Metalloproteinases, Mechanical Factors and Vascular Remodeling

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ABSTRACT

Chronic increases in arterial blood flow elicit an adaptive response of the arterial wall, leading to vessel enlargement and reduction in wall shear stress to physiological baseline value. Release of nitric oxide from endothelial cells exposed to excessive shear is a fundamental step in the remodeling process, and potentially triggers a cascade of events, including growth factor induction and matrix metalloproteinase activation, that together contribute to restructuralization of the vessel wall. NO synthesis blockade in vivo inhibits adaptive wall shear stress regulation in vessels subjected to chronic increased blood flow. This effect is partial, indicative that other factors are probably involved. The pathways by which the remodeling action of NO is mediated include metalloproteinase activation and possibly implicate the induction of growth factor mitogenic activity as well. Furthermore, matrix metalloproteinase (MMP) activation is required for adaptive arterial remodeling (IEL fragmentation and arterial enlargement) to occur. These observations are significant since adaptive vascular enlargement and remodeling are known to accompany early human coronary atherosclerosis, and exaggerated expression of MMPs, in particular MMP-2, is now known to be a ubiquitous marker of aortic aneurysms, and could reflect abnormal flow-induced vessel remodeling. Hence understanding the process of vascular remodeling could help explain how changes in blood vessel wall structure occur in the context of atherosclerosis or aortic aneurisms.

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