Structural Bioinformatics unveils insights in SARS-CoV-2 Susceptibility and Transmissibility

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Abstract

The COVID-19 pandemic has caused a substantial global impact on both public health and socioeconomic since its emergence in 2019. Many countries are still experiencing an intermittent rise in the number of infections due to the emergence of Variants of Concern (VOCs) within the SARS-CoV-2 virus. Despite the availability of vaccines, re-infection is common.

The mechanism by which SARS-CoV-2 gains entry into host cells involves its spike protein (S-protein) binding to the ACE2 receptor. Beyond the receptor binding domain of spike proteins, many VOCs are known to harbour novel mutations within the N-terminal domains of spike protein. Studies suggest that the N-terminal domain might have a role in facilitating virus entry via binding to sialic-acid receptor. We structurally characterized the sialic acid binding pockets, explored whether variants could enhance the binding to sialic acids and therefore to the host membrane, thereby contributing to increased transmissibility.

Certain populations or clinical groups could exhibit an increased susceptibility to COVID-19. Whilst socioeconomic and cultural differences are likely significant important, human genetic factors could influence susceptibility. Experimental studies indicate SARS-CoV-2 uses innate immune suppression as a strategy to speed-up entry and replication into the host cell. In light of this, we employed a structural bioinformatics approach to analyse the impact of missense variants from human and viral proteins, utilizing the 3D structures of SARS-CoV-2: human protein complexes.

Our studies demonstrate the power of bioinformatics in deepening the understanding of SARS-CoV-2. This information may be useful for vaccine/drug design.