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The Effect of Combined Fluid Shear Stress and Cyclic Stretch on Endothelial Cells

Authors : Daphne Meza, Louie Abejar, David A. Rubenstein, Wei Yin

Abstract : Endothelial cell (ECs) morphology and function is highly impacted by the mechanical stresses these cells experience in vivo. Any change in the mechanical environment can trigger pathological EC responses. A detailed understanding of EC morphological response and function upon subjection to individual and simultaneous mechanical stimuli is needed for advancement in mechanobiology and preventive medicine. To investigate this, a programmable device capable of simultaneously applying physiological fluid shear stress (FSS) and cyclic strain (CS) has been developed, characterized and validated. Its validation was performed both experimentally, through tracer tracking, and theoretically, through the use of a computational fluid dynamics model. The effectiveness of the device was evaluated through EC morphology changes under mechanical loading conditions. Changes in cell morphology were evaluated through: cell and nucleus elongation, cell alignment and junctional actin production. The results demonstrated that the combined FSS-CS stimulation induced visible changes in EC morphology. Upon simultaneous fluid shear stress and biaxial tensile strain stimulation, cells were elongated and generally aligned with the flow direction, with stress fibers highlighted along the cell junctions. The concurrent stimulation from shear stress and biaxial cyclic stretch led to a significant increase in cell elongation compared to untreated cells. This, however, was significantly lower than that induced by shear stress alone, indicating that the biaxial tensile strain may counteract the elongating effect of shear stress to maintain the shape of ECs. A similar trend was seen in alignment, where the alignment induced by the concurrent application of shear stress and cyclic stretch fell in between that induced by shear stress and tensile stretch alone, indicating the opposite role shear stress and tensile strain may play in cell alignment. Junctional actin accumulation was increased upon shear stress alone or simultaneously with tensile stretch. Tensile stretch alone did not change junctional actin accumulation, indicating the dominant role of shear stress in damaging EC junctions. These results demonstrate that the shearing-stretching device is capable of applying well characterized dynamic shear stress and tensile strain to cultured ECs. Using this device, EC response to altered mechanical environment in vivo can be characterized in vitro.

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