Understanding SARS CoV-2: A Sequence and Structural Analysis of the Evolution of Non-Structural Protein 9, Nsp9

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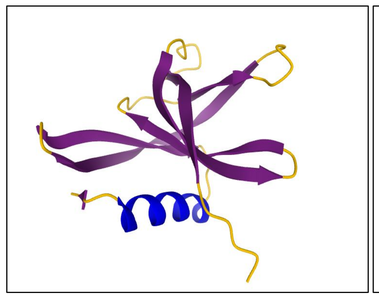
OVERVIEW

In January 2020, the World Health Organization (WHO) issued an announcement declaring COVID-19 (coronavirus disease 2019) a public health emergency of global concern. COVID-19 is an acute respiratory disease that is caused by the SARS CoV-2 virus. SARS CoV-2 has a large RNA viral genome that encodes many nonstructural and structural proteins.

The focus of this poster is SARS CoV-2 nonstructural protein 9,(Nsp9). Nsp9 is one of 16 nonstructural proteins represented within the SARS CoV-2 proteome. Research suggest that Nsp9 plays an important role in viral replication by acting as a single stranded RNA binding protein. Researchers are racing to visualize and understand the proteins used by SARS-CoV-2 in an effort to understand their mechanistic pathways and develop methods to inhibit the enzyme.



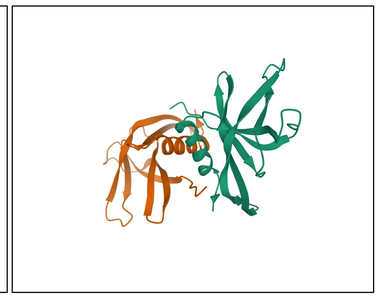


Figure 1a: Model of Nsp9 Monomer (beta sheets:purple, alpha helix:blue, random coils: gold)
Figure 1b: Model of proposed Nsp9 Homodimer

METHODOLOGY

- We explored 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.

Models and Preliminary Results

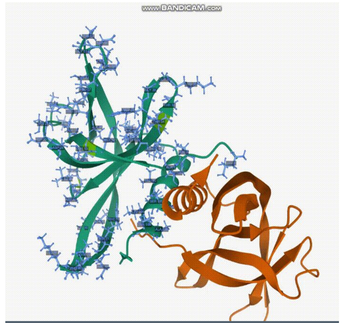


Figure 2: Distribution of Mutated Amino Acids

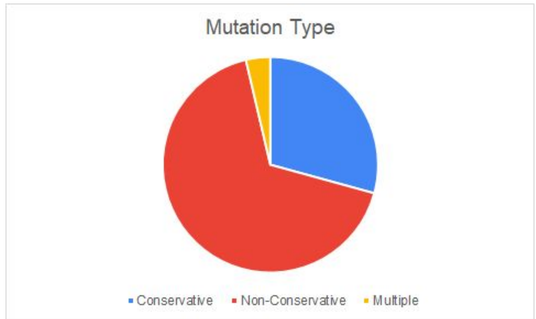


Chart 1:Mutation Type Analysis (Non-Conservative v. Conservative)

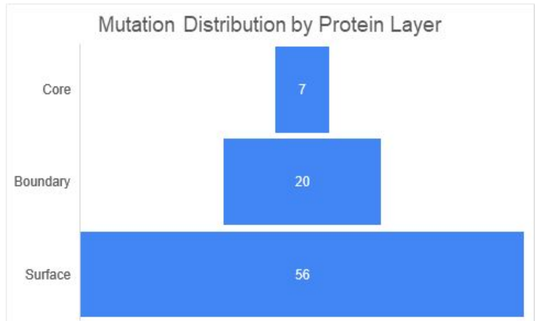


Chart 2: Mutation Distribution Analysis (Protein Layer)

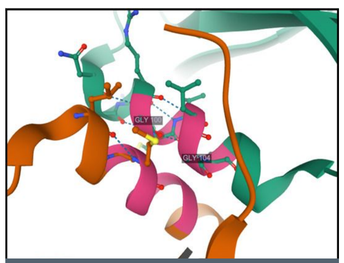


Figure3: Important Dimer Interface Residues G100 and G104

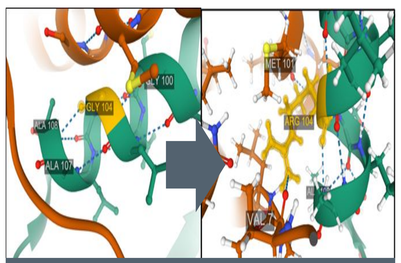


FIgure 4a and 4b: G104R Substitution at the Dimer Interface; Most energetically unfavorable mutant

Conclusion

- The data generated will be used in a scientific manuscript submitted after the conclusion of the RISE program.

Acknowledgements

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