Statement of the WHO Working Group on COVID-19 Animal Models (WHO-COM) about the UK and South African SARS-CoV-2 new variants.

Background

The WHO-COM is an expert group of more than 150 scientists around the world with expertise in animal models of viral diseases. Since February 2020 the group has met weekly to discuss advances, foster collaborations, share resources and reagents and avoid duplication of effort. The WHO-COM met on 22 December 2020 to discuss current knowledge and action plans about the emerging SARS-CoV-2 variants containing multiple mutations in the viral spike protein and that are currently circulating in the UK and South Africa. The UK variant was identified through genomic sequencing and reported to WHO on 14 December 2020 and is referred to as SARS-CoV-2 VUI 202012/01 (B.1.1.7). The South African variant is characterized by eight lineage-defining mutations in the spike protein including three key residues in the receptor binding domain (K417N, E484K and N501Y) and is referred to as lineage 501Y.V2. Epidemiological data suggests that these two variants may be associated with increased transmissibility. It is not known whether they may also result in increased pathogenicity, immune escape from current COVID-19 vaccines or lack of detection by established diagnostic methods. The WHO-COM group provides here a high-level summary of the deliberations and recommends action points to test these hypotheses experimentally.

155 scientists participated in the meeting of Tuesday 22 December, 2020 to discuss the SARS-CoV-2 variants.

Meeting minutes

- Simon Funnell, co-chair of the WHO-COM group presented a summary of the current knowledge regarding the B.1.1.7 variant in the UK including: i) Specific mutations in the spike, ORF1ab, ORF8 and N genes, ii) S gene target failure in diagnostic tests, iii) unanswered questions and iv) possible approaches. As it is being generated, information about this clade is being regularly updated at the following UK Government website location. https://www.gov.uk/government/collections/new-sars-cov-2-variant
- Public Health England and the University of KwaZulu-Natal are working as fast as possible to distribute the UK and South African variants respectively via dedicated repositories such as BEI, NIBSC, and EVA.
- Additional resources available immediately to the group are plasmids to encode the mutant spike RBD. These plasmids generated by Florian Krammer (Mount Sinai) will be distributed to group members without the need of an MTA and may help immediately to assess important questions such as possible evasion from neutralizing antibodies present in convalescent or vaccinee sera.
- The group agreed that a high priority is to test the new variant against existing COVID-19 sera. This could be done with existing non-human primate (NHP) sera or with vaccinee sera. Regarding the latter, PHE will seek collaborators to test the new variant against sera from test vaccines where permissions allow.
- With respect to the latter point, the group discussed ways to speed up sharing of sera without the need to execute new MTAs with developers. Rather than obtaining sera from clinical trials, the proposal would be to obtain and share sera from vaccinees receiving EUA vaccines. Collection

of these sera by key laboratories of the WHO-COM distributed worldwide would ensure rapid testing of possible immune escape by emerging SARS-CoV-2 variants.

- With respect to pathogenicity testing, the WHO-COM agreed that, based on the fact that both variants include the N501Y mutation commonly seen in mouse-adapted SARS-CoV-2, it is likely that these viruses infect regular laboratory mice. In addition, hamster studies to compare the pathogenicity of these new variants with that of previous SARS-CoV-2 isolates was suggested.
- With respect to transmission studies, the group agreed that these experiments are important but that they may be very difficult. Transmission studies give usually yes/no results with little room for comparison. Yet, the WHO-COM has outstanding expertise in transmission studies including different models (cats, hamsters, ferrets, NHPs) as well as other experimental setups to assess airborne transmission, fomite transmission and direct contact transmission.

Critical outcome

The WHO-COM agrees that, setting up a mechanism to study the impact of emerging SARS-CoV-2 variants on transmission, pathogenicity and viral escape from vaccines and therapeutics is a high operational research priority.

Suggested Action points

1) Identify methods for rapid collection of vaccinee sera and distribution across key WHO-COM laboratories around the world.

2) Establish a task-force among the WHO-COM to design studies to test differences in transmission among SARS-CoV-2 variants.

3) Test the pathogenicity of the new SARS-CoV-2 variants in animal models.

4) Determine the protection exerted by current vaccines and monoclonal antibody-based therapies against newly emerging SARS-CoV-2 variants.