



## Department of Chemical Engineering Seminar Series

Tuesday, October 20, 2009

Presentation: 1:30 p.m., 1017 H.H. Dow

Refreshments to Follow: 3158 H.H. Dow (Pod Room)

### Larry V. McIntire

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#### *Role of Mechanical Forces in Vascular Biology*

Understanding the molecular basis of the modulation of vascular phenotype by mechanical forces (stresses induced by blood flow and vessel wall strain) is an area of great significance in vascular biology. It is hypothesized that certain flow environments (arterial flow, non-reversing) lead to anti-atherogenic endothelium, while low mean wall shear stress reversing flows promote a pro-atherogenic endothelium. We examined in a flow chamber human endothelial cells exposed to high (15 dynes/cm<sup>2</sup>) and low (1 dyne/cm<sup>2</sup>) steady shear stress and a reversing waveform characteristic of the carotid sinus (time average 1 dyne/cm<sup>2</sup>) using whole human genome microarray studies. We demonstrated unique sets of genes controlled by both low average shear stress and by reversing flow, with more genes controlled by low average stress. Functional studies confirmed that reversing flow increases cell proliferation and monocyte adhesion. Detailed studies of two cytochrome P450 genes that are maximally up-regulated by steady arterial levels of shear stress (CYP1A1 and CYP 1B1) demonstrated strong attenuation by reversing flows. Furthermore, CYP1A1 protein and AhR nuclear localization correlate with flow patterns in the mouse aortic arch in vivo. Finally, as a result of changes observed in zinc-binding and zinc transporter proteins, changes in free zinc were measured under different shear stresses. High steady shear stress exposure dramatically increases the levels of free zinc in endothelial cells.

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