



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Understanding variants of SARS-CoV-2

Many variants of SARS-CoV-2 are emerging, but will they have different clinical effects? A new consortium is trying to find out. Talha Burki reports.

For more on the importance of genomic sequencing and surveillance in the COVID-19 response see [Editorial](#) page 445

All viruses mutate. But three variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have raised particular concerns. On Jan 21, 2021, the UK New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) issued a paper outlining the results from several preliminary analyses of B.1.1.7. The variant, which is highly transmissible, was initially identified in the south of England in September 2020, and has since spread to dozens of countries around the world. It carries 17 mutations in its genome, including eight in the spike protein, which forms the basis of the three COVID-19 vaccines that have been licensed in the UK. NERVTAG concluded that there was a “realistic possibility” that infection with B.1.1.7 is associated with an increased risk of death, compared with infection with the parental virus. The group stressed that its assessment was based on limited preliminary data and even if the results were confirmed, the overall risk of death would still be low.

Another extremely infectious variant, P.1, has been circulating in Brazil since the middle of 2020. This variant has been implicated in the surge of infections that has struck Manaus, in the Brazilian Amazon, leaving the health-care system on the brink of collapse. B.1.351 was first detected in South Africa late last year. On Jan 25, Moderna said that in-vitro studies indicated that its vaccine would be effective against B.1.351 and B.1.1.7. However, the South African variant was associated with a substantial reduction in neutralising antibodies. Pfizer has revealed that laboratory tests suggested that its vaccine would work against B.1.1.7. The studies have not been peer reviewed. Both companies have said that they are investigating booster

shots to protect against variants of SARS-CoV-2.

Making sense of how the variants will influence the pandemic is the task of the newly formed G2P-UK National Virology Consortium. Its remit is to use cell cultures and animal models to examine how the mutations affect the transmissibility of the virus, the severity

“It is great to see a serious attempt to try to understand these variants”

of the disease, and the effectiveness of the vaccines and treatments. The initiative brings together researchers at ten academic institutions in the UK, who will work alongside the COVID-19 Genomics UK Consortium.

The UK has generated almost half of the approximately 400 000 genomic sequences of SARS-CoV-2. “We have really good infrastructure to identify variants of interest”, explained Massimo Palmarini, director of the Medical Research Council–University of Glasgow Centre for Virus Research and co-lead of the new consortium. “The question is: what do you do when you have found a new variant? You need experimental evidence that the variant is something to be concerned about”, he added. The G2P Consortium aims to provide this information.

“We want to put all the different variants of interest into the laboratory and determine whether they have different properties, whether they replicate in distinctive ways, and whether they escape neutralising antibodies from people who have previously been infected, or from others who have been vaccinated”, said Palmarini. The Brazilian, UK, and South African variants do not seem to be associated with more severe disease. The G2P Consortium will look

for signs of different pathogenesis in experimental models.

“Any given variant will have several mutations, and we can make educated guesses as to which of these will be important”, said Palmarini. “However, we need experimental data to determine which mutation or combinations of mutations lead to particular phenotypes.” The goal is to arrive at a point at which the researchers can identify mutations of concern. The spike protein is crucial, given its interaction with the immune system and its role in the vaccines, but the viral phenotype can also be driven by mutations in other proteins.

Martin Hibberd, professor of emerging infectious diseases at London School of Hygiene & Tropical Medicine, London, UK, welcomed the initiative. “It is great to see a serious attempt to try to understand these variants”, he told *The Lancet*. The potential for vaccine escape is a major issue, although Hibberd points out that the existing variants have evolved in relation to transmissibility, rather than in response to the vaccines. He added that adjusting mRNA vaccines such as the Pfizer and Moderna products when necessary should be relatively straightforward.

The consortium’s work will entail creating standardised versions of SARS-CoV-2, with or without each mutation, and observing how the virus’s behaviour changes. It is a huge task. But as countries around the world prepare to roll out the COVID-19 vaccines, it is essential to get an idea of how the virus is changing. “The more we integrate the epidemiological data with laboratory experimental data on the strains and mutations, the more we increase our ability to predict what this virus will do”, said Palmarini.

Talha Burki