Vascular Mechanobiology in Health and Disease

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Atherosclerosis, a disease of arteries that is responsible for most cardiovascular-related morbidity and mortality, develops predictably in regions of the arterial tree in which wall shear stresses are generated by complex patterns of blood flow. It has been recognized that hemodynamic characteristics determine the location of lesions and contribute to the pathogenesis of atherosclerosis. The key cells involved in atherogenesis include vascular endothelial cells (ECs), smooth muscle cells (SMCs), and different types of leukocytes including T-lymphocytes and monocytes/macrophages. Recent evidence suggests that laminar blood flow in the straight part of the arterial tree and high shear stress modulate cellular signaling and EC function, and protect against atherogenesis. In contrast, disturbed flow in bifurcations of the arterial tree and the associated oscillatory low shear stress enhance leukocyte infiltration of the arterial wall and thus are atherogenic. Although the effect of laminar shear stress on ECs has been intensively studied, little is known about the effect of disturbed flow on ECs, especially on their interactions with circulating leukocytes in bloodstream, as well as with the underlying SMCs, whose phenotypic switching is significantly implicated in the initiation of atherosclerosis. These interactions between ECs, leukocytes, and SMCs with different phenotypes generated in response to different types of flow can modulate gene expression and function of these cells and consequently contribute to development of atherosclerotic lesions. Understanding of the effects of different patterns of flows and shear stresses on these cell-cell interactions can provide mechanistic insights into the role of complex flow patterns in pathogenesis of vascular diseases, and help to elucidate the phenotypic and functional differences between quiescent (non-atherogenic/non-thrombogenic) and activated (atherogenic/thrombogenic) cells. Such information can contribute to our understanding of the etiology of lesion development in vascular niches with disturbed flow and help to generate new approaches for therapeutic interventions.