Omicron Variant Primer

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[Note: Sources and additional readings are located in the comments section of this post]

As of today (November 30, 2021), the Delta variant remains the world's most prevalent mutation of the original SARS-CoV-2 virus first identified in January 2020 that is responsible for the global COViD-19 pandemic.

The previously named B.1.1.529 variant now known as the Omicron variant was first reported by South African scientists on 9 November 2021 and then quickly visualized (see image below) by researchers at the Bambino Gesu hospital in Rome. This does not mean that the variant necessarily first arose in South Africa. Variants can also arise independently and spontaneously in multiple locations.

On November 26, the WHO designated the Omicron variant a variant of concern (VOC) subject to special reporting and investigation. The Omicron variant is the most mutated form of SARS-CoV-2 yet sequenced.

Variants of concern

The WHO has identified five VOCs to date. They are named according to the Greek alphabet in the order they were designated VOCs, not in the order they were first identified). The current VOCs include the Alpha variant first identified in the United Kingdom in September 2020; the Beta variant first identified in South Africa in May 2020; the Gamma variant first identified in Brazil in November 2020; the Delta variant first identified in India in October 2020; and now the Omicron variant first identified in South Africa in November 2021.

The Epsilon, Zeta, Eta , Theta and Iota variants were designated only as variants of interest to monitor. The letters Nu and Xi were deliberately skipped by the WHO reportedly because they thought Nu could easily be confused with "new" and Xi is common last name in China.

Mutations

Mutations may change fitness, and are part of the normal mechanisms of evolution. Mutations during replication are usually random and provide genetic variability that other evolutionary mechanisms act upon. (See a primer on evolution and evolutionary mechanisms linked in comments below). Mutations often change molecular shape (conformation) and other attributes of proteins and, in so doing, may increase or decrease certain observable and/or functional attributes or specific proteins that can, in turn, change the fitness or attributes of an organism or virus (e.g., attributes like viral transmissibility or virulence).

Scientists usually can't make high-confidence predictions regarding transmissibility and other elements of pathogenicity based solely on sequence and conformational analysis. It takes clinical data as well as controlled analysis and testing to make such determinations.

It is often difficult to predict functional changes due to a single mutation and nearly impossible to precisely predict net changes in functional attributes due to multiple changes. Uncertainty grows with the number of mutations. The effects of mutations are also modulated by epistasis and additional genetic and physiological factors.

Variants arise because of mutations in nucleic acids during replication (are the result of changes in the nucleic acid sequence. In the case of the SARS-CoV virus responsible for the 2003 SARS outbreak and SARS-CoV-2 responsible for the current outbreak of COVID-19, the nucleic acid is single-stranded ribonucleic acid (RNA). In addition to structural, membrane, nucleocapsid, envelope, and accessory proteins that are also susceptible to mutation, the virus has so-called “spike proteins” located on its source that are key to its ability to infect human cells.

The spike protein is a key to SARS-CoV-2 pathogenicity, including transmissibility and so changes in the spike protein caused by mutations can alter transmissibility and the efficacy of vaccines designed to produce antibodies that bind to specific sequences on the spike protein.

Antibody production and binding is, however, only one facet of the immune response to viral infection.

Mutations are denoted by the change in amino acid in the sequence as well as position. In mutation D614G, for example, there is an exchange of amino acids at position 614 on the spike protein where glycine (G) is exchanged for asparate (D). The N501Y mutation discussed below involves the substitution of tyrosine (N) for asparagine (Y) at position 501 in the receptor binding domain of the spike protein (see a reference linked in comments to help better understand mutation nomenclature)

Omicron's mutations

Scientists are concerned that the number and location of mutations would make the Omicron variant more transmissible and possibly better equipped to evade current vaccines. It may take weeks to make high-confidence assessments regarding those concerns.

The Omicron variant has about 50 mutations, of which about 30 are scattered on three major conformational prongs of the spike protein.

Mutations, especially in the SARS-CoV-2 spike protein, may increase or decrease attributes like transmissibility.

Some of the mutations are, in fact, actually useful. For example, two deletions near the middle of the spike protein allow the PCR tests to to definitively discern the omicron variant from other variants without resorting to full genomic sequencing

In essence it is a unique combination of mutations from other VOCs (variants of concern), especially the Alpha, Beta, Gamma , and Delta variants along with the 26 or so mutations unique to Omicron.

Some of the Omicron mutations are familiar. For example , the Omicron variant carries a N501Y mutation previously observed in the Alpha variant. The mutation was thought to increase transmissibility. The Delta variant, which proved more transmissible than the Alpha variant, lacked the N501Y mutation but had other mutations that greatly enhanced its transmissibility.

The Omicron variant's 26 unique mutations are far more than previously observed in other VOCs.

Mutations of concern

Still, what is it about the Omicron's mutations -- and attendant changes to the conformation of the SARS-CoV-2 variant -- that has put scientists on alert?

Three mutations located near the middle of the spike protein near the furin cleavage site may make Omicron more transmissible. While not definitive, given the evolutionary advantages omicron seems to enjoy with regard to its ability to infect humans, a cluster of 15 mutations in the receptor domain area of the protein may also facilitate attachment to human cells.

Two groups, each consisting of four mutations, one at a tip, the other located near the middle of the spike protein may inhibit antibody binding and three deletions observed on

proteins not a part of the spike protein may potentially decrease vaccine efficiency by reducing known vaccine targets.

Prevalence

The Omicron variant is currently reported in about a dozen countries but this number is sure to grow. According to the WHO reports, the Alpha variant has been reported in 197 countries, the Beta variant in 146 countries; Gamma in 103 countries; and the Delta variant in at least 196 countries. The Delta variant currently (as of November 30, 2021) accounts for 99.8% of all analyzed sequences.

Other Epidemiological and Clinical Reports

As of November 28, 2021, no deaths had been attributed to COVID cases arising from the Omicron variant. Death is, however, a lagging indicator to cases.

Multiple news sources have quoted physicians in South Africa to the effect that, as with other variants, many infections with Omicron are reportedly asymptomatic. They have also quoted physicians saying that, of those who do show symptoms after Omicron variant infection, most suffer only a mild illness not requiring hospitalization.

What is notably different in quoted physician observations regarding the Omicron variant are demographic cohorts reportedly being hospitalized. In South Africa, people under 35 apparently represented the bulk of new cases, but this data could, at least partly be attributed to the fact that the elderly are, as a group, more vaccinated and less likely to engage in behaviors that expose them to the omicron variant.

What is also notable about observations thus far is that joining those over 65 as the most likely to be hospitalized after contracting COVID are an apparently higher number of very young children requiring hospitalization after infection with the Omicron variant . This is interesting because thus far throughout the pandemic and across prior variants, the young and healthy have been far less susceptible to severe illness (as defined by the need for hospitalization) after contracting COVID.

Physicians in South Africa have not yet raised red flags with regard to a loss of efficacy in currently approved treatments.

My Comments

Even if Omicron's mutations allow it to be evasive of current vaccines, It does NOT mean that the vaccines won't still be highly effective compared to vaccines for other diseases. Out of an abundance of caution, given that the Delta variant resulted in slightly lowered vaccine efficacy, vaccine researchers and manufacturers are already

investigating potential changes to vaccines and boosters to better protect against the Omicron variant.

While much of what is known about the Omicron variant is based on preliminary and anecdotal observations, as I have maintained since the emergence of SARS-CoV-2, this would have been a very different pandemic in terms of public response had it posed a greater threat to children and young people. An evolutionary imperative, people and societies are usually most protective of their young. If the largely anecdotal data, not yet subject to more sophisticated statistical and experimental analysis as well as clinical verification, shows that the young are more vulnerable to the Omicron variant, it could radically change people's attitudes toward compliance with recommended public health measures.

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"Recognized for his use of language, accuracy, and balanced presentation, K. Lee Lerner's portfolio covering science and global issues has garnered respected writing, book and media awards, including books on climate change, infectious diseases, and biotechnology named as Outstanding Academic Titles. His dossier spans every continent, includes two global circumnavigations, and features coverage from areas suffering civil war, violent protests, drought, famine, and disease outbreaks. Centering on the plight of displaced and vulnerable populations, Lerner's work at Harvard treated both the humanitarian and security facets inherent in responding to both man-made and natural disasters. That experience, built on a scholarly foundation in science, allows his evidence-based writing to bring clarity to chaotic and complex issues.

Contributing editor of more than 40 academic books and producer and/or contributing editor of more than two dozen major media projects, for more than three decades — across print, broadcast media, and digital platforms -- Lerner's 'Taking Bearings,' essays have ranged across the human intellectual enterprise. He has served on the board of advisors for the venerable *American Men and Women of Science* since 2003 and his Academia site consistently ranks among those most frequently accessed by students, scholars, and decision makers from around the world."

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