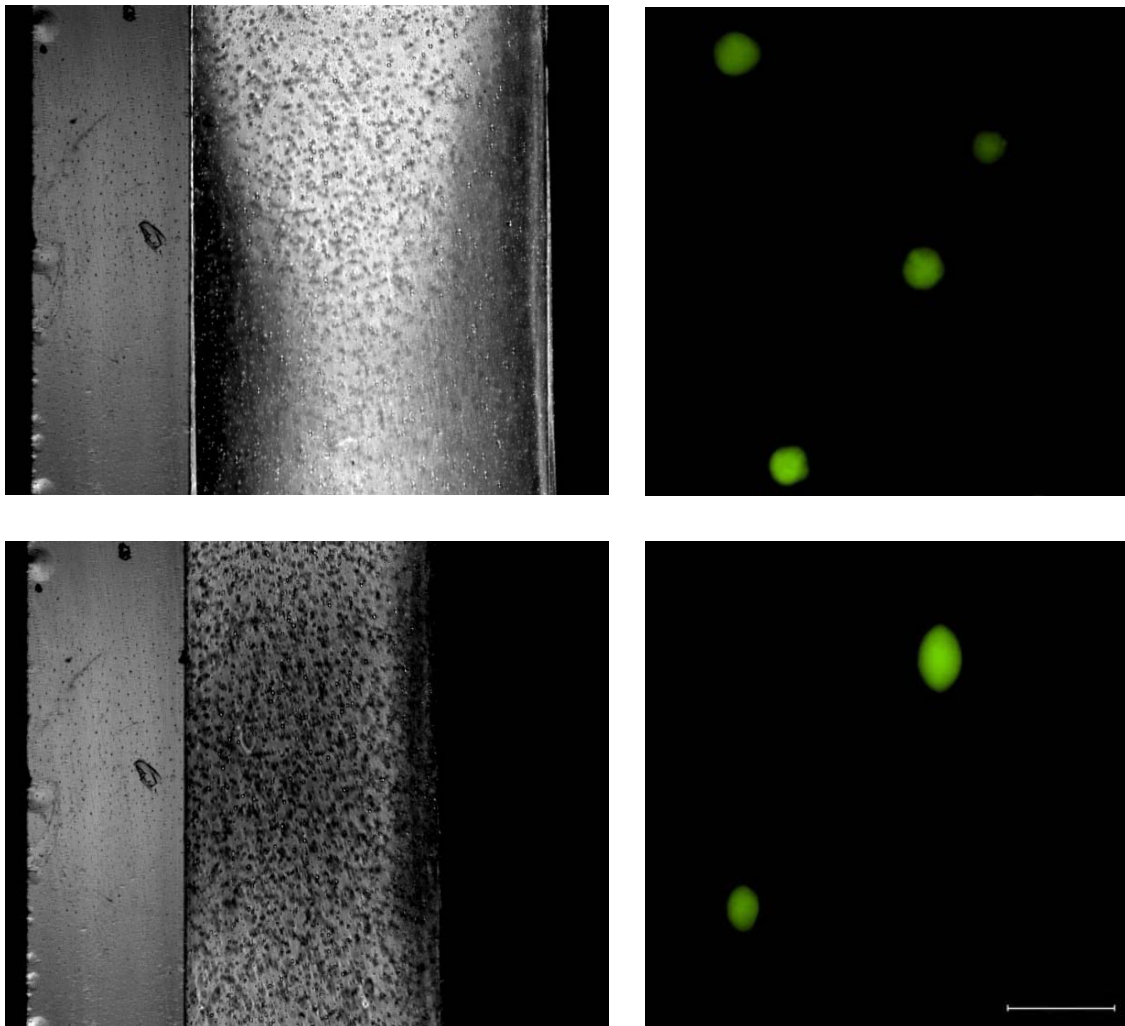
Mesenchymal stem cells (MSCs) are a clinically attractive alternative to chondrocytes for the development of engineered cartilage tissue owing to their ease of isolation and chondrogenic potential. However, the mechanical properties of MSC-based constructs have yet to match those of native cartilage or of chondrocyte-based constructs that have been cultured similarly. We hypothesize one reason for the disparity seen in the mechanical properties of MSC-based constructs is the heterogeneity in chondrogenic potential of the starting MSC population. Several groups have identified heterogeneity of isolated stem cell populations with respect to morphology, proliferation rate, and differentiation potential, but these differences have not yet been specifically correlated to chondrogenesis in 3D culture. As the pericellular matrix of chondrocytes is crucial for interpretation of biochemical and biomechanical cues in native cartilage tissue, we work to analyze the differences in the establishment of a robust pericellular matrix of clonally derived MSC subpopulations cultured within 3D hydrogels. Furthermore, we use advanced microscopy techniques to analyze how the development of this pericellular matrix modulates cell deformation when the bulk 3D environment is deformed. We have shown that clonal subpopulations do in fact differ in their ability to produce robust PCM at early times in culture, and that these differences are paralleled by the micromechanical properties of the cell and its microenvironment. The overall goal of this work is to better understand matrix deposition and differentiation by adult stem cells so as to improve the properties of engineered MSC-based cartilage replacements.



**Figure 1.** Differences in morphology, proliferation, and migration of MSC colonies are apparent. Phase images are of colonies located within the same tissue culture plate from a single donor isolation at day 11 (10x objective).



**Figure 2.** Alcian blue staining of proteoglycan deposition (C1, C2: clonal subpopulations; H: heterogeneous population). (Blue box indicates high pericellular staining; Red box indicates weak pericellular staining). Scale Bar: 200  $\mu$ m



**Figure 3.** Left) Phase contrast of gel at 0% (top) and 30% (bottom) bulk strain; Right) MSCs at 0% (top) and 30% (bottom) strain. Scale = 50  $\mu$ m.

**Recent Publications:**

1. Farrell MJ, Perreira JD, Mauck RL. Micromechanical Heterogeneity of Chondrogenic Mesenchymal Stem Cell Subpopulations in 3D Culture. Orthopaedic Research Society Annual Meeting 2010, New Orleans, LA.
2. Huang AH, Farrell MJ, Mauck RL. Mechanics and Mechanobiology of Mesenchymal Stem Cell-based Engineered Cartilage. J Biomech. 2009; 43: 128-136.

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