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Scientific Literacy - Coronavirus

There are many variants that have emerged from Coronavirus, also known as SARS-CoV-2. Of all the variants, there are five main ones that are distinguished as concerning. The five variants include: Delta, Gamma, Omicron, Beta, and Alpha. Within these five variants, there are five notable mutations that have been observed on the spike protein and those include: L452R, E484K, E484Q, N501Y, and P681H (Wikipedia, 2022). These mutations cause the amino acid structures to change in different positions on the spike protein structure. The first letter of the mutation states the beginning amino acid, while the second letter of the mutation states which amino acid replaced the beginning amino acid. The number in the middle defines which position the amino acid was in on the spike protein (Wikipedia, 2022).

Mutation L452R started as leucine (L) and was replaced by arginine (R) on amino acid number 452 on the spike protein (Wikipedia, 2022). Leucine is a nonpolar amino acid that contains a side chain consisting of only Carbons and Hydrogens. It is hydrophobic and does not interact well with water. This amino acid gets replaced by arginine which is a polar and charged amino acid. It has a side chain consisting of a charged nitrogen. Arginine is very likely to form hydrogen bonds and interacts very well with water. Since the amino acid had a mutation going from nonpolar to polar, its structure changed quite a bit.

Mutation E484K started as glutamic acid (E) and was replaced by lysine (K) on amino acid number 484 (Wikipedia, 2022). Glutamic acid is a polar and charged amino acid. Lysine is

also a polar and charged amino acid. Glutamic acid has a charged oxygen on its side chain, while lysine has a charged nitrogen on its side chain. Since both of these amino acids are polar there is not as big of a structure change as L452R but does have a structure change due to it mutating from a negatively charged oxygen, to a positively charged nitrogen.

Mutation E484Q started as glutamic acid (E) and was replaced by glutamine (Q) on amino acid number 484. This mutation occurred on the same amino acid as E484K and started off as the same original amino acid – glutamic acid. The difference between these two mutations is what glutamic acid was replaced by (Wikipedia, 2022). In this mutation it was replaced by glutamine which is a polar and uncharged amino acid. It consists of a side chain with a nitrogen, but the nitrogen is not charged. This mutation went from having a charged oxygen, to having an uncharged nitrogen. Both of these amino acids are polar and will react highly with hydrogen and water.

Mutation N501Y started as asparagine (N) and was replaced by tyrosine (Y) on amino acid number 501 (Wikipedia, 2022). Asparagine is a polar uncharged amino acid that has a side chain consisting of a nitrogen that is not charged. Tyrosine is also a polar uncharged amino acid that has a side chain consisting of an oxygen. There is structural change going from the asparagine to the tyrosine but since they are both polar, they will be highly reactive with hydrogens and appear on the outer shell of the protein.

Mutation P681H started as proline (P) and was replaced by histidine (H) on amino acid number 681 (Wikipedia, 2022). Proline is a bigger amino acid that is unique and tends to bend and form a 90-degree structure. Its side chain consists of only carbons and hydrogens and is therefore nonpolar. Histidine is a polar and charged amino acid that has a side chain consisting of a charged nitrogen. The mutation of proline to histidine goes through a pretty big structural

change as it is going from nonpolar to polar and from having only carbons and hydrogens to having a charged nitrogen. Histidine is also not in a 90-degree angle structure so the layout of the molecule's protein structure changes significantly.

The spike protein in SARS-CoV-2 plays a big role in the spread of coronavirus throughout the human body and spreading to other people. The protein gets its name spike from the spiky appearance it portrays on the surface of the protein, looking like a crown. The spike protein consists of single stranded RNA on the inside enclosed by an envelope which is constituted of a protein and lipid-based membrane. (de Kok-Mercado, F., O'Hearn, A. and Basta, H. 2021. Biology of SARS-CoV-2: Infection. In: O'Hearn, A., Basta, H., Bonetta, L., Conneely, B., de Kok-Mercado, F. and Shyu, E. (eds.)) The coronavirus spike protein can first enter the human body through either the nose or mouth and travels into the body where the spikes on the protein can then attach to other proteins on the surface of cells. Once the proteins are attached to each other, the spike protein's membrane can then intermingle with the cell membrane of the other cell which allows it to insert the single stranded RNA genome into the cell. (de Kok-Mercado, F., O'Hearn, A. and Basta, H. 2021. Biology of SARS-CoV-2: Infection. In: O'Hearn, A., Basta, H., Bonetta, L., Conneely, B., de Kok-Mercado, F. and Shyu, E. (eds.))

With the spike proteins genome now inside the cell of a human body, the RNA actually gets translated by the ribosome of the cell into proteins including RNA polymerase which is viral or infected. The infected RNA polymerase can have the spike proteins genome undergo transcription and translation which then leads to even more copies of the infected or viral proteins and genome. (de Kok-Mercado, F., O'Hearn, A. and Basta, H. 2021. Biology of SARS-CoV-2: Infection. In: O'Hearn, A., Basta, H., Bonetta, L., Conneely, B., de Kok-Mercado, F. and Shyu, E. (eds.)) All of this ultimately leads to replication of even more spike proteins that can go

on to infect other cells in the body or can leave the human body that is infected already, which can then spread to others through the nose or mouth as well. This cycle of the spike protein infecting and spreading in someone's human body is a continuous cycle until the infection can get eliminated by the immune system fighting it off. (de Kok-Mercado, F., O'Hearn, A. and Basta, H. 2021. Biology of SARS-CoV-2: Infection. In: O'Hearn, A., Basta, H., Bonetta, L., Conneely, B., de Kok-Mercado, F. and Shyu, E. (eds.))

The protein or receptor that the spike protein initially binds to is angiotensin-converting enzyme 2, also known as ACE2. ACE2 is the only protein that the spike protein can bind to, as it fits perfectly in it, allowing it to enter the cell and therefore is a receptor. (Sriram, K., Insel, P. and Loomba, R. 2020) The ACE2 protein is found in many different cells in the human body such as cells associated with the liver, heart, blood vessels, lungs, and more. It is also found in the cells of epithelium for the lungs, mouth, and nose. When SARS-CoV-2 binds to ACE2, it prevents ACE2 from performing its normal functions which include regulating many different processes including inflammation, blood pressure, and wound healing. (Sriram, K., Insel, P. and Loomba, R. 2020) It also helps with regulating the protein ANG II, which is responsible for damaging blood vessel linings, damaging other tissues, and increasing inflammation and blood pressure. Without ACE2, ANG II can also harm or kill the cells that are responsible for transporting oxygen into the body, which is critical for living. (Sriram, K., Insel, P. and Loomba, R. 2020)

Sometimes, the viral RNA genome replication can lead to different mutations. These mutations can include substituting a nucleotide for another nucleotide, the insertion of an extra nucleotide, or deletion a nucleotide. Mutations cause the spike protein to act or infect in different ways than the original virus did. A mutated virus cannot go back to its original state and will

then infect other cells and only spread the newly mutated RNA going forward. (de Kok-Mercado, F., O'Hearn, A. and Basta, H. 2021. Biology of SARS-CoV-2: Infection. In: O'Hearn, A., Basta, H., Bonetta, L., Conneely, B., de Kok-Mercado, F. and Shyu, E. (eds.)) With the change in the spike protein, it may alter the ability of the virus to bind to its receptor and infect a cell depending on the types of mutation or location of mutation. Some mutations can help the virus replicate and spread to infect other cells which allow for the mutation to become more common in people as it spreads. There can also be mutations that do the opposite of this and give it a disadvantage of replicating and spreading. This would restrict the spike protein from binding to the receptor protein. Lastly, there are some mutations that have no effect on the virus and will act the same way as if the virus does not have a mutation at all. (de Kok-Mercado, F., O'Hearn, A. and Basta, H. 2021. Biology of SARS-CoV-2: Infection. In: O'Hearn, A., Basta, H., Bonetta, L., Conneely, B., de Kok-Mercado, F. and Shyu, E. (eds.))

Recently there was a new discovery of a mutation or variant of the SARS-CoV-2 called B.1.640.2. Studies have shown that this variant is not one leading to much concern as there have not been many people affected by this variant, but there is also not enough data to note for sure if it is one that will spread heavily or not. Many professionals in the field believe that based off of current numbers and studies, this mutation is not one that will spread heavily or cause an outbreak that is worrisome. The omicron variant has produced way more numbers in data that are worth noting and worrying about than the B.1.640.2. (Freund, A. 2022) In conclusion, this currently shows us that the impact of the mutation could either have a disadvantage of replicating and spreading or has a neutral effect and allows the spike proteins to continue to act in the same way they would if they were not mutated at all.

Resources:

de Kok-Mercado, F., O'Hearn, A. and Basta, H. 2021. Biology of SARS-CoV-2: Infection. In: O'Hearn, A., Basta, H., Bonetta, L., Conneely, B., de Kok-Mercado, F. and Shyu, E. (eds.) Biology of SARS-CoV-2. Biology of SARS-CoV-2 (biointeractive.org): HHMI Biointeractive.

Freund, A. (2022) ‘Coronavirus: Health experts not alarmed by new variant identified in France’, DW Made for minds.

Sriram, K., Insel, P. and Loomba, R. (2020) 'What is the ACE2 receptor?', ASBMB Today, ASBMB Today, Available: American Society for Biochemistry and Molecular Biology.

Wikipedia (2022). Variants of SARS-CoV-2. Wikipedia.org, https://en.wikipedia.org/wiki/Variants_of_SARS-CoV-2#L452R