The virus SARS-CoV-2 is a coronavirus that infects cells in the body that, among other things, are necessary for respiration. The virus consists of a lipid membrane that encases the viral RNA that is necessary for reproduction (Yang, 2). The lipid membrane is lined with spike glycoproteins that are equally spaced out across the entire virus. These spike glycoproteins consist of transmembraneous homotrimers with the active binding site located at the end of the extracellular portion of the protein (Yang, 2), and resemble those that bind to the ACE2 receptors of some cells in the body, including the lung, heart, kidney, and intestines (Goodsell). ACE2 is a receptor enzyme that is part of the B0AT1 complex located within the cell membrane of the affected cells (Goodsell). Normally, these are responsible for the activation of the signal cascade that controls the synthesis of angiotensin II which is important for blood pressure regulation and a number of other processes. These spike proteins share the same receptor as the SARS CoV virus, and the relation was first identified in 2003 (Davison, 2). When the ACE2 receptor is activated by the CoV spike protein, it causes angiotensin II to break down and leads to inflammation and death in the alveolar cells (Sriram)

Changes in the structure of spike proteins can affect its ability to bind to the receptor of a cell, for the better or for the worse. Because it is a virus, SARS-Cov-2 mutates at a much higher frequency than living cells. Some mutations can affect the amino acids that make up the spike protein, and these affect the rate at which the spike protein successfully binds to the receptor of the cell (Wikipedia). This is because, like all chemical reactions, they are done by chance bumping between the different reactants in just the right way to allow it to bind. Structural changes in the spike protein amino acid sequence that rarely but sometimes result in different configurations in which the chance of a successful binding configuration is increased. In general, these mutations can result in spatial differences in the protein, some examples of which are the movement of the active site to a more exposed position or the movement of portions of the protein that might get in the way of the active site.

The L452R mutation happens when a leucine is replaced by an arginine at position 452, which changes the physical structure of the protein (Wikipedia). The section of the protein on which this amino acid is found is rotated away from the rest of the spike, which has multiple effects.This increases the rate of ACE2 binding, causing an increased rate of infection, as well as decreases binding to select antibodies, which increases the virus's resistance to the immune system (Cherian,1). This mutation can be found in both the Delta and Kappa variants (Hodcroft).

The E484K mutation to its spike proteins gives the virus a higher chance to bind with human cells, making it more contagious (Freund, 2). In this mutation, glutamic acid at position 484 is replaced by lysine. Because the negatively charged glutamic acid is replaced by a positively charged lysine, this section of the protein is repelled away from the rest of the protein (Wikipedia). This change positions one of the binding locations on the spike protein to be in a higher, more exposed position that gives it an advantage over other strains (Hodcroft). Consequently, the change in shape alters the virus's contact with the ACE-2 receptors of antibodies, meaning the body must develop a new resistance to this strain. This mutation can be found in the Beta, Gamma, and Kappa variants, which have been mostly outcompeted globally (Hodcroft).

The E484Q mutation is a change from glutamic acid to lysine at position 484 of the amino acid (Wikipedia). This causes changes in the physical structure of the protein, giving it slight improvements to both binding to host cells and resisting antibodies similar to those of the E484K mutation. This mutation is present in the Kappa variant, which has since been outcompeted by other variants (Hodcroft).

The N501Y variant allows the virus to have an easier time binding to human cells, which allows it to spread faster in the body (Feund, 2). This is caused by a mutation in the spike protein that causes the asparagine at amino acid position 501 to become a tyrosine (Wikipedia). This mutation is also suspected to be one which allows the virus to spread from humans to

rodents and mustelids. Variants that include this mutation are the Gamma, Alpha, and Beta strains (Hodcroft).

The P681H mutation involves the exchange where proline is replaced by arginine, located at amino acid position 681 (Wikipedia). This mutation causes the structure of the spike near the furin cleavage site to change slightly which results in the decreased ability of the immune system to detect the receptor. This mutation can be found in the Alpha, Delta, and Kappa variants (Hodcroft).

In order to get an understanding of how these mutations and resulting structural differences impact the larger pandemic as a whole, the B.1.640.2 will be discussed in greater detail. This variant of SARS-CoV-2 is a recently discovered strain that was first identified in the Republic of the Congo in November 2021 (Wikipedia), and was later identified in multiple different countries including France, the United Kingdom, United States, and others. Today however, this variant of SARS-CoV-2 is no longer recorded in any country in the world (cov-lineages). This means that this variant of the virus was outcompeted by other more successful variants. This means that this variant had a mutation that caused the spike protein to change in a way that made it bind to cell receptors at a lower rate than other lineages, or in a way that increased the change of binding, but not by more than an alternate lineage. This variant was reported at the time to be milder than previous variants because the mutation caused it to be resistant to antibodies designed for other variants of SARS-Cov-2 but is not 100% effective, which is what causes more mild symptoms (Freund).

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