

Perspective

Impacting the COVID-19 Pandemic by Inducing Temporary Non-Specific Immunity

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The COVID-19 pandemic is a human tragedy and has a growing global impact. It is crucial to find innovative approaches to reduce the severity of the pandemic particularly in low resource countries, which will be significantly affected in the near future resulting in a massive loss of life.

Following viral interference, “a state of temporary immunity from infection,” which is induced by respiratory viral infections, there is a brief window in which a host has less susceptibility to other respiratory viruses [1]. This viral intervention seems to be independent of any antigenic analogy among the viruses [1]. Viral infections that share epitopes may limit cross-reactive immune responses [2]. The host is protected from subsequent unrelated respiratory virus infections for a temporary period, which is antigen independent [2]. This can promote an antiviral environment in the respiratory system.

After an influenza or a rhinovirus infection is established in the host body, infected cells start producing interferon and other cytokines, which causes the cells to enter an antiviral state [3]. After influenza infection, antigen-nonspecific immunity will remain for a period of a few weeks [2]. This immunity may be able to decrease the risk of infection with SARS-CoV-2 due to a cytokine-mediated phenomenon [4].

The impact of this temporary immunity can be seen in reality since the Respiratory Syncytial Virus (RSV) season was postponed due to the 2009 pandemic Influenza A Viruses (IAV) outbreak [2]. The interference of temporary nonspecific antiviral immunity on epidemics of respiratory viruses can have important implications [5] such as protecting the host against COVID-19. We suggest the application of temporary enhanced cross-protective immune responses, which can limit the scale of viral infection that share epitopes [1]. This is essential, particularly in the current situation in which it may take up to 1 year to develop an adequate vaccine that can be available to the public.

Previous pandemics have shown that recent infection with any strain of a viral infection like influenza [6] can provide ‘temporary-immunity to infection with any other strain’, such as RSV [7] or

Rhinoviruses, regardless of antigenic distance [4].

Any vaccination would not provide protection unless the vaccine and current strains are antigenically comparable. It is worth considering that the current influenza vaccination would not grant temporary non-specific protection [4] against COVID-19, as the vaccine and circulating SARS-CoV-2 are not antigenically similar. Therefore, we propose to induce infections with other types of viral respiratory infections such as strains causing common colds including non-fatal typically mild and self-limited Rhinoviruses or Coronavirus (OC43, 229E or NL63), prior to exposure to COVID-19. These viruses can also include other non-fatal respiratory viruses such as influenza, respiratory Enteroviruses (EV-D68) and adenoviruses (types 3, 4).

It is important to consider that the desired outcome of inducing temporary immunity theory may vary based on: i) the combination of virus and the interval between initial infection and reinfection; ii) the extent and exact duration of the temporary immunity⁽¹⁾; and iii) age, since the temporary protection may differ by age but is greater than that provided by antibody-mediated cross-protection alone [4].

While we are waiting for a vaccine, eliciting nonspecific immunity would be beneficial for surrounding community members of individuals who have COVID-19 [4]. It may take up to 3 days after primary infection to initiate nonspecific immunity to protect the host against secondary infection shown in Ferrets [4]. Inducing vulnerable populations may protect people, particularly those who are in close contact and direct exposure to individuals who have recently been infected by the SARS-CoV-2 at home. Aggressive implementation of lockdown policy, which is beneficial to reduce general exposure to the virus, less likely reduces the level of exposure for the relatives living or interacting with the infected patients. The scope and scale of the benefit of this new application is significant since most people get SARS-CoV-2 infection from their infected relatives at home, particularly during the first two weeks after exposure to infected people. The duration of ‘temporary immunity’ is essential since short-lived immunity is needed to last around two weeks, which is necessary to protect people during the transmissible period of the SARS-CoV-2 to others. In addition, according to studies in animal models and in humans [2], the new infection may happen at least 10 and 14 days after the first infection [1]. Inducing immediate family members of recently infected individuals with benign respiratory viral infections such as Rhinovirus during early stages of the exposure, when they are at maximum risk, would be able to reduce their chance of infection. This is very important since infected individuals can transmit infection to their relatives mainly during the first two weeks after their infection. If we can protect these non-infected relatives for two weeks, the likelihood that they get infected from their infected relatives after this golden time would be very low.

The induced temporary immunity may limit the incidence and severity of the COVID-19 pandemic. It gives countries enough time

to respond and reduces the overload of hospitals related to severe cases. The proposed strategy is very critical, particularly in developing countries, such as those in Africa. These countries have poor health care systems along with limited access to intensive care. They haven't been significantly affected by COVID-19 yet, however they will be affected soon.

In conclusion, we may be able to protect immediate relatives who interact with infected individuals for at least two weeks. This may significantly reduce the level of exposure or severity of the COVID-19 among activated hosts. Therefore, during proactive case findings, where there is an active screening of immediate relatives of a person infected with COVID-19, we can induce temporary nonspecific immunity by administering non-fatal, mild respiratory viruses like Rhinoviruses, Coronavirus or influenza viruses *via* internal or external administrations (for instance intranasal [8], sublingual, or inhalation). This timely, cost-effective intervention can reduce the incidence and burden of the disease by promoting an antiviral respiratory environment against SARS-CoV-2 for those whose test has been initially negative without previously encountering the virus. Inducing Temporary Non-Specific Immunity may be a good way to suppress the spread of the virus but more should be considered such as its operability level and operating effect when compared with individual exercise for preventing and enhancing self-immunity.

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