

MECHANISM OF MATRIX METALLOPROTEINASE-14 (MMP-14) EXPRESSION DURING ATHEROSCLEROSIS

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ABSTRACT

Atherosclerosis is characterized by the narrowing of the arterial lumen due to formation of the plaque within the intimal layer of the arterial wall resulting in the impaired flow of blood to the target organs. Most severe consequences of atherosclerosis arise due to the rupture of the atherosclerotic plaque, which is the cause of stroke, myocardial infarction, etc. Rupture of the plaque occurs due to the thinning of the fibrous cap of the plaque. Increased expression of matrix metalloproteinases (MMPs), including MMP-14, the enzymes which can cause degradation of many components of the extracellular matrix, is the cause of thinning and rupture of the fibrous cap of the atherosclerotic plaque. Increased expression of MMP-14 is due to its transcriptional upregulation during inflammatory conditions such as atherosclerosis. In a recent study, we have shown that serum amyloid A-activating factor-1 (SAF-1) is involved in the increased expression of MMP-14 in the atherosclerotic lesion area. This discovery is a major breakthrough in understanding the regulation of MMP-14 gene expression during inflammatory conditions. However, we still do not have a clear understanding of the regulatory processes that are involved in the expression of MMP-14 during physiological and pathological conditions. We here show that another transcription factor, octamer binding protein-1 (Oct-1) may be involved in the regulation of MMP-14. We have here shown that there is physical interaction between SAF-1 and Oct-1, and Oct-1 may be involved in controlling SAF-1 mediated expression of MMP-14 gene. The crucial finding that Oct-1 is a downregulator of MMP-14 gene may be an important target for developing new therapeutic measures for the treatment of atherosclerosis.