

Structure-based Modeling COVID-19

Emerging WuHan (COVID-19) coronavirus: glycan shield and structure prediction of spike glycoprotein and its interaction with human CD26section

The study modelled homo-trimer structure of COVID-19 spike glycoprotein in both closed (ligand-free) and open (ligand-bound) conformation, which is involved in host-cell adhesion.

<https://pubmed.ncbi.nlm.nih.gov/32178593/>

Modeling

- **SwissModel:** <https://swissmodel.expasy.org/>

Protein-Protein docking:

- **Cluspro:** <https://cluspro.bu.edu/login.php>

COVID-19 spike-host cell receptor GRP78 binding site prediction

<https://pubmed.ncbi.nlm.nih.gov/32169481/>

- DOI: [10.1016/j.jinf.2020.02.026](https://doi.org/10.1016/j.jinf.2020.02.026)COV

The study has modeled the COVID-19 spike binding site to the cell-surface receptor (Glucose Regulated Protein 78 (GRP78)) is predicted using combined molecular modeling docking and structural bioinformatics. The COVID-19 spike protein is modeled using its counterpart, the SARS spike.

A comparative analysis for SARS-CoV-2

<https://arxiv.org/pdf/2004.04281.pdf>

The report provides further insights into how the SARS-CoV-2 surface glycoprotein mutated for higher binding affinity to human ACE2 receptors, compared to the SARS-CoV protein, by integrating existing 3D protein models.

2019-nCoV (Wuhan virus), a novel Coronavirus: human-to-human transmission, travel-related cases, and vaccine readiness

<https://pubmed.ncbi.nlm.nih.gov/32088679/>

Protein-protein docking of Receptor Binding Domain, Phylogenetic analysis and docking

Software used:

- **Phyre2** was used for protein modeling
- **Haddock2** was used for docking

The potential chemical structure of anti-SARS-CoV-2 RNA-dependent RNA polymerase.

<https://pubmed.ncbi.nlm.nih.gov/32167173>

RNA-dependent RNA polymerase (RdRp) is an important protease that catalyzes the replication of RNA from RNA template and is an attractive therapeutic target. In this study, we screened these chemical structures from traditional Chinese medicinal compounds proven to show antiviral activity in severe acute respiratory syndrome coronavirus (SARS-CoV) and the similar chemical structures through a molecular docking study to target RdRp of SARS-CoV-2, SARS-CoV, and Middle East respiratory syndrome coronavirus (MERS-CoV).

Simulation of the Clinical and Pathological Manifestations of Coronavirus Disease 2019 (COVID-19) in Golden Syrian Hamster Model: Implications for Disease Pathogenesis and Transmissibility section

<https://pubmed.ncbi.nlm.nih.gov/32215622/>

Molecular docking on the binding between ACE2 of common laboratory mammals and the RBD of the surface spike protein of SARS-CoV-2 suggested that the golden Syrian hamster is an option.

Software Used:

I-TASSER: <https://zhanglab.ccmb.med.umich.edu/I-TASSER/>

Rosetta: <https://www.rosettacommons.org/software>

Structural modeling of 2019-novel coronavirus (nCoV) spike protein reveals a proteolytically sensitive activation loop as a distinguishing feature compared to SARS-CoV and related SARSlike coronavirusesUntitled section

<https://arxiv.org/ftp/arxiv/papers/2002/2002.06196.pdf>

Protein structure and sequence re-analysis of 2019-nCoV genome does not indicate snakes as its intermediate host or the unique similarity between its spike protein insertions and HIV-1

<https://arxiv.org/ftp/arxiv/papers/2002/2002.03173.pdf>

Based on our analyses and existing data of coronaviruses, we concluded that the intermediate hosts of 2019-nCoV are more likely to be mammals and birds than snakes, and that the "novel insertions" observed in the spike protein are naturally evolved from bat coronaviruses

Comparing the binding interactions in the receptor binding domains of SARS-CoV-2 and SARS-CoV

<https://arxiv.org/ftp/arxiv/papers/2004/2004.02158.pdf>

we used molecular dynamics simulations and Monte Carlo sampling to compare the binding affinities of the spike proteins of SARS-CoV and SARS-CoV-2 to the ACE2. We found that the SARS-CoV-2 binds to ACE2 stronger than SARS-CoV by 7 kcal/mol, due to enhanced electrostatic interactions

Genomics-guided molecular maps of coronavirus targets in human cells: a path toward the repurposing of existing drugs to mitigate the pandemic

<https://arxiv.org/ftp/arxiv/papers/2003/2003.13665.pdf>
(Pathway based analysis)

Gene set enrichment analyses (GSEA) of genomic features associated with the ACE2 and FURIN genes

Structural analysis of SARS-CoV-2 and prediction of the human interactome

<https://arxiv.org/ftp/arxiv/papers/2003/2003.13655.pdf>

In-Silico evidence for two receptors based strategy of SARS-CoV-2

<https://arxiv.org/pdf/2003.11107.pdf>

We propose a novel numerical method able to determine efficiently and effectively the relationship of complementarity between portions of protein surfaces

Computational Design of Peptides to Block Binding of the SARS-CoV-2 Spike Protein to Human ACE2

<https://doi.org/10.1101/2020.03.28.013607>

Peptide design

Structure-Based Design, Synthesis and Biological Evaluation of Peptidomimetic Aldehydes as a Novel Series of Antiviral Drug Candidates Targeting the SARS-CoV-2 Main Protease

<https://doi.org/10.1101/2020.03.25.996348>

Recognition of potential Covid-19 drug treatments through study of existing protein-drug structures: an analysis of thermodynamically active residues

<https://arxiv.org/ftp/arxiv/papers/2004/2004.10233.pdf>

We report results of our study of approved drugs as potential treatments for COVID-19 based on the application of various bioinformatics predictive methods. The drugs studied include hydroxychloroquine, ivermectin, remdesivir and α -difluoromethylornithine (DMFO). Our results indicate that these small drug molecules selectively bind to thermodynamically active residues on protein surfaces, and that some prefer hydrophobic over other active sites. Our approach is not restricted to viruses and can facilitate rational drug design, as well as improve our understanding of molecular interactions, in general.

SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor

[https://www.cell.com/cell/pdf/S0092-8674\(20\)30229-4.pdf](https://www.cell.com/cell/pdf/S0092-8674(20)30229-4.pdf)

(shows the benefit of inhibiting TMPRSS2)

Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein

[https://www.cell.com/cell/fulltext/S0092-8674\(20\)30262-2](https://www.cell.com/cell/fulltext/S0092-8674(20)30262-2)

(provides proof of the importance of ACE2 receptor)

Decoding SARS-CoV-2 transmission, evolution and ramification on COVID-19 diagnosis, vaccine, and medicine

<https://arxiv.org/pdf/2004.14114.pdf>

(interesting paper that connects the mutation in the COVID-19 genome to infection)

Structural and Functional Implications of Non-synonymous Mutations in the Spike protein of 2,954 SARS-CoV-2 Genomes

<https://www.biorxiv.org/content/10.1101/2020.05.02.071811v1.full.pdf>

CoV-Seq: SARS-CoV-2 Genome Analysis and Visualization

<https://www.biorxiv.org/content/10.1101/2020.05.01.071050v1.full.pdf>

In-silico nucleotide and protein analyses of S-gene region in selected zoonotic coronaviruses reveal conserved domains and evolutionary emergence with trajectory course of viral entry from SARS-CoV2 genomic data

<https://arxiv.org/ftp/arxiv/papers/2005/2005.02809.pdf>

Conserved domains with antagonistic action on host innate antiviral cellular mechanisms in SARS-CoV 2 include nsp 11, nsp 13 etc. Also, multiple sequence alignments of the spike [S] gene protein of selected candidate zoonotic coronaviruses alongside the S gene protein of the SARs-CoV2 revealed closest evolutionary relationship [95.6%] with pangolin coronaviruses [S] gene

Impact of Thiol-Disulfide Balance on the Binding of Covid-19 Spike Protein with Angiotensin Converting Enzyme 2 Receptor

<https://www.biorxiv.org/content/10.1101/2020.05.07.083147v1.full.pdf+html>

A modified ACE2 peptide mimic to block SARS-CoV2 entry

<https://www.biorxiv.org/content/10.1101/2020.05.07.082230v1.full.pdf>

Table 1: **Systems simulated in this study. The last 3 systems feature mutated peptides. The points of mutation have been mentioned in red in the peptide sequence.**

S.no	Simulation Model	Peptide Sequence
1	Wild type (WT)	IEEQAKTFLDKFNHEAEDLFYQS
2	WT-S	TFLDKFNHEAED
3	E17L	IEEQAKTFLDKFNHEAredLDLFYQS
4	D18L	IEEQAKTFLDKFNHEAredLLFYQS
5	N13E-E17L	IEEQAKTFLDKFredEHEAredLDLFYQS

Bulk and single-cell gene expression profiling of SARS-CoV-2 infected human cell lines identifies molecular targets for therapeutic intervention

<https://www.biorxiv.org/content/10.1101/2020.05.05.079194v1>

In summary, our study established in vitro cell culture models to study SARS-CoV-2 infection and identified HSP90 protein as potential drug target for therapeutic intervention of SARS-CoV-2 infection.

Coarse-grained molecular simulations of the binding of the SARS-CoV 2 spike protein RBD to the ACE2 cell receptor

<https://www.biorxiv.org/content/10.1101/2020.05.07.083212v1>

In silico comparison of spike protein-ACE2 binding affinities across species; significance for the possible origin of the SARS-CoV-2 virus

<https://arxiv.org/ftp/arxiv/papers/2005/2005.06199.pdf>

CoV3D: A database of high resolution coronavirus protein structures

<https://www.biorxiv.org/content/10.1101/2020.05.12.091983v1.full.pdf>

Drug targets for corona virus: A systematic review

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7074424>

The 2019-novel coronavirus (nCoV) is a major source of disaster in the 21st century. However, the lack of specific drugs to prevent/treat an attack is a major need at this current point of time. In this regard, we conducted a systematic review to identify major druggable targets in coronavirus (CoV). We searched PubMed and RCSB database with keywords HCoV, NCoV, corona virus, SERS-CoV, MERS-CoV, 2019-nCoV, crystal structure, X-ray crystallography structure, NMR structure, target, and drug target till Feb 3, 2020. The search identified seven major targets (spike protein, envelop protein, membrane protein, protease, nucleocapsid protein, hemagglutinin esterase, and helicase) for which drug design can be considered. There are other 16 nonstructural proteins (NSPs), which can also be considered from the drug design perspective. The major structural proteins and NSPs may serve an important role from drug design perspectives. However, the occurrence of frequent recombination events is a major deterrent factor toward the development of CoV-specific vaccines/drugs.

Expression of ACE2, the SARS-CoV-2 receptor, and TMPRSS2 in prostate epithelial cells

<https://www.biorxiv.org/content/10.1101/2020.04.24.056259v2.full.pdf>

A comparison of ACE2 expression in lung tissue between males and females showed higher expression in males and a larger proportion of ACE2+ cells in male type II pneumocytes, with preliminary evidence that type II pneumocytes of all lung epithelial cell types showed the highest expression of ACE2. These results raise the possibility that sex differences in ACE2 expression and the presence of doublepositive cells in the prostate may contribute to the observed disparities of COVID-19