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Short Communication

Matrix Metalloproteinases Enzyme and Risk for HIV-Associated Neurocognitive Disorders

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Abstract

The severity of HIV-associated neurocognitive disorder (HAND) is modulated by various genetic factors including Matrix metalloproteinase (MMPs). Thus, the aim of short review was to present the association of MMPs polymorphisms with development of HAND and modulation of HAND severity. MMPs have been explained with reference to extracellular matrix remodelling, which occurs throughout life and ranges from tissue morphogenesis to wound healing in various processes. MMP are inhibited by endogenous tissue inhibitors of metalloproteinase's (TIMPs). Matrix metalloproteases act as an interface between host's assault by Tat protein of HIV-1 virus and extracellular matrix which cause breaches in endothelial barriers by degradation of ECM, thus facilitating viral dissemination in tissues as a result there is a progress in HIV-1 infection. MMPs are diverse and are highly polymorphic in nature, hence associated with many diseases. In this short review, we presented here correlation between MMP& TIMPs polymorphism with HIV-related neurological disease (HAND) date suggests that MMPs polymorphism (MMP1, MMP2, MMP3 and MMP9) play an important role in modulation of pathogenesis in HIV disease. Further research is required to explore the role of MMPs and TIMPs variation in modulation of pathogenesis of HAND.

Keywords: MMP; Genetic Polymorphism; HAND; TIMP; HAND

Background

Neurological complications associated with HIV-1 are major health problem among AIDS patients and long-term HIV survivors. Antiretroviral treatment (ART) has improved the morbidity and mortality in HIV-1 infected individuals, however, neurocognitive impairments continue to present >50% in these patients. Neurotoxicity is considered as the major contributing factor for neuro AIDS which might be due to toxic effect of ART metabolite and persistence of a chronic state of immune activation, cytokine dysregulation and immune dysfunction. HIV infection is associated with an altered production and secretion of Matrix Metalloproteinases Enzymes (MMPs) and tissue inhibitory Matrix Metalloproteinases Enzymes (TIMPs) which contribute to immunopathology, dysregulation in T-cell, monocyte/macrophage and cellular trafficking and viral dissemination.

Matrix Metalloproteinases Enzyme in HIV-Related Neurological Disease (HAND)

HIV-related neurological disease is an important co-morbidity of HIV, recognized by globally. More than 55% advanced stage of HIV-patients manifests the HAND. The prevalence of HAND in India is 32.5%. The pathogenesis of HAND is still not clear. Dysregulation of MMPs and TIMPs pathway alter the inflammatory pathway. MMP degrades the extracellular matrix of collagen and proteoglycan, rupture the blood brain barriers thus play an important role in viral dissemination from cell to cell. Hence study of genetic polymorphism of Matrix metalloproteinase enzyme and TIMPS genes in HAND patients may provide the genetic risk for HAND. Also, finding of these kind studies may provide the genetic marker for incidence of HAND in susceptible individuals.

Some of the findings are given here. MMP-2-735TT genotype was associated with development of HAND [1]. MMP-9-1562C>T polymorphism enhanced the risk of development of HAND reported [1]. MMP-3 -18125A5A genotype was found to be associated with protection modulation of HAND pathogenesis reported [2], MMP-1-16072G/1G polymorphism represented higher risk for the development of HAND [2]. MMP-8 -799C/T polymorphism increased the risk for development of HAND and its severity in alcohol user [3]. TIMP-2-418G/C polymorphism independent and its haplotype with-303 G/A polymorphism were associated with the HAND severity (under communication in BMC infectious disease). Also finding suggested that HIV-patients on ART with MMP8 -799TT & TIMP-2-418CC genotypes may recommend for the neurological examination in susceptible individuals. MMP-7-181A>G polymorphism had no impact on development of HAND and its severity reported [4]. MMP-21 572, C/T polymorphism increased the risk for development of HAND in tobacco and alcohol users [5].

In conclusion, association of MMP8-799C/T, MMP-2-735C/T and TIMP-2-418G/C polymorphisms with HAND patients suggested that study need to be validated in larger samples size with other populations. Further studies are required up to level.

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