Relevance of HLA-KIR Genes in Chronic Hepatitis C Virus Infection Outcome

Ileana Constantinescu1,2, Larisa Denisa Ursu2
1Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
2Centre for Immunogenetics and Virology, Fundeni Clinical Institute, Bucharest, Romania

Corresponding author: Ileana Constantinescu, Department for Immunogenetics and Virology, Fundeni Clinical Institute, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Received date: July 02, 2018; Accepted date: July 06, 2018; Published date: July 11, 2018

Editorial

Hepatitis C Virus (HCV) is responsible for over 170 million chronically infected worldwide people, most patients develop a lifetime chronic infection that can lead to severe liver pathology [1].

Substantial research evidences suggest that the innate immune response significantly contributes to HCV outcome [2,3]. Natural killer (NK) cells have efficient anti-viral functions including direct cytotoxicity of infected cells and production of inflammatory cytokines [4]. Killer cell immunoglobulin-like receptors (KIRs) play a major role in regulating the activity of NK cells involved against viral infections, autoimmune diseases, cancers or post-transplantation [5-7].

Many recent studies have reviewed the importance of NK cells in chronic HCV infection outcome and the interactions between the KIR and HLA genes. Both molecules have structural polymorphisms which could be referred to a particular clinical condition [5-11].

Interaction between KIR and HLA-C molecules is the dominant control mechanism of the host NK cells. Genetic studies reveal that, in the early phase of HCV infection, specific KIR and HLA-C pairs are associated with the spontaneous resolution of HCV infection [8,9].

KIR2DL1 receptors recognize HLA-C group 2 antigens (lysine in position 80), KIR2DL2/3 receptors recognizes HLA-C group 1 antigens (asparagine in position 80) and KIR3DL1 is the receptor for HLA Bw4 molecules [10,11].

KIR2DL3-mediated inhibition of NK cells protects from HCV persistence, since KIR2DL3 has a lower affinity for its HLA-C ligand than other KIRs [12]. KIR2DL3 binds HLA-C1 with a weaker affinity compared with KIR2DL2 binding of HLA-C1. NK cells in HCV carriers with this combination of receptors and ligands could be more easily activated during HCV infection resulting in a better outcome [8,11].

Activatory KIR2DS3 gene interaction with HLA-C2 is significantly increased in HCV patients having a role in the development of chronic viral infection [12]. The authors of this study identify a strong influence of KIR B haplotype (and HLA-C2) for the activation of NK cells. In other previous study, a beneficial effect of a KIR A haplotype (with HLA-C1) was observed [8,13].

The role of KIR genes in susceptibility to chronic HCV infection and viral load level variations were revealed in different KIR2DS3- KIR2DS5 genotypes combinations.

Kusnierczyk et al. have found that in patients with KIR2DS3+/ KIR2DS5- the HCV viremia levels was 2.6 times lower than in patients with other KIR genotypes [14]. In contrast, a study conducted by Podhorzer et al. has shown that KIR2DS3 expression was correlated with high viral load levels [15].

Our unpublished data, show on HCV Romanian infected patients, that in KIR2DS3+/KIR2DS5- genotype HCV viremia mean values were 2.2 times lower than in other genotypes.

All these evidence-based results underline that the immune response against HCV is complex. Interactions between NK activatory-inhibitory KIR genes and HLA alleles are important and challenging. These insights could offer more information related to different outcomes in HCV chronically infected individuals. Variable interactions between KIRs and HLA class I and class II molecules have a relevant influence on immunopathogenesis of HCV and have a significant impact on NK cells function.

Understanding HCV immunopathogenesis for an improved clinical management of chronic hepatitis C is further required.

References


Citation: Constantinescu I and Ursu LD (2018) Relevance of HLA-KIR Genes in Chronic Hepatitis C Virus Infection Outcome. Immunogenet Open Access 2: e104.