Characterization of connective tissue progenitors through phase contrast and multicolor fluorescence time-lapse microscopy

Edward Kwee\textsuperscript{1,3}, Kimerly Powell\textsuperscript{2}, George Muschler\textsuperscript{3}
\textsuperscript{1}Department of Biomedical Engineering
Case Western Reserve University
Cleveland, OH, USA
edward.kwee@case.edu

\textsuperscript{2}Department of Biomedical Informatics
The Ohio State University Medical Center
Columbus, OH, USA
kimerly.powell@osumc.edu

\textsuperscript{3}Department of Biomedical Engineering
Cleveland Clinic
Cleveland, OH, USA
muschlg@ccf.org

Abstract—Connective tissue progenitors (CTPs) are defined as the heterogeneous population of tissue resident stem and progenitor cells capable of proliferating and differentiating into connective tissue phenotypes. The prevalence and variation in clonal progeny of CTPs can be characterized using a colony formation assay. However, colony assays do not directly assess the characteristics of the colony founding CTP. We developed a large field of view, time lapse microscopy system with phase contrast and fluorescence capabilities that enables tracking from seeding through colony formation. Colonies were identified and characterized using automated image processing and quantitative analysis methods. Following colony identification, the time lapse was reversed to identify and characterize the colony founding CTP according to morphology and marker expression. We found that established markers for mesenchymal stem cells demonstrated low positive predictive value for CTPs and colony formation. This method can be used to study CTPs and other stem and progenitor cell populations to benefit point-of-care methods for assay and isolation in cell based therapies.

Index Terms—Stem and progenitor cells, colony forming assay, time lapse, phase contrast, fluorescence