

## Monitoring SARS-CoV-2 variants: how and why?

Press release of the French National Academy of Medicine

March 16, 2021

Since the start of the Covid-19 pandemic, SARS-CoV-2 had acquired a reputation for a low variability, the only event that caught the attention of virologists being the D614G mutation that appeared at the end of January 2020, giving rise to the more infectious and transmissible variant that, in six months, replaced worldwide initial strain identified in Wuhan. This relative stability has been challenged since December 2020 by the emergence of variants from different lineages of SARS-CoV-2. The three main variants (variants of interest) are the 501Y.V1 "British" variant, the 501Y.V2 "South African" variant and the 501Y.V3 "Brazilian" variant. Carrying several mutations, mainly in the "S" (spike) protein, these variants have a better transmission potential and are supplanting the SARS-CoV-2 strain that had been circulating for 10 months. In France, the 501Y.V1 variant is suspected in 66% of the cases and the 501Y.V2 and 501Y.V3 variants in more than 5 % of the cases, exceeding 45% in Moselle [1]. This pattern is very heterogeneous across the country, with a high prevalence of variants often correlated with a high incidence rate, except in some regional departments.

The emergence of multiple variants, which occurs independently in several parts of the world, is a new challenge in the fight against the pandemic, while vaccination is being developed throughout the world. The selection of these variants is thought to be facilitated in immunocompromised patients, in whom the infection is more prolonged and viral loads higher, when they are treated with convalescent serum [2].

The impact of these new variants, which have become dominant in the current epidemic landscape, remains to be clarified, but several threats must already be considered: in addition to their greater contagiousness, it seems that the 501Y.V2 and 501Y.V3 variants, which carry the same E484K mutation, have the capacity to escape, at least partially, to the immune response induced by vaccination. Some mutations also affect genes encoding viral proteins other than S protein and could lead to increased virulence in some variants. It is therefore necessary to intensify the epidemiological surveillance of this epidemic at the

molecular level to detect the presence of new more pathogenic viruses escaping vaccine immunity. The two methods available are the targeted RT-PCR, which detects variants of interest with known mutations, and the sequencing (of the whole genome or of the gene encoding S protein), that identifies known or unknown variants. The sequencing data can be used for molecular epidemiology and viral phylo-dynamics that is analyzing the geographical factors of propagation of the different variants over the territory (climates, population densities, international exchanges, etc.).

Concerned by the progression of SARS-CoV-2 variants, whose worsening could jeopardize the effectiveness of the national vaccination campaign, **the French National Academy of Medicine recommends:**

- to increase the vaccination coverage against Covid-19 as quickly as possible;
- to intensify the application of barrier measures by recalling that they are still effective in preventing the transmission of the different variants of SARS-CoV-2;
- to strengthen high-throughput sequencing capacities to maintain the permanent monitoring of representative samples of human and environmental origins (wastewater);
- to develop molecular phylo-dynamics techniques applied to SARS-CoV-2 by cross-comparing genomic analyses with international epidemiological data;
- to share all the data collected by public and private institutions by considering them as public goods to be shared by all the research structures involved in the fight against the pandemic;
- to stimulate the research and development effort about variant-vaccine, particularly within the framework of the European HERA incubator program.

[1] Advice from the Scientific Council of February 12, 2021: "South African variant" 501.YV2 and departments in Eastern France.

[2] Kemp SA et al. SARS-CoV-2 evolution during treatment of chronic infection. Nature. 2021 Feb 5.