Delving Into COVID-19 “Seams”: Examining the Structural Fabric of SARS-CoV-2

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The year 2019 and 2020 took an unprecedented turn as SARS-CoV-2 (COVID-19) ravaged the world, taking over half a million lives (as of July 2020), leaving vulnerable communities to take the hardest hits, exacerbating systemic injustices towards minorities (including decreased access to healthcare), and damaging economies. By examining proteins and their respective mutations in SARS-CoV-2, a better understanding of its structural biology can aid in drug and vaccine discovery. Further applications of a deepened structural understanding of SARS-CoV-2 include assisting in broader research efforts and valuable public health efforts to mitigate and prevent harm caused by SARS-CoV-2 and other coronaviruses worldwide. As part of a virtual summer research experience with the RCSB PDB, we studied how SARS-CoV-2 proteins protein evolved during the first six months of the COVID-19 pandemic by exploring amino acid sequence and 3D atomic-level structure using various structural bioinformatics tools, including Clustal Omega (www.ebi.ac.uk/Tools/msa/clustalo/) for sequence alignments and phylogenetic trees; Mol* (molstar.org) for 3D molecular visualization; and Foldit (fold.it) for structural/energetic effects of sequence mutations. The focus of this poster is SARS-CoV-2 Orf7a, a viral protein that interferes with N-linked glycosylation of the cellular protein BST-2, an inhibitor of coronavirus release (Taylor et al. 2015). Orf7a has also been shown to arrest cells in the G0/G1 cell checkpoint during SARS-CoV infection, thereby preventing cell cycle progression. The G0/G1 cell checkpoint is a phase in the cell division process wherein DNA is checked for damage before allowing progress into the S phase. If DNA damage cannot be repaired cell death ensues. Prevention of cell cycle progression is thought to provide more time for coronaviruses to replicate at higher rates with increased nucleotide pools and allow for higher virus pathogenicity (Yuan et al. 2005). Studying Orf7a can provide insights into SARS-CoV-2 pathogenesis, including what proteins are involved in regulating viral propagation and what SARS-CoV-2 proteins affect host cell cycle regulation. RCSB PDB is funded by the National Science Foundation (DBI-1832184), the US Department of Energy (DE-SC0019749), and the National Cancer Institute, National Institute of Allergy and Infectious Diseases, and National Institute of General Medical Sciences of the National Institutes of Health under grant R01GM133198.

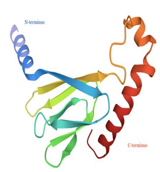

Figure 1