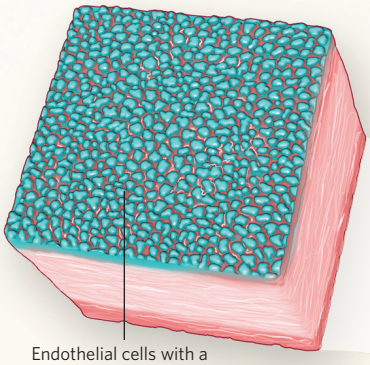
ANDREW SWIFT, FOR THE SCIENTIST, FEBRUARY 2011

STRESS AND INFLAMMATION

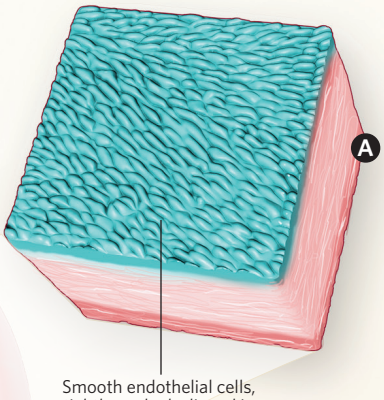
Cardiovascular disease, including coronary artery disease and stroke, is the single greatest cause of death worldwide and is a major burden on health services and society. Most resources are currently directed towards surgical intervention and management of advanced disease; recently, however, research has revealed molecular mechanisms that could lead to better treatment and prevention strategies.



Endothelial cells with a cobblestone morphology

B LOW SHEAR STRESS

Atherosclerotic lesions develop predominantly at branches, bends and bifurcations in the arterial tree. These sites are exposed to slow or disturbed blood flow which exerts low/oscillatory shear stress on the vessel wall. Without input from the mechanosensor complex 1 to dampen inflammatory signaling, this environment primes endothelial cells for inflammation by inducing adhesion molecule expression (VCAM-1, ICAM-1, and E-selectin) on the endothelial surface 2. These "sticky" molecules facilitate the recruitment of leukocytes to the vessel wall. Once there, they pass between the endothelial cells and accumulate within the intima, driving plaque formation. The compound sulforaphane, a naturally occurring antioxidant found in broccoli and other green vegetables, activates Nrf2 and limits inflammation, representing a novel therapeutic strategy against cardiovascular disease 3.



Smooth endothelial cells, tightly packed, aligned in direction of blood flow

A HIGH SHEAR STRESS

Regions of the arterial tree that are exposed to uniform, unidirectional blood flow experience high shear stress which is sensed by a mechanosensory complex on the endothelial surface. This mechanical signal is transduced into biochemical signaling events resulting in activation of KLF-2 and Nrf2 transcription factors 1. These suppress proinflammatory signaling pathways and prevent expression of adhesion molecules, protecting against the development of atherosclerotic plaques within the vessel wall 2.