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Pan Variant SARS-CoV-2 Common Interactions and Drug Candidates

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Introduction

The SARS-CoV-2 pandemic has impacted billions of lives on the global scale: directly, indirectly, financially, emotionally, and physically. Much research has investigated drug candidates for SARS-CoV-2 that have shown to be effective, however, are these drug candidates effective for all strains? Research into drug candidates that consider multiple variants of SARS-CoV-2 has not been found and the primary goal of this research.

Knowledge of domains-functional subunits of proteins- and interologs-interacting orthologs- of virus proteins in question can be leveraged to make predictions for these novel SARS-CoV-2 variants. Online databases containing domain-domain interactions and protein-protein interactions will be utilized to predict the interactions of the new variant's proteins with human proteins. A set of common interactions-interactions shared between all variants can then be made, characterized, and analyzed.

Ultimately, drug candidates will be identified based on the common interactions found in all variants, signifying the potential as drug candidates for current and future variants that have yet to emerge. Identifying these drug candidates is the primary goal of this research, along with characterizing the interactions via functional enrichment, subcellular localization, tissue expression and network analysis.

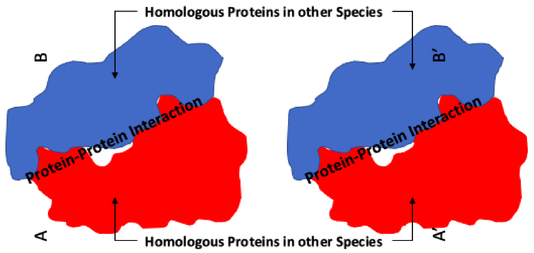

Figure 1. General example of interologs.

Methods

Figure 1 depicts the pipeline utilized in this research and summarized as follows:

- Retrieve orthologs/domains of proteins
- Query DDI and PPI databases
- Create common set of interactions
- Interaction characterization and drug candidate identification

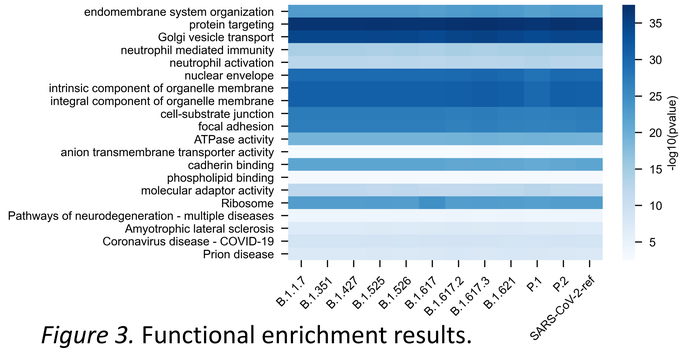

Figure 3. Functional enrichment results.

Results

- 8963 common interactions
- Gene Ontology, KEGG, subcellular localizations, tissue expressions seen in *Figures 3* and *2B*, respectively.
- High degree drug candidates in *Figure 4*
  - Fostamatinib
  - NADH
  - Glutamic acid
  - Zinc derivatives

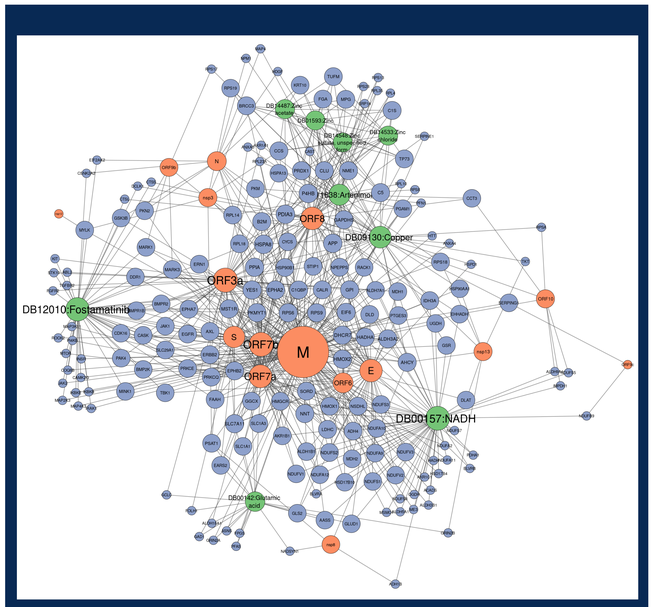

Figure 4. Interaction network involving drug candidates, viral and human proteins. Green: drug candidates, red: viral proteins, blue: human proteins.

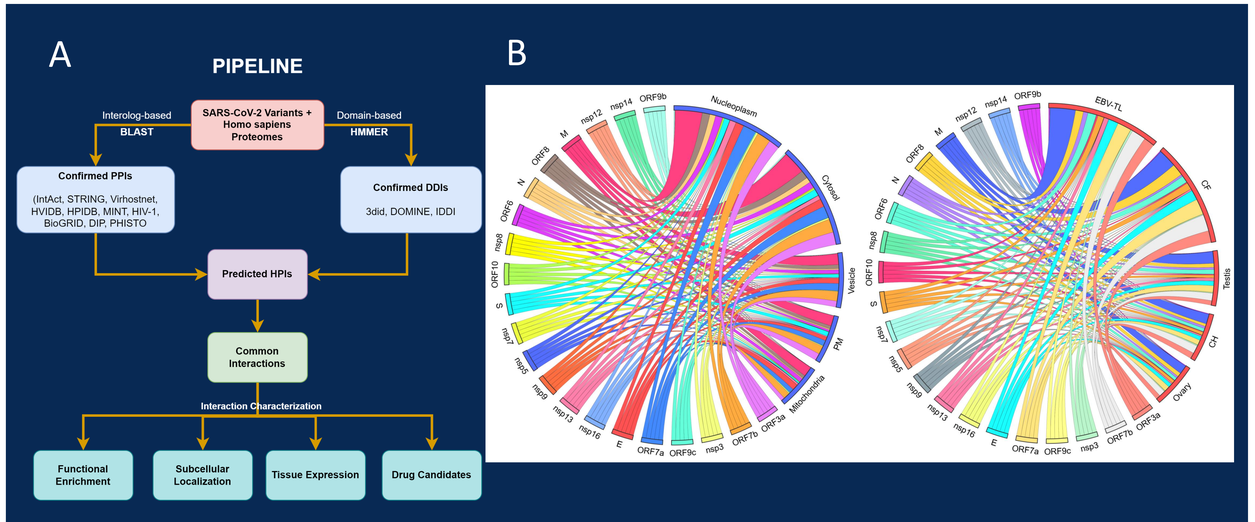

Figure 2. A) Pipeline utilized in this research. B) Viral protein distributions for subcellular localization and tissue expression. EBV-TL: EBV transformed lymphocytes, CF: cultured fibroblasts, CH: cerebellar hemisphere

Conclusions

The common PPI interactions involved in the variants of SARS-CoV-2 and human proteins have been characterized. Drug candidates have been identified. Several of these have been identified in other research, signifying the importance of these drug candidates in treating COVID-19.

Emphasis should be placed on these drug candidates for future research in treating COVID-19.

1. https://cytoscape.org/
2. https://www.genome.jp/kegg/
3. https://go.drugbank.com/
4. https://go.drugbank.com/

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