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The outbreak of COVID-19 across the world has posed unprecedented and global challenges on multiple fronts. Till now, approximately more than 22 million cases have been reported worldwide with around 800 thousand deaths. Although the virus has infected a lot of people, lethality remains low and skewed by confounding factors like age and comorbidities. All major economies have suffered economically, socially, politically, and scientifically as they had to implement nation-wide lockdown. A race for the identification and production of vaccines has taken over resulting in the identification of numerous targets and possible therapies. Most of the vaccine and drug development so far has focused on the spike proteins and viral RNA-polymerases and the main protease for viral replication. The virus uses the spike glycoprotein on its surface to bind to Ace2 receptors on the human cells. Thus begins an evolutionary “arms race” between the virus and the humans.

In our present study, we focus on an entirely different approach to understand the nature of the virus and its pathogenicity. A small yet enigmatic protein in the virus is the envelope protein, which we have identified to demonstrate lower disparity in their sequence, and hence, lower mutability. Therefore, the envelope protein could be an attractive avenue to crack the game of the evolutionary “arms race”. Using the bioinformatics and structural modeling approach, we modeled the structure of this protein of the novel SARS-CoV-2. Moreover, we found that the most favorable structure could function as a gated ion channel conducting H⁺ ions. We identified and classified many distinct structural regions in the protein: the hydrophobic core, the central core, a bottleneck, and a gate region. These suggest that the envelope protein might show viral ion channeling activity (viroporin) which plays a critical role in viral infection and pathogenesis.

We provide a structural basis and additional avenues for vaccine development and generating therapeutic interventions against the virus. But more importantly, we are just beginning to understand this novel virus and its complexities.