Antiviral Targeting against SARS-CoV2 Present in the Nonstructural Protein 14 (NSP14)

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The rapidly evolving SARS-CoV-2, commonly known as COVID-19, continues to pose as a public health crisis, motivating the pharmaceutical industry to better understand the virulence and infection process of the virus, as well as develop drug therapies that may decrease its mortality and infection rate. The purpose of this study is to investigate the Nonstructural protein 14 (NSP14) accessibility, druggability and conservation, with the objective of finding a good drug binding pocket that can work for current and future SARS-CoV-2 variants. Druggability scores reflect the potential of a protein binding to drug-like molecules. A low evolutionary rate and high conservation score is important when considering drug binding sites. NSP14 plays an important role in SARS-CoV-2 replication and transcription by proofreading RNA degradation and capping mRNA. The Basic Local Alignment Search Tool (BLAST) was used to identify NSP14 sequences for different coronaviruses and build a Multiple Sequence Alignment (MSA). The MSA was used to build phylogenetic trees and calculate the evolutionary rate of NSP14. Results demonstrated that NSP14 had a high conservation, which is important in the role of a successful drug target. PockDrug was used to determine potential drug binding sites, yielding a total of seven pockets with a druggability probability > 0.8. One pocket was found to have a high conservation score and low evolutionary rate, as well as a druggability probability of 0.93. Overall, we found good potential antiviral targets within NSP14 that should be further investigated and considered for SARS-CoV-2 drug therapies.