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SARS-CoV-2: A Biochemical Treatise on its Past, Present & Future

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The SARS-CoV-2 pandemic is unprecedented but equally unprecedented is the contribution of scientists who have helped us in understanding the mechanisms by which it infects human beings and also, developing a variety of vaccines to protect the masses, in a year's time, which can be called truly groundbreaking. This article gives an overview of the progress made by scientists around the world working round the clock in developing an understanding of the SARS-CoV-2 evolution and COVID-19 disease pathogenesis, and also makes an attempt to suggest the possible ways of coping with this pandemic if we have to co-exist with it forever!

As per the figures disclosed by the National Health Ministry (NHM), India has witnessed 400,000 excess deaths in April and May, 2021 in comparison with April and May 2020. And the surge in COVID-19, cases in Europe, the US and neighbouring countries reveals that the coronavirus is still amidst us and is thriving well! Since December 2019, with more than 188 million confirmed cases and more than 4.0 million deaths worldwide, as recorded on July 16, 2021, COVID-19 has severely disrupted human life, and we still don't know for sure. The reasons why COVID-19 drastically affects some people, but the majority recovers whilst remaining largely asymptomatic. 'How long will the immunity acquired after infection or the vaccination driven adaptive immunity be able to save us from re-infection?' is a million-dollar question.

Why is SARS-CoV-2 so contagious?

Expedited sequencing of the viral genome, which proved that SAR-CoV-2 is similar to SARS (Severe Acute Respiratory Syndrome), the infection broke out in China between 2002 and 2004, also provided a clear understanding about the nature

and mechanism by which SARS-CoV-2 spikes bind with Angiotensin-Converting Enzyme-2 (ACE-2), 10-20 times more effective than its predecessor, and how it gets quickly detached with the help of a protease allowing the lipid layer to fuse with the cell membrane and releasing its RNA into the host cell. Once inside, the virus replicates by simply hijacking the machinery of the host cells, thus spreading further and infecting more cells and eventually other organs, the transmission contaminating the environment and thus infecting more people. It's again the understanding of the spike glycoproteins, which formed the basis for developing novel vaccines, in record times.

The reasons for loss of smell and neurological problems associated with COVID-19, NRP-1, a protein receptor in the host, not only helps SARS-CoV-2 to attach to a host cell but also invading the nervous system resulting in the loss of taste and smell, as generally experienced by most of the COVID-19 patients. TMPSSR2 and Furin, two proteases present in the host cells, activate and facilitate the cleavage of spikes after they get bounded to ACE-2. This activation is key to the fusion and subsequent entry of the virus into the cell.

Breaking of young hearts!

The recent studies carried out by Kory. J. Lavine et al. at Washington University School of Medicine have shown that SARS-CoV-2 infects heart muscle cells and fibres directly, causing heart failure or cardiac injury in generally healthy people. It is important to note that this effect is independent of inflammation level, which means that inflammation is not the initial cause for this damage.

Previous studies have already demonstrated that apart from wreaking havoc on the respiratory system, heart, brain and kidneys, SARS-CoV-2 impairs insulin-producing beta cells of the Pancreas, leading to diabetes in COVID-19 patients and thus ensuring that nothing remains unaffected by this deadly virus, as far as the vital organs of a human body, are concerned, provided they are susceptible.

The way forward

The damaging effects of COVID-19, discussed above are mainly due to the presence of ACE-2 guarded multiple entry gates, available in high numbers on the cells in upper airways as well as in all the vital organs of our body including lungs, heart, kidney, digestive system and brain. The efficient transmission and spread of the virus is further facilitated by NRP-1 and two proteases, namely TMPRSS2 and Furin, as discussed above. The Furin cleavage site in the spike protein of SARS-CoV-2 responsible for high infectivity, transmissibility and disease pathogenesis is absent in other lineage B beta coronaviruses, such as SARS-CoV.

It becomes pretty clear from the understanding developed so far, that once the SARS-CoV-2 affects the targeted organs the only option left with doctors is to symptomatically handle the damage. Since the extent of the damage appears to be directly proportional to the overall weakness of the immune system and/or a particular organ affected with co-morbidities, it unveils the mystery why COVID-19 is non-symptomatic in many but deadly in some isolated patients.

There is nothing new about the speed with which most of the RNA viruses mutate but the way SARS-CoV-2 is mutating to evolve into more transmissible and infectious versions and spreading across the globe, it is difficult to believe that it could soon be possible to eradicate it completely.

It may be possible to keep people safe by timely providing vaccines, capable of inducing required antibodies, to protect masses from infection and the studies carried out by researchers at Washington University confirming the presence of antibody producing cells against the virus in the bone marrow of COVID-19 patients gives hope that the SARS-CoV-2 induced immune response may be robust enough to provide long-lasting protection against the virus.

The findings that vaccines may elicit a similar immunological response further increase hopes to contain the virus. However, one has to wait and see how these vaccines will tackle SARS-CoV-2 and also the continuously emerging novel variants in the long run. A recent study, published in Lancet on July 15, 2021 finds that vaccine antibody levels drop substantially over the course of 2-3 months and can reduce by more than 50 per cent over 10 weeks. If the levels continue dropping at this rate, it is very likely that current vaccines may not be able to provide desired protection against future variants.

Wearing masks appears to help a bit in keeping SARS-CoV-2 infections at bay and the strength of an individual's immunity in avoiding the severity due to COVID-19, but believing and feeling confident that someone will not get the infection, is as good as living in delusion. Also, knowing the facts that even those who had taken vaccines have succumbed to COVID-19, it is

important for scientists to find out a method to detect the infection soon after it sets in, rather than after few days or a week, so as to handle the COVID-19 well before it travels down and infects vital organs of a person. Further, a foolproof treatment to immediately restrict and neutralise the virus before it travels down from the upper respiratory to the lower respiratory system and other vital organs is highly warranted.

Dr Ashok Kumar, President, Centre for Research and Development, Ipca Laboratories Ltd, Mumbai