428c Perfusion Flow Affects Human Mesenchymal Stem Cell Expansion, Ecm Structure, and Progenicity in 3d Scaffolds

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Human mesenchymal stem cells (hMSCs) have great clinical potential for a wide range of diseases. However, these cells are rare in adults and require extensive expansion for clinical usage. HMSCs are highly sensitive to the in vivo physiological environment such as chemical gradients and mechanical cues, and in vitro culture environments greatly influence their expansion and construct development. Elucidating the regulatory mechanisms of these parameters is an important step in developing a strategy to support 3D hMSC construct formation. Using the perfusion system developed in our lab, we have shown that hMSCs grown in the perfusion system have greatly increased metabolic rates, oxygen consumption, and uniform cellularity in the 3D constructs compared to static-culture, which is partially attributed to the improved nutrient transport in the perfusion system (Zhao and Ma, 2005; Zhao et al, 2005). The phenotype and tissue-morphogenesis patterns of hMSC grown in 3D PET matrices are also significantly affected by the different mechanical and biochemical cues inherent in static and perfusion systems. We have found that ECM structure and expression, and cell nuclear morphology, which correlated with cellular traits such as proliferation, differentiation, and progenicity, are significantly influenced by perfusion. To further understand the role of shear stress on construct development, we will investigate the effects of shear stress in the perfusion system on hMSC expansion, ECM formation, and progenicity of the cells. The perfusion system will be operated under flow rates in the range of 0.1 to 1.5 mL/min and the cell expansion, progenicity, and ECM secretion and structure will be evaluated. These results will provide experimental evidence on the mechanism of the effects of perfusion flow on hMSC tissue development characterized by expansion, ECM structure and progenicity in the 3-D constructs.