COVID-19 AND IMMUNOLOGICAL RESPONSES & PATHWAYS

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The current and ongoing COVID-19 pandemic, caused by the SARS-CoV-2 coronavirus, began with the first reported cases in Wuhan, China, in December 2019, which has expanded dramatically throughout the globe. SARS-CoV-2 or COVID-19 belongs to the family Coronaviridae and has high transmissibility and a degree of lethality not yet established globally. As there is no medicine or vaccine against COVID-19, our immune system is the best defense. The immune system is pathogen-resistant and resistant to infection. As a pathogen penetrates our body, a ferocious response to eradicate it is delivered by our body's immune system. The first and foremost physical barrier to any external factors affecting our body is the skin and; the virus renounces it while crossing the nostrils. The hairy structures; of the nostrils; are responsible for cleaning the air but do not do much to clean the air of microscopic pathogens, especially against viruses. This work is supported by mucus in the nostrils that act as a trapping mechanism for dirt and particles but not effective against a minuscule virus.

The virus then enters the lungs. The lungs are the most vulnerable organs as they face multiple viruses, and many of them do substantial damage to them. Thus, as a defense mechanism, they have ciliated epithelium, mucosal lining, and cells that can help initiate an immune response from the body and numerous defense mechanisms to prevent lung damage. Mucocilian elimination is a principal defensive mechanism. The lungs also secrete A-immunoglobulins that protect from respiratory infections. The goblet cells secreting mucus also secrete defensins, antiproteases, and antioxidants. Further, lungs have macrophages, dendritic cells that activate the responsive immune system like B and T cells by presenting antigens. Now, we shall go in-depth on the cellular level of immune responses. For any virus to be detected, innate immunity plays a significant role.

Innate immune response-

When the host is infected with SARS-CoV-2, it infects macrophages which in turn presents the CoV antigen to T lymphocytes and causes differentiation of T lymphocytes. After T cell differentiation, various chemicals, Cytokines, are released. It comprises cytokines related to T lymphocyte subsets such as Th17. Cytokine storm occurs when there is an over expression of antigen and immune response. The continued release of these chemicals leads to a negative effect on CD8 cells and NK cells and their activation processes. CD8 T cells do produce chemicals to clear out CoV. The viral fixation to the host cells results in the emergence of pathogenic genomic RNA in the host cytoplasm.

SARS CoV-2 is an RNA virus. Hence, the body needs to have a complex recognition system for the virus to be recognized, targeted, and exterminated systematically. Innate immunity is required when the pathogen is recognized on a genetic level. The body recognizes the pathogens as something foreign and done by the pathogen recognizing receptors (PRR). They are to detect and proofread whether the particulate, organism, or molecule is a pathogen or not. They identify nucleic acids as a molecular profile associated with pathogens present in RNA viruses. They restrict unintentional activation of the pathways. They also describe ligands and routes associated with the RNA helix of innate antiviral immunity as RIG, MDA5, and sentinel sensors as LGP2, SNRNP200. PRRs are a part of the innate immunity of human beings.

As the RNA virus is recognized, a large amount of secretions of chemokines and cytokines IL-1, IL-6, IL-8, IL-21, TNF-β and MCP-1) is seen in infected cells in retaliation to CoV. These chemicals then recruit lymphocytes and leukocytes to the infection sites. There are many receptors which are responsible for the recognition of the viral genomic material, like RIG like receptors, the H family, Toll like receptors, etc.

The following immunologic response is due to type 1 interferences. These interferons are synthesized for the first time when RRPs recognize viral nucleic acids. After that, the next step is the collection of specific adapter proteins and the activation of IRF3 and IRF7. (IRF- interferon regulatory factor). Interferons are the body's principal antiviral molecules, restricting the spread of the pathogen. Interferon production has a direct impact on the propagation of the virus. It has been reported that the N protein of the virus nullifies the effect of interferon and therefore the virus is still pathogenic even after the attack of interferon.

The next best cells to negate the virus spread are the dendritic cells also termed to be the best antigen-presenting cells. These cells activate T and B cells, gathering inborn and adaptive immunity. But attempts at DCS are counteracted by the receptor-blocking proteins in the virus. These proteins block the receptor that starts maturing and differentiating dendritic cell precursors. These proteins also block prime receptors like CC chemokine receptor, hindering the more controlled adaptive immune response of dendritic cells.

The body does not have one cell to defend it. Several cells, molecules are acting altogether. A group of molecules comes into play in the fight against the virus. They are known as defensins. These molecules are endogenous antibiotic peptide molecules that come under innate immunity. These molecules can kill almost any pathogenic organism that enters our body and is found in the neutrophil granules. But these being potent against fungi, bacteria, etc., they do nothing much against the virus.

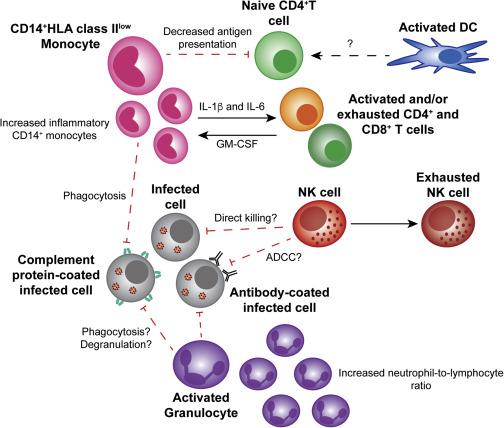


Figure 1: The peripheral Innate immune response to severe SARS CoV-2

Source: Chowdhury, M. A., Hossain, N., Kashem, M. A., Shahid, M. A., & Alam, A. (2020). Immune response in COVID-19: A review. *Journal of Infection and Public Health*.

Adaptive immune response:

One of the many important cells that make up the adaptive immune system is the T-cell. These cells cause immune responses specific to pathogens. Against β coronaviruses like SARS CoV T cells, CD4+ T cells, CD8+ T cells have a major antiviral role. CD4+ T cells promote virus-specific antibody production by activation of T dependent B cells. CD8+ T cells being cytotoxic, kill infected cells. The only concern is that CD4+ T cells are more vulnerable to the virus. The reduction in CD8+ T lymphocytes does not affect virus growth or spread. However, the depletion of CD4+ T cells means that fewer cells are brought to the infected site, the lungs. This leads to highly immunized interstitial pneumonitis and delayed lung clearance.

Humoral immunity response:

The immune system is controlled by macromolecules and extracellular fluids like secreted antibodies also known as antibody-mediated immunity. It is seen that the complement system responds to a foreign antigen. Due to the possibility of damaging body tissues and organs, the complement system is underneath a tight leashBut even after these virus-encoded proteins help the pathogen evade the complement system and continue to develop. But humoral immunity is important in the fight against the virus as it is a deterrent for the virus.

Antibody Response:

Human monoclonal antibody m336 does reduce the RNA titre of the lungs. Monoclonal antibodies in vitro have shown substantial resistance to the viral proteins thus reducing the viral growth. There is much to learn about the antibody response to the virus in concern, be that as it may, it has been suggested that prolonged production of IgG does have some relevance in the immune response of the body

When our body encounters any germs or viruses for the first time, the immune system cannot work properly and we become sick. The same thing has happened in the case of COVID-19. When the cells of the immune system become educated, it completes its jobs by recirculating between central and peripheral [lymphoid organs](https://www.sciencedirect.com/topics/medicine-and-dentistry/lymphoid-organ) and migrating it and from sites of injury via blood. Blood carries naïve and educated immune cells from one site to another, as it flows throughout the body, it acts as a pipeline for the immune system. The cells again enter into the bloodstream to be transported to tissues throughout the body after exiting these nodes through outgoing lymphatic vessels.

Thus, we shall conclude that the body’s combined immune responses are repeatedly thwarted and there is no cure or even a vaccine for the disease caused by SARS CoV 2.

Reference:

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