

Unveiling the Role of Cellular Mechanical Oscillation in Vascular Smooth Muscle Cell Migration

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Aberrant cell proliferation and migration contribute significantly to diseases like atherosclerosis, vascular restenosis, and cancer metastasis. Cell migration involves dynamic cytoskeletal changes that drive membrane extension and exploration. Our research suggests that cell migration is linked to cellular mechanical oscillations, not static mechanics. Therefore, targeting these oscillations could be a promising strategy to treat migration-related diseases, including cardiovascular diseases (CVD).

We studied vascular smooth muscle cells (VSMCs) that were isolated from the descending thoracic aorta of male ApoE^{-/-} and male WT mice. An Atomic Force Microscope (AFM) (MFP-3D-BIO, Asylum Research, Santa Barbara, CA) was used to examine the oscillation in VSMC mechanics. Live VSMC submembranous cytoskeleton architecture was assessed with AFM and confocal microscopy (IX83 FV1200, Olympus, USA). Real-time cellular mechanics and cytoskeleton architecture data were analyzed using an in-house data-driven mathematical model. Statistical significance was determined by two-way ANOVA for all experiments.

We observed that ApoE^{-/-} VSMCs exhibited significantly higher E-modulus compared to WT VSMCs. This increased stiffness correlated with more pronounced stress fiber alignment, evident from AFM-generated force maps and stress fiber topography images. Additionally, ApoE^{-/-} VSMCs displayed notably greater mechanical oscillation amplitude than WT cells. This outcome can be attributed to differential cholesterol loading between ApoE^{-/-} and WT cells following high-fat diet exposure, leading to modified VSMC adhesion and heightened cell migration, as previously demonstrated in our study. These findings shed light on the dynamic cellular mechanism associated with cell migration in CVD and offer insights for a novel therapeutic approach to atherosclerosis treatment.