Structural analysis of Fab fragment from the human anti-SARS CoV-2 neutralizing antibody

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INTRODUCTION

The current pandemic COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

The SARS-CoV-2 was presumed to infect the human cells by spike glycoprotein binding to its cellular receptor, angiotensin-converting enzyme 2 (ACE2). And current evidence supports this idea. COVID-19 effects the lungs by causing inflammation and leads to alveolar damage.

The COVID-19 outbreak was first reported in Wuhan, China.Later spread to other provinces. At early stage, it was reported that most patients had the contact history with Huanan seafood market, where various wild animals like poultry and bats were on sale. According to WHO , the environmental samples taken from Huanan seafood market, China, were tested positive for SARS-CoV-2 but the specific animals associated with the virus have not been identified. Based on current evidence, bats are the probable origin.

COVID-19 has spread widely around the world, affecting more than seventy countries.[1]

Statistics- (as of 13 December 2020) [2]

Global -

Corona Virus cases - 72,646,648

Deaths- 1,618,908 ; Recovered- 50,864,820

Active cases- 20,162,920

In mild condition- 20,056,741(99.5%)

Serious or critical- 106,179(0.5%)

India -

Corona Virus cases - 9,884,716

Deaths- 143,393 ; Recovered- 9,388,159

It was found that Remdesivir which is a nucleotide analogue RNA polymerase inhibitor with broad spectrum antiviral activity , as highly effective in the control of SARS-CoV-2 infection in vitro.

The worldwide endeavour to create a safe and effective vaccine is ongoing. At present Clinical trials are being conducted. Vaccine will be out soon.[3]

EXPERIMENTALS

Protein of interest is chosen from Protein Data Bank(PDB) after applying following refinements - Scientific name of source organism - Homo sapiens ; Experimental method- X -Ray diffraction,NMR, Electron microscopy ; Refinement Resolution-1.5 – 2.0; Release date – 2020-2024 ;

PDB ID - 7K8P

Name - Crystal structure of an anti-SARS-CoV-2 human neutralizing antibody Fab fragment, C110.

Function - Human neutralizing antibody that targets the host ACE2 receptor-binding domain of the SARS-CoV-2 spike protein.

Classification: IMMUNE SYSTEM

Organism(s): Homo sapiens

Expression System: Homo sapiens; Mutation(s): No

Experimental Data –

Method: X-RAY DIFFRACTION; Resolution: 1.80 Å

R-Value Free: 0.229 ;R-Value Work: 0.196

The quality of protein structure is analysed by performing two tests- 1) The difference between R- Value Free and R-Value Work should be less than or equal to 0.05(5%). 2)R-Value Work should be roughly equal to one tenth of resolution.

Literature Citation-SARS-CoV-2 neutralizing antibody structures inform therapeutic strategies.

PubMed: 33045718

Macromolecules –Entity ID: 1 C110 Fab Heavy Chain

Entity ID: 2 C110 Fab Light Chain

Using PyMOL Secondary structure of Protein is analysed.

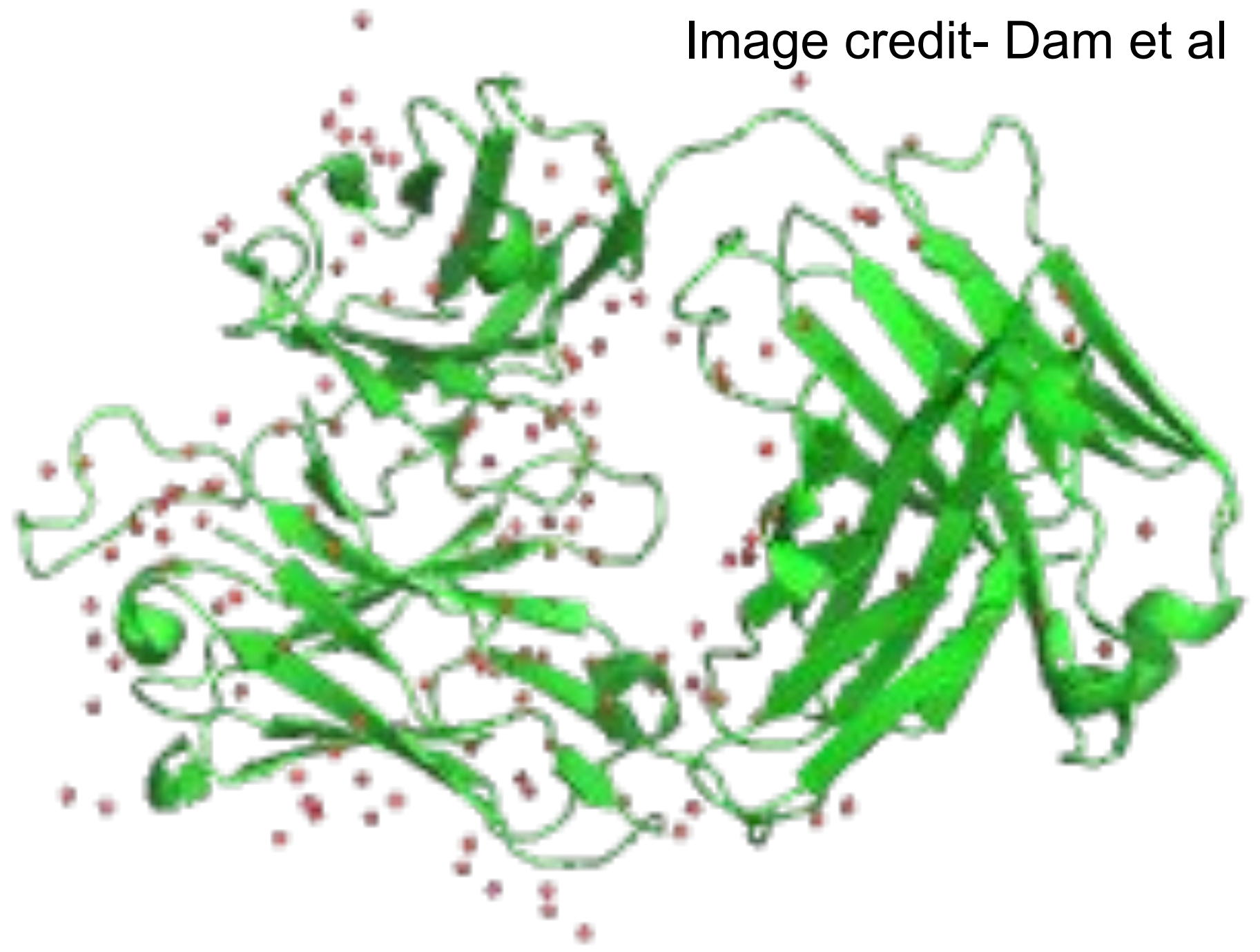

Image credit- Dam et al

Figure 1- 7K8P Structure.

Image credit- Google.

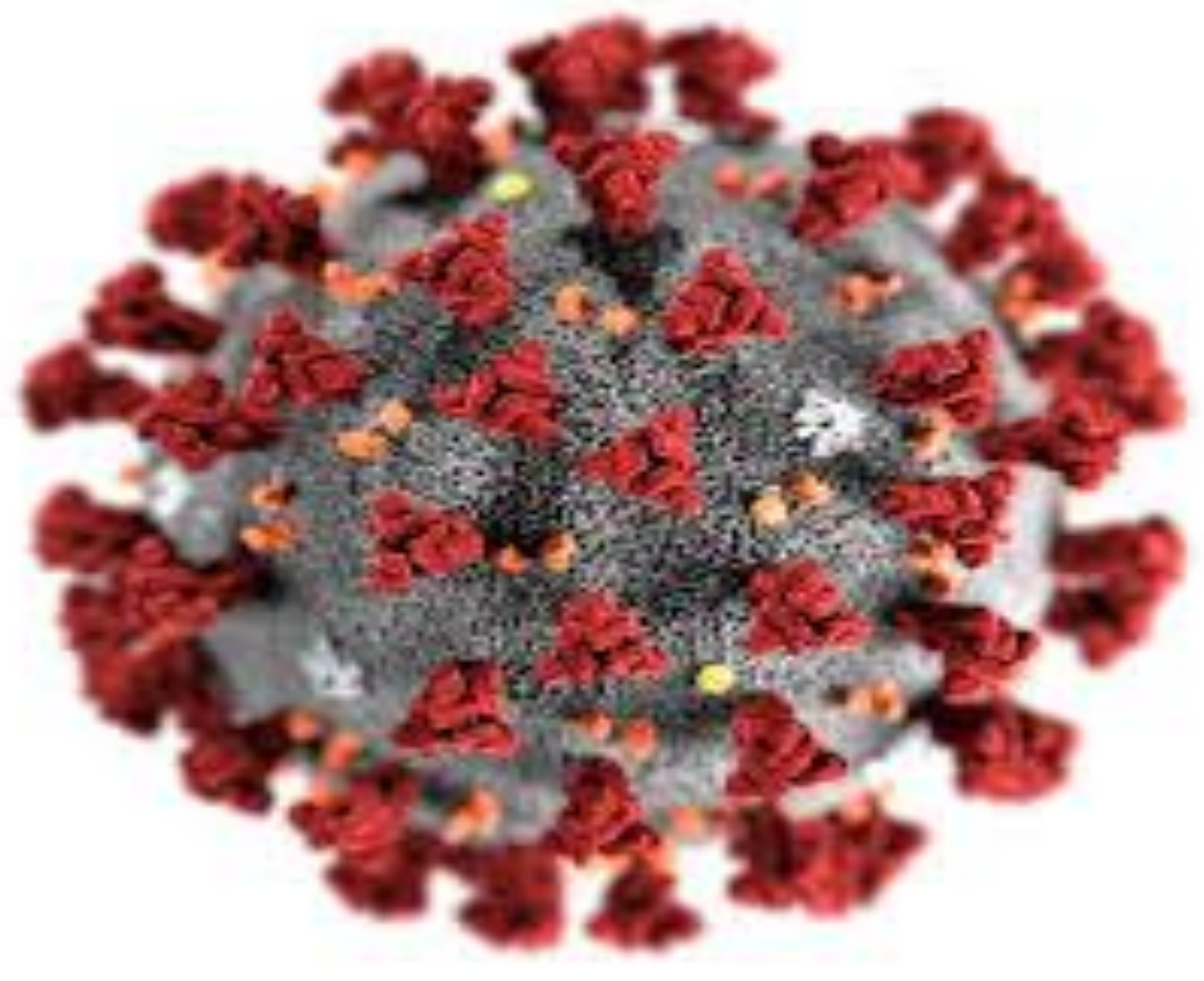

Figure 2 - Virus Structure

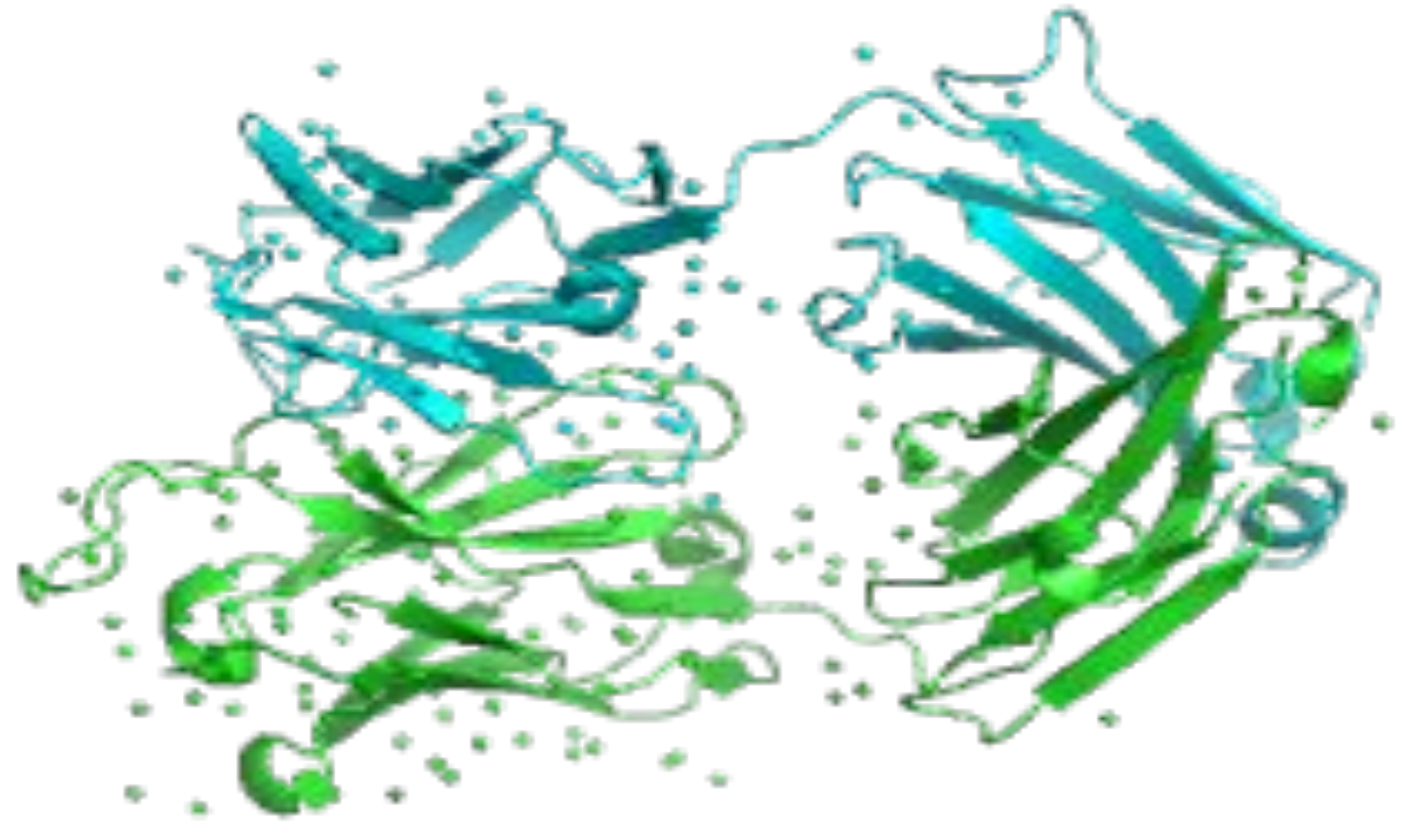

Figure 3 - 7K8P. Showing two chains - Cyan chain
and Green chain

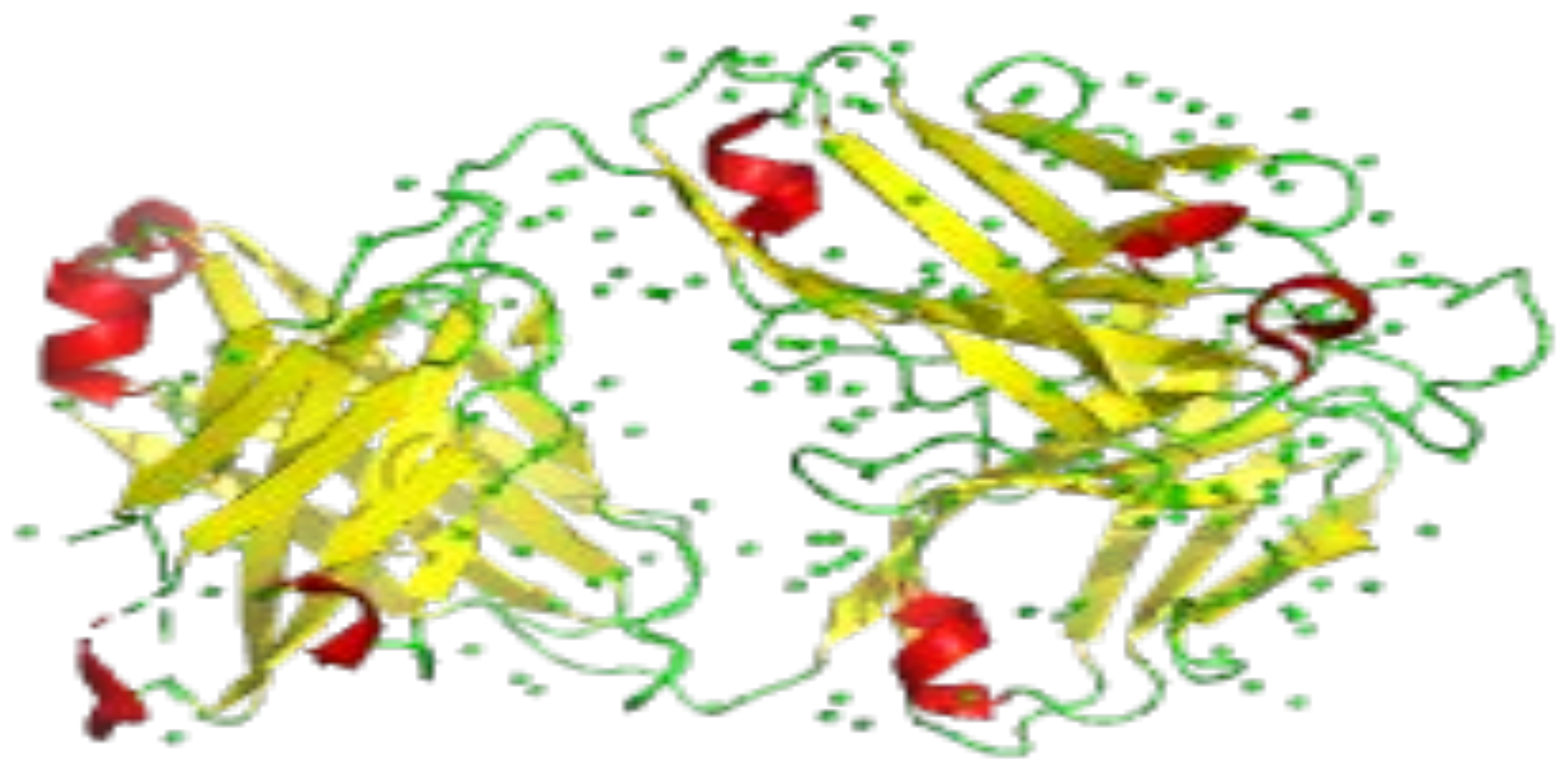

Figure 4 - 7K8P. Showing Alpha helices (Red) and Beta strands (yellow).

RESULTS AND DISCUSSION

Quality Analysis of protein structure-

1) The difference between R-Value Free and R-Value Work (0.229-0.196) is 0.03.
2) R-Value Work is 0.19 which is roughly equal to one tenth of resolution which is 0.18

Conclusion- The quality of crystal structure of the protein is good.

Secondary Structure analysis of protein-

Number of Alpha helices- 8

Number of Beta strands- 38

This protein is a dimer. That is , it consists of two monomers.

Hence Two chains are Observed-

Cyan Chain -

Number of Alpha helices- 3

Number of Beta strands- 19

Green Chain-

Number of Alpha helices- 5

Number of Beta strands- 19

Small Molecules- There are no small molecules.

REFERENCES

1) Ge et al, 2020, The epidemiology and clinical information about COVID-19 , Eur J Clin Microbiol Infect Dis.
2) Coronavirus Update (Live): 73,202,281 …
3) Jeff Craven,2020, Regulatory Affairs Professionals Society (RAPS).

e-poster presented online at the ABFR-2020.