Difference in the mechanics of vascular smooth muscle cells from wild type and apolipoprotein-E knockout mice

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Introduction: Cardiovascular disease, a major cause of mortality worldwide, is primarily caused by atherosclerosis [1]. Vascular smooth muscle cells (VSMCs) comprise the medial layer of the arterial wall and undergo phenotypic switching during atherosclerosis to a synthetic phenotype capable of proliferation and migration. The surrounding environment undergoes alterations in extracellular matrix (ECM) stiffness and composition in addition to an increase in cholesterol content [2]. Our work is committed to investigating and analyzing difference in the mechanics of VSMCs isolated from western diet fed apolipoprotein-E knockout ($ApoE^{-/-}$) and wild type (WT) mice during atherosclerosis.
Materials and methods: VSMCs were isolated from the descending thoracic aorta of male $ApoE^{-/-}$ and male WT mice. VSMCs were cultured on elastically tunable substrates. Atomic force microscope (AFM) was employed to study N-cadherin (N-Cad) mediated cell-cell adhesion, integrin mediated cell-ECM adhesion forces, and stiffness of VSMCs. AFM was also used to examine live VSMC submembranous cytoskeleton architecture. Two-way ANOVA was used to infer statistical significance for all experiments.
Results and Discussion: $ApoE^{-/-}$ VSMCs were found to have a significantly higher E-modulus compared to WT VSMCs (Figure 1). 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 had a significantly lower adhesion force to N-Cad compared to WT on the 28 and 103 kPa substrates.

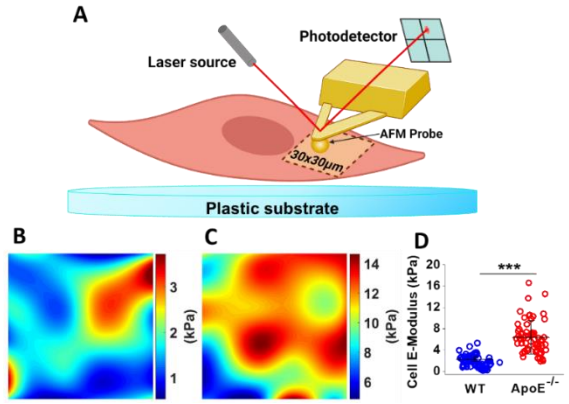

Fig. 1. Live WT and $ApoE^{-/-}$ VSMC stiffness maps. (A) 30 × 30 μm cell surface areas were automatically scanned and indented at 6×6 positions with a glass bead. **(B, C)** Stiffness force maps for WT and $ApoE^{-/-}$ VSMCs, respectively. **(D)** Average stiffness for WT and $ApoE^{-/-}$ VSMCs.

Conclusion: The results demonstrated a significant difference in cell mechanics, cytoskeletal organization, and migratory behavior of VSMCs isolated from WT and $ApoE^{-/-}$ mice. This supports our hypothesis that atherosclerosis alters the mechanical properties of VSMCs and provide insight into underlying mechanisms that may lead to future novel therapeutic approaches.

References:

1. Lusis, A. J. Nature (2000) 407, 233–241
2. Raines, E. W. Int J Exp Pathol. (2000) 81(3), 173-182.