NERVTAG

Brief note on SARS-CoV-2 variants

13th January 2021

Signed off by Chair

1. In the last two months several SARS-CoV-2 variants with a large number of mutations have been identified that are concerning since they appear to have rapid epidemiological growth. This rapid growth may relate to biological properties of the virus that confer a competitive advantage over other virus variants.

2. The UK variant (B.1.1.7; VOC 202012/01) appears to have increased transmissibility compared to other variants and has grown quickly to become the dominant variant in much of the UK. It possesses several changes in the spike glycoprotein that may individually or in combination contribute to increased transmissibility. Although mutations in spike such as N501Y may contribute to some antigenic distance between this variant and older viruses, there is no evidence that this variant is associated with changes in disease severity or antigenic escape from naturally, monoclonal or vaccine acquired immunity. [1,2]

3. A different variant (B.1.351; VOC 202012/02) has shown rapid epidemiological growth in South Africa. It possesses the N501Y substitution in spike and well as an E484K substitution. The rapid growth could be related to increased transmissibility, antigenic escape or both. There are reasons to be concerned about the possibility of antigenic escape:

    a. In vitro data showing weaker neutralisation of viruses with the E484K substitution with polyclonal serum. [3]

    b. In vitro data showing that variants with the E484K substitution show weaker neutralisation with some monoclonal antibodies (bamlanivimab – Eli Lily; REGN10933 – Regeneron [also K417E]).[4,5]

    c. A report at the WHO virus evolution meeting on Monday 11th January of in vitro data (n=6) showing weaker neutralisation of VOC 202012/02 with polyclonal serum from South Africa.

    d. Rapid epidemiological growth in an area (Nelson Mandela Bay) with reported high levels of seropositivity. [6]

4. Viruses in the lineage B.1.1.28 have emerged in Brazil with the E484K substitution, without (VUI 202101/01) and with the N501Y (VUI 202101/02) substitution. Data are limited but there may be rapid growth of these variants (low confidence). VUI 202101/02 has been identified in Manaus which is experiencing a rapid growth in numbers of COVID hospitalisations. SARS-CoV-2 seroprevalence in Manaus has previously been reported to be high [7]. If present, this rapid growth could be related to increased transmissibility, antigenic escape or both. There are reasons to be concerned about the possibility of antigenic escape:

    a. In vitro data showing weaker neutralisation of viruses with the E484K motif with polyclonal serum. [3]

    b. In vitro data showing that variants with the E484K substitution show weaker neutralisation with some monoclonal antibodies (bamlanivimab Eli Lily, >100 fold; REGN10933 Regeneron, 25-fold [also K417N, 7-fold]). [4,5]

    c. Identification in an area (Manaus) with rapid growth in COVID hospitalisations and previously reported high levels of seropositivity. [7]

5. A small number of South African and Brazilian and other genomes with the E484K substitution have been identified in the UK as of 12 January 2021 (50-100 genomes).

6. Variants with the combined N501Y and E484K substitutions have been shown to have enhanced ACE2 receptor binding. [6,8]

Conclusion

7. The emergence and spread of SARS-CoV-2 virus variants which may have either increased transmissibility or antigenic escape or both is a significant concern.

8. The following actions should be considered:

    a. Minimise spread of these and other variants by reducing overall infection transmission in the UK.

    b. Minimise introduction of VOCs into the UK by enhanced border measures.

    c. Enhance case detection, contact tracing and quarantine related to any viruses with the E484K substitution in order to minimise spread.

    d. Analyse whether UK cases with the E484K substitution are enriched in reinfection or vaccine breakthrough cases.

e. Conduct neutralisation assays to assess antigenic properties of variants with the E484K substitution.

f. Establish / agree a critical cut off value or drop in in vitro measured neutralisation that correlates with a meaningful loss of protection.

g. Specify additional substitutions of concern and establish systemic genomic surveillance and phenotypic evaluation of these substitutions.

h. Undertake a review of vaccine development pipelines and, if needed, provide support to identify antigens for accelerated antigenic update.

i. Undertake a review of monoclonal antibody formulations and, if needed, provide support to identify monoclonal antibodies for updated monoclonal therapeutics.

References:

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