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OMICRON SUB-LINEAGE BA.2

We need to optimise genome surveillance and tracing of SARS-CoV-2 variants

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Whole genome sequencing has been crucial in studying the evolution and genetic diversity of SARS-CoV-2 during the pandemic, and it had an important role in identifying the omicron variant.[1 2]

Earlier in the pandemic, the alpha variant was found to result in an undetectable S gene on reverse transcription polymerase chain reaction (S gene target failure (SGTF))—a feature of considerable diagnostic value.[3 4] The South African investigations that led to announcement of the omicron variant of concern found SGTF in more than 50% of all tested specimens, supporting SGTF as a proxy for this variant too.[5] This aligns with the World Health Organization's recommendations for early detection of the omicron variant, which calls for diagnostic test kits containing two confirmatory genes, at least one of which is the S gene, pending sequencing confirmation.[2]

Now the SARS-CoV-2 omicron (B.1.159) lineage is thought to be split into two sub-lineages: BA.1 and BA.2 (www.gisaid.org). These sub-lineages share several common defining mutations and seem to be co-circulating, but the BA.2 sub-lineage does not carry the del69-70 mutation in the spike region, and recently sequenced cases belonging to the BA.2 sub-lineage have not been flagged by SGTF.[6] The UK Health Security Agency[7] and the American Medical Association[8] have expressed concerns over this new "stealth" sub-lineage, which also seems to be more transmissible, a trait likely to affect the current trend of declining cases.

Detection of SGTF seemed to be an effective strategy to contain omicron through targeted contact tracing and isolation, but the rapid evolution of variants and sub-lineages, and the unfolding data regarding their genetic profiles, need to be incorporated into our diagnostics tools if we are to succeed in overcoming SARS-CoV-2.

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All authors contributed equally to this letter.

1 Umair M, Ikram A, Salman M, etal. Whole-genome sequencing of SARS-CoV-2 reveals the detection of G614 variant in Pakistan. *PLoS One* 2021;16:e0248371. doi: 10.1371/journal.pone.0248371 pmid: 33755704

2 World Health Organization. Enhancing readiness for omicron (B.1.1.529): technical brief and priority actions for member states. 28 Nov 2021 https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states

3 Migueres M, Lhomme S, Trémeaux P, etal. Evaluation of two RT-PCR screening assays for identifying SARS-CoV-2 variants. *J Clin Virol* 2021;143:104969. doi: 10.1016/j.jcv.2021.104969 pmid: 34509927

4 Brown KA, Gubbay J, Hopkins J, etal. S-gene target failure as a marker of variant B.1.1.7 among SARS-CoV-2 isolates in the Greater Toronto area, December 2020 to March 2021. *JAMA* 2021;325:2115-6. doi: 10.1001/jama.2021.5607 pmid: 33830171

5 European Centre for Disease Prevention and Control. Implications of the emergence and spread of the SARS- CoV-2 B.1.1. 529 variant of concern (omicron), for the EU/EEA. 26 Nov 2021. https://www.ecdc.europa.eu/sites/default/files/documents/Implications-emergence-spread-SARS-CoV-2%20B.1.1.529-variant-concern-Omicron-for-the-EU-EEA-Nov2021.pdf

6 European Centre for Disease Prevention and Control, World Health Organization Regional Office for Europe. Methods for the detection and characterisation of SARS-CoV-2 variants—first update. 20 Dec 2021. https://www.ecdc.europa.eu/en/publications-data/methods-detection-and-characterisation-sars-cov-2-variants-first-update

7 Mahase E. Omicron sub-lineage BA.2 may have "substantial growth advantage," UKHSA reports. *BMJ* 2022;376:o263. doi: 10.1136/bmj.o263 pmid: 35101887

8 American Medical Association. What is the BA.2 or "stealth" omicron subvariant? https://www.ama-assn.org/delivering-care/public-health/what-ba2-or-stealth-omicron-subvariant