Acta Scientific Microbiology (ISSN: 2581-3226)
Volume 1 Issue 6 June 2018
Mini Review

Host Immune Responses to the Infections Caused by the Infectious Viruses

Modhusudon Shaha[1]*, Bithi Roy[2], Tanzina Akter[3], Md. Ekramul Karim[3] and Md Mizanur Rahaman[4]

[1]*Microbial Biotechnology Division, National Institute of Biotechnology, Dhaka, Bangladesh*
[2]*Department of Agronomy, Bangladesh Agricultural University, Mymensingh, Bangladesh*
[3]*Environmental Biotechnology Division, National Institute of Biotechnology, Dhaka, Bangladesh*
[4]*Department of Microbiology, University of Dhaka, Dhaka, Bangladesh*

***Corresponding Author:** Modhusudon Shaha, Microbial Biotechnology Division, National Institute of Biotechnology, Dhaka, Bangladesh.

Received: April 20, 2018; **Published:** May 10, 2018

Abstract

Evasion of host immune systems has become a norm for infectious viruses. However, host system also plays defensive games to combat and inhibit virus establishment in the body. Components of the innate immune system such as cytokines, interferon, complements, etc. act as the first and furious defense against these pathogens upon sensation. If the pathogen sustains longer, the adaptive immune system wakes up and eliminates it protecting the body. The combined actions of innate and adaptive immunity use several immune cells and components and determine the fate of an antigen.

Keywords: Viruses; Host Immunity; Evasion

Introduction

Viruses are obligate intracellular parasites that need to find a preferred way to enter into the susceptible host cell by crossing cellular membrane and exploit the usual cellular processes such as capsid destabilization, and uncoating along with the proper action of nucleic acids to initiate the infection cycle in the human body [1,2]. Furthermore, it is well known that the initial mode of viral entry is the identification and recognition of host pattern recognition receptors (PRRs), for instance, toll-like receptors (TLR) [3,4].

Human body usually responses to the viruses by activating the immune system [1,5]. After the entry of the virus into the cell, host downstream signals try to combat the virus. The process includes initiation of a cascade pathway to secrete pro-inflammatory cytokines and interferon, body's first-line defense against viral infections [3,6]. However, viruses are sometimes able to hide themselves from the adverse effects of host immune cells, and cause disease progression, especially if the host is immunocompromised [7]. On the other hand, protection to the host itself is gained by either gaining tolerance to the caused infections or through activating the immune defense mechanisms [8,9].

Actions of innate immunity to defend virus establishment

Innate immunity starts activation and defends the host to the infections as soon as after the adhesion of viral protein with the PRRs [3,4]. Different types of PRR are engaged in this recognition process [3,4]. These include TLR3, which is specific for double-stranded RNA and normally recognizes virus-infected cells in the body; on the other hand, TLR7 and TLR8, detect only single-stranded RNA and detect and bind to the viral RNA present in the infected sentinel cells; furthermore, retinoic acid inducible gene- I (RIG-I) detects and locate viruses in the cytosol of virus-infected cells [4,8]. A cascade pathway is activated by TLR producing pro-inflammatory molecules (IL-1 and IL-18) as well as three classes of interferon, firstly, interferon type I (composed of IFN-α and IFN-β), secondly, type II interferon (IFN-γ) and finally, newly reported type III interferon (IFN-λ1, IFN-λ2, and IFN-λ3) [3,10-12]. A new class of interferon, type III interferon, identified by Durbin research group [13], was found to have antiviral activity as like as type I interferon located in the mucosal surfaces, e.g., respiratory tract and gut [14-16]. However, antiviral activity of type III interferon has been documented to be limited to respiratory syncytial virus, influenza A virus and rotavirus [14].

Furthermore, several IFN-stimulated genes (ISGs) is triggered by activated interferon produced by the infected host cells, which later function to inhibit the virus replication, to promote immune systems to the antiviral state and finally to activate the adaptive immune response [3,17,18]. Some of these ISGs include viperin, a virus inhibitory protein modulating IFN-β production by activating signaling pathways, IRF3, IRF7 and PRRs (activation of this protein is distinctly induced by Sinbis virus, human cytomegalovirus, Sendai virus, etc.) [3,17,19]; tetherin, another IFN-induced protein that is composed of an unusual structure with three domains (two membrane-anchoring domains at both N-termini and C-termini, and a middle coiled domain) that act to make a link between virus and cellular membrane and thereby can capture the enveloped pathogens, for example, human immunodeficiency virus-1 [3,17,18]; another protein, SAMHD1 (sterile alpha motif and histidine-aspartic domain - 1), plays an antiviral activity by inhibiting transcriptions of both non-retroviruses and retroviruses such as herpes simplex virus type I and vaccinia virus [3,20]. Furthermore, protein kinase R, a detector protein that is capable to detect dsRNA in the cytosol, which uniquely provide signals to activate Nuclear factor (NF)-kB and thus, to inhibit the initiation of translation [21]. Defense by innate immune system of the host is not limited to the functioning proteins; however, a small portion of siRNAs and miRNAs also act to prevent virus infection [3].

Several immune cells such as neutrophils, Natural killer cells, dendritic cells, mast cells, etc. are activated to prevent the virus infections in innate system [22-24]. Neutrophils play an important role in combatting acute inflammatory infections which finally migrate to the virus infected sites rapidly [25,26]. They are activated by signals conveyed by TLRs and damage-associated molecular patterns (DAMPs) upon the infection caused by virus [26,27]. Another potent immune cell, NK cell is involved with the cellular innate immune response to viral infections [28-30]. Furthermore, NK cell functions as an effector cell possessing the both cytokine and cytotoxicity productions, and maintain a balance between the activation and inhibitory signaling [28]. For instance, during viral hepatitis, in the presence of IL-10, NK cells seem to produce less IFN-γ (anti-inflammatory cytokine) with a relatively increased cytotoxicity to the host cells [28,30].

Activation of adaptive immunity to prevent viral infections

In addition to function in allergic responses, mast cells play important role as cellular component of innate immune systems to viral infections [23,24,31]. After activation by cytokines they release pro-inflammatory cytokines, followed by stimulating other immune cells, for example, phagocytes to be recruited to the infection site [23,24,31]. Mast cells can also activate and promote adaptive immune responses by activation of T and B cell [23,31]. Additionally, another immune cell, plasmacytoid dendritic cell was documented to have antiviral response to influenza A virus [21,32]. Activation of these cells are occurred by TLR7-dependent manner and they are reported to produce type I interferon acting against the viral infection [16,21].

Adaptive immune response is essential for the inhibition of viral infections and to keep a memory to prevent the repeated infections caused by the same pathogen [33]. The activation of adaptive immune responses to viral infections needs a few days to weeks [33,34]. This activation process involves some antigen presenting cells (APC) such as neutrophils (later differentiated into muscles macrophages and dendritic cells, which act as bridges between the adaptive and innate immunity), which up regulate co-stimulatory molecules, for instance,CD80 and CD86, and pro-inflammatory cytokines, e.g., interferon (IFN), tumor necrosis factor (TNF) and interleukin (IL)-1, IL-6, IL-12 [26,33,35,36]. These induced immune components further activate other immune cells such as dendritic cells, and promote migrations to the secondary lymphoid tissues [33,35,37,38]. Peptides derived from the virus are presented on the activated cells surface by major histocompatibility complex (MHC) class II [39]. These peptides provide co-stimulatory signals to activate CD4+ T cells from the naïve state [35,39].

Differentiation of the activated CD4 + T cells results into T helper (H) 1, TH2, TH4, TH17, TFH (follicular) and regulatory T cells (Treg) cells [35,40,41]. Furthermore, these cells function differently as their nature of communications, where TH1 and TH2 produces IFN-γ and IL-4 respectively to help the macrophages activation and B cells differentiation respectively [35,42]. Additionally, TFH enter into the B cell follicles and helps to activate the B cells with interacting with CD40, which later produce specific antibody against viral infections [43,44]. On the other hand, TH17 acts against some of the deadly viruses such as vaccinia virus, influenza viruses, HSV, etc.), and Treg cells regulate the functions of other T cells and inflammatory substances from over-exuberant immune responses as well as immunopathology [35,45]. Additionally, by the help of IL-2, CD4+ T cells are activated and differentiated into cytolytic T cells (CTL) to kill viral infected cells directly [35,46,47].

On the other hand, Virus infected cells express antigens in association with MHC class I on its surface and activate CD8+ T cells [39,46]. MHC I carrying the antigenic determinant binds to the TCR (T cell receptor) and through CD80 and CD86, it provides signals to CD8+ T cells [39,46]. After receiving the signals from the infected cells, CD8+ T cells are started proliferation and differentiation into CTL and if necessary, it can lyse the infected cells by secreting perforin and granzymes, and activates cytokines like TNF-α, IL-2 and IFNγ to promote apoptosis by the macrophages [46,48,49]. At the same time, few differentiated CTLs, THs and plasma cells turn into the memory cells which further provide rapid and robust immune responses if re-infection happens [8,50].

Innate and adaptive immune systems co-stimulate each other

Both innate and adaptive immunity are the ultimate counterpart for each other and are needed to control viral infection effectively [8,51]. Innate immunity control viruses defending in the early phase infections such as virus entry, replication, and if pathogens manage to evade such responses, innate immune cells generate co-stimulatory signals to the adaptive system using pro-inflammatory molecules [8]. Then T and B cells are activated and differentiated. Furthermore, immunoglobulin that are specific to the virus infections bind and block the viral spread [8,52]. On the other hand, CTL eliminates the cells infected by viruses [8,44]. Later, some of these immune cells act as memory cells in the immune system to prevent further infections.

Conclusions

To combat the immune responses, viruses are making changes to their genome regularly which in turn upgrading their infection causing mechanisms Further studies are needed to understand the molecular mechanisms of viral evasion and the defense systems against the host immunity. Furthermore, to develop vaccines against deadly viral infections, it is essential to study the continuous modifications of virus proteins which play vital role to evade the host immunity.

Bibliography

1. Kalia M and S Jameel. "Virus entry paradigms". *Amino Acids* 41.5 (2011): 1147-1157.

2. Da Silva Santos C., *et al*. "A Novel Entry/Uncoating Assay Reveals the Presence of at Least Two Species of Viral Capsids During Synchronized HIV-1 Infection". *PLOS Pathogens* 12.9 (2016): e1005897.

3. Freed EO and M Gale Jr. "Antiviral innate immunity: editorial overview". *Journal of Molecular Biology* 426.6 (2014): 1129-1132.

4. Thompson MR., *et al*. "Pattern Recognition Receptors and the Innate Immune Response to Viral Infection". *Viruses* 3.6 (2011): 920-940.

5. Pichlmair, A and C Reis e Sousa, "Innate recognition of viruses". *Immunity* 27.3 (2007): 370-383.

6. Jarczak J., *et al*. "Impaired Expression of Cytokines as a Result of Viral Infections with an Emphasis on Small Ruminant Lentivirus Infection in Goats". *Viruses* 8.7 (2016): 186.

7. Oldham ML., *et al*. "A mechanism of viral immune evasion revealed by cryo-EM analysis of the TAP transporter". *Nature* 529.7587 (2016): 537-540.

8. Iwasaki A and PS Pillai. "Innate immunity to influenza virus infection". *Nature Reviews Immunology* 14.5 (2014): 315-328.

9. Ayres JS and DS Schneider. "Two ways to survive an infection: what resistance and tolerance can teach us about treatments for infectious diseases". *Nature Reviews Immunology* 8.11 (2008): 889-895.

10. McNab F., *et al*. "Type I interferons in infectious disease". *Nature Reviews Immunology* 15.2 (2015.): 87-103.

11. de Castro IF., *et al*. "First evidence of a pro-inflammatory response to severe infection with influenza virus H1N1". *Critical Care* 14.1 (2010): 115.

12. Thanawongnuwech R., *et al*. "Increased Production of Proinflammatory Cytokines following Infection with Porcine Reproductive and Respiratory Syndrome Virus and Mycoplasma hyopneumoniae". *Clinical and Diagnostic Laboratory Immunology* 11.5 (2004): 901-908.

13. Durbin RK., *et al*. "Interferon induction and function at the mucosal surface". *Immunological Reviews* 255.1 (2013): 25-39.

14. Braciale TJ and YS Hahn. "Immunity to viruses". *Immunological Reviews* 255.1 (2013): 5-12.

15. Samuel CE., *et al*. "Antiviral Actions of Interferons". *Clinical Microbiology Reviews* 14.4 (2001): 778-809.

16. Markušić M., *et al*. "Induction of IFN-α Subtypes and Their Antiviral Activity in Mumps Virus Infection". *Viral Immunology* 27.10 (2014): 497-505.

17. Schoggins JW and CM Rice. "Interferon-stimulated genes and their antiviral effector functions". *Current Opinion in Virology* 1.6 (2011): 519-525.

18. Schneider WM., *et al*. "Interferon-Stimulated Genes: A Complex Web of Host Defenses". *Annual review of Immunology* 32 (2014): 513-545.

19. Fitzgerald KA., *et al*. "The Interferon Inducible Gene: Viperin". *Journal of Interferon and Cytokine Research* 31.1 (2011): 131-135.

20. Ballana E., *et al*. "SAMHD1 Specifically Affects the Antiviral Potency of Thymidine Analog HIV Reverse Transcriptase Inhibitors". *Antimicrobial Agents and Chemotherapy* 58.8 (2014): 4804-4813.

21. Kane M and T Golovkina. "Realities of virus sensing". *Microbes and Infection* 14.12 (2012): 1017-1025.

22. Newton AH., *et al*. "The host immune response in respiratory virus infection: balancing virus clearance and immunopathology". *Seminars in Immunopathology* 38.4 (2016): 471-482.

23. Urb M and DC Sheppard. "The Role of Mast Cells in the Defence against Pathogens". *PLOS Pathogens* 8.4 (2012): e1002619.

24. Krystel-Whittemore M., *et al*. "Mast Cell: A Multi-Functional Master Cell". *Frontiers in Immunology* 6 (2015): 620.

25. Jenne CN and P Kubes. "Virus-induced NETs--critical component of host defense or pathogenic mediator?". *PLOS Pathogens* 11.1 (2015): e1004546.

26. Roberts RL., *et al*. "Antiviral properties of neonatal and adult human neutrophils". *Pediatric Research* 36.6 (1994): 792-798.

27. de Oliveira S., *et al*. "Neutrophil migration in infection and wound repair: going forward in reverse". *Nature Reviews Immunology* 16.6 (2016): 378-391.

28. Shin EC., *et al*. "Immune responses and immunopathology in acute and chronic viral hepatitis". *Nature Reviews Immunology* 16.8 (2016): 509-523.

29. Waggoner SN., *et al*. "Roles of natural killer cells in antiviral immunity". *Current opinion in virology* 16 (2016): 15-23.

30. Vidal SM., *et al*. "Natural Killer Cell Responses during Viral Infections: Flexibility and Conditioning of Innate Immunity by Experience". *Current Opinion in Virology* 1.6 (2011): 497-512.

31. Abraham SN and AL St John. "Mast cell-orchestrated immunity to pathogens". *Nature Reviews Immunology* 10.6 (2010): 440-452.

32. Fei, T., *et al.* "Plasmacytoid dendritic cells in antiviral immunity and autoimmunity". *Science China Life Sciences* 53.2 (2010): 172-182.

33. Libbey JE and RS Fujinami. "Adaptive immune response to viral infections in the central nervous system". *Handbook of Clinical Neurology* 123 (2014): 225-247.

34. Miao H., *et al*. "Quantifying the Early Immune Response and Adaptive Immune Response Kinetics in Mice Infected with Influenza A Virus". *Journal of Virology* 84.10 (2010): 6687-6698.

35. Swain SL., "Expanding roles for CD4(+) T cells in immunity to viruses". *Nature Reviews Immunology* 12.2 (2012): 136-48.

36. Cox JH., *et al*. "Antigen presentation requires transport of MHC class I molecules from the endoplasmic reticulum". *Science* 247.4943 (1990): 715-718.

37. Bordería AV., *et al*. "Antiviral Activated Dendritic Cells: A Paracrine Induced Response State". *Journal of Immunology* 181.10 (2008): 6872-6881.

38. Ludewig B., *et al*. "Dendritic Cells Efficiently Induce Protective Antiviral Immunity". *Journal of Virology* 72.5 (1998): 3812-3818.

39. Andrews NP., *et al*. "Generation of Antiviral Major Histocompatibility Complex Class I-Restricted T Cells in the Absence of CD8 Coreceptors". *Journal of Virology* 82.10 (2008) 4697-4705.

40. Velu V., *et al*. "Induction of Th1 biased Tfh (Tfh1 cells) in lymphoid tissues during chronic SIV infection defines functionally distinct germinal center Tfh cells". *Journal of Immunology* 197.5 (2016): 1832-1842.

41. Muranski P. and NP Restifo. "Essentials of Th17 cell commitment and plasticity". *Blood* 121.13 (2013): 2402-2414.

42. Mosser DM and JP Edwards. "Exploring the full spectrum of macrophage activation". *Nature reviews Immunology* 8.12 (2008): 958-969.

43. Miles B., *et al*. "CD4 T Follicular Helper and Regulatory Cell Dynamics and Function in HIV Infection". *Frontiers in Immunology* 7 (2016): 659.

44. Ayala VI., *et al*. "CXCR5-Dependent Entry of CD8 T Cells into Rhesus Macaque B-Cell Follicles Achieved through T-Cell Engineering". *Journal of Virology* 91.11 (2017): e02507-e02516.

45. Martinez NE., *et al*. "Regulatory T cells and Th17 cells in viral infections: implications for multiple sclerosis and myocarditis". *Future virology* 7.6 (2012): 593-608.

46. Tscharke DC., *et al*. "Sizing up the key determinants of the CD8(+) T cell response". *Nature reviews Immunology* 15.11 (2015): 705-716.

47. Freigang S., *et al*. "DC infection promotes antiviral CTL priming: the 'Winkelried' strategy". *Trends Immunology* 26.1 (2005): 13-18.

48. Cao Y., *et al*. "Effects of different cytokines on immune responses of rainbow trout in a virus DNA vaccination model". *Oncotarget* 8.68 (2017): 112222-112235.

49. Ruby J., *et al*. "Antiviral Activity of Tumor Necrosis Factor (TNF) Is Mediated via p55 and p75 TNF Receptors". *The Journal of Experimental Medicine* 186.9 (1997): 1591-1596.

50. Chen HD., *et al*. "Memory CD8+ T cells in heterologous antiviral immunity and immunopathology in the lung". *Nature Immunology* 2.11 (2001): 1067-1076.

51. Chew T., *et al*. "Innate and Adaptive Immune Responses to Herpes Simplex Virus". *Viruses* 1.3 (2009): 979-1002.

52. Frenzel K., *et al*. "Antiviral function and efficacy of polyvalent immunoglobulin products against CMV isolates in different human cell lines". *Medical Microbiology and Immunology* 201.3 (2012): 277-286.

Volume 1 Issue 6 June 2018