Mini Review

HIV-1 Immune evasion: The main obstacle toward a successful vaccine

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It is estimated that there are 36.9 million individuals living with HIV-1 from who 21.7 million patients receiving antiretroviral therapy (ART) [1,2]. ART has had a significant effect on the patients' quality of life recently, however, its global coverage declines to 16-35% in low or middle income parts of Africa [3]. ART is unable to eliminate the virus from the infected individuals despite the fact of great impact on virus life cycle. There is no doubt that vaccination is considered as the most important medical strategy to prevent and suppress the infectious diseases. Nevertheless, there are many difficulties toward the cure or prevention of HIV-1 including the virus characteristics, lack of ideal animal model and funding [4-7].

As the infection is caused by HIV-1, a burst of viremia happens and consequently specific CD8+ and CD4+ T cells are generated. Consequently, the viral load decreases according to T-cell mediated pathway and antibodies can be detectable by six months after infection [8-10]. The virus is capable to escape from human immune system recognition due to its genetically variable glycoprotein on the envelope and also diverse virus protein products which can effect on the host cell cycle [11,12]. HIV-1 genome encodes Gag, Pol and Env as its three main proteins and also some accessory proteins in an open reading frame. Each of these proteins acts differently among the virus establishment in host cell and also immune evasion. The ability of genetic diversity of HIV-1 is one of the crucial immune evasion approaches for the virus. The HIV-1 RNA genome is capable of mutation randomly which contributes to evade the host immune recognition. All HIV-1 products have been widely investigated toward achieving an effective vaccine candidate [13-15].

The virus enters through the mucosal surfaces of genital tissues during sexual transmission. Indeed mucosa is the first line of physical defense against the pathogens.

One of the proposed mechanisms to avoid this barrier is that HIV-1 crosses the mucosal surface by capturing intraepithelial DCs [16,17]. Moreover, the tight junction proteinsand the integrity of the monolayer mucosal epitheliummight be disrupted according to the exposure of the viral protein gp120 (processed by Env) and due to the upregulating inflammatory cytokines which then leads to the increase of virus particles permeability. HIV-1 establishes acute infection in present immune cells within the mucosa following mucosal breaking step from which the resting CD4+ T cells are the main targets [17,18]. After penetration of the mucosal barrier, a major host defense mechanism is conferred by complement system which contributes to the restriction of viral replication by bursting plasma membranes of undesired cellsand also recruitment of inflammatory cells. Despite this, HIV-1 is able to overcome the complement mediated response by activating the classical pathway of complement system by ability of envelope protein gp41 binding. Capsid or p24, a Gag product, also contributes to immune evasion by hiding HIV-1 nucleic in order to mimic the cellular proteins [19-23].

Moreover, Cytokines and chemokines have significant impact on HIV-1 pathogenesis since the infection results in the activation of NK cells, macrophages, DCs, and the activation of B cells. Attachment of HIV-1 envelope protein through gp120 provokes the production of CC chemokines which are chemoattractants for lymphocytes, DCs and macrophages. In addition to main HIV-1 proteins, HIV-1 uses different mechanisms to escape this cytokine networks by its accessory products [14,20]. For instance, HIV-1 Tat (transactivator of transcription) protein imitates β-chemokines and that leads to increased activation and infection. Furthermore, Nef (HIV-1 negative regulatory factor) leads to rise of production and the stimulatory function of proinflammatory cytokines such as IL-12 and IL-15. Nef also it is the main protein which downregulates HLA-A and HLA-B on target cells and inhibits the cytotoxicity of NK cells [15,17].

The interaction between this intelligent virusand the host cells is complicated. The host system attempts to use its machinery to overcome HIV-1 infection progression, whereas the virus manipulates the host tools to its own propagation. By looking at clinical trials, many kinds of vaccines have been investigated including protein, peptide and DNA or RNA based vaccines which try to make use of the most important HIV-1 products in order to recall immune system. Although neither of them has been successful. Indeed, a therapeutic vaccine against HIV-1 is a priority with the aim of eliminating the virus from cells due to this fact that transmission of it is preventable and possible. Therefore, understanding of the way that HIV-1 overcomes host immune defense and targeting the virus products which are more conserved among different clades and are crucial for the virus life cycle will improve our knowledge toward developing a therapeutic approach to HIV-1 infection and spreading.

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