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Editorial Open Access

HLA-G and Virus Infection

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Editorial

Various viruses have evolved multiple mechanisms to escape the host immune recognition and innate or adaptive immune responses, such as strategies to modulate the expression and/or function of human leukocyte antigens (HLA) on the surface of infected cells. Among HLA family, HLA-G is commonly up-regulated and plays critical roles during virus infection [1,2].

HLA-G is a member of the non-classical HLA class I antigen, due to its primary mRNA alternative splicing, seven different HLA-G isoforms (HLA-G1~-G7) could be generated. HLA-G1, -G2, -G3 and -G4 are membrane-bound and HLA-G5, -G6, and -G7 are soluble isoforms [3].

The immunosuppressive function of HLA-G is through binding to its receptors including ILT-2/CD85j, ILT-4/CD85d, KIR2DL4/CD158d expressed on different types of immune cells. KIR2DL4 is expressed on NK cells and ILT-2 is expressed on B cells, some T cells and NK cells, and all monocytes and dendritic cells, ILT-4 is expressed only by monocytes, dendritic cells and neutrophils [4-6]. HLA-G could induce immune inhibition including (a) direct immuno-inhibitory functions through inhibiting effector cells, (b) indirect immuno-suppressive functions through the generation of regulatory cells, and (c) other functions of HLA-G that have immunoinhibitory consequences such as inhibit phagocytosis and reactive oxygen species production of neutrophils, proliferation and immunoglobulin production of B cells, and impairment of chemotaxis of different immune effectors [6-8].

HLA-G has been involved in various physiological and pathological conditions including reproduction, transplantation, autoimmune, infectious and malignant diseases. For its immune tolerant property, HLA-G expression was believed to be beneficial in pregnancy, organ transplantation and autoimmune disease by promoting embryo implantation, accepting allografts and turning down immune reaction. However, it becomes deleterious in cancer and viral infection by permitting evasion of malignant or virus-infected cells from antitumor or antiviral responses [9].

In the scenario of virus infection, significance of both HLA-G polymorphism and protein expression were addressed in previous studies. HLA-G was considered as an important genetic susceptible factor for virus infection such as human immunodeficiency virus (HIV), human papillomavirus (HPV), human cytomegalovirus virus (HCMV), and even for the vertical transmission of HIV [10]. Both membrane-bound and peripheral blood soluble HLA-G was markedly increased in virus infected patients or host cells [2,11]. For an example, HLA-G expression was upregulated in CD8+ T cells and monocytes in patients with AIDS [12]. HLA-G+ CD4 Treg were found highly susceptible to HIV-1 infection and significantly reduced in persons with progressive HIV-1 disease courses and HLA-G$^+$ CD4 and CD8 T cell proportion was inversely correlated to HIV-1 associated immune activation [13]. Moreover, sHLA-G levels were significantly higher in AIDS patients before treatment and significantly decreased after antiretroviral therapy. The decrease of sHLA-G was correlated with the decrease of plasma HIV-RNA level and CD8+ T lymphocytes number and with the increase of CD4+ T lymphocytes number [14].

Induction of HLA-G expression after virus infection was also observed in other virus infection such as influenza A virus [15,16], HCMV [17,18], HIV [13,19], hepatitis B and C virus [20,21], herpes simplex virus and rabies virus [22,23], etc.

The significance of HLA-G genetic and expression in virus infection susceptibility, virus replication, and disease progression could provide an advantage for infection by subverting host's antiviral defenses; however, modulate HLA-G production could lead us to seek HLA-G as either a useful therapy target or a marker for viral infection and drug treatment.

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