Harnessing immune checkpoint blockade and hyper-inflammation: A viable option for therapeutically tackling COVID-19 severity

At DBT’s National Institute of Biomedical Genomics (NIBMG), Kalyani, recent research findings pointed towards decreased T cell counts (the key players that attack the virus infected cells) and T cell exhaustion (loss of effector function of T cells, i.e., inability to attack the infected cells) among COVID-19 patients. With cues from cancer studies and mouse models of various infections, it is seems plausible that T cell exhaustion could also result due to overexpression of immune checkpoint molecules such as PD-1, CTLA-4, TIM3 etc., for which, effective inhibitory molecules are available that have shown success in case of cancer immunotherapy.

Furthermore, cytokine storm syndrome (CRS) is another phenomenon that contributes to disease aggravation in COVID-19 pathogenesis through elicitation of acute respiratory distress with co-existence of venous thromboembolism and multiple organ dysfunctions. A number of therapeutic options for reducing hyper inflammation or CRS are being considered worldwide, some of which are already in clinical trials. Of these, tocilizumab has an FDA approval for treatment of rheumatoid arthritis and related diseases, as well as an oncology supportive care drug. Therefore, it is tempting to propose that a combination therapy could be designed to counteract CRS on one hand, together with reversal of immune checkpoint blockade, as an antiviral for tackling severe COVID-19 pathogenesis.

The latter phenomenon could bolster the activation of effector T cells to specifically target the virus infected cells, as well as act to prevent future infections through generation of memory T cells. However, such translational insights could be implemented only after examining the spectrum of host immune related factors such as, antigen presentations, immune activations and inhibitions, cytokine profiles etc. associated with the various stages of COVID-19 pathogenesis, i.e., SARS-COV-2 positive asymptomatic individuals,
individuals with mild symptoms (not required to be transferred to ICU) and individuals with severe disease (admitted in ICUs, succumbing to death or recovering).

COVID-19, the disease caused by the RNA virus SARS-CoV-2, has a spectrum of effects in different patients. This is suggestive of the key role played by host immunity in COVID-19 pathogenesis. Some of the thrust areas of therapeutically tackling severe cases of COVID-19 are development of antiviral drugs, monoclonal antibodies, use of convalescent plasma from recovered severe patients and prophylactic vaccines against SARS-CoV-2.

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