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COMMENTARY

# The Newly Detected B.1.1.529 (Omicron) Variant of SARS-CoV-2 With Multiple Mutations

## *Implications for transmission, diagnostics, therapeutics, and immune evasion*

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Keywords: COVID-19; SARS-CoV-2; B.1.1.529; Omicron Variant; VBM: Variant Being Monitored; VOI: Variant of Interest; VOC: Variant of Concern; VOHC: Variant of High Concern; SDFT: S-gene target failure; ACE2: Angiotensin-converting Enzyme 2; CDC: Center for Disease Control and Prevention

The global and regional impact of SARS-CoV-2 pandemic continues to be a source of grave concern. While the availability of vaccines against the SARS-CoV-2 virus may have partially assuaged this anxiety in certain parts of the world, it remains a prevailing and unpretentious global public health crisis. The latter outcome is fueled by the convergence of several factors which include (but not limited to) the lack of availability of adequate number of vaccines; poor socio-economic conditions; vaccine hesitancy; and rampant proliferation of misinformation on the social media.

To date, SARS-CoV-2 pandemic has infected over 48 million people in the United States resulting in the death of over 777 thousand (1). It is noteworthy that to a large extent, refusal by hominoid to get vaccinated in the United States continues to be a source of much consternation. Not only do unvaccinated people have a much higher rate of infection and hospitalization, but they are also a very fertile source for generation of SARS-CoV-2 variants. Since the identification of the first infected case of COVID-19 in Wuhan, China in December 2019, the world has witnessed multiple peaks of resurgence of COVID-19 pandemic largely as a consequence of mutations in the SARS-CoV-2 with enhanced transmissibility and infectivity.

The US SARS-CoV-2 Interagency Group (SIG) has delineated SARS-CoV-2 variants into four distinct categories (Table 1). To date, the most impactful in terms of its transmissibility and infectivity has been the Delta (B.1.617.2) variant of SARS-CoV-2. First identified in India in December 2020, the Delta variant swept rapidly through that country and Great Britain before reaching the U.S., where it quickly surged. It is now the predominant SARS-CoV-2 variant, accounting for more than 99% of COVID-19 cases and leading to an overwhelming increase in hospitalizations in some states (2). The Delta variant was believed to be more than five times as contagious as previous variants, and studies have shown that it may be more likely than the original virus to put infected people in the hospital. People who are not vaccinated are most at risk, and the highest spread of cases and severe outcomes is happening in states with low vaccination rates.

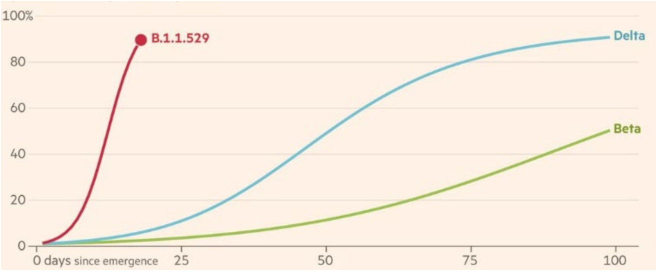
Table 1: US Government SARS-CoV-2 Interagency Group Classification of SARS-CoV-2 Variants (as of November 26, 2021; 1400 hrs.)

| **CLASSIFICATION** | **DEFINITION** | **VARIANTS IDENTIFIED** |
|---|---|---|
| Variant Being Monitored (VBM) | Variant for which there is data indicating a potential or clear impact of approved or authorized medical countermeasures; OR that has been associated with more severe disease or increased transmission but are no longer detected or are circulating at very low levels in the United States, and as such, do not pose a significant and imminent risk to public health in the United States. | • Alpha (B.1.1.7 and Q lineages)<br>• Beta (B.1.351 and descendent lineages)<br>• Gamma (P.1 and descendent lineages)<br>• Epsilon (B.1.427 and B.1.429)<br>• Eta (B.1.525)<br>• Iota (B.1.526)<br>• Kappa (B.1.617.1)<br>• 1.617.3<br>• Mu (B.1.621, B.1.621.1)<br>• Zeta (P.2) |
| Variant of Interest (VOI) | Variant with specific genetic markers that have been associated with changes to receptor binding; reduced neutralization by antibodies generated against previous infection or vaccination; reduced efficacy of treatments; potential diagnostic impact; or predicted increase in transmissibility or disease severity | • None |
| Variant of Concern (VOC) | Variant for which there is evidence of an increase in transmissibility; more severe disease (e.g., increased hospitalizations or deaths); significant reduction in neutralization by antibodies generated during previous infection or vaccination; reduced effectiveness of treatments or vaccines; or diagnostic detection failures | • Delta (B.1.617.2 and AY lineages)<br>• Omicron (B.1.1.529) |
| Variant of High Consequence (VOHC) | Variant of high consequence has clear evidence that prevention measures or medical countermeasures (see below) have significantly reduced effectiveness relative to previously circulating variants. Possible attributes of a variant of high consequence (in *addition to the possible attributes of a variant of concern):*<br>• Demonstrated failure of diagnostic test targets<br>• Evidence to suggest a significant reduction in vaccine effectiveness; a disproportionately high number of infections in vaccinated persons; or very low vaccine-induced protection against severe disease<br>• Significantly reduced susceptibility to multiple Emergency Use Authorization (EUA) or approved therapeutics<br>• More severe clinical disease and increased hospitalizations | • None |

On November 13, 2021, Thomas Peacock, a post-doctoral fellow in the Division of Infectious Diseases, Imperial College London, London, United Kingdom submitted a sequence to GitHub of a new variant (B.1.1.529) of SARS-CoV-2 isolated from an immunocompromised patient in South Africa (3). According to the available data, the new variant has 32 mutations in the conserved domain of the Spike protein which, is the region of the SARS-CoV-2 that binds to the Angiotensin-converting enzyme 2 (ACE2) allowing for the conformational change that facilitates its entry into host cells and is the target of immune responses. Additionally, 19 mutations were also identified in the conserved non-Spike region of the B.1.1.529 variant which, are assumed to be of less significance in terms of the transmissibility and infectivity of the SARS-CoV-2.

While most of the mutations in the Spike region of B.1.1.529 were similar to that in the Delta variant, some were unique which raised serious concerns about the transmissibility of this variant. In fact, the B.1.1.529 is now the most dominant variant identified in patients with COVID-19 in South Africa and has already been isolated from patients with COVID-19 in other Southern African countries (Lesotho, Botswana, Namibia, Eswatini and Zimbabwe), Belgium, Israel, and Hong Kong (5). According to the modelling using S-gene target failure (SDFT) data, the rate of infection from the B.1.1.529 will be 100-fold higher as compared to that to the Delta variant of SARS-CoV-2 (Figure 1).

Figure 1: Modeling of Spread of COVID-19 Cases in South Africa from Infection with B.1.1.529 Variant of SARS-CoV-2 Using S-gene Target Failure Data*



*Source: Financial Times analysis of data from Global Initiative on Sharing Avian Influenza Data (GISAID) and the South African National Health Laboratory Service

Given these alarming observations, the Technical Advisory Group of the World Health Organization (WHO) met on November 26, 2021, and classified the B.1.1.529 as the Variant of Concern and named it "Omicron" (6). It is also unclear at this moment if the immunity acquired against SARS-CoV-2 following natural infection and/or vaccination would be effective against this variant. Equally, disconcerting is the possibility that the existing molecular tests that are commonly used to diagnose infection with SARS-CoV-2 might be less effective in identifying the B.1.1.529 variant. Nevertheless, to contain the spread of Omicron, United States has banned flights from seven high-risk countries effective Monday, November 29, 2021 (7). Similar travel restrictions have also been implemented by many other countries around the globe.

In conclusion, the identification of a new potentially more dangerous variant is a somber reminder that the world is still living under the umbrella of a pandemic and remains highly vulnerable to another wave of SARS-CoV-2 infection. Despite these travel restrictions, it is only a matter of time that the B.1.1.529 variant will be identified in patients in the US. **In fact, we predict that the B.1.1.529 variant has already penetrated the US eco-system.** While it must be confirmed unequivocally, given some similarities of observed mutations in B.1.1.529 to that to the Delta variant, we envisage that the immune responses raised by the currently available vaccines will be effective in protecting against this variant. It is the degree of protection afforded by these vaccines against Omicron which is the focus of studies currently underway. Hence the need for universal vaccination all around the world otherwise, the threat of evolving new and more dangerous SARS-CoV-2 variants will always be lurking in the background. Recent affirmative news about the gradual decline in the rate of infection and hospitalization in some states has perhaps bestowed false reassurance prompting many to abandon US Centers for Disease Control & Prevention guidelines for limiting the spread of COVID-19**. It is, therefore, imperative that we continue to exercise extreme caution in our social congregations and all those who are eligible must get vaccinated including the third and/or the booster doses.**

## Diclosures

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