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Evasion of host immune system by new SARS-CoV-2 variant of concern omicron: A review

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Abstract
On 26 November 2021, WHO designated the variant B.1.1.529 a variant of concern (VOC), following advice from the WHO's Technical Advisory Group on Virus Evolution. The variant has been given the name Omicron. Omicron is a highly divergent variant with a high number of mutations, including 26-32 mutations in the spike protein, some of which may be associated with humoral immune escape potential and higher transmissibility. The current global epidemiology of SARS-CoV-2 is characterized by the global dominance of the Omicron variant. All other variants, including variants of concerns (Alpha, Beta, Gamma and Delta) and variants of interest (Lambda and Mu) continue to decline in all six WHO regions. Among the 432 470 sequences uploaded to global Initiative on Sharing All Influenza Data (GISAID) with specimens collected in the last 30 days, 425 227 (98.3%) were Omicron, 7 191 (1.7%) were Delta and one (<0.1%) was Lambda. During this same period, there was no Alpha, Beta, Gamma or Mu sequences reported. The purpose of this review was to summarize the structural characteristics, epidemiology of the Omicron variant and its potential to evade the immune response.

Keywords: corona virus, immune response, omicron, variant of concern

Introduction
Coronavirus disease 2019 (COVID-19) first emerged in Wuhan city in December 2019, and became a grave global concern due to its highly infectious nature [1–3]. The Severe Acute Respiratory Coronavirus-2 (SARS-CoV-2), with its predecessors (i.e., MERS-CoV and SARS-CoV) belongs to the family of Coronaviridae. Reportedly, COVID-19 has infected 344,710,576 people around the globe and killed nearly 5,598,511 persons in the short span of two years [4]. As with other viruses, coronavirus constantly changes through genetic mutations, which have posed new challenges in the road to recovery. According to the United States (U.S.) government-led SARS-CoV-2 Interagency Group (SIG), SARS-CoV-2 variants can be categorized into four classes: Variant Being Monitored (VBM), Variant of Interest (VOI), Variant of Concern (VOC), and Variant of High Consequence (VOHC) [5].
Among the VOC class, variants such as Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2 and AY lineages) evolved, and recently a new variant, B.1.1.529, was detected in several countries [5]. It quickly became a subject of discussion and exploration among the scientific community. The variant B.1.1.529 was first detected in Botswana, followed by South Africa between 11 November 2021 and 14 November 2021 [6]. It is a VOC due to its high transmissibility and less susceptibility to neutralization by antibodies produced either by previous viral exposure or vaccine administration [5, 6]. According to the estimates, the cases of B.1.1.529 in South Africa grew by over fivefold in one week from 16 November to 25 November 2021 [7, 8]. These upward trends remained for four weeks, followed by a rapid decline by 48% from 27 December 2021 to 2 January 2022 [7, 8]. Other countries to report cases of infection by B.1.1.529 include, but are not limited to, France, The Netherlands, Germany, Portugal, Italy, the United Kingdom (U.K.), Canada, Hong Kong, Australia, and the United States. On 25 November, the B.1.1.529 variant was termed a Variant Under Monitoring by the United Kingdom Health Security Agency, and was considered as the maximally mutated variant amongst the other variants [7, 8]. A day after, on 26 November 2021, this variant was designated as an official Variant of Concern by the World Health Organization (WHO) and named Omicron [9]. Omicron created chaos around the world and different studies are being conducted to study its presenting symptoms, transmission, risk of reinfection, severity, and its tendency to evade immune responses [10–13]. There are concerns related to its rampant transmission, which could hinder containment efforts, such as vaccine effectiveness. The surging trend in Omicron cases is worrisome, because this could cause an overwhelming demand on health care systems which have not yet completely recovered from the health and financial damages caused by the initial virus outbreak [13, 14].

Omicron (B.1.1.529)

On Friday 26 November 2021, the WHO announced [15] that a new SARS-CoV-2 Variant of Concern, named Omicron (initially named B.1.1.529), appeared to be increasing in almost all of South Africa's provinces, particularly Gauteng. The rapid spread, especially among the younger age group, in Gauteng, South Africa, has placed WHO and global health systems on high alert. The SARS-COV-2 VOC was first reported to the WHO from South Africa on 24 November, 2021. Cases of VOC Omicron had also been identified in Botswana, Belgium, Hong Kong and Israel. On 29 November, 2021, three days after the announcement by WHO, cases of VOC Omicron have been detected in Austria, Australia, Belgium, Canada, Czech Republic, Denmark, France, Germany, Italy, the Netherlands and the United Kingdom. The global public health community applauds scientists in South Africa and other countries which have reported the new VOC for the speed with which they have identified, sequenced and characterized SARS-CoV-2 strains, and their transparency and openness in reporting quickly to WHO [15]. Their SARSCoV-2 sequencing work has been exemplar [16, 17]. As of November 28, 2021, 17:00 CET, 127 viral genomes (VOC Omicron GR/484A) have been entered into the GISAID databases [18]. Several receptor binding domains (RBD) and N-terminal domains (NTD) mutations hypothesized to be associated with resistance to neutralizing antibodies and increased transmissibility are of concern.

The Omicron lineage (B.1.1.529) has split into three divergent sub-lineages (BA.1, BA.2 and BA.3) of which BA.1 has spread rapidly around the world. The BA.1 Omicron genome encodes 30 amino acid substitutions relative to Wuhan-Hu-1 within the spike glycoprotein, 15 of which are in the receptor-binding domain (RBD) and 9 within the receptor-binding motif (RBM), the RBD subdomain that interacts with the human ACE2 receptor. Six of these mutations (G339D, N440K, S477N, T478K, Q498R and N501Y) enhance binding affinity to the human ACE2 receptor. Combinations such as Q498R and N501Y may enhance ACE2 binding additively. Overall, the Omicron RBD binds to the human ACE2 with approximately double the affinity (x2.4) of the Wuhan RBD9. Seven Omicron RBD mutations (K417N, G446S, E484A, Q493R, G496S, Q498R and N501Y) are associated with decreased antibody binding, importantly falling in epitopes corresponding to the three principal classes of RBD-specific neutralizing antibodies [19].

Epidemiology of B.1.1.529

The prevalence of BA.2 among sequenced Omicron cases globally submitted to GISAID has been steadily increasing [20] reaching 21.09% in week 5 of 2022 [21]. As of 14 February, 10 countries reported a predominance of BA.2 (>50%): Bangladesh, Brunei Darussalam, China, Denmark, Guam, India, Montenegro, Nepal, Pakistan, Philippines. However, there are differences between regions observed, with the South-East Asia Region reporting the highest prevalence of BA.2 among Omicron sequences (44.7%) and the Region of the Americas reporting the lowest prevalence (1%). This analysis is based on all sequences submitted to GISAID with samples collected from 13 January to 11 February 2022. These trends should be interpreted with due consideration of the limitations of surveillance systems, including differences in sequencing capacity and sampling strategies between countries, as well as laboratory turn-around times for sequencing and delays in reporting. Additionally, it is important to consider the relative proportions of the BA.2 sequences in the context of the case incidence when interpreting the spread and relative growth of different lineages.

Examples of countries which have seen an increase in the prevalence of BA.2 include: South Africa where the prevalence rose from 27% on 4 February 2022 [22] to 86% by 11 February 2022 [23]; the United Kingdom [24] where the prevalence increased six-fold from 17 to 31 January 2022 (from 2.2% to 12%); Denmark where the prevalence doubled from week 52 of 2021 to week 2 of 2022 (from 20% to 45%) and became the dominant variant (66% of sequenced by week 3 of 2022) [25] and the United States of America where the prevalence tripled from 1.2% during the week ending 29 January 2022 to 3.6% during the week ending 5 February 2022 [26]. The prevalence of BA.2 appears to be increasing both in countries experiencing a decline in Omicron cases and in countries that are in the growing phase of the wave.

Structure of Omicron

The Omicron variant, which is a derivative of the Pango lineage B.1.1.529, exhibiting a variation in the 21 amino acid pertaining to the spike protein with the majority residing in the receptor binding domain (RBD) (residues 319–541) compared with the original strain [16–21]. SARS-CoV-2 has continuously undergone a series of unprecedented mutations and evolved to exhibit varying characteristics [16–21]. These mutations have largely occurred in the spike (S) protein (which is the site for antibody binding), which attribute high infectivity and transmissibility properties to Omicron variant [27-32]. According to the genomic reports, the S protein of Omicron has a total of 30 amino acid substitutions, 3 deletions, and 1 small insertion [32]. About 50% (n = 15) of amino acid substitutions occur exclusively in the receptor binding domain (RBD) [27-32]. Among the 15 RBD substitutes, N501Y and Q498R have a stronger affinity towards the angiotensin-converting enzyme (ACE-2 receptors), which explain the high transmissibility of the Omicron variant [27-33]. The ACE-2 receptors play a significant role in COVID-19 pathogenesis, which may involve serious organ failure [34].

Potential for Immune Escape by Omicron Variant

The population-level evidence from South Africa estimated that the hazard ratio for Omicron reinfection and primary infection was 2.39, suggestive of a possible evasion from natural immunity gained from previous infections [11, 35]. This is consistent with the general premise that antibodies generated following the natural

response have a lower titer and greater dissipation, thereby reducing immunity over time [11, 35]. It is important to explore the dimensions of vaccine effectiveness, especially between countries which have used different types of vaccines. Given the genetic divergence of Omicron with its predecessors, its emergent genetic sequence coding the spike protein has been documented to sheath away from the respective immunoglobulins or humoral response [36]. Upon analyzing the titers of neutralizing antibodies of sera from vaccinated individuals, the neutralization capacity was lower for Omicron [36–42]. However, the neutralization capacity was maintained among vaccinated individuals, who also had a history of prior infection [37, 38].

Interestingly, one study by Cele *et al.* [43] reported high levels of neutralizing antibodies in the plasma of subjects who had a history of previous infection and were fully vaccinated. According to an (unpublished) report by Andrew *et al*., the vaccine effectiveness was raised by 75–80% following the administration of a booster dose [44]. This might be relatively lower than the Delta variant, but still encouraging to deal with the unknowns of Omicron. Some studies have compared the immunogenic properties of homologous and heterologous vaccinations, and found that the heterologous prime-boost regimens exhibited higher neutralizing activity compared with the homologous vaccinations [45]. More data will be needed to confirm this finding. Existing data suggest a reduced efficiency of vaccines in antibody neutralization; however, the cell-mediated immunity remains resilient in offering protection from severe illness [36–42, 46]. T cells offer cell-mediated immunity and have an ability to recognize mutated virus through multiple sites beyond the spike protein [36–46]. In addition, T cells provide long-lasting immunity which does not fades as quickly as natural antibodies [44–46].

Conclusion

The major reason that Omicron raised a great concern is its accumulated mutations, including more than 30 of those in the spike (S) protein. More importantly, 15 of those mutations occurs on receptor-binding domain (RBD), which is not only the vital binding site to the host receptor angiotensin-converting enzyme 2 (ACE2) for the entry of SARS-CoV-2, but also the key target of neutralizing antibodies produced by immune response and therapeutics antibodies. By contrast, other VOCs including Alpha, Beta, Gamma, and Delta possess 9–12 mutations on their S protein regions. Even so, some crucial mutations like D614G, N501Y, K417N, and E484A in these known VOCs have been reported about the effect on viral infectivity and transmission

References

1. Centers for Disease Control and Prevention Transmission of Coronavirus Disease 2019 (COVID-19). Available online: https://www.cdc.gov/coronavirus/2019-ncov/index.html.
2. Ali M, Nas FS, Abdallah MS, Mu'azu L, Yahaya GM. Global Geographical Distribution of COVID-19 A: Review. Annals of Geographic Studies,2020;3(3) Pp 36-423. Wax RS, Christian MD. Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patients. Can. J. Anesth. 2020, 67, 568–576.
3. The Worldometers. COVID-19 Coronavirus Pandemic. 2022. Available online: https://www.worldometers.info/coronavirus/.
4. Centers for Disease Control and Prevention. SARS-CoV-2 Variant Classifications and Definitions. 2021. Available online: https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-info.html
5. Centers for Disease Control and Prevention. Omicron Variant: What You Need to Know. 2021. Available online: https://www.cdc.gov/coronavirus/2019-ncov/variants/omicron-variant.html.
6. Boynton S. When Will the Omicron Wave End? Data Suggests It Could Be Soon, but Experts Are Wary. Available online: https://globalnews.ca/news/8494760/omicron-wave-end-covid/.
7. Government of South Africa. Cabinet Approves Several Changes to the Adjusted Alert Level 1 COVID19 Regulations 2021. Available online: https://www.gov.za/speeches/cabinet-approves-several-changes-adjusted-alertlevel-1-covid-19-regulations-30-dec-2021.
8. European Centre for Disease Prevention and Control. Epidemiological Update: Omicron Variant of Concern (VOC)-Data As of 11 December 2021.
9. Liu L, Iketani S, Guo Y, Chan JF, Wang M, Liu L, Luo Y, Chu H, Huang Y, Nair MS. *et al*. Striking Antibody Evasion Manifested by the Omicron Variant of SARS-CoV-2. Nature 2021.
10. Pulliam JRC, van Schalkwyk C, Govender N, von Gottberg A, Cohen C, Groome M.J, Dushoff J, Mlisana K, Moultrie H. Increased risk of SARS-CoV-2 reinfection associated with emergence of the Omicron variant in South Africa. Medrxiv 2021
11. McCreesh N, Dlamini V, Edwards A, Oliver S, Dayi N, Dikgale K, *et al*. Impact of the COVID-19 epidemic and related social distancing regulations on social contact and SARS-CoV-2 transmission potential in rural South Africa: Analysis of repeated cross-sectional surveys. BMC Infect. Dis. 2021, 21, 928.
12. Mohiuddin M, Kasahara K. Investigating the aggressiveness of the COVID-19 Omicron variant and suggestions for possible treatment options. Respir. Med,2021:191:106716.
13. French G, Hulse M, Nguyen D, Sobotka K,Wedster K, Corman J, Aboagye-Nyame B, Dion M, Johnson M, Zalinger B, *et al*. Impact of Hospital Strain on Excess Deaths During the COVID-19 Pandemic-United States, July 2020–July 2021. MMWR Morb. Mortal. Wkly. Rep,2021:70:1613–1616.
14. WHO (2021c) WHO 2nd Global consultation on assessing the impact of SARS-CoV-2 variants of concern on Public health interventions. https://www.who.int/publications/m/item/2nd- global- consultation- on-assessing- the impact-of- sars- cov- 2- variants- of- concern- on- public- health- interventions

15. Wilkinson E, Giovanetti M, Tegally H, San JE, Lessells R, Cuadros D, *et al*. A year of genomic surveillance reveals how the SARS-CoV-2 pandemic unfolded in Africa. Science,2021:374:423–31. doi: 10.1126/science.abj4336.
16. Tao K, Tzou PL, Nouhin J, Gupta RK, de Oliveira T, Kosakovsky Pond SL, *et al*. The Biological and clinical significance of emerging SARS-CoV-2 variants. Nat Rev Genet,2021:22:757–73. doi: 10.1038/s41576-021-00408-x
17. Inzaule SC, Tessema SK, Kebede Y, Ogwell Ouma AE, Nkengasong JN. Genomic informed pathogen surveillance in Africa: opportunities and challenges. Lancet Infect Dis 2021;21:e281–9. doi: 10.1016/S1473-3099(20)30939-7.
18. US COVID-19 Cases Caused by Variants. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html..
19. GISAID. Time-course of Omicron variant sublineage distribution: analysis update (2022-02-08). Accessed February 9, 2022. https://www.epicov.org/epi3/frontend#
20. World Health Organization. Weekly epidemiological update on COVID-19 - 8 February 2022. Published online 2022
21. Network for Genomic Surveillance in South Africa. SARS-CoV-2 Sequencing Update: 4 February 2022. Published online 2022. Accessed February 9, 2022. https://www.nicd.ac.za/wp-content/uploads/2022/02/Update-of-SA-sequencing-data-from-GISAID-4-Feb-2022.pdf
22. Network for Genomic Surveillance in South Africa. *SARS-CoV-2 Sequencing Update: 11 February 2022*, 2022. Accessed February 14, 2022. https://www.nicd.ac.za/wp-content/uploads/2022/02/Update-of-SA-sequencing-data-from-GISAID-11-Feb-2022.pdf
23. United Kingdom Health Security Agency. Technical briefing 35: SARS-CoV-2 variants of concern and variants under investigation in England. Published online 2022.
24. Statens Serum Institute. Risk assessment of Omicron BA.2. Published online 2022. Accessed February 8, 2022. https://en.ssi.dk/-/media/arkiv/subsites/covid19/risikovurderinger/2022/risk-assesment-of-omicron-ba2.pdf?la=en
25. CDC. COVID Data Tracker. Centers for Disease Control and Prevention. Published March 28, 2020. Accessed December 21, 2021. https://covid.cdc.gov/covid-data-tracker
26. Kannan SR, Spratt AN, Sharma K, Chand HS, Byrareddy SN, Singh K. Omicron SARS-CoV-2 variant: Unique features and their impact on pre-existing antibodies. J. Autoimmun. 2022, 126, 102779
27. Lubin JH, Markosian C, Balamurugan D, Pasqualini R, Arap W, Burley SK, Khare SD. Structural models of SARS-CoV-2 Omicron variant in complex with ACE2 receptor or antibodies suggest altered binding interfaces. bioRxiv,2021:12:472313.
28. Saxena SK, Kumar S, Ansari S, Paweska JT, Maurya VK, Tripathi AK, Abdel-Moneim AS. Characterization of the novel SARS-CoV-2 Omicron (B.1.1.529) variant of concern and its global perspective. J. Med. Virol. 2021
29. Mannar D, Saville JW, Zhu X, Srivastava SS, Berezuk AM, Tuttle KS, Marquez AC, Sekirov I, Subramaniam S. SARS-CoV-2 Omicron variant: Antibody evasion and cryo-EM structure of spike protein-ACE2 complex. Science 2022
30. Kumar S, Thambiraja TS, Karuppanan K, Subramaniam G. Omicron and Delta variant of SARS-CoV-2: A comparative computational study of spike protein. J. Med. Virol. 2021.
31. Centers for Disease Control And Prevention. Science Brief: Omicron (B.1.1.529) Variant. 2021. Available online: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/scientific-brief-omicron-variant.html (accessed on 31 December 2021).
32. Scialo F, Daniele A, Amato F, Pastore L, Matera MG, Cazzola M, Castaldo G, Bianco A. ACE2: The Major Cell Entry Receptor for SARS-CoV-2. Lung,2020:198:867–877.
33. Joseph S, Nair B, Nath LR. The Ineluctable Role of ACE-2 Receptors in SARS-CoV-2 Infection and Drug Repurposing as a Plausible SARS-CoV-2 Therapy: A Concise Treatise. Curr. Mol. Med,2021:21:888–913.
34. Poudel S, Ishak A, Perez-Fernandez J, Garcia E, León-Figueroa DA, Romaní L, *et al*. Highly mutated SARS-CoV-2 Omicron variant sparks significant concern among global experts—What is known so far? Travel Med. Infect. Dis, 2021.
35. Ahmed SF, Quadeer AA, McKay MR. SARS-CoV-2 T Cell Responses Elicited by COVID-19 Vaccines or Infection Are Expected to Remain Robust against Omicron. Viruses,2022:14:79.
36. Wilhelm A, Widera M, Grikscheit K, Toptan T, Schenk B, Pallas C, *et al*. Reduced neutralization of SARS-CoV-2 Omicron variant by vaccine sera and monoclonal antibodies. medRxiv, 2021.
37. Roessler A, Riepler L, Bante D, von Laer D, Kimpel J. SARS-CoV-2 Omicron Variant Neutralization in Serum from Vaccinated and Convalescent Persons. N. Engl. J. Med, 2022.
38. Planas D, Saunders N, Maes P, Guivel-Benhassine F, Planchais C, Buchrieser J, *et al*. Considerable escape of SARS-CoV-2 Omicron to antibody neutralization. Nature, 2021.
39. Krammer FA correlate of protection for SARS-CoV-2 vaccines is urgently needed. Nat. Med. 2021, 27, 1147–1148. Available online: https://www.nature.com/articles/s41591-021-01432-4 (accessed on 10 January 2022).
40. Hartley GE, Edwards ES, Aui PM, Varese N, Stojanovic S, McMahon J, *et al*. Rapid generation of durable B cell memory to SARS-CoV-2 spike and nucleocapsid proteins in COVID-19 and convalescence. Sci.

Immunol. 2020, 5, eabf8891. Available online: https://immunology.sciencemag.org/content/5/54/eabf8891/43 (accessed on 10 January 2022).
41. Lau EH, Tsang OT, Hui DS, Kwan MY, Chan W, Chiu SS, *et al*. Neutralizing antibody titres in SARS-CoV-2 infections. Nat. Commun. 2021, 12, 1–7. Available online: https://www.nature.com/articles/s41467-020-20247-4 (accessed on 10 January 2022).
42. Cele S, Jackson L, Khoury DS, Khan K, Moyo-Gwete T, Tegally H, *et al*. SARS-CoV-2 Omicron has extensive but incomplete escape of Pfizer BNT162b2 elicited neutralization and requires ACE2 for infection. medRxiv 2021.
43. Andrews N, Stowe J, Kirsebom F, Toffa S, Rickeard T, Gallagher E, *et al*. Effectiveness of COVID-19 vaccines against the Omicron (B.1.1.529) variant of concern. medRxiv 2021.
44. Barros-Martins J, Hammerschmidt SI, Cossmann A, Odak I, Stankov MV, Morillas Ramos G, *et al*. Immune responses against SARS-CoV-2 variants after heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination. Nat. Med,2021:27:1525–1529.
45. Hoffmann M, Krüger N, Schulz S, Cossmann A, Rocha C, Kempf A, *et al*. The Omicron variant is highly resistant against antibody-mediated neutralization: Implications for control of the COVID-19. Cell 2021.