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Letter to the Editor

Introduction of the South African SARS-CoV-2 variant 501Y.V2 into the UK



The current surge of COVID-19 cases across the UK is now thought to be mostly driven by a new, highly transmissible SARS-CoV-2 variant (B.1.1.7/ VUI-202,012/01),¹ but another highly transmissible SARS-CoV-2 variant (B.1.351/501Y.V2) from South Africa has already been detected in the UK population [https://cov-lineages.org/global_report.html].

This South African 501Y.V2 variant is characterised by three mutations in the SARS-CoV-2 spike (S) protein: K417N (a lysine to asparagine substitution at amino acid position 417 in the S protein), E484K (a glutamic acid to lysine substitution at amino acid position 484 in the S protein) and N501Y (an asparagine to tyrosine substitution at amino acid position 501 in the S protein). This last mutation is also present in the UK VUI-202,012/01 variant.¹

This 501Y.V2 variant likely emerged from the first wave of the South African COVID-19 epidemic in the hardest hit Nelson Mandela Bay metropolitan area of the Eastern Cape Province in early October 2020, then spread quickly to become the predominant virus lineage in the Eastern and Western Cape Provinces by the end of November 2020.²

This virus variant soon spread to neighbouring Botswana in December 2020, as well as several other countries worldwide including England, Scotland, France, Sweden, Switzerland, South Korea during December 2020, and Australia in January 2021 (Fig. 1). This phylogenetic reconstruction of the whole genome viral sequences suggests that there may have been up to 8–9 independent introductions of the 501Y.V2 variant into England and 2 into Scotland, though the details of the epidemiological linkage between these cases is unknown.

One hypothesis about the origins of this variant is through intra-host viral evolution due to prolonged infection in an immunocompromised host.³ Indeed, in this case report, the appearance of the E484K and N501Y mutations were described after 75 and 128 days of infection, respectively. However, this cannot be the only mechanism, as multiple other mutations are present that would require contributions from other viral lineages.² Additional mutations in other viral genes may also be secondary mutations that may have arisen as 'compensatory' mutations to reduce any fitness penalty resulting from these S protein changes (K417N, E484K, N501Y).⁴

Currently, the 501Y.V2 variant is considered to be a more highly transmissible strain due to the rapidity with which it became predominant in this South African population over just a few weeks.²

There are also some real concerns that the mutations in the S protein (K417N, E484K, N501Y) may result in conformation changes that may impact on the effectiveness of COVID-19 vaccines developed based on earlier SARS-CoV-2 strains. However a recent small study examining the impact of the N501Y mutation on the recently licensed Pfizer-BioNTech vaccine did not show any loss of antibody neutralisation efficacy,⁵ though similar further studies examining the impact of this N501Y and the other mutations (K417N, E484K) on the various other COVID-19 vaccines are also required.

There appears to be no indication of increased severity of illness, as yet, though research is ongoing in both the UK and South Africa to further characterise the phenotype of this South African 501Y.V2 variant.⁶

Despite the presence of these two more transmissible SARS-CoV-2 variants, the public health messaging remains the same to reduce the spread of these viruses: to maintain social distancing, including masking in crowded indoor areas, and limit the number of contacts that we have each day.



Fig. 1. A maximum likelihood tree of South African variant B.1.351/501Y.V2 (downloaded 7 January 2021, from GISAID: <https://www.gisaid.org/>). Sequences were aligned using MAFFT: <https://mafft.cbrc.jp/alignment/software/> and manually edited using BioEdit v7.2.5. Phylogenetic tree construction was performed using FastTree v2.1.11 and displayed using FigTree v1.4.4. We gratefully acknowledge and thank all the teams and laboratories that have deposited these sequences into GISAID to make this analysis possible. Red and blue brackets denote 501Y.V2 viruses detected in England or Scotland, respectively, together with any closely related sequences from elsewhere. The larger, bold red bracket indicates a larger cluster of possibly linked viruses that are closely related to viruses from France. Note that this tree is intended to be illustrative and not comprehensive.

Declaration of Competing Interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.jinf.2021.01.007](https://doi.org/10.1016/j.jinf.2021.01.007).

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