Cellular intrinsic immunity of SAMHD1 to retroviruses

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Human SAMHD1 possesses dual enzymatic functions. It acts as both a dGTP-dependent triphosphohydrolase and as an exoribonuclease. The dNTPase function depletes the cellular dNTP pool which is required for retroviral reverse transcription in differentiated myeloid cells and resting CD4+ T cells; thus this activity mainly plays a role in SAMHD1-mediated retroviral restriction. However, a recent study demonstrated that SAMHD1 directly targets HIV-1 genomic RNA via its RNase activity and that this function (rather than dNTPase activity) is sufficient for HIV-1 restriction. While HIV-1 genomic RNA is a potent target for SAMHD1 during viral infection, the specificity of SAMHD1-mediated RNase activity during infection by other viruses is unclear. The results of the present study showed that SAMHD1 specifically degrades retroviral genomic RNA in monocyte-derived macrophage-like cells. Consistent with this, SAMHD1 selectively restricted retroviral replication but did not affect the replication of other common non-retro RNA genome viruses suggesting that the RNase mediated antiviral function of SAMHD1 is limited to retroviruses. In addition, neither inhibiting reverse transcription by treatment with several reverse transcriptase inhibitors nor infection with reverse transcriptase-defective HIV-1 altered RNA levels after viral challenge indicating that the retrovirus-specific RNase function is not dependent on processes associated with retroviral reverse transcription.

Genetic association study of MBL-2 gene polymorphisms with RA

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Mannose Binding Lectin-2 (MBL-2) is a C-type serum lectin synthesized by the liver as an acute phase protein. MBL-2 gene is located on chromosome 10q11.2- q21. Mannose-binding lectin gene polymorphisms have been associated with a number of autoimmune disorders. The objective of the present study was to investigate promoter as well as structural polymorphisms of MBL-2 gene in RA patients and healthy controls. Further objective was to asses and compare serum MBL-2 levels between cases and controls. The present case-control study included 200 RA patients and a cohort of 200 age, gender and ethnicity matched controls. The study was approved by institutional ethical committee in accordance with declaration of Helsinki. The genotyping of SNPs rs5030737, rs1800451, rs1800450, rs7096206, rs11003125, rs70958912 were done by ARMS-PCR method. Serum MBL-2 levels were estimated in cases and controls using ELISA kits. Genotypic and allelic frequencies were compared between RA patients and controls by odds ratio using Medcal software. Genotypic and allelic distribution of rs11003125 showed significant differences between cases and controls (p<0.01). Furthermore, there was suggestive evidence of association of this SNP with dominant as well as co-dominant model (p<0.01). However, significant differences in allelic frequencies of rs1800450 were observed between patients and controls. Genetic analysis indicated dominant mode of association of rs1800450 with RA. Significantly lower serum MBL-2 levels were observed in RA patients than controls (p<0.01). Polymorphism in promoter region of gene may act as genetic marker associated with susceptibility towards RA.

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