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"Convergence of Biology and Biomechanics in the Pathogenesis of Vascular Disease"

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Suddath Seminar room (IBB 1128)
Georgia Institute of Technology

Abstract:

Cardiovascular disease remains the number one cause of death in the United States today. In addition to a plethora of genetic and environmental factors, the diet and lifestyle of Western populations continues to have a profound negative impact on the prevalence of atherosclerotic disease. Significant advances have been made in the management and treatment of the clinical sequalae of this disease process. However, many of these treatments are geared towards the management of catastrophic clinical events, and our appreciation of the basic pathophysiology of atherosclerosis is still lacking in terms of our understanding of the fundamental biology and biomechanics of the atherosclerotic lesion.

Intense efforts have been made over the past decade to identify the factors responsible for the initiation, development, and rupture or erosion of atherosclerotic lesions. Several central theses have emerged from these studies. Mechanical factors impinging on the arterial wall are of major pathophysiologic importance throughout the atherosclerotic disease process. This includes both the effects of fluid shear stress as well as physical stress within the arterial wall and atherosclerotic lesions. Second, inflammatory mechanisms involving the production of reactive oxygen species, expression of pro-inflammatory gene products, apoptosis, and mononuclear infiltration of the arterial wall appear to be central pathogenic mechanisms in all stages of atherogenesis. What is lacking is a comprehensive understanding of the potential convergence of fluid shear forces and physical stresses within the arterial wall and the combinatorial impact of these forces on inflammatory

responses within the arterial wall.

Our laboratory has a global focus on the role of vascular inflammation in the pathogenesis of vascular disease. In this seminar I will provide an integrative view of how biological and mechanical stimuli converge to promote a proinflammatory state within the arterial wall. Using a combination of in vivo and in vitro studies, we have shown that several critical signaling pathways are convergnetly regulated by mechanical and biological stimuli to produce inflammation in the vascular wall. This inflammation is the critical step in the pathogeneis of atherosclerosis, aneurysm formation and other vascular diseases.