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.

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EDITORIAL

The evolution of SARS-CoV-2 variants and their clinical and healthcare implications☆

La evolución en variantes del SARS-CoV-2 y su repercusión clínica y sanitaria

It is well-documented that genetic expression is the most complex and varied process in the various animal viruses[1]. It is an issue of special focus for virologists and as a consequence, it is one of the most studied and better-defined areas, with widespread repercussions on clinical pathology.

Viruses develop a multitude of strategies to achieve the expression of their genes and efficient replication of their genomes. To do so, they depend on the possibilities offered by the parasitized cells[2]. From a practical point of view, they have short generation times and, at least in the case of RNA viruses, have replication enzymes that are prone to making mistakes. In consequence, they evolve much more quickly than other organisms, which provides unique opportunities to study changes in circulating virus populations[3].

Though SARS-CoV-2 undergoes mutations every time it performs an intracellular replication process, the stability of its sequence is greater than that of other riboviria because it has an intrinsic error correction mechanism. This is based on a protein codified in the ORF1ab gene called nsp14 (ExoN), with 3′–5′ exonuclease activity that maintains stability of the virus genome by minimizing modifications. Therefore, coronaviruses generally accumulate mutations much more slowly than other RNA viruses[4]. Even still, genomic variation regarding complete genomes, analyzed according to place and time, allow for analyzing the chain of transmission of isolates.

In the process of host cell recognition, SARS-CoV-2 uses the S protein, which binds to the host cell's angiotensin-converting enzyme 2 receptor[5]. In addition, this protein, and in particular the S1 subunit, has a receptor-binding domain that is an essential element with regard to inducing an immune response to both natural infection and vaccination strategies[6,7]. It has been noted that variability in the gene that codifies this protein would affect both vaccine effectiveness, the response to the use of monoclonal antibody therapies, and innate immunity[8].

The study of evolution by means of SARS-CoV-2 genome sequencing in order to quickly identify substitutions, insertions, or deletions that may induce a change in viral behavior is an essential task in monitoring the pandemic and its consequences for clinical management and the approach to prevention. This task includes at least five areas[9].

First, it is important to describe phenotypic modifications that lend the virus greater capacity for transmission and, in consequence, increase the speed of its spread. Second, it is necessary to determine its pathogenic power in terms of severity and thus define its potential to cause not only infection, but also to cause disease and lead to severe illness and death. Third, its interference in the immune response after natural infection and in various vaccination models should be defined. Fourth, it should be evaluated whether they entail some type of change in the use of diagnostic tests, whether these tests are direct, based on antigen detection or molecular techniques, or indirect, which indicate the innate or adaptive response. Lastly, its repercussions on treatment with antivirals or monoclonal antibodies prescribed to those infected or those who have the disease should be established.

A temporal description of virus mutations in different geographical areas can contribute to monitoring its propagation and determining possible routes and dynamics of transmission. It is possible to reconstruct a pathogen's evolutionary history by means of phylogenetic and phylodynamic studies that generate information which serve to guide the healthcare response to epidemic outbreaks and pandemics. In this scenario, massive sequencing and bioinformatics emerge as essential elements for its study[10].

After having designated variants in accordance with their geographical origin, in order not to stigmatize countries or areas of the planet, an agreement was adopted to establish their names using letters of the Greek alphabet[11], as is

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done in other sciences. Thirteen variants have been designated to date: alpha (B.1.1.7), beta (B.1.351), gamma (P.1), delta (B.1.617.2), epsilon (B.1.427/B.1.429), zeta (P.2), eta (B.1.525), theta (P.3), iota (B.1.526), kappa (B.1.617.1), lambda (c.37), mu (B.1.621), and omicron (B.1.1.529).

The first recognized variant appeared in September 2020 and was designated the British or alpha variant (B.1.1.7). It was described as a ''variant of concern'' (VOC) on December 18, 2020. Two other variants from Commonwealth countries caused high levels of concern. They are the South African or beta variant (B.1.351), which was detected in May 2020 and designated a VOC on January 14, 2021, and the first Indian or delta (B.1.617.2) variant, which was detected in October 2020 and designated a VOC on May 6, 2021. It displaced the alpha variant in our country during the summer of 2021 and became responsible for practically 100% of cases. In addition to these three VOC, the Brazilian or gamma variant (P.1), first detected on January 6, 2021, merits mention. It has not spread as extensively worldwide and is the only one of these four that had its origin outside of countries of British influence.

The new South African strain called omicron (B.1.1.529) emerged on November 9, 2021 and was designated a VOC by the WHO on November 24. Experts predict its spread given the large number of mutations that have accumulated in the gene that codes the spike (between 26 and 32). In this regard, it must be clarified that although a set of mutations defines a line, different genomes of a single strain contain mutations that differentiate them. In fact, two sublines of this new omicron variant have already been proposed: BA.1 and BA.2, with 20 and 27 characteristic mutations, respectively. It is notable that the new BA.2 subline does not have the 69/70del deletion and therefore, it is not detectable due to a failure in the S gene target used in the PCR detection system.

Though it is true that the importance of this new variant will be determined by the repercussion it has on the five aforementioned areas, the real evaluation of its impact on the disease and public health requires a certain amount of time and the launch of cohort studies that allow for adding knowledge in this field.

Meanwhile, in our setting, continuing with established vaccination plans and maintaining the healthcare measures of precaution, social distancing, and healthcare where required will be decisive[12]. At the same time, we must not overlook the profound changes in the composition of the virus' genome that condition its structure and functionality, given that they will cause the current vaccines and acquired immunity to lose effectiveness[13]. Therefore, it is necessary to minimize virus replication by limiting new infections, maintain virological surveillance of cases by means of massive sequencing and reporting of the results[14], and promote the development of effective antiviral treatments as much as possible.

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