The Mechanical Contribution of Vascular Smooth Muscle Cells in Atherosclerosis

Nisha Khatiwada[1,2], Alex P. Rickel[1], Zhongkui Hong[1,2]*
1. Department of Biomedical Engineering, University of South Dakota
2. Department of Mechanical Engineering, Texas Tech University

Cardiovascular disease remains primary cause of death worldwide. During atherosclerosis, vascular walls accumulate cholesterol and cause plaque formation. Vascular smooth muscle cells (VSMCs) undergo phenotypic switching to a synthetic phenotype capable of proliferation and migration. This leads to arterial wall stiffening and thus alter micromechanical environment of VSMCs. In this study, we analyzed how the mechanics of VSMCs isolated from Western diet-fed apolipoprotein-E knockout ($ApoE^{-/-}$) and wild-type (WT) mice were altered during atherosclerosis. VSMCs were isolated from the descending thoracic aorta of male $ApoE^{-/-}$ and WT mice and were cultured on elastically tunable substrates mimicking variation in environmental stiffness experienced by VSMCs in atherosclerosis. Stiffness of VSMCs, N-cadherin mediated cell-cell adhesion, and integrin mediated cell-ECM adhesion forces were measured using atomic force microscope (AFM). AFM and image processing was used to examine live VSMC cytoskeleton architecture. Significant results were obtained from the experiments performed. $ApoE^{-/-}$ VSMCs were found to have a significantly higher E-modulus compared to WT VSMCs. Increased stiffness of $ApoE^{-/-}$ VSMCs correlated with a greater degree of stress fiber alignment as evidenced by AFM-generated force maps and stress fiber topography images. $ApoE^{-/-}$ VSMCs migrated longer distance but had a significantly lower adhesion for both N-Cad and COL-1 compared to WT. The results demonstrated a significant alteration in cell mechanics, cytoskeletal organization, and migratory behavior of VSMCs isolated from $ApoE^{-/-}$ and WT mice. This provides a further insight into VSMC behavior during the progression of atherosclerosis.