Biomedical Engineering

Seminar

Hemodynamics and the Functional Compartmentalization of Vascular Endothelium

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11:00am-12:00 pm

Abstract:

Functional Compartmentalization (adjacent regions with altered cell function) of vascular endothelium is apparent in atherogenesis-prone regions of the human vasculature.

The localization of atherosclerotic lesions coincides with regions of disturbed blood flows where endothelial cells of altered phenotype are found adjacent to normal endothelium in undisturbed flow where the vessel is relatively protected from lesion development.

The cellular and molecular mechanisms by which hemodynamics might alter endothelial cell function leading to lesion development remain unclear. The direct passage of small molecules (<1 kD) through endothelial gap junctions is important for the function and homeostasis of the vessel wall. We hypothesize that gradients in fluid shear stress associated with disturbed flows, induce regional changes in endothelial gap junctional communication (GJIC) which in turn, affect cell phenotype, contributing to "functional compartmentalization" of the endothelial monolayer in vivo and in vitro.

We are investigating endothelial GJIC in in vitro model systems in which all of the hemodynamic features of atherosclerotic lesion-prone regions of the vasculature can be recreated. The fluid dynamic environment is controlled and its effect on cell function and contribution to endothelial "functional compartmentalization" is evaluated. Endothelial cell morphology, proliferation, migration, monolayer permeability, and regulation of intercellular adhesion molecules are evaluated as biological features associated with altered endothelial phenotype. These cell functions are correlated with alterations in vascular gap junction expression (gene, protein, macromolecular assembly, and functional GJIC). To evaluate the physiological relevance of our in vitro findings, we are investigating gap junction expression in vivo by en face immunostaining of rat aorta at vascular sites of disturbed and undisturbed flow.

Our results suggest a prominent role for hemodynamics in regulating endothelial cell communication and determining regional differences in cell function that may contribute to the vascular pathophysiological changes found at sites of atherosclerotic lesion development.

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