Role of Mechanosensor in Endothelial Cells

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Vascular endothelial cells (ECs), which form the innermost layer of the blood vessel, are constantly exposed to hemodynamic forces, including blood flow-induced shear stress. From the early 1960s when associations between flow characteristics, particularly blood flow–induced wall shear stress, and the localization of atherosclerotic plaques were uncovered. Atherosclerotic lesions preferentially develop in regions of arterial branches and curvatures, where the local flow is disturbed with low and oscillatory shear stress. In contrast, the straight part of the artery, where the flow is laminar with higher levels of shear stress, is generally spared from atherosclerosis. These observations suggest that hemodynamic forces play important roles in the formation and progression of atherosclerosis. Recent data have highlighted the potential EC mechanoreceptors that may mediate EC responses to different flow patterns and shear stresses, and they may mediate mechanobiological coupling that leads to exquisite alterations of the component cells down to the level of gene expression networks. A mechanosensory complex on the endothelial cell surface has been identified as an initial transducer of mechanical forces consisting of the adhesion molecules PECAM-1 (platelet endothelial cell adhesion molecule-1), which is the mechanosensor, and VE-cadherin and VEGFR-2 (vascular endothelial growth factor receptor-2), which, once activated, stimulate a host of downstream signaling pathways. Mechanotransduction via this trimolecular complex mediates integrin activation, which causes elongation and alignment of cells in the direction of flow, characteristic of cells in high-shear, protected regions. This is an adaptive response that redistributes and reduces the local mechanical load experienced by the cell, reducing subsequent injury, and is dependent on anchoring of endothelial cells to the ECM via integrins. High laminar shear stress induces rapid conformational activation of integrins leading to remodeling of endothelial attachment sites and increased binding to the ECM, triggering cytoskeletal rearrangement and cell alignment.
The knowledge gained on mechanotransduction in ECs in response to shear stress will advance our understanding of the physiological and pathophysiological processes that contribute to the progression of vascular diseases.