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Letter to the Editor

Emergence of a new SARS-CoV-2 variant in the UK

An earlier article described how new SARS-CoV-2 synonymous nucleotide mutations (which had no impact on the amino acid coding) may have arisen with its move into the human population, but reported no 'beneficial' mutations.¹

Subsequent to this, Korber et al.² reported on the spread of a SARS-CoV-2 spike (S) protein mutation, D614G (i.e. an aspartic acid to glycine amino acid substitution at position 614 in the viral S gene) across multiple countries, suggesting that it was a more 'transmissible' form of the virus. This was based on higher viral loads found during in vitro replication studies, as well as in clinical samples containing this mutation and animal studies suggesting this.³ However, others cautioned this interpretation, stating that 'founder' effects could not be entirely ruled out to explain the ubiquity of this virus in the global population,⁴ and other teams did not find evidence of enhanced transmission of the D614G strain when analysing the frequency of recurrent mutations.⁵

Since then a new, rapidly spreading variant in the UK ('VUI-202012/01' i.e. 'variant under investigation') has been reported in the UK in recent weeks.^{6,7} This variant is derived from the SARS-CoV-2 20B/GR clade (lineage B.1.1.7) and contains multiple mutations, including a combination of the N501Y (i.e. an asparagine to tyrosine amino acid substitution at position 501 in the viral S gene) and the 69–70del (i.e. a deletion of 6 bases coding for histidine and valine at positions 69 and 70, respectively, in the viral S gene) mutations, both of which have been circulating, separately and independently, globally for many months previously.^{8,9}

Fig. 1 shows an illustrative maximum likelihood phylogenetic tree of selected SARS-CoV-2 full genome sequences, highlighting the diversity and timeline of globally circulating strains containing the N501Y (red) and 69–70del (green) mutations that have been existing separately and independently prior to the emergence of the new B.1.1.7 (variant) (pink), after August 2020, that contains both of these characteristic mutations. Note that some of the earliest N501Y-containing viruses originated from Brazil (April 2020) and Australia (June–July 2020), and as early as March 2020 from Slovenia for the 69–70del mutation, though we know that this 69–70del mutant was circulating as early as January in Thailand and February in Germany.⁹ Most of the sequences containing both of these mutations (pink) are from the UK during October–November 2020, though there is at least one sequence from Denmark from November 2020.

Early investigations from the UK suggest an increased transmissibility of up to 71% over and above the previous circulating strains of SARS-CoV-2, which may contribute 0.39–0.93 to the R_0 value estimates of the virus, and ongoing monitoring of the situation is in progress.⁶ However, so far there is no evidence that this new B.1.1.7 (variant) demonstrates any increased clinical severity of illness, or vaccine escape capability. The fact that these mutations have been

reported since October before the surge in test positivity noted in the Southeast of England also raises the question as to whether this is also a founder effect.

The practical risk of a more rapidly spreading virus is the potential impact on healthcare services especially if seasonal influenza were to return. If more people are infected over a similar time period compared to other virus strains, potentially more patients may need hospitalisation, with a danger that healthcare services may be overwhelmed. A more rapidly spreading virus will also accelerate the need to reach the COVID-19-vulnerable populations (the elderly and those with multiple comorbidities) with the new COVID-19 vaccines to stay 'ahead' of the virus. At the same time, deferring elective surgeries or resources for other illnesses may have unintended consequences if the rapidly spreading virus does not behave as predicted.

At the time of writing, further investigations are ongoing of this virus to determine more clearly its impact on society and healthcare capacity. In addition, the impact of the mutation on the effectiveness of vaccines or prior immunity are being explored. Another intriguing question is whether the mutation has arisen from an immunocompromised host,¹⁰ or through an animal source such as mink.⁷ Many countries have decided to close the borders to visitors from the UK even though the impact of the new B.1.1.7 (variant) is not fully known. It is critical to have updated and transparent information from across the world to answer these questions.

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Fig. 1. Maximum likelihood phylogenetic tree of selected SARS-CoV-2 full genome sequences rooted against the original Wuhan SARS-CoV-2 reference strain (NC_045512_Wuhan_Hu_1, blue), highlighting the diversity and timeline of globally circulating strains containing the N501Y (red) and 69-70del (green) mutations that have been existing separately and independently prior to the emergence of the new B.1.1.7 (variant) (pink), after August 2020, that contains both of these characteristic mutations. All sequences were downloaded from GISAID (<https://www.gisaid.org/>) and were aligned using BioEdit v.7.2.5., the tree was constructed using FastTree v.2.1.11 and displayed in FigTree v.1.4.4. We gratefully acknowledge and thank the various laboratories and contributors of these GISAID for providing these SARS-CoV-2 sequences. Note that this tree is illustrative and not intended to be comprehensive.

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