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Research Article

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Role of changes in SARS-CoV-2 spike protein in the interaction with the human ACE2 receptor: An in silico analysis Role of changes in SARS-CoV-2 spike protein in the interaction with the human ACE2 receptor: An *in silico* analysis

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Abstract

Many human viral diseases are the result of zoonotic diseases. Some of the diseases caused by these zoonotic events have affected millions of people worldwide, some of which have resulted in high human morbidity/mortality rates. Changes in viral proteins that act as ligands to host receptors may promote interspecific spillover. The most recent of these zoonotic events that have caused an ongoing large-scale epidemic are the SARSCoV2-caused Covid19 epidemics..The purpose of this study was to identify mutations in the SARSCoV2 peaplomer sequence that could promote human-to-human transmissionTo identify modifications in the S1 subunit of the spike receptor binding domain, an in silico method has been used. The observed changes have a significant effect on the SARSCoV2 spike / ACE2 interaction, causing a decrease in binding energy compared to the binding energy of BatCoV to this receptor. The data presented in this study suggest a higher affinity of the SARS-Cov-2 spike protein to the human ACE2 receptor, compared to the one of Bat-CoV spike and ACE2This may be responsible for the rapid viral spread of SARSCoV2 in humans.

Keywords: Spike, SARS-CoV-2, ACE2, Coronavirus, outbreak

Introduction

Acute Respiratory Syndrome with Severity SARS (Middle Eastern Respiratory Syndrome) Coronavirus Coronavirus (MERS-CoV) and the newly discovered novel Coronavirus (SARS-CoV-2) are both members of the Coronaviridae family, genus Betacoronavirus, which have been linked to major epidemic outbreaks. These are enveloped viruses with a 32-kilobyte positive-sense single-strand RNA. The spike, membrane, envelope protein, and nucleocapsid are the four primary structural proteins found in viral particles. The spike protein protrudes from the virion's envelope and is important for receptor host selection and cellular attachment.

SARS and SARS-CoV-2 spike proteins interact with angiotensin-converting enzyme 2 (ACE2), according to strong scientific data (Chen et al 2020 Wan et al.). Other cellular receptors, including as the C-type lectin CD209L and DC-SIGN, also play a secondary role in viral attachment However, contact between viral proteins and their cell membrane receptors appears to be an important step in the reproductive cycle of SARS-CoV and possibly SARSCoV2. (Walls et al.). Furthermore, the effectiveness of viral infection is highly reliant on this procedure. Protein-protein interactions are linked to a number of physicochemical parameters.

The nature of residues and the sort of chemical interactions that occur between ligand and receptor define these parameters. As a result, the presence of residues that provide a more energetically favourable contact (lower free energy) may drive binding kinetics and eventually lead to fusion. As a result, the goal of this research was to assess the energetic profile of the interaction between the SARS-CoV-2 spike protein and the human cell receptor ACE2.

Materials and Methods

NCBI:

NCBI is database which is used to charged with creating automated systems for storing and analyzing knowledge about molecular biology, biochemistry, and genetics. NCBI is now a leading source for publicbiomedical databases, software tools for analyzing molecular and genomic data, and research in computational biology.

PUBCHEM:

PUBCHEM is the database which is used to drug discovery and many aspects such as lead identification and optimization, compound-target profiling, polypharmacology studies and unknown chemical identityelucidation. PubChem has also shown to be a useful tool for creating secondary databases, software tools, and online applications..

PROTEIN DATA BANK:

PROTEIN DATA BANK (PDB) is the database which is used find 3D structure of the protein. The PDB is a key in areas of structural biology, such as structural genomics. Most major scientific journals and some funding agencies now require scientists to submit their structure data to the PDB.

UNIPROT:

UNIPROT also called as SWISSPROT It provides an up-to-date, comprehensive bodyof protein information at a single site.It aids scientific discovery by collecting, interpreting andorganising this information so that it is easy to access and use.

SWISSMODEL

SWISSMODEL is the online web server dedicated to homology modeling of 3D protein structures. Homology modeling is currently the most accurate method to generate reliable three-dimensional protein structure models and is routinely used in many practical applications.

TCOFFEE Alignment:

T-Coffee is a multiple sequence alignment program.

Phylogenetic analysis:

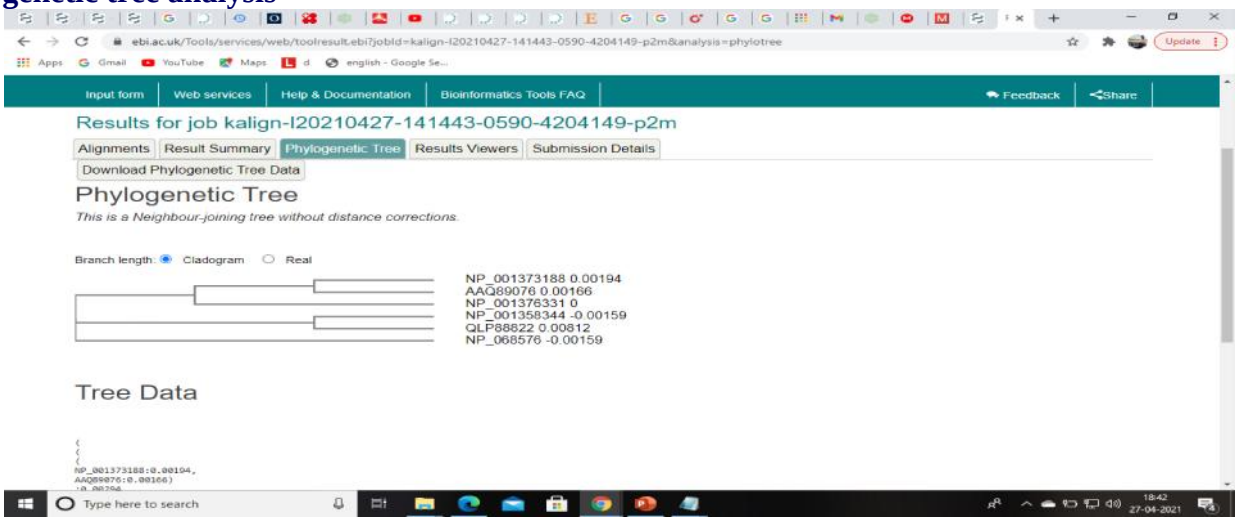
A phylogenetic tree is a diagram that represents evolutionary relationships among organisms.

Protein sequence:

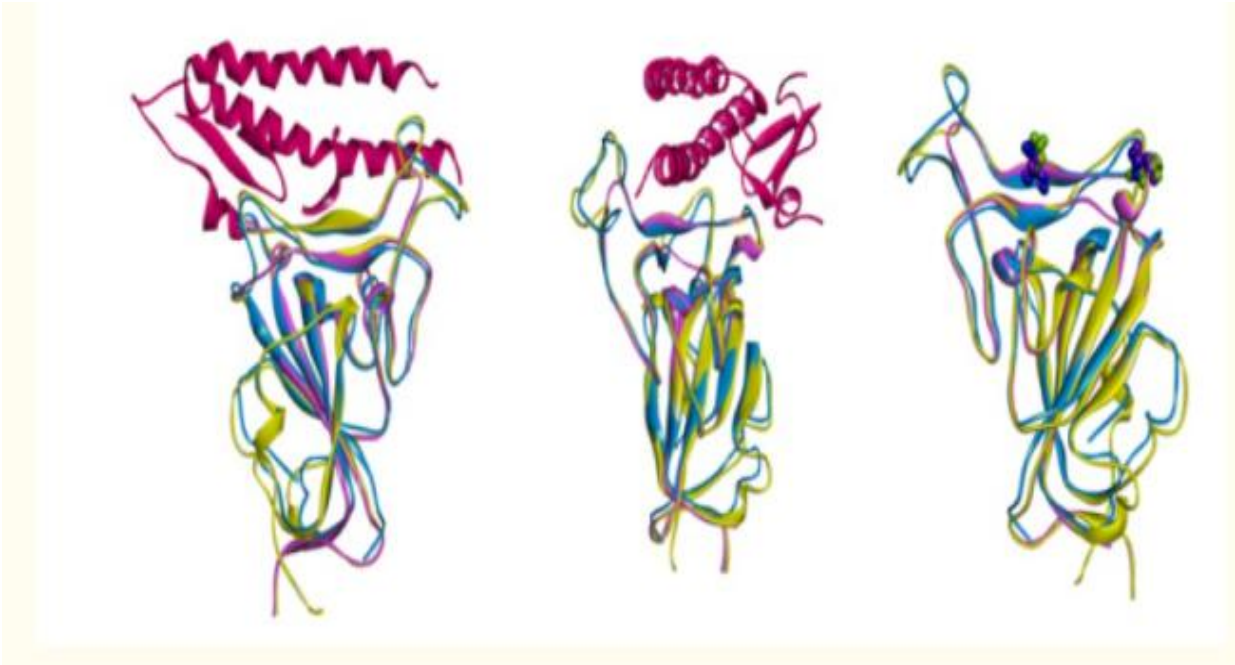
▶ >tr|A0A7I2V4H0|A0A7I2V4H0_HUMAN Angiotensin-converting enzyme 2 OS=Homo sapiens OX=9606 GN=ACE2 PE=4 SV=1
▶ MSSSSWLLLSLVAVTAAQSTIEEQAKTFLDKFNHEAEDLFYQSSLASWNYNTNITEENVQ
▶ NMNNAGDKWSAFLKEQSTLAQMYPLQEIQNLTVKLQLQALQQNGSSVLSEDKSKRLNTIL
▶ NTMSTIYSTGKVCNPDNPQECLLLEPGLNEIMANSLDYNERLWAWESWRSEVGKQLRPLY
▶ EEYVVLKNEMARANHYEDYGDYWRGDYEVNGVDGYDYSRGQLIEDVEHTFEEIKPLYEH
L
▶ HAYVRAKLMNAYPSYISPIGCLPAHLLGDMWGRFWTNLYSLTVPFGQKPNIDVTDAMVDQ
▶ AWDAQRIFKEAEKFFVSVGLPNMTQGFWENSMLTDPGNVQKAVCHPTAWDLGKGDFRIL
M
▶ CTKVTMDDFLTAHHEMGHIQYDMAYAAQPFLLRNGANEGFHEAVGEIMSLSAATPKHLKS
▶ IGLLSPDFQEDNETEINFLLKQALTIVGTLPFTYMLEKWRWMVFKGEIPKDQWMKKWWEM
▶ KREIVGVVEPVPHDETYCDPASLFHVSNDYSFIRYYTRTLYQFQFQEALCQAAKHEGPLH
▶ KCDISNSTEAGQKLFNMLRLGKSEPWTLALENVVGAKNMNVRPLLNYFEPLFTWLKDQNK
▶ NSFVGWSTDWSPYADQSIKVRISLKSALGDKAYEWNDNEMYLFRSSVAYAMRQYFLKVK
N
▶ QMILFGEEDVRVANLKPRISFNFFVTAPKNVSDIIPRTEVEKAIRMSRSRINDAFRLNDN
▶ SLEFLGIQPTLGPPNQPPVSIWLIVFGVVMGVIVVGIVILIFTGIRDRKKPTPLLGKSWL
TAILKD

Results and Discussion

Phylogenetic tree analysis



Protein Data Bank



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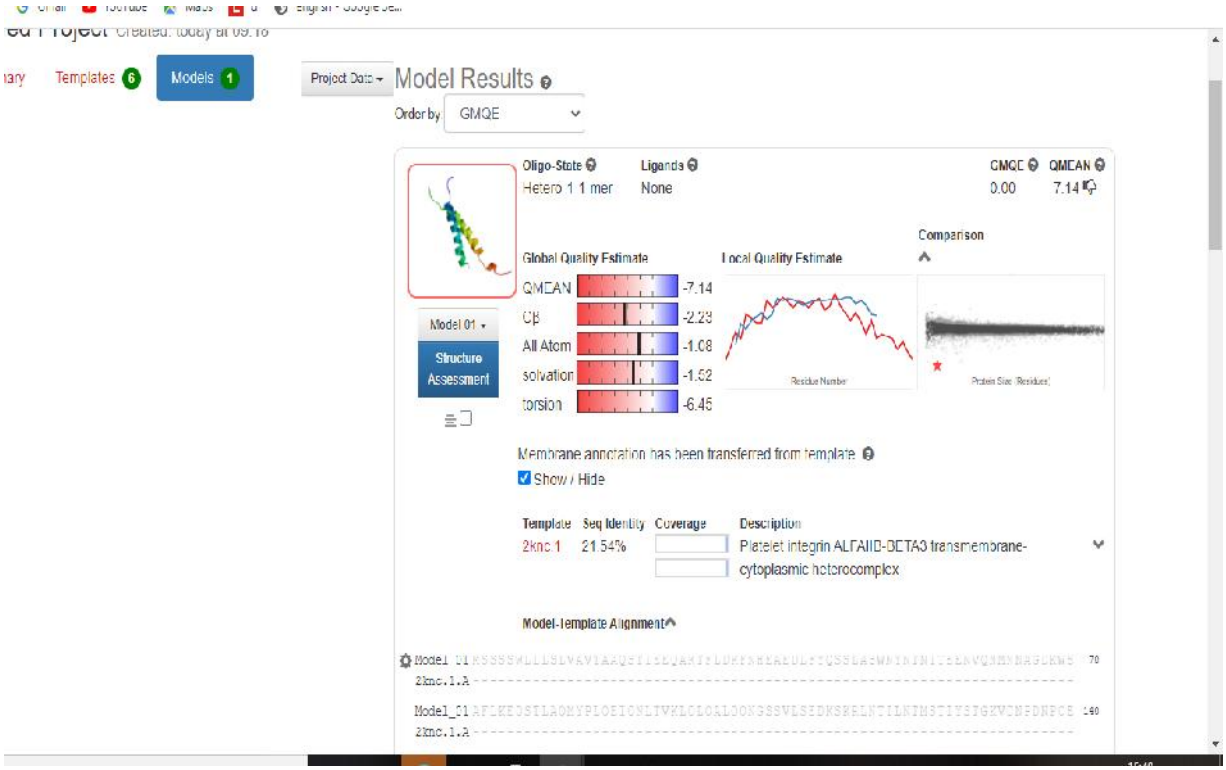

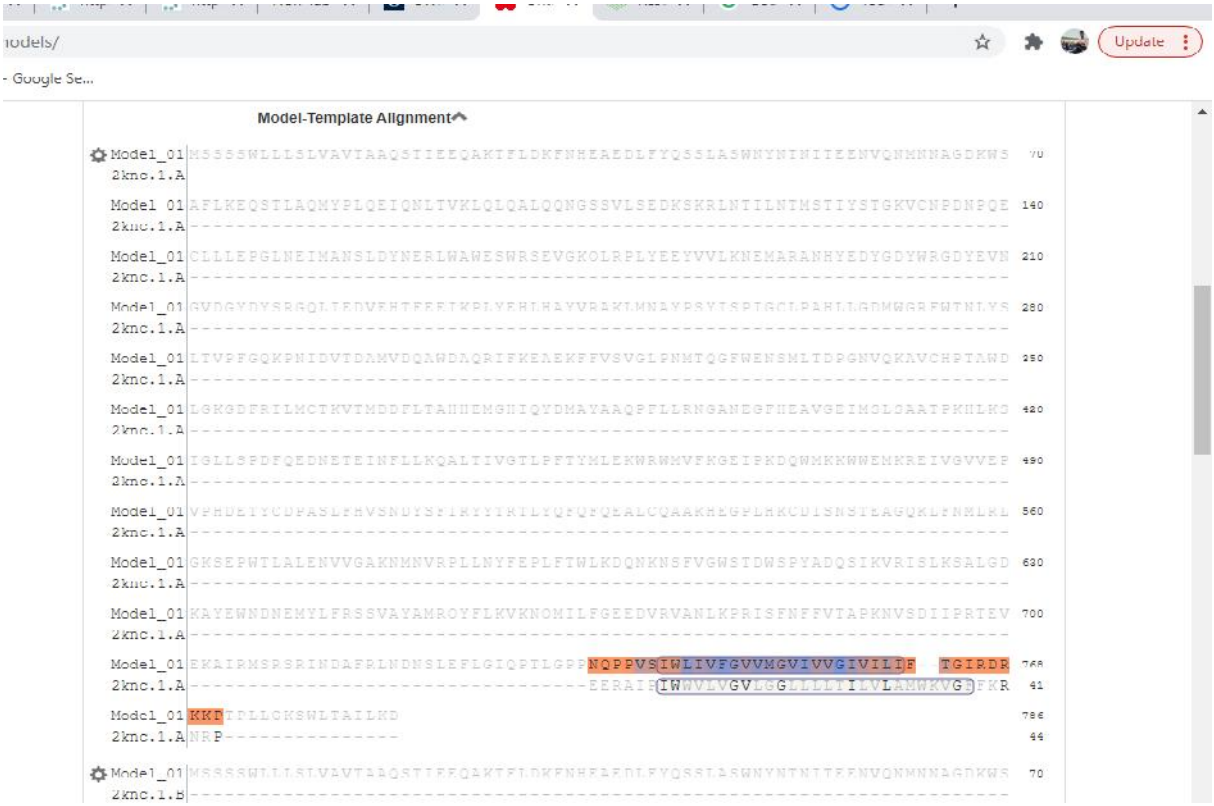
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Model_01
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2knc.1.A
Model_01
2knc.1.A
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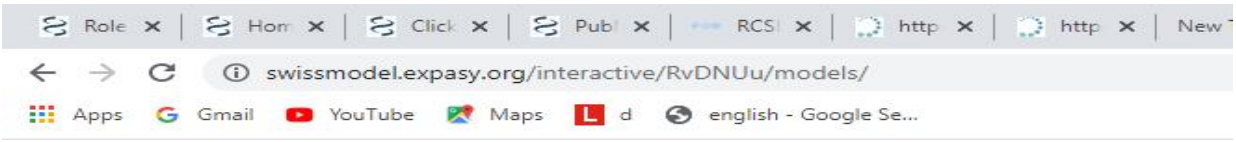
2knc.1.B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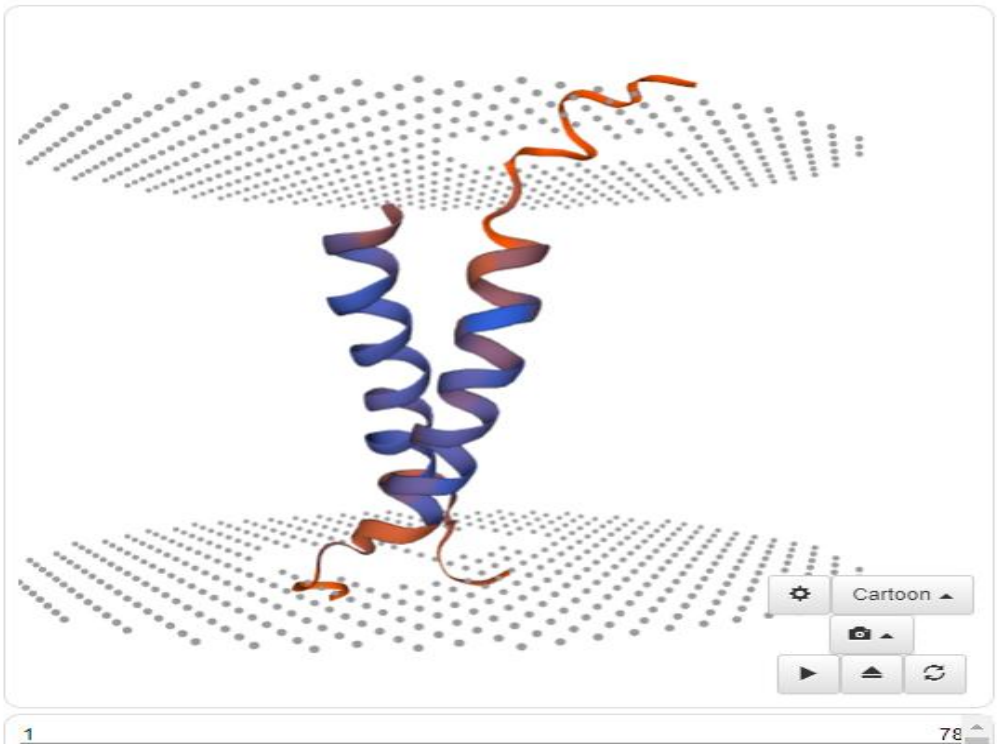
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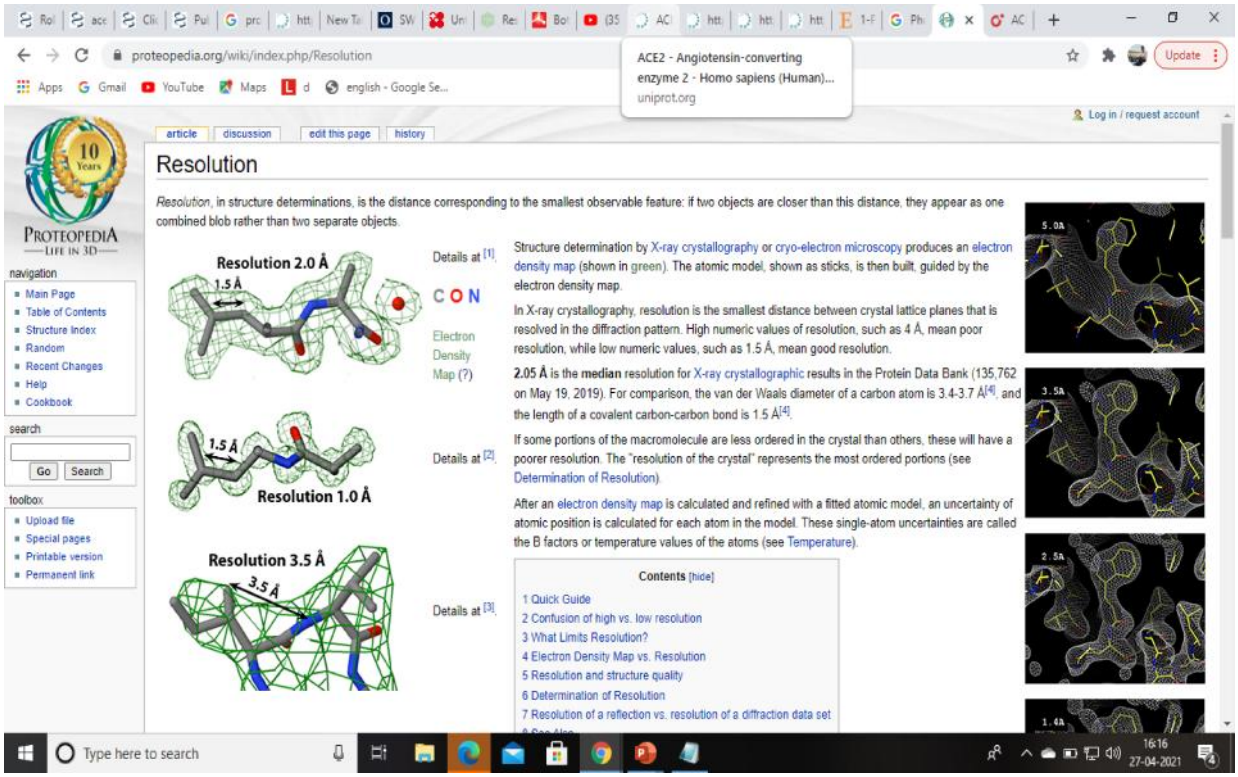

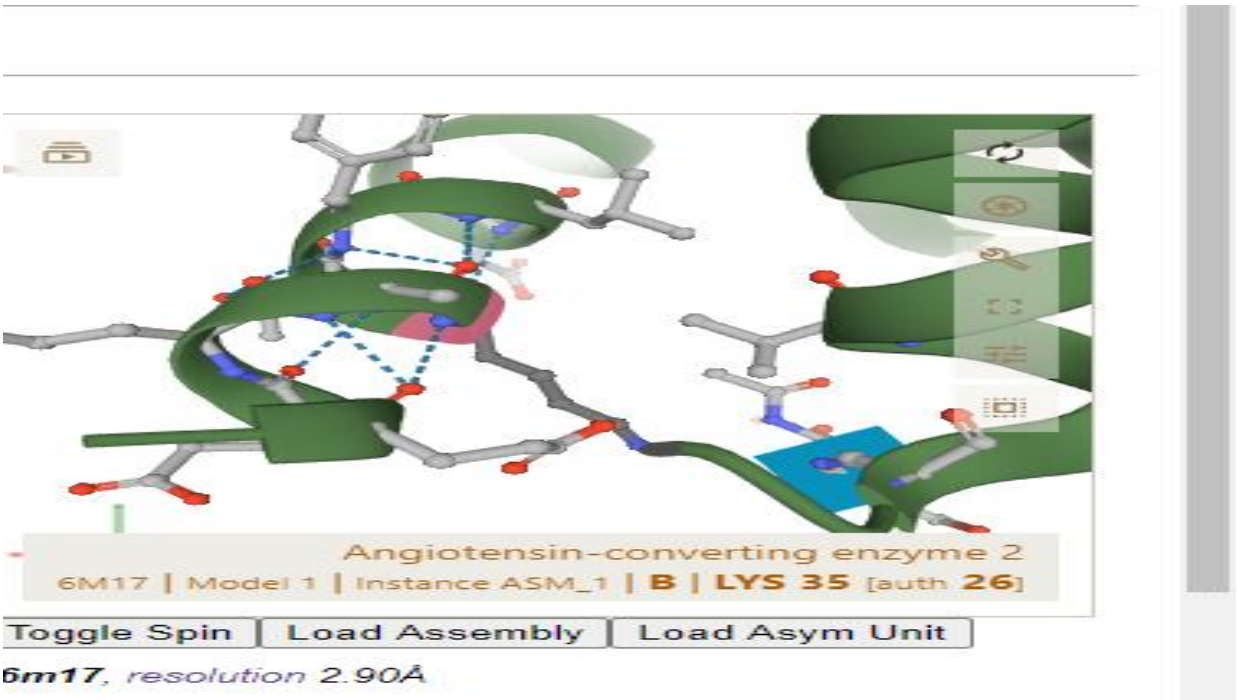

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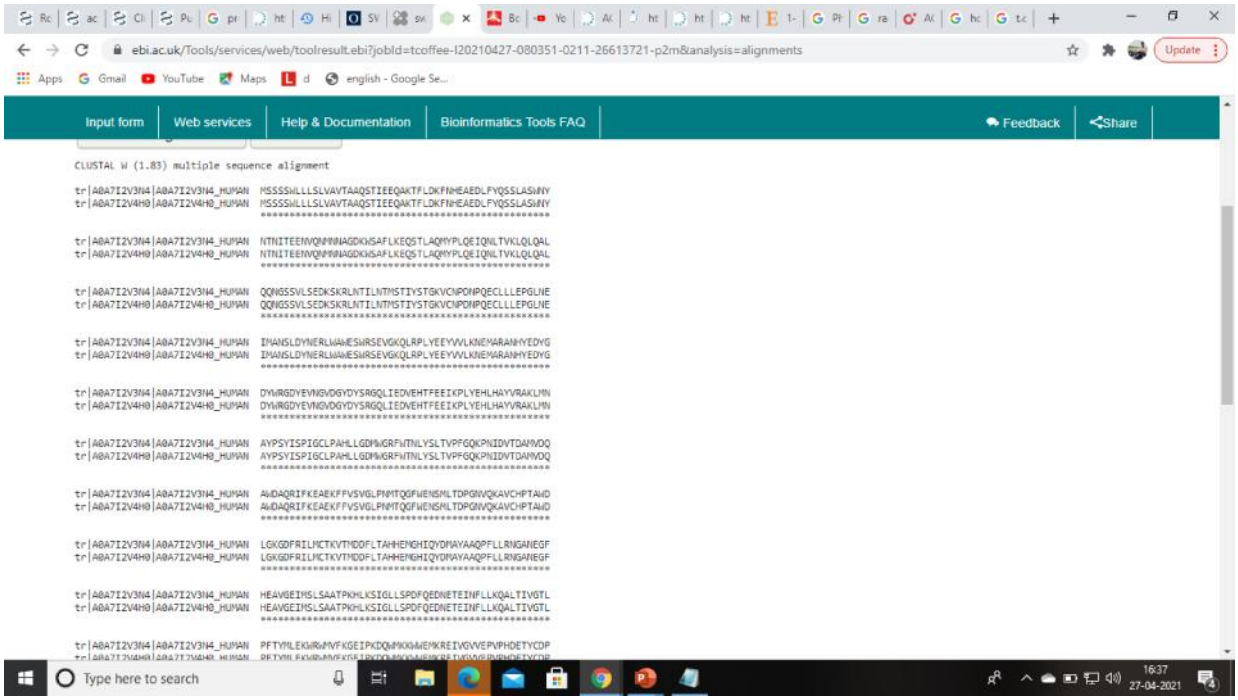

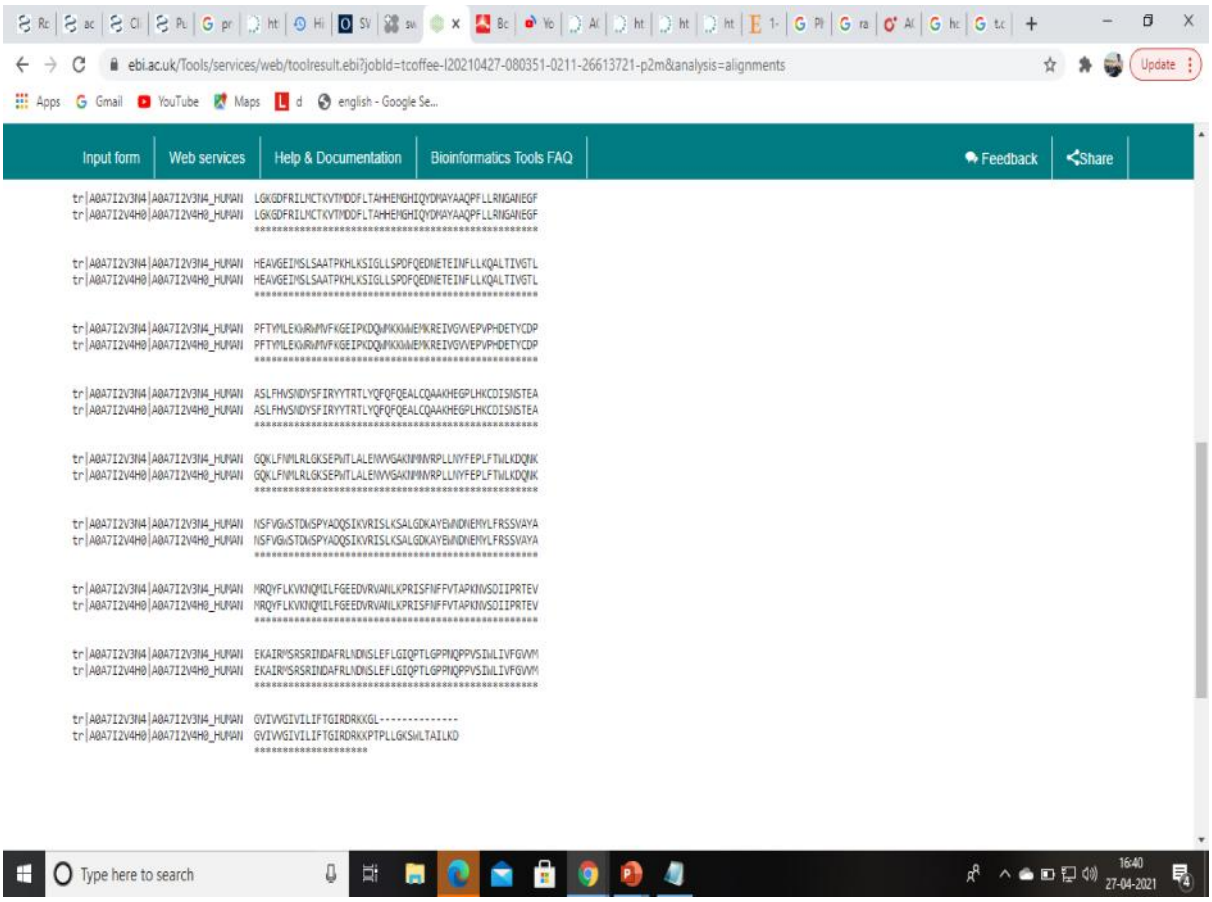

Conclusion

The SARS-CoV-2 S protein is highly conserved among all human Coronaviruses (HCoVs) and is involved in receptor recognition, viral attachment, and entry into host cells. Due to its indispensable functions, it represents one of the most important targets for COVID-19 vaccine and therapeutic research

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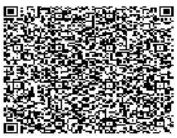	Website: www.ijarbs.com
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