

## **MECHANICAL STRAIN-SENSITIVE TRANSCRIPTOME PROFILES IN HUMAN MESENCHYMAL STEM CELLS AND VASCULAR SMOOTH MUSCLES CELLS**

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**INTRODUCTION:** Human adult mesenchymal stem cells (MSCs) have been proposed for use in cardiovascular cell-based therapies. MSCs have the potential to home to sites of injury, recruit vascular cells and stabilize vessel formation, and secrete cytokines and growth factors to promote cell survival. While this data supports a role for MSCs in vascular therapies, little is known about the response of MSCs to physical cues inherent to the vasculature. Vascular smooth muscle cells (SMCs) are exposed to cyclic mechanical strain due to the pulsatile nature of blood flow. Cyclic strain alters smooth muscle cell proliferation, migration, and alignment via a range of gene and protein cell signaling molecules, affecting cell proliferation, migration, and alignment. The objective of this study was to profile the response of the MSCs transcriptome to physiologically-relevant applied cyclic strain, in comparison with that of SMCs.

**METHODS:** MSCs and SMCs were subjected to applied equibiaxial cyclic strain (10%, 1 Hz) or parallel static culture for 24 hours using a custom-built bioreactor. Gene expression was assessed using whole human genome microarrays or standard qPCR. Statistical and ontology analysis were completed using GeneSpring and Ingenuity Pathways Analysis.

**RESULTS:** Microarray analysis showed more genes had significant ( $p \leq 0.05$ ,  $n=3$ ) expression differences due to cell type than force condition (16983 vs. 633 genes), determined via two-factor ANOVA. Approximately 500 genes showed significant ( $p \leq 0.05$ ,  $n=3$ ) differences in strain vs. static culture for MSCs and SMCs. Of these, 142 genes exhibited a conserved strain-response in both cell types. Strain-responsive gene expression was primarily associated with NRF2-mediated oxidative stress response, a defense mechanism important for normal cardiovascular function. Kinetic assessment of NRF2-related signaling components after 0, 2, 6, 12, and 24 hours applied strain identified HMOX1 as significantly ( $p \leq 0.005$ ,  $n \geq 3$ ) upregulated within 6 hours in both cell types.

**CONCLUSION:** This study highlights the unique nature of cellular response to mechanical strain and identifies a subset of genes with conserved mechanosensitivity.