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COMPUTATIONAL METHOD FOR PROTEIN STRUCTURE PREDICTION AND DRUG DESIGN AGAINST COVID -19

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Abstract- In modern drug discovery, a detailed understanding of interactions between small chemical compounds and biomolecular macromolecules (e.g. medicinal agents and their targets) is of crucial importance.1 The search for drug-like compounds that selectively bind to a molecular target and interfere with its receptor function or enzymatic activity demands a multi- and interdisciplinary approach. Hereby, computer modeling serves as an important tool to understand the relevant ligand-receptor or ligand-enzyme interactions. Nowadays, it is difficult to imagine drug discovery without computation. Almost all critical function in cell rely on specific protein. Understanding these is therefore crucial in investigation of biological system Drug design and drug discovery are critical importance in human health care, Computational approaches have become a major part of structure based drug design. In this review computational method for prediction of protein structure are described and their use toward drug design is discovered.

I. INTRODUCTION

Coronaviruses are a family of viruses that can cause illnesses such as the common cold, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). In 2019, a new coronavirus was identified as the cause of a disease outbreak that originated in China.

The virus is now known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease it causes is called coronavirus disease 2019 (COVID-19). In
March 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic Coronaviruses (CoVs) (order Nidovirales, family Coronaviridae, subfamily are enveloped viruses with a positive sense, single-stranded RNA genome. With genome sizes ranging from 26 to 32 kilobases (kb)\in length, CoVs have the largest genomes for RNA viruses. Based on genetic and antigenic criteria, CoVs have been organised into three groups: α-CoVs, β-CoVs, and γ-CoVs. The corona virus family is a positive-stranded RNA virus, which mainly causes respiratory and central nervous system disease in humans and animals].

There is an urgent need for the development of anti-viral drugs and vaccines against the 2019-nCov virus due to the high mortality rate of patients. The aim of the study is to use to computational approach to design both anti-viral drug and vaccine candidates. The spike protein in the novel coronavirus sequence is used to design both anti-viral drug and vaccine candidates.

II. MATERIAL & METHOD

NCBI protein database – 6M03-A PDB ID For further analysis the sequence was downloaded as the FASTA sequence.
Homology Modeling using Phyre software
Ligand predicted by Galxey tool, ProBis

III. EXPERIMENT AND RESULT

- analysis show how virus is evolutionary history with bats coronavirus
- Homology modeling using phyre indicate identity with 3C like proteinase
- Ligand predicted by Galxy web – D3F, RFM
- Using probis predicted- Small molecule ligand – 4 Methylbenzene diaminozinc.

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BLAST SEQUENCE ANALYSIS

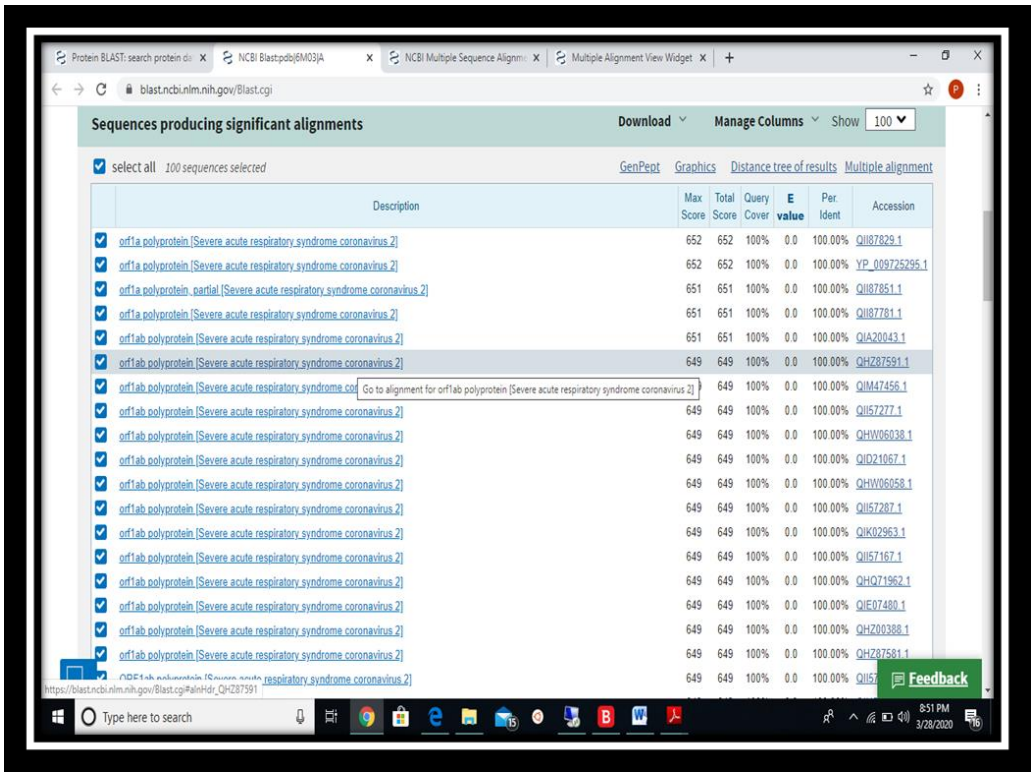

Fig 1 - blast sequence alignments

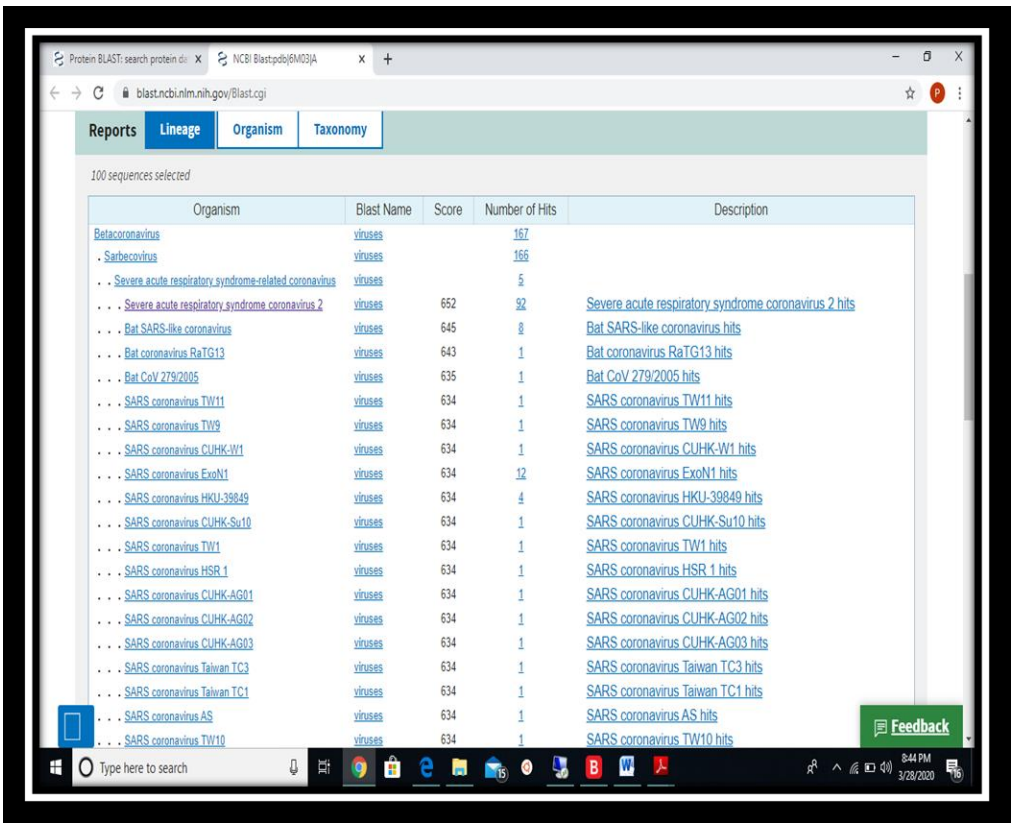

Fig 2- top sequence similarities

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HOMOLOGY MODELING USING PHYRE

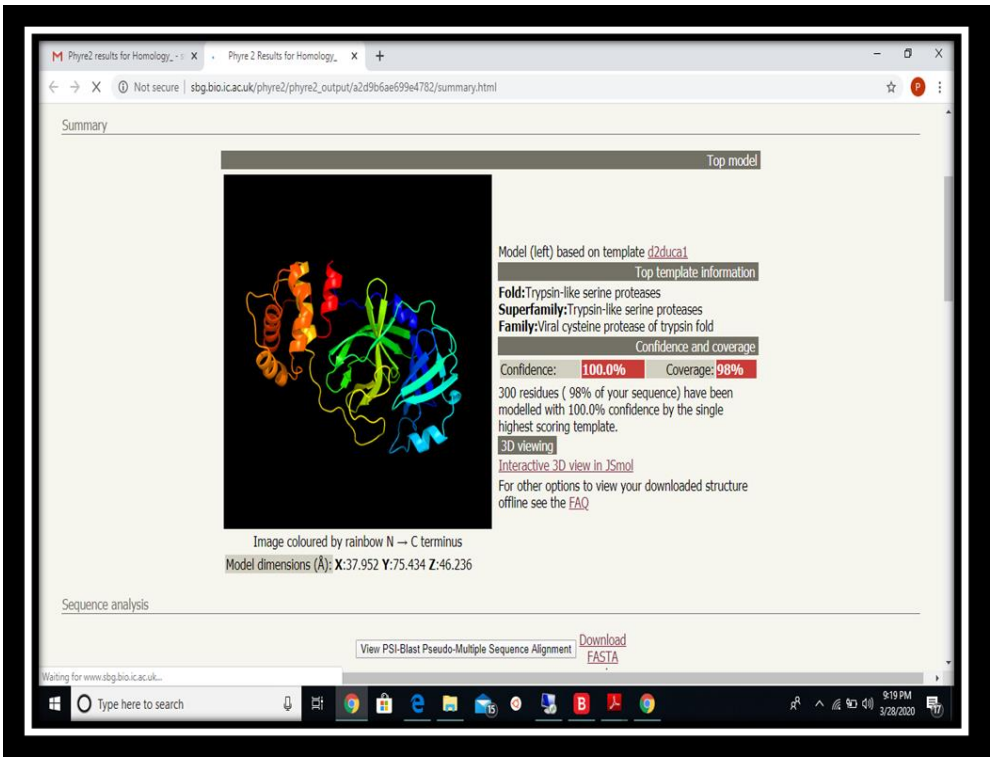

Fig 3 - Homology modeling structure

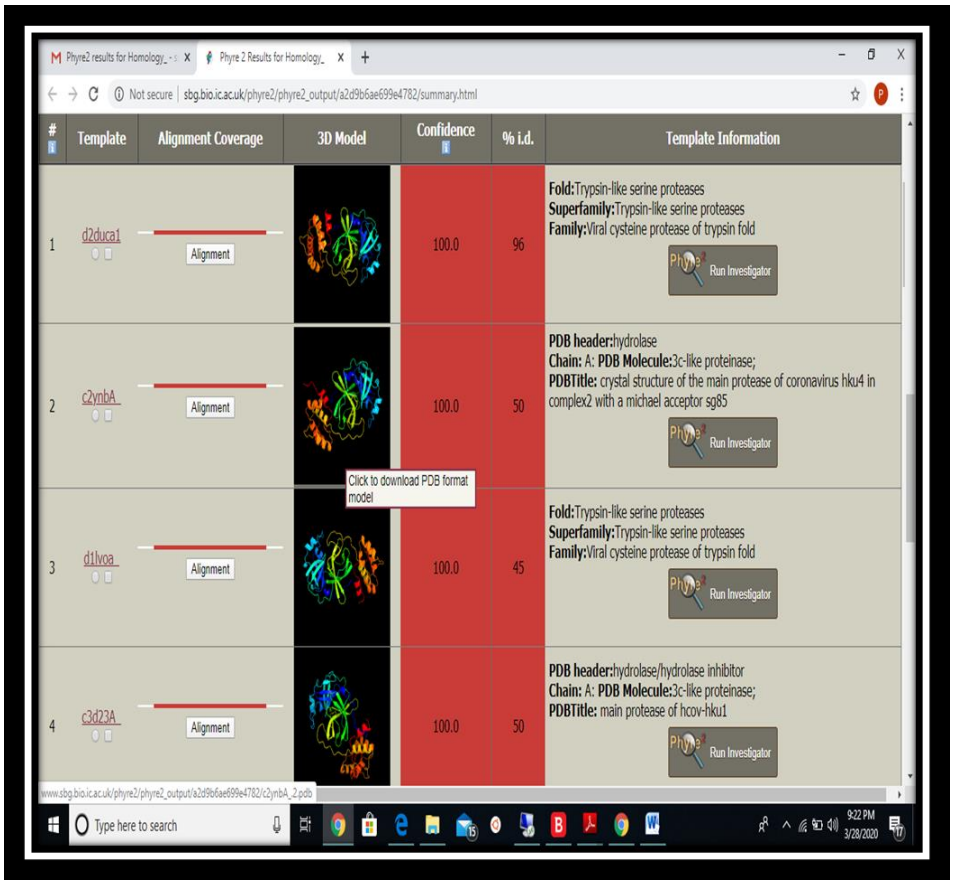

Fig 4 -top rated alignments

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LIGAND BINDING USING GALAXY

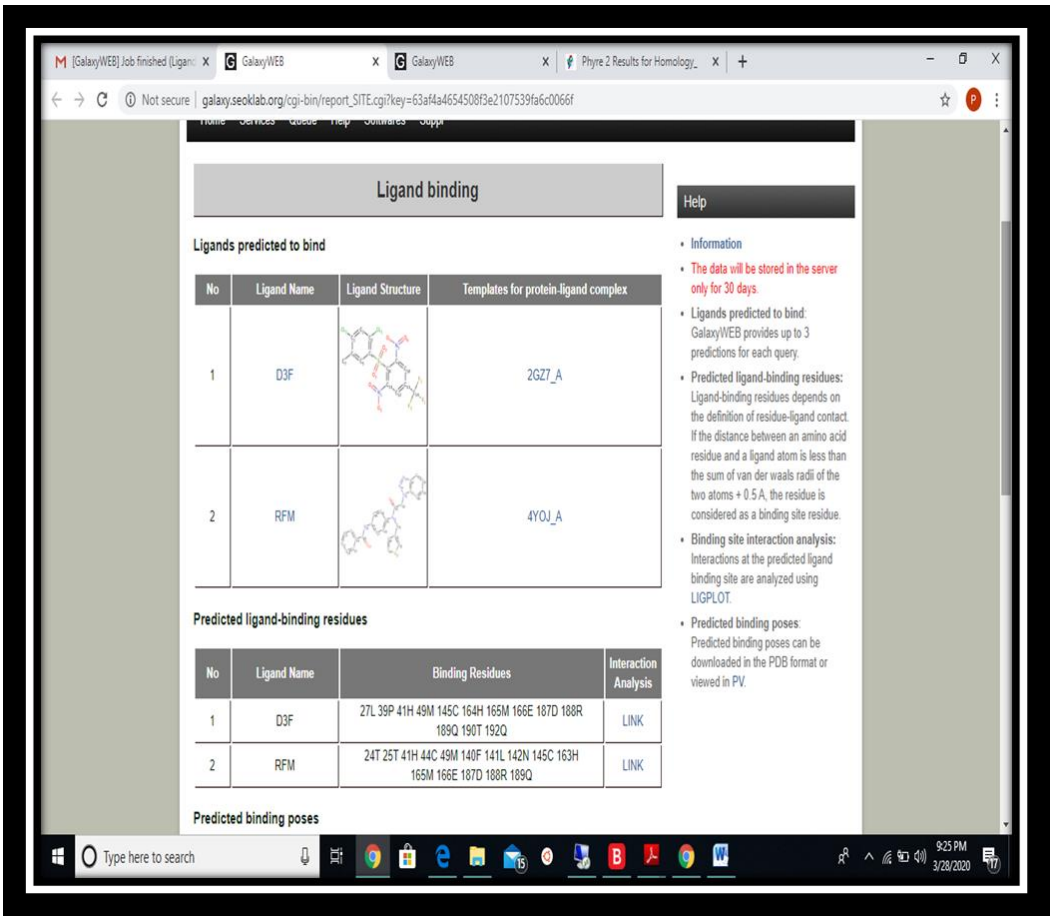

Fig 5-ligand predicted by galxy web

PREDICTED BINDING POSES

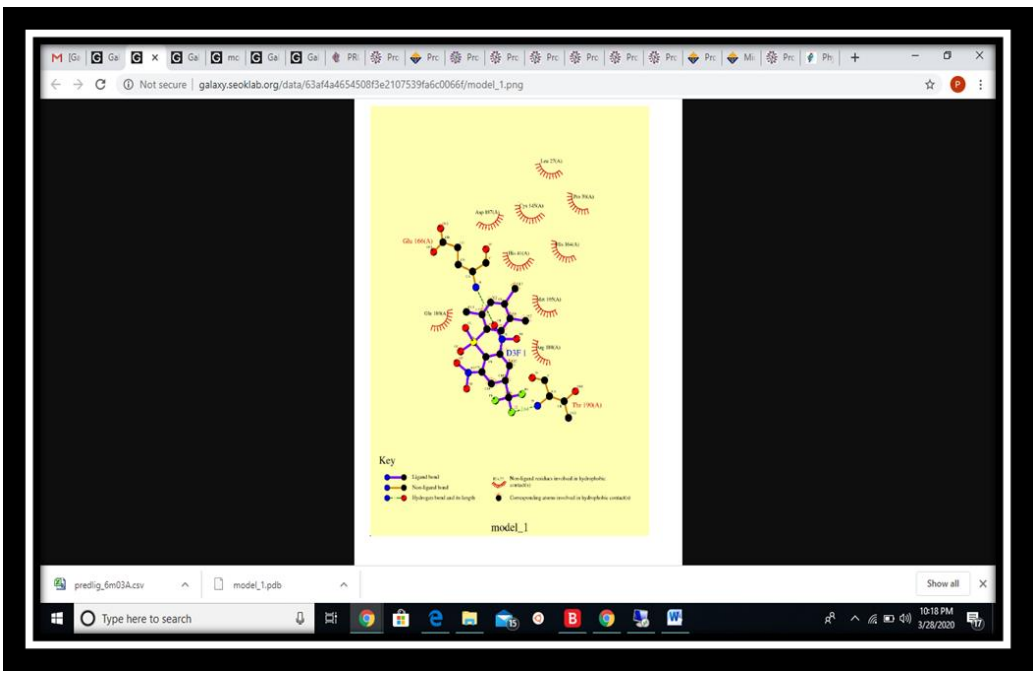

Fig 6 -site predicted by galaxy web model 1

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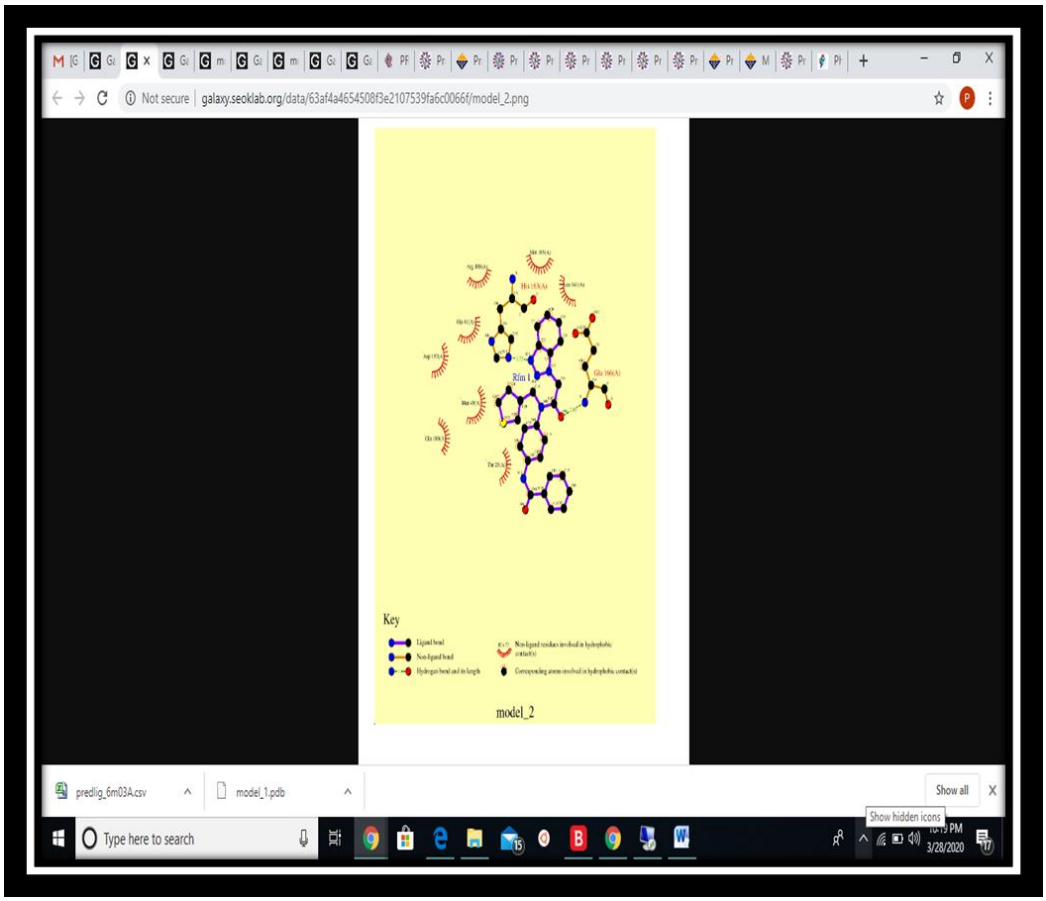

Fig 7 -site predicted model 2

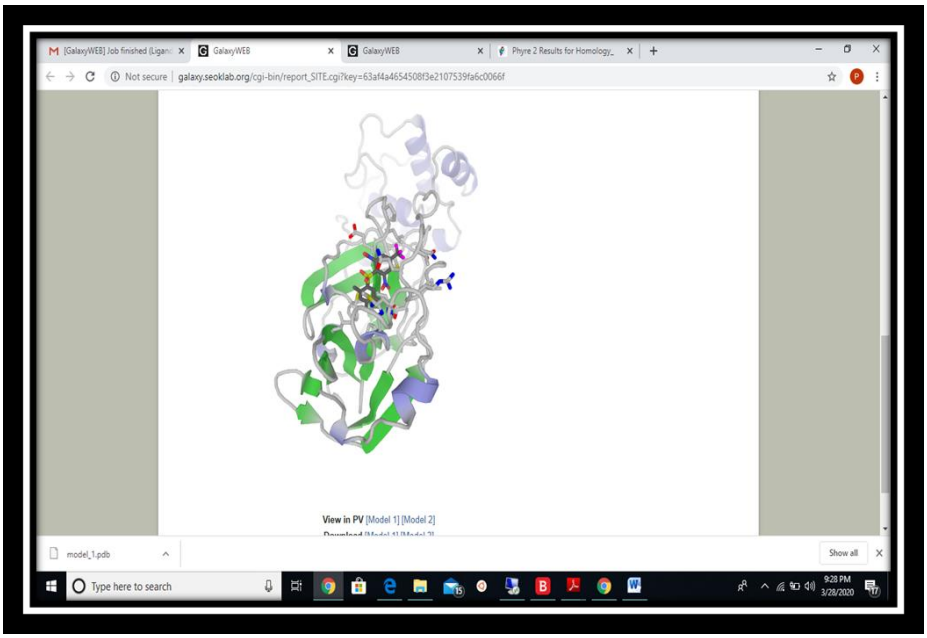

Fig 8 -predicted model

proBis web servers into one functional unit that enables prediction of protein–ligand complexes and allows for their geometry optimization and interaction energy calculation. The ProBiS web server predicts ligands (small compounds, proteins, nucleic acids, and single-atom ligands) that may bind to a query protein

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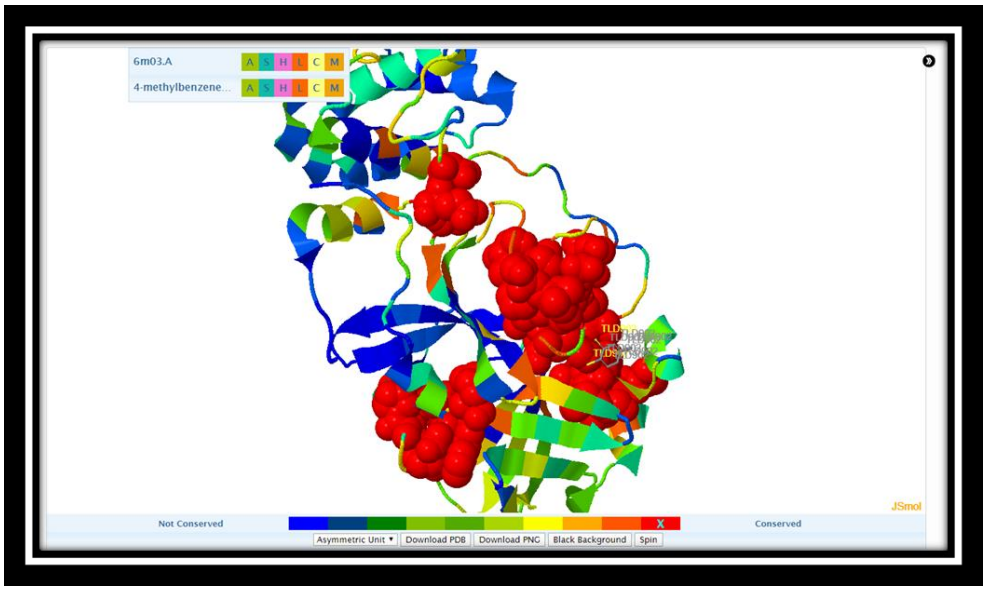

Fig 9- showing 4 methylbenzene binding geometry

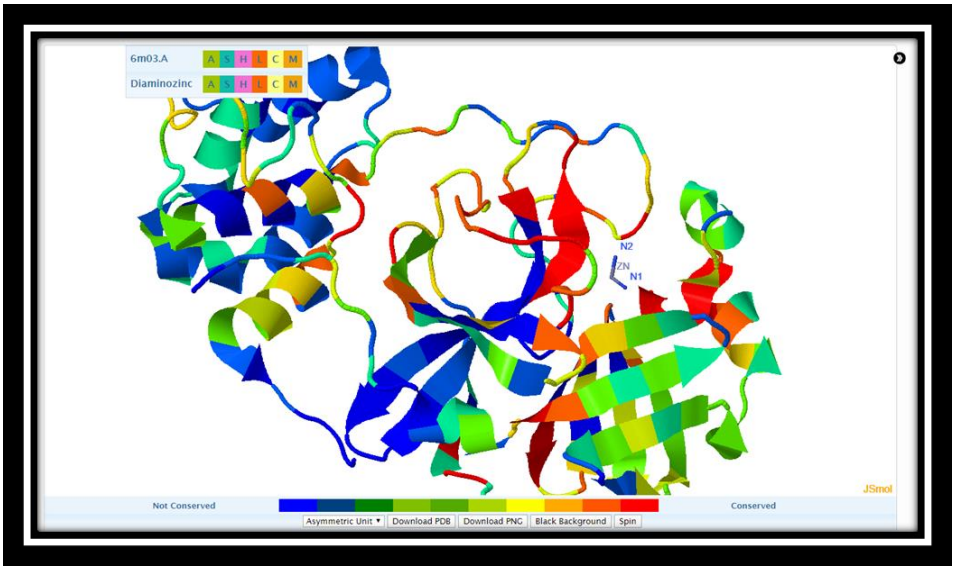

Fig 10 - showing diaminozinc binding geometry

IV. CONCLUSION

Due to the scarcity of experimental and clinical data, as well as the urgency to understand the infectivity of the deadly coronaviruses. computational analyses to study the 2019-nCoV virus in terms of protein structures, functions, phylogeny, and interactions at both molecular and organismal levels. In the present study, both drug and vaccine design was applied to identify drug and vaccine this approach will be cost effective and can save time in the design of drugs.

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