Druggable target pockets in non-structural proteins of sars-cov-2 polyprotein 1ab

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19. Since the proteins encoded in the SARS-CoV-2 genome mutate, highly conserved pockets in said proteins are ideal for broadly neutralizing antiviral drug targets. Though research has been done on the subject, there is much to be proposed regarding a broadly neutralizing antiviral for SARS-CoV-2. This work aimed to find the nonstructural protein (NSP) encoded in the polyprotein most suitable for further testing based on conservation and number of pockets deemed suitable based on druggability. Thus, the SARS-CoV-2 polyprotein was investigated, a Multiple Sequence Alignment was made using Jalview, and the protein's evolutionary history was determined using a phylogenetic tree. ConSurf helped determine the conservation of the NSPs and statistical analysis was done using boxplots. PockDrug, a webserver that predicts the pocket's ability to bind a drug with high affinity measured as druggability, found 154 pockets across the proteome. In NSP12 and NSP14, 27 and 17 pockets, respectively, had a druggability score ≥ 0.5. Increasing the druggability cutoff to 0.8, left two pockets in NSP12 and four in NSP14. These proteins had the greatest number of pockets, and the NSPs had high conservation rates. This indicates that these pockets could be used as drug targets for SARS-CoV-2 and its current and future variants. Further testing of the pockets' location, conservation, amino acids, and post-translational modifications would allow for a better understanding of these pockets as targets for new antiviral drugs against coronaviruses.