

Public Abstract

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Title: Mechanism of matrix metalloproteinase-14 (MMP-14) regulation during atherosclerosis.

Atherosclerosis is the most common cause of morbidity and mortality in the developed countries including the US. Atherosclerosis is a chronic inflammatory disease characterized by the build up of plaques in the lumen of the arteries. During the pathogenesis of atherosclerosis, the cap of the atherosclerotic plaque is degraded due to the action of proteases including matrix metalloproteinases (MMPs). The degradation of the cap of the atherosclerotic plaque leads to the plaque rupture. It also causes the release of the contents of plaque which form emboli and block the flow of blood supplying the vital organs leading to conditions such as stroke and myocardial infarction.

Among these MMPs, MMP-14 is an important protease involved in the degradation of the atherosclerotic plaque. MMP-14 is expressed as membrane bound MMP and is involved in the activation of other members of MMP family including MMP-2 and MMP-13. The expression of MMP-14 is primarily regulated at the level of transcription. We here show that an inflammation responsive transcription factor, Serum Amyloid A Activation Factor-1 (SAF-1) is involved in the upregulation of MMP-14 expression during atherosclerosis. We also show that an ubiquitously expressed transcription factor, Octamer binding protein-1 (Oct-1) downregulates the SAF-1 mediated expression of MMP-14 gene. The crucial finding that Oct-1 is involved in downregulating SAF-1 mediated expression of MMP-14, may be the target of future therapeutic measures for the treatment and control of atherosclerosis.