NSP5- SARS-CoV-2 potential antiviral target with conserved pockets

Patricia Fonseca Cruz, under the direction of Dr. Jessica Liberles, Biology
Florida International University, Miami, Fl.

Abstract:

The COVID-19 pandemic, caused by SARS-CoV-2, has impacted millions of people around the world. SARS-CoV-2 is a fast-evolving virus with a high rate of mutations and different variants. Due to the often lengthy process of developing new antiviral drugs, we decided to investigate if conserved pockets that could serve as drug targets were present across a broad range of coronaviruses including SARS-CoV-2 and its variants. This study focuses on the analysis of critical regions within SARS-CoV-2 NSP5's structure that could potentially serve as antiviral targets. NSP5 is a non-structural protein that functions as a protease and plays a crucial role in the organism's viral replication and immune system evasion. We used BLAST to create a protein sequence dataset for NSP5 from SARS-CoV-2 and other coronaviruses. A total of 24 sequences were aligned and used for phylogenetic reconstruction. A Consurf evolutionary analysis revealed high conservation scores and low evolutionary rates across all lineages. Furthermore, a biochemical characterization on Pockdrug revealed the presence of five protein pockets with druggability potential. These findings highlight the value of NSP5 as an antiviral target. Aiming at the potential druggable pocket regions within the conserved NSP5 protein could disrupt the assembly of the viral complex not just in SARS-CoV-2 but also in other coronaviruses.