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Title: Inflammation in atherosclerosis: innate immunity on track or off-piste?

Abstract: Atherosclerosis on vascular walls is believed to be an inflammatory disease, but it is not fully understood whether inflammation is there to help in the removal of accumulated lipids or causative for the disease. We have analyzed the expression of complement genes and protein interactions in atherosclerotic walls and adipose tissues. Compared to controls (n= 25) coronary vessel walls from atherosclerotic individuals (n=50) showed upregulation of complement C1q, ficolin-1 and ficolin-3, as well as of complement receptor (CR1, CR3, C1qR, C5aR1, C5aR2, C3aR) genes. In contrast the genes for C3, factor D and the terminal pathway components were down-regulated. These results point towards an ongoing recognition of nonviable structures by sensors of the complement system and their clearance by complement receptors expressed on macrophages. The expression of factor H, a key factor in regulating complement activation, was also upregulated in atherosclerotic lesions. Its genetic variant Ile62Val has been found to be strongly associated with high levels of the matrix metalloproteinase 8 (MMP8) in atherosclerotic individuals. Factor H interacts with some key players related to atherosclerotic inflammation, like C3b, C-reactive protein (CRP) and apolipoprotein E (apoE). Together they regulate opsonophagocytosis of modified lipoprotein particles and cholesterol by macrophages. The results reveal the intricate network of inflammatory and anti-inflammatory interactions, where the complement system appears to be the cohesive system linking together lipid metabolism, inflammation and innate immune clearance functions.

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