SARS–CoV-2 3-chymotrypsin-like protease and its affinity to human STAT2 protein can possibly alter type 1 Interferon signaling, an in silico based study

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ABSTRACT

To understand a plausible antagonistic role played by the SARS-CoV-2 viral protease in type 1 interferon signaling, we performed an interaction analysis focused on STAT2 and protease 3CLpro. STAT2 is crucial in producing a cellular antiviral state. RNA-seq data analysis of severe Covid-19 patients compared with moderate and healthy specimens has shown a significant down regulation of STAT2 along with its pathway associated proteins. To elaborate on the role of 3CLpro in this dysregulation, a protein-protein interaction analysis between the two was performed. The 3CLpro-STAT2 docked complex displayed a stable binding affinity score of -10.4. 62 residues constituted the protein-protein interface and 8 hotspot residues were identified. ARG188, ASP187, PRO168, HIS172 were amongst the H-bonding residues in 3CLpro. A total of 13 H-bonds was observed between the two proteins. 15 residues from 3CLpro and 11 from STAT2 were involved in hydrophobic interactions as well. Next, for better understanding the binding affinity we induced mutation in the unconserved regions of 3CLpro and observed an interaction profile similar to the wild type complex. Out of 26 mutant complexes three even had a higher docking score than the wild type while a majority showed stable binding. The inhibition of STAT2 via 3CLpro could explain the viral immune evasion studies that are currently being reported.

Keywords: 3CLpro, STAT2, Gene Expression Profile, Docking, Protein-Protein Interaction

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