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Mechanisms of host immune responses to human immunodeficiency virus (HIV): A mini review

Farouk S Nas[1], Muhammad S Abdallah[2], Lurwanu Mu'azu[3], Muhammad Ali[4]*
[1] Department of Biological Sciences, Bayero University Kano, Nigeria
[2] Desert Research Monitoring and Control Centre, Yobe State University Damaturu, Nigeria
[3] Department of Biological Sciences, Federal University Gusau, Nigeria
[4] Department of Microbiology, Federal University Gusau, Nigeria

Abstract
In order to survive, the host has developed distinct strategies to recognize and respond effectively and rapidly to invading microorganisms present within the environment. Two types of immunity are utilized to protect the host against microbial pathogens: innate and adaptive (acquired) immunity. HIV can be transmitted via four major routes: through sexual contact, blood, perinatally (mother-to-child transmission) or via breast milk. HIV can be found as cell-free viral particles or in infected immune cells such as dendritic cells, macrophages and CD4+ T cells. Innate immune cells (e.g., dendritic cells and natural killer cells) are the first line of defence which HIV encounters upon entry to the body. The cellular immune response is induced upon the entry of HIV into the target cells (e.g., T cells) and synthesis of viral proteins. Major Histocompatibility Complex (MHC) class I on the cell surface displays the intracellularly degraded HIV peptide fragments for recognition by T-cell receptors (TCR) on CD8+ T cells. The paper was aimed to review host immune response to Human Immunodeficiency Virus (HIV).

Keywords: human immunodeficiency virus (hiv), virus, innate immunity, adaptive immunity

Introduction
Over the years, a great amount of progress has been accomplished in the understanding of the relationship between the host and invading pathogens [1]. In order to survive, the host has developed distinct strategies to recognize and respond effectively and rapidly to invading microbes present within the environment. The immune system is classically divided into innate and adaptive (acquired) immunity [1]. During the early phase of infection, hosts mount innate immune response that comprises defense mechanisms to protect the hosts from invading pathogens in an antigen independent manner. This immune response is the first and a rapid response launched against a variety of microorganisms. The innate immune system can distinguish between self and foreign proteins and responds accordingly [2]. This nonspecific immune response is activated primarily by the structural motifs of invading pathogens. The major cell types that play key roles in innate immune response against invading pathogens include macrophages, dendritic cells, neutrophils, natural killer cells, mast cells, eosinophils, and basophils [3]. Most of the innate effector cells produce inflammatory factors that function as chemical messengers. Among these molecules, IFNs are the most effective in elucidating antiviral immune responses [4]. Additionally, cytokines and chemokines also play important roles as chemo-attractants controlling leukocytes trafficking [5]. Innate immune response operates through the steps of recognition of the pathogen, Signal transduction, and subsequent gene expression to produce the innate immune effector molecules [6]. The adaptive immunity in mammals is characterized by two types of lymphocytes, T and B cells, clonally expressing a large repertoire of antigen receptors that are produced by site-specific somatic recombination, i.e., T cell receptor (TCR) and antibody B cell receptor [7]. Functionally, naive T and B cells encounter antigens in specialized lymphoid organs and undergo a process of cell division and maturation before exerting their effector function [8].

Human Immunodeficiency Virus (HIV)
Human Immunodeficiency Virus (HIV) is a member of the Lentiviruses genus and is known to cause the acquired immunodeficiency syndrome (AIDS). HIV was discovered by one group in early 1983 from human patients [9]. It was first isolated from the lymph node of a patient with lymphadenopathy, a syndrome that was considered to be a precursor of AIDS [10, 11]. Two species of HIV, which are known to infect humans, are commonly found throughout the world. HIV-1 (HIV type 1) and HIV-2 (HIV type 2) have been shown to have arisen from several cross-species transmission from primates in Africa to humans. They have been shown to have evolved from a related simian immunodeficiency virus (SIV) that mainly infects African monkeys [12]. HIV-1 has evolved from an SIV strain namely SIVcpz, found in chimpanzees (Pantroglodytes troglodytes) from West central Africa. HIV-2 appears to be closely related to the SIVsmm strain found in sooty mangabeys from West Africa [13]. HIV-1 has spread in most part of the world including North America, central Europe, and Asia, whereas HIV-2 has remained mainly prevalent in West Africa [14]. Although, both viruses are associated with the development of progressive immunological

deterioration, HIV-1 is more virulent, highly transmitted and is the cause of the AIDS pandemic [15]. By the end of 2008, the number of people worldwide living with AIDS was estimated to 33.4 million, and in North America about 1.4 million of individuals are living with HIV-1 [16]. On the other hand, HIV-2 is known to be less transmittable, has lower virulence and has an incubation period for the progression of the disease longer than HIV-1, thus people tend to live longer. HIV-2 has largely remained confined to West Africa and is rarely found elsewhere [17, 18]. Number of people worldwide living with AIDS was estimated to 33.4 million, and in North America about 1.4 million of individuals are living with HIV-1 [16]. On the other hand, HIV-2 is known to be less transmittable, has lower virulence and has an incubation period for the progression of the disease longer than HIV-1, thus people tend to live longer. HIV-2 has largely remained confined to West Africa and is rarely found elsewhere [19].

Molecular Biology of HIV

HIV is an enveloped virus that has a spherical shape of approximately 120-140nm in diameter. The mature virion is composed of two identical 9.2 kb positive single-stranded RNA molecules that are surrounded by cone-shaped core that is composed of more than 1000 capsid (CA) proteins [20]. Within the core, the viral genomic RNA molecules are tightly bound by nucleocapsid (NC) proteins and also present are the virally encoded enzymes required for the replication of the virion such as reverse transcriptase (RT), protease (PR), and integrase (IN). Several viral proteins including Vpu, Vif, Vpr and Nef as well as some cellular factors can be also found in the viral particles (reviewed in [21, 22]. To ensure the integrity of the virion, the core is surrounded by a matrix coat that consists of the viral MA protein or p17, which is in turn surrounded by lipid bilayer membrane that is derived from the host cell membrane after budding. Also, embedded within the membrane are the viral Env glycoproteins [23]. The Env protein is a heterodimer of the glycoprotein (gp) 120 that is attached to a stem which consists of three molecules of gp41 that anchors the structure into the envelop of the virion [24]. Gp41 also forms a pore in the plasma membrane, which enables gp120 to be anchored in both the virion and infected cells [25].

HIV Infection

HIV can be transmitted via four major routes: through sexual contact, blood, perinatally (mother-to-child transmission) or via breast milk. HIV can be found as cell-free viral particles or in infected immune cells such as dendritic cells, macrophages and CD4+ T cells. A great percentage of HIV infections occur through unsafe sexual intercourse, whereby bodily fluids such as semen, vaginal fluids or blood from an infected individual come into contact with the mucous membranes of the genitals, mouth or rectum of an uninfected person [26]. In general, the mode of infection, either through mucosal surfaces or through direct contact with blood, can often determine the target cells that will be initially infected by the virus. Upon viral entry in the mucosa, the first encountered cells are the antigen-presenting cells, including different subsets of dendritic cells or macrophages. HIV infected dendritic cells or macrophages will subsequently migrate to the lymphoid tissue, where infection of CD4+ T cells will then take place [26]. Upon HIV infection, a host cellular immune response is triggered to eradicate the HIV infected cells; a cell-mediated immune response mediated by cytotoxic CD8+ T lymphocytes (CTL), as well as a humoral immune response. CD8+ T cells play a pivotal role in the control of HIV-1 replication. They can destroy HIV infected cells through different mechanisms. Detection of infected antigen-presenting cells by CTL occurs through an MHC-I dependent manner. CTL recognize infected cells presenting the HIV antigen via MHC-I molecules and induce the production of perforin and granzymes which lead to the destruction of infected cells [27]. In addition, CTL can also induce apoptosis of the infected cells by interaction of the death inducing ligand, FasL, Sexpressed on their surface with the death receptor, Fas, present on the infected cells [27]. CTL also induce the expression of chemokines such RANTES and MIP-1α/β, which are the ligands of the coreceptor CCR5. Binding of these chemokines to CCR5 has been shown to interfere with HIV entry into target cells [28]. HIV infection induces the production of HIV-1 specific antibodies; however the contribution of the humoral response in the inhibition of viral replication appears to be relatively minor. Non-neutralizing antibodies directed against the envelope glycoprotein are produced during the early stages of the infection, while neutralizing antibodies that would normally neutralize HIV, are delayed and arise few months after the initial infection and can no longer control viraemia [29, 30] HIV has developed several strategies to evade detection by CD8+ T cells and antibody neutralization. HIV has a high degree of genetic variations that result in viral escape from the immune system. Several factors contribute to production of HIV variants; in particular the rapid replicative cycle of HIV, the high maturation rate of the RT, the lack of exonuclease proof-reading activity, and the propensity of the RT to promote recombination of different viral strains [31, 32, 33]. Consequently, these HIV-1 variants expose different epitopes that can no longer be recognized by the CTL and neutralizing antibodies. Thus, the host immune response cannot control HIV infection and disease progression.

Host Immunity

Protection against invading pathogens is essential for host survival. In vertebrates, two types of immunity are utilized to protect the host against microbial pathogens: innate and adaptive immunity [1]. The innate immune response acts as the sentinel for the immune system and is characterized by a rapid detection of specific features of micro-organisms. Upon recognition of pathogens, innate immune cells such as macrophages, dendritic cells (DCs) and neutrophils are activated to produce cytokines that will directly inhibit spreading of invading microbes and simultaneously regulate a pathogen-specific adaptive immune response, mediated by the T and B lymphocytes [1, 5].

Innate immune response to HIV

Innate immune cells (e.g., dendritic cells and natural killer cells) are the first line of defence which HIV encounters upon entry to the body.

Macrophages

Tissue macrophages are one of the target cells for HIV. These macrophages harbor the virus and are known to be the source of

viral proteins. However, the infected macrophages are shown to lose their ability to ingest and kill foreign microbes and present antigen to T cells. This could have a major contribution in overall immune dysfunction caused by HIV infection [34].

Dendritic cells (DCs)

DCs are large cells with dendritic cytoplasmic extensions. These cells presented processed antigens to T lymphocytes in lymph nodes. Epidermal DCs, expressing CD1a and Birbeck granules, are probably among the first immune cells to combat HIV at the mucosal surfaces [29]. These cells transport HIV from the site of infection to lymphoid tissue. The follicular DCs, found in lymphoid tissue, are also key antigen-presenting cells that trap and present antigens on their cell surfaces. In the lymph node follicles, DCs provide signals for the activation of B lymphocytes [34].

Natural killer (NK) cells

NK cells have lytic activity against cells that have diminished expression of major histocompatibility complex (MHC) I antigens. Because the presence of MHC class I is required for peptide presentation to T cell receptors, NK cells are important line of defence when HIV escapes the cellular immune response. NK cells proliferate in response to type 1 interferon secreted by DCs. These stimulated NK cells release cytokines such as interferon γ (IFN-γ), tumour necrosis factor α (TNF-α), and chemokines to activate T-cell proliferation (cellular immune response). NK cells also inhibit viral replication by releasing IFN-γ [34].

Adaptive immune response to HIV

The cellular immune response is induced upon the entry of HIV into the target cells (e.g., T cells) and synthesis of viral proteins. MHC class I on the cell surface displays the intracellularly degraded HIV peptide fragments for recognition by T-cell receptors (TCR) on CD8+ T cells [34]. CD8+ T cells lyse HIV infected cells and secrete cytokines, i.e. interferon-γ (IFN-γ), tumor necrosis factor α (TNF-α), and chemokines, i.e. MIP-1 α, MIP β and RANTES, that inhibit virus replication and block viral entry into CD4+ T cells [27]. Development of CD8+ T cells is crucial for control of HIV replication. This results in declining viraemia after primary infection. In the early stages of infection, CD4+ T cells lose their proliferative capacity and therefore their contribution to viral control is minor. However, during chronic infection CD4+T cells are present and secrete interleukin-2 (IL-2) or cytokines, such as IFN-γ, to control viraemia [34].

Humoral response to HIV

The humoral immune response occurs later in infection; therefore, the level of antibodies during the acute infection is very low. Non-neutralizing antibodies to structural proteins (i.e. P17 and P24) are first to appear and generally do not persist. Later neutralizing antibodies specific to proteins, involved in the entry of the virus into the cells, will be generated. These antibodies are specific to: The variable region of gp120 (V3); CD4 binding sites and chemokine receptors (i.e., CXCR4 and CCR5) and the trans-membrane protein gp41. Potent neutralizing antibodies have been shown to play a major role in controlling HIV infection in a few symptom-free HIV+ individuals who maintain high level of CD4+ T cells and low viral load [11, 34].

Evasion of host immunity by HIV

Viruses have evolved distinct mechanisms to evade the innate immune response by directly inhibiting the activation of specific signaling pathways in order to promote their replication and transmission [1]. Retroviruses, for example, have developed several ways to subvert immune detection by these pathogen-recognition receptors, or in contrast favor the activation of certain pathways to promote their replication. There are various reasons which can contribute to the failure of the immune system to control HIV infection and prevent AIDS development. By infecting CD4+ T cells, HIV is able to replicate predominantly in activated T cells and paralyze one of the main components of adaptive immune system. HIV can also establish latent infection in CD4+ T cells and remain invisible to CD8+ T cells and therefore replication can occur later in the infection and generate new virions. Antigenic mutation within the T-cell epitopes can affect the binding capacity of MHC molecules to the viral peptides, resulting in the inability of the TCRs to recognize the MHC-peptide complex. Finally, HIV is able to hide from anti-HIV antibodies by expressing non- immunogenic glycans on key antibody epitopes [34].

Conclusion

The interaction between HIV and the host cells is complicated. The host system attempts to use its machinery to overcome HIV infection. Both innate and adaptive immune induced response upon the entry of HIV into the target cells.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Beutler B. Innate immunity: An overview. Mol Immunol. 2004; 40:845-59.
2. Renjifo B, Gilbert P, Chaplin B, Msamanga G, Mwakagile D, Fawzi W, *et al*. Preferential in-utero transmission of HIV-1 subtype C as compared to HIV-1 subtype A or D. AIDS. 2004; 18:1629-36.
3. Chieux V, Hober D, Chehadeh W, Wattr´e P. “Anti-viral proteins: from interferon α toitsreceptor,” Annalesde Biologie Clinique. 1999; 57(3):283–290.
4. Richter S, Ping YH, Rana TM. TAR RNA loop: a scaffold for the assembly of a regulatory switch in HIV replication. Proc Natl Acad Sci USA. 2002; 99:7928-33.
5. Ridky T, Leis J. Development of drug resistance to HIV-1 protease inhibitors. J Biol Chem. 1995; 270:29621-3.
6. Robins T, Plattner J. HIV protease inhibitors: their anti-HIV activity and potential role in treatment. J Acquir Immune Defic Syndr. 1993; 6:162-70.
7. Roeth JF, Collins KL. Human immunodeficiency virus type 1 Nef: adapting to intracellular trafficking pathways. Microbiol Mol Biol Rev. 2006; 70:548-63.
8. Rich EA, Chen IS, Zack JA, Leonard ML, O'Brien WA. Increased susceptibility of differentiated mononuclear phagocytes to productive infection with human immunodeficiency virus-1 (HIV-1). J Clin Invest. 1992; 89:176-83.

9. Lever RA, Lever AML. "Intracellular defenses against HIV, viral evasion and novel therapeutic approaches," Journal of the Formosan Medical Association. 2011; 110(6):350–362.
10. Barre-Sinoussi FJC, Chermann F, Rey MT, Nugeyre S, Chamaret J, Gruest C, *et al*. Isolation of a T- lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science. 1983; 220:868-71.
11. Barro M, Patton JT. Rotavirus NSP1 inhibits expression of type I interferon by antagonizing the function of interferon regulatory factors IRF3, IRF5, and IRF7. J Virol. 2007; 81:4473-81.
12. Ganser-Pornillos BK, Yeager M, Sundquist WI. The structural biology of HIV assembly. Curr Opin Struct Biol. 2008; 18:203-17.
13. Gao F, Bailes E, Robertson DL, Chen Y, Rodenburg CM, Michael SF. Origin of HIV-1 in the chimpanzee Pan troglodytes troglodytes. Nature. 1999; 397:436-41.
14. Gao F, *et al*. Human infection by genetically diverse SIVSM-related HIV-2 in west Africa. Nature. 1992; 358:495-9.
15. Clerzius G, Gelinas JF, Gatignol A. Multiple levels of PKR inhibition during HIV-1 replication. Rev Med Virol. 2011; 21:42-53.
16. Hosmalin A, Lebon P. Type I interferon production in HIV-infected patients. J Leukoc Biol. 2006; 80:984-93.
17. United Nation AIDS. http//www.unaids.org, posting date. UNAIDS December update, 2009. [Online]
18. Marlink R. Lessons from the second AIDS virus, HIV-2. AIDS. 1999; 10:689-99.
19. Reeves JD, Doms WR. Human immunodeficiency virus type 2. J Gen Virol. 2002; 83:1253-65.
20. Briggs JA, Wilk T, Welker R, Krausslich HG, Fuller SD. Structural organization of authentic, mature HIV-1 virions and cores. EMBO J. 2003; 22:1707-15. 498.
21. Ott DE. Cellular proteins detected in HIV-1. Rev Med Virol. 2008; 18:159-75.
22. Sierra S, Kupfer B, Kaiser R. Basics of the virology of HIV-1 and its replication. J Clin Virol. 2005; 34:233-44.
23. Marschang P, Sodroski J, Wurzner R, Dierich MP. Decay-accelerating factor (CD55) protects human immunodeficiency virus type 1 from inactivation by human complement. Eur J Immunol. 1995; 25:285-90.
24. Panne D, McWhirter SM, Maniatis T, Harrison SC. Interferon regulatory factor 3 is regulated by a dual phosphorylation- dependent switch. J Biol Chem. 2007; 282:22816-22.
25. Helseth E, Olshevsky U, Furman C, Sodroski J. Human immunodeficiency virus type 1 gp120 envelope glycoprotein regions important for association with the gp41 trans-membrane glycoprotein. J Virol. 1991; 65:2119-23.
26. Coffin JM. Retroviruses. Cold Spring Harbor Laboratory Press, Plainview, New York, 1997.
27. Gulzar N, Copeland KF. CD8+ T-cells: function and response to HIV infection. Curr HIV Res. 2004; 2:23-37.
28. Sheehy AM, Gaddis NC, Malim MH. The antiretroviral enzyme APOBEC3G is degraded by the proteasome in response to HIV-1 Vif. Nat Med. 2003; 9:1404-7.
29. Tomaras GD, Yates P, Liu L, Qin GG, Fouda LL, Chavez AC, *et al*. Initial B-cell responses to transmitted human immunodeficiency virus type 1: virion-binding immunoglobulin M (IgM) and IgG antibodies followed by plasma anti-gp41 antibodies with ineffective control of initial viremia. J Virol. 2008; 82:12449-63.
30. Wei X, Decker S, Wang H, Hui JC, Kappes X, Wu JF. Antibody neutralization and escape by HIV-1. Nature. 2003; 422:307-12.
31. Coffin JM. HIV population dynamics in vivo: implications for genetic variation, pathogenesis, and therapy. Science. 1995; 267:483-9.
32. Jetzt AE, Yu H, Klarmann GJ, Ron Y, Preston BD, Dougherty JP. High rate of recombination throughout the human immunodeficiency virus type 1 genome. J Virol. 2000; 74:1234-40.
33. Kirchhoff F. Immune evasion and counteraction of restriction factors by HIV-1 and other primate lentiviruses. Cell Host Microbe. 2010; 8:55-67.
34. Nejad SM. Human Immunodeficiency Virus (HIV), University of Oxford, British Society for Immunology, 2018.