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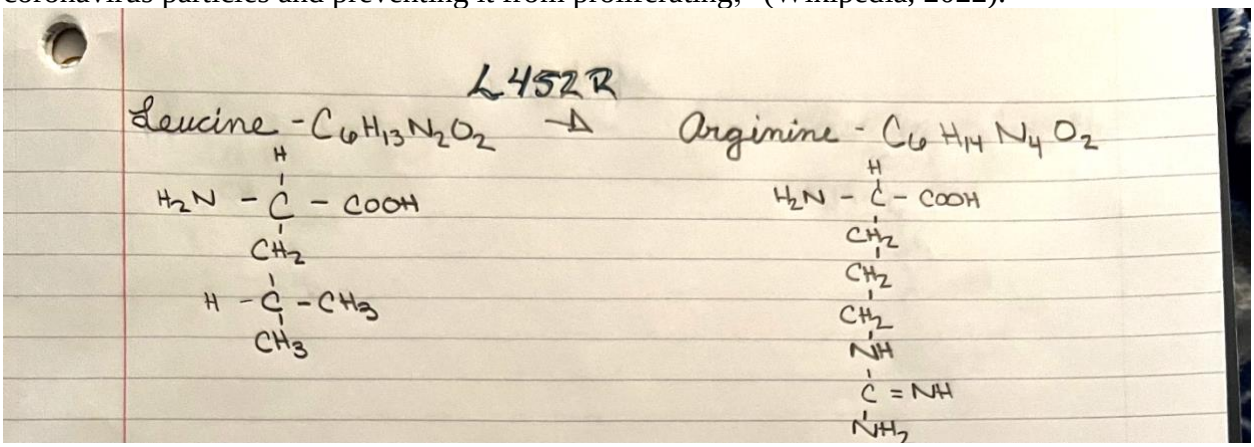
The Variants of SARS-CoV-2

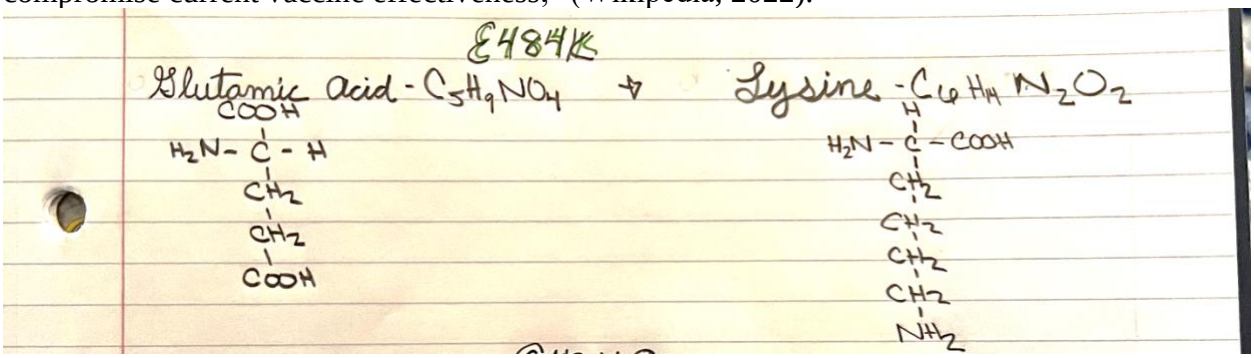
What makes these variants trigger and/ or indicate red flags is the amino acids that are found within the variants; they are L452R (delta), E484K (alpha, beta, gamma), E484Q (delta), N501Y (alpha, beta, gamma), and P681H (delta). "The signature mutations possessed by these strains were L452R, T478K, E484Q, D614G and P681R in the spike protein, including within the receptor-binding domain (RBD). Of these, the mutations at residue positions 452, 484 and 681 have been reported in other globally circulating lineages. The structural analysis of RBD mutations L452R, T478K and E484Q revealed that these may possibly result in increased ACE2 binding while P681R in the furin cleavage site could increase the rate of S1-S2 cleavage, resulting in better transmissibility. The two RBD mutations, L452R and E484Q, indicated decreased binding to select monoclonal antibodies (mAbs) and may affect their neutralization potential," (article). "An amino acid is an organic molecule that is made up of a basic amino group (−NH2), an acidic carboxyl group (−COOH), and an organic R group (or side chain) that is unique to each amino acid. The term amino acid is short for α-amino [alpha-amino] carboxylic acid," (Reddy, 2020).

"The name of the mutation, L452R, refers to an exchange whereby the leucine (L) is replaced by arginine (R) at position 452. L452R is found in both the Delta and Kappa variants which first circulated in India but have since spread around the world. L452R is a relevant mutation in this strain that enhances ACE2 receptor binding ability and can reduce vaccine-stimulated antibodies from attaching to this altered spike protein. L452R, some studies show, could even make the coronavirus resistant to T cells, that are class of cells necessary to target and destroy virus-infected cells. They are different from antibodies that are useful in blocking coronavirus particles and preventing it from proliferating," (Wikipedia, 2022).

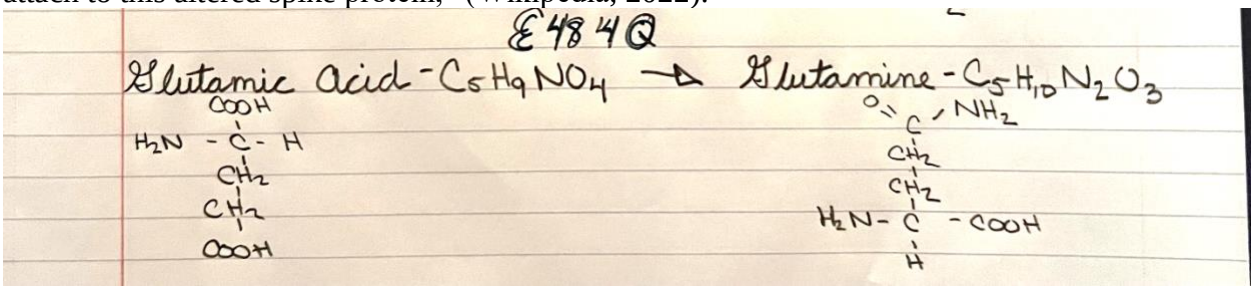


"The name of the mutation, E484K, refers to an exchange whereby the glutamic acid (E) is replaced by lysine (K) at position 484. E484K has been reported to be an escape mutation (i.e.,

a mutation that improves a virus's ability to evade the host's immune system) from at least one form of monoclonal antibody against SARS-CoV-2, indicating there may be a "possible change in antigenicity". The Gamma variant (lineage P.1), the Zeta variant (lineage P.2, also known as lineage B.1.1.28.2) and the Beta variant (501.V2) exhibit this mutation. A limited number of lineage B.1.1.7 genomes with E484K mutation have also been detected. Monoclonal and serum-derived antibodies are reported to be from 10 to 60 times less effective in neutralising virus bearing the E484K mutation. On 2 February 2021, medical scientists in the United Kingdom reported the detection of E484K in 11 samples (out of 214,000 samples), a mutation that may compromise current vaccine effectiveness," (Wikipedia, 2022).

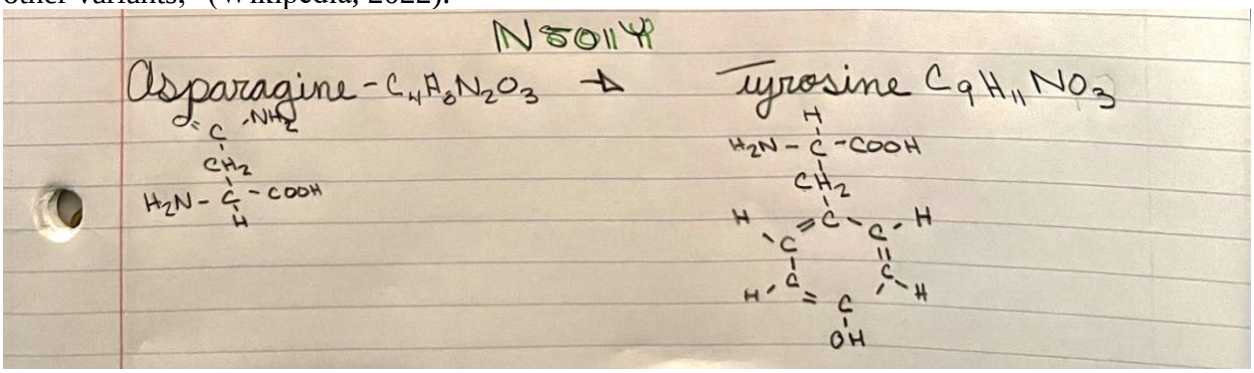


"The name of the mutation, E484Q, refers to an exchange whereby the glutamic acid (E) is replaced by glutamine (Q) at position 484. The Kappa variant circulating in India has E484Q. These variants were initially (but misleadingly) referred to as a "double mutant". E484Q may enhance ACE2 receptor binding ability and may reduce vaccine-stimulated antibodies' ability to attach to this altered spike protein," (Wikipedia, 2022).

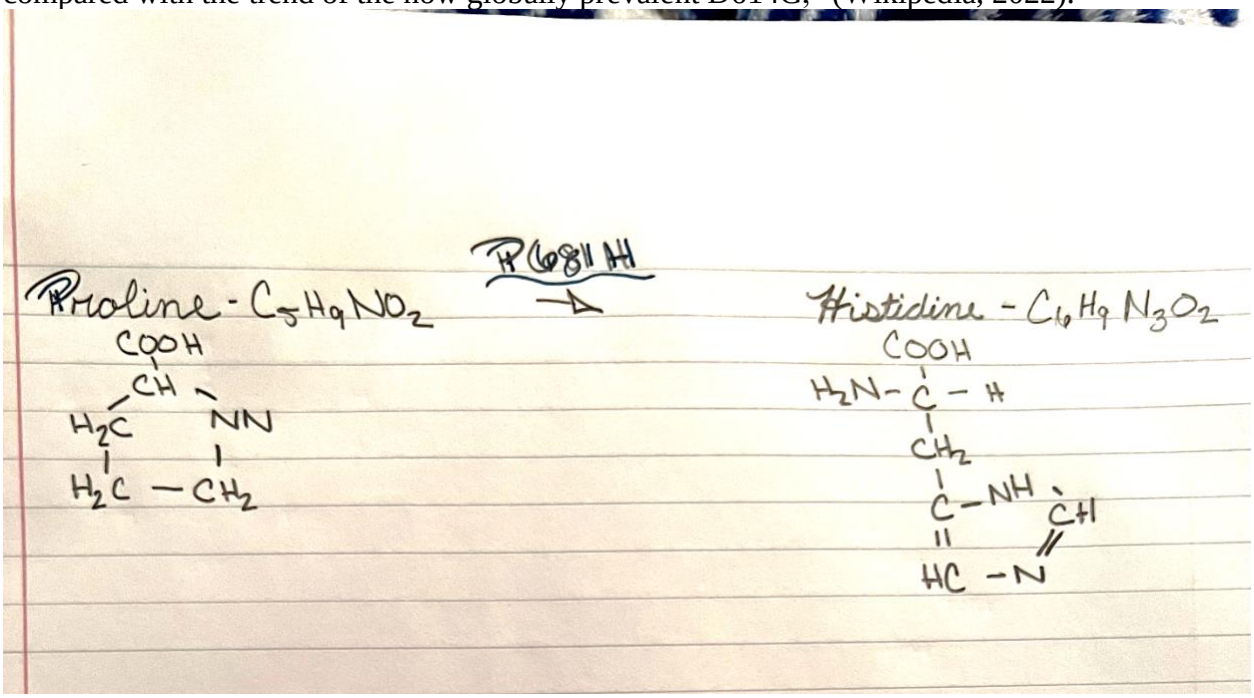


"N501Y denotes a change from asparagine (N) to tyrosine (Y) in amino-acid position 501. N501Y has been nicknamed "Nelly". This change is believed by PHE to increase binding affinity because of its position inside the spike glycoprotein's receptor-binding domain, which binds ACE2 in human cells; data also support the hypothesis of increased binding affinity from this change. Molecular interaction modelling and the free energy of binding calculations has demonstrated that the mutation N501Y has the highest binding affinity in variants of concern RBD to hACE2. Variants with N501Y include Gamma, Alpha (VOC 20DEC-01), Beta, and COH.20G/501Y (identified in Columbus, Ohio). This last became the dominant form of the virus in Columbus in late December 2020 and January and appears to have evolved independently of

other variants," (Wikipedia, 2022).



"The name of the mutation, P681H, refers to an exchange whereby the proline (P) is replaced by histidine (H) at position 681. In January 2021, scientists reported in a preprint that the mutation P681H, a characteristic feature of the Alpha variant and lineage B.1.1.207 (identified in Nigeria), is showing a significant exponential increase in worldwide frequency, thus following a trend to be expected in the lower limb of the logistics curve. This may be compared with the trend of the now globally prevalent D614G," (Wikipedia, 2022).



The SARS-CoV-2 Variant:

The Structural and Function Description

The spike protein of SARS-CoV-2 has been said to bind to the host cell by recognizing the receptor ACE2, which is a homolog that converts angiotensin I to angiotensin 1-9. Also, the S1 subunit that connected to the SARS-CoV-2 S protein "...binds with ACE2 to promote the formation of endosomes, which triggers viral fusion activity under low pH" (Zhang H, 2020) It has been said that the total length of the SARS-CoV-2 S is 1273 aa and consists of a signal peptide located at the N-terminus, the S1 subunit, and the S2 subunit; the last two regions are necessary for receptor binding and membrane fusion. Overall, to ignite an infection, the spike has to connect to the ACE2 receptor, which results in dramatically changing by folding itself so it can combine its membrane with our cells' membrane.

The normal function of a cell receptor can be compared to the analogy of a lock and key; the receptor being the lock and the material substance, obviously, being the key. However, the only key, substance, which can fit in the lock, the receptor, is the key that is made for that particular receptor. The cell receptor is a known as a protein molecule substance such as antigens, hormones, etc. can bind together which allows the change of activity within the cell. Although cell receptors may take part in damaging in the autoimmune diseases, cell receptors can help medication bind to cells to treat certain conditions.

The variant (B.1.640.2) has not been around enough do more damage than the original. The name the scientist has given it is "IHU." To say how this variant act, as of now, when it comes to the infection and protection from the infection, such as vaccines, is too soon to say. However, the B.1.640.2 variant has 46 mutations and 37 deletions which ends in 30 amino acids substitutions and 12 deletions. Surprisingly, I have also found out that the vaccines have its scope targeted on that spike protein of SARS -CoV- 2, which gives the IHU viruses wiggle room to enter and infect the cell (ET Oline, 2022).

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References

ET Oline, 2022. *All about the new Covid variant - IHU,* s.l.: EconomicTimes.

Zhang H, P. J. L. Y. Z. N. S. A., 2020. *Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target,* s.l.: Intensive Care Med.

Anon, 2021. SARS-COV-2 variant classifications and definitions. *Centers for Disease Control and Prevention*. Available at: https://www.cdc.gov/coronavirus/2019-cov/variants/variant-classifications.html [Accessed February 7, 2022].

Anon, 2022. Variants of SARS-COV-2. *Wikipedia*. Available at: https://en.wikipedia.org/wiki/Variants_of_SARS-CoV-2 [Accessed February 7, 2022].

Cherian, S. et al., 2021. SARS-COV-2 spike mutations, L452R, T478K, E484Q and P681R, in the second wave of covid-19 in Maharashtra, India. *Microorganisms*. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8307577/ [Accessed February 7, 2022].

Reddy, M.K., 2020. Amino acid. *Encyclopedia Britannica*. Available at: https://www.britannica.com/science/amino-acid [Accessed February 7, 2022].