Matrix metalloproteinase

Matrix metalloproteinases (MMPs) are zinc-dependent endopeptidases; other family members are adamalysins, serralysins, and astacins. The MMPs belong to a larger family of proteases known as the metzincin superfamily, which are involved in the remodeling of vascular walls.

Collectively, these enzymes are capable of degrading all kinds of extracellular matrix proteins, but also can process a number of bioactive molecules. They are known to be involved in the cleavage of cell surface receptors, the release of apoptotic ligands (such as the FAS ligand), and chemokine/cytokine inactivation.

They were first described in vertebrates (1962), including humans, but have since been found in invertebrates and plants. They are distinguished from other endopeptidases by their dependence on metal ions as cofactors, their ability to degrade extracellular matrix, and their specific evolutionary DNA sequence.

Proteins of the matrix metalloproteinase (MMP) family are involved in the breakdown of extracellular matrix (ECM) in normal physiological processes, such as embryonic development, reproduction, and tissue remodeling, as well as in disease processes, such as arthritis and metastasis. Most MMP's are secreted as inactive proproteins which are activated when cleaved by extracellular proteinases. This gene encodes an enzyme which degrades type IV collagen, the major structural component of basement membranes. The enzyme plays a role in endometrial menstrual breakdown, regulation of vascularization and the inflammatory response.

MMPs are also thought to play a major role on cell behaviors such as cell proliferation, migration (adhesion/dispersion), differentiation, angiogenesis, apoptosis, and host defense.

A study investigated a joint contribution of matrix metalloproteinases (MMPs) genes to ischemic stroke (IS) development and analyzed interactions between MMP genes and genome-wide associated loci for IS. A total of 1288 unrelated Russians (600 IS patients and 688 healthy individuals) from Central Russia were recruited for the study. Genotyping of seven single nucleotide polymorphisms (SNPs) of MMP genes (rs1799750, rs243865, rs3025058, rs11225395, rs17576, rs486055, and rs2276109) and eight genome-wide associated loci for IS were done using Taq-Man-based assays and MALDI-TOF mass spectrometry iPLEX platform, respectively. Allele - 799T at rs11225395 of the MMP8 gene was significantly associated with a decreased risk of IS after adjustment for sex and age (OR = 0.82; 95%CI, 0.70-0.96; P = 0.016). The model-based multifactor dimensionality reduction method has revealed 21 two-order, 124 three-order, and 474 four-order gene-gene (G×G) interactions models meaningfully (Pperm < 0.05) associated with the IS risk. The bioinformatic analysis enabled establishing the studied MMP gene polymorphisms possess a clear regulatory potential and may be targeted by gene regulatory networks driving molecular and cellular pathways related to the pathogenesis of IS. In conclusion, the present study was the first to identify an association between polymorphism rs11225395 of the MMP8 gene and IS risk. The study findings also indicate that MMPs deserve special attention as a potential class of genes influencing the multistep mechanisms of cerebrovascular disease including atherosclerosis in cerebral arteries, acute cerebral artery occlusion as well as the ischemic injury of the brain and its recovery [1)].

Matrix metalloproteinases may play a role in the development of Failed Back Surgery Syndrome (FBSS) Spinal Cord Stimulation (SCS) increases the already elevated MMP-2 serum levels which are associated with Neuroinflammation in FBSS patients [2].

They play a pivotal role in regulating the biology of stem cells, and play the important role in the process of glioblastoma cell invasion through 3D matrices. However, the effects of MMP inhibitors used in the treatment of malignant gliomas are unsatisfactory.

(MMP) plays a pivotal role. MMPs have long been linked to tumor invasion owing to their crucial involvement in the breakdown of the extracellular matrix and in the proteolytic activation of various classes of tumor progression factors. Accordingly, increased expression and activation of MMPs are found in almost every type of human cancer compared with normal tissue, and this has been associated with poor patient prognosis [3] [4] [5].

see Matrix metalloproteinase 2

see Matrix metalloproteinase 9.

Data suggest that macrophage-derived MMP-2 and -9 may play an important role in the progression of intracranial aneurysms. The findings will shed a new light into the pathogenesis of cerebral aneurysms and highlight the importance of inflammatory response causing the degeneration of extracellular matrix in the process of this disease [6].

1)
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