Cell Migration and Mechanical Oscillations: Implications for Cardiovascular Diseases

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Cell proliferation and migration are pivotal in the pathogenesis of diseases like atherosclerosis, vascular restenosis, and cancer metastasis. Cell migration, driven by dynamic cytoskeletal changes, involves membrane extension and exploration. Our research highlights the intricate connection between cell migration and cellular mechanical oscillations, emphasizing their significance over static mechanics. Targeting these oscillations holds promise as a strategy for treating cell migration-related diseases, including cardiovascular diseases (CVD).

In our study, we investigated vascular smooth muscle cells (VSMCs) isolated from the descending thoracic aorta of male ApoE$^{-/-}$ and male WT mice. Using an Atomic Force Microscope (AFM) (MFP-3D-BIO, Asylum Research, Santa Barbara, CA), we explored VSMC mechanics' oscillations. Live VSMC submembranous cytoskeleton architecture was examined through 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, with statistical significance determined by two-way ANOVA.

Our findings revealed that ApoE$^{-/-}$ VSMCs exhibited significantly higher E-modulus compared to WT VSMCs. This increased stiffness correlated with more pronounced stress fiber alignment, demonstrated by AFM-generated force maps and stress fiber topography images. Additionally, ApoE$^{-/-}$ VSMCs displayed notably greater mechanical oscillation amplitude than WT cells. This outcome stemmed from differential cholesterol loading between ApoE$^{-/-}$ and WT cells following high-fat diet exposure, modifying VSMC adhesion and enhancing cell migration, as demonstrated in our study.

These results shed light on the dynamic cellular mechanism associated with cell migration in CVD, offering valuable insights for a novel therapeutic approach to atherosclerosis treatment.