# Understanding The Increased Aggressiveness of N501Y-SARS-CoV-2 Mutant: A call to Personal Protection

The second wave of COVID-19 is underway; boasting of more deaths and infection than the parent pandemic. In the heart of this wave is mutation to the genetic material of the parent virus SARS-CoV-2; although, quite a number of mutations exit with us now, of higher importance is the spike-glycoprotein N501Y mutation. The spike glycoprotein is responsible for recognizing and binding of human cells at the angiotensin converting enzyme 2 surface (ACE2); thus, making human vulnerable to the infection. But residue 501 is located at the epicenter of the binding activity called receptor-binding domain (RBD).

The Bio-medical scientists at Chemo-Genomics Research Institute Afe Babalola University (CRIA) led by Dr. I. Omotuyi in collaboration with ABUAD Multisystem Hospital (MSH) have obtained novel insights into the mechanism responsible for increased human infectivity of N501Y SARS-CoV-2 mutant.

The researchers had taken advantage of the cutting-edge Bio-computing platform at CRIA to calculate the re-evaluate the interaction between SARS-CoV-2 spike glycoprotein RBD and ACE2 for the wildtype in comparison with the mutant.

One of the surprising discovery is the improved RBD binding with ACE2 following N501 mutation. This can be understood from the critical node interaction diagram below in which only Q325 (ACE2) forms critical interaction with Q506 RBD) in the wildtype virus. In the mutant however, in addition to this interaction, three (L79/L486, H34/Q493, T324/G502, Q325/Q506, Fig. 1.0) other interactions were established; thus making recognition and binding with ACE2 more efficient.

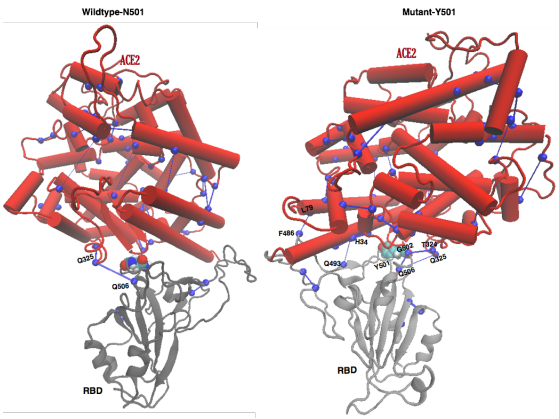


Fig. 1.0 Critical interaction node between RBD and ACE2 is altered in N501Y mutant SARS-CoV-2.

Another critical insight gained in the study is the role of N501Y mutation in altering the interface water dynamics (Fig. 2.0). It should be noted that interface water acts as a stabilizing force for protein-protein interaction through enhanced hydrophobic attractions.

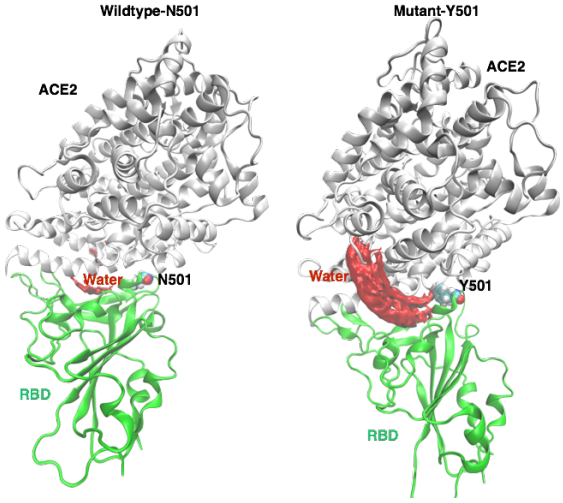


Fig. 2.0 water occupancy within RBD/ACE2 interface in wildtype and mutant RBD bound to ACE2

The energy of binding was also calculated based on the MMGBSA end-point free energy model.

Table 1.0 End-point energy of binding RBD/ACE2

| Biosystem | INT | ELE+dSol | VDW+dSol | d-BIND |
|---|---|---|---|---|
| WT | $8.78e^{-4}$ | 23.14 | $-1.04e^{2}$ | -80.88 |
| MT | $8.59e^{3}$ | $-1.30e^{4}$ | $-2.12e^{3}$ | -6533.98 |

The free energy calculation showed that N501Y-SARS-CoV-2 spike glycoprotein RBD would bind ACE2 80-times more efficiently compared to the wildtype.

In conclusion, N501Y mutant will be more effective at binding ACE2, and will be characterized by rapid clinical episodes, human-to-human transmission and death.

Recommendation:

These findings should therefore serve as a wake up call for enforcement of COVID-19 protocol by all institutions.

On personal level; personal protection must be enforced at all levels of society.

**Watch out therefore for Indigenous solution to COVID-19 by ABUAD**