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SARS COV-2 GENOME AND IT'S ROLE IN PANDEMIC

Epidemiology

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ABSTRACT

For past two years, world has been fighting against Covid-19. Many vaccines have been developed across the world against it but mutations happening in its form have been a real concern which has lead to spread as well as 'waves' of pandemic. After its discovery in Wuhan, China, various genomic changes have happened in the original form of virus leading to origin of VOC (Variants of concern). Different VOCs have lead to many 'waves' in various countries. Genomic surveillance has played an essential role in identifying and monitoring novel variants in SARS-CoV-2 that have had a direct impact on the control and spread of the virus. Although there are many variants already detected, some of the variants which are not yet found out have to be isolated in time for prevention of future outbreaks of SARS CoV-2. For this, the co operation among countries is important to win the war against the invisible enemy

KEYWORDS

SARS -COV-2, VOC, Mutation

Viruses are constantly changing, and this includes SARS-CoV-2, the virus that causes COVID-19. These genetic variations occur over time and can lead to the emergence of new variants that may have different characteristics.

The SARS-CoV-2 genome encodes instructions organized into sections, called genes, to build the virus. Scientists use a process called genomic sequencing to decode the genes and learn more about the virus. Genomic sequencing allows scientists to identify SARS-CoV-2 and monitor how it changes over time into new variants, understand how these changes affect the characteristics of the virus, and use this information to better understand how it might impact health.

Researchers isolated the virus causing the pneumonia in December 2019 and found it to be a strain of β-coronavirus (CoV). The virus showed a high nucleotide sequence homology with two severe acute respiratory syndrome (SARS)-like bat coronaviruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21 (88% homology) and with SARS-CoV (79.5% homology), while only 50% homology with the Middle East respiratory syndrome coronavirus (MERS) CoV. The virus, now named SARS-CoV-2, contains a single positive stranded RNA (ribonucleic acid) of 30 kilobases, which encodes for 10 genes.Researchers have shown that the virus can enter cells by binding the angiotensin-converting enzyme 2 (ACE2), through its receptor binding domain in the spike protein

Mutations are changes in the genetic code of a virus that naturally occur over time when an animal or person is infected. While a certain amount of genetic variation is expected to occur as SARS-CoV-2 spreads, it's important to monitor circulating viruses for key mutation(s) that happen in important regions of the genome. Many mutations do not affect the virus's ability to spread or cause disease because they do not alter the major proteins involved in infection; eventually these are outcompeted by variants with mutations that are more beneficial for the virus

Community transmission of the virus, as well as anti-viral treatments, can engender novel mutations in the virus, potentially resulting in more virulent strains with higher mortality rates or emergence of strains resistant to treatment. Therefore, systematic tracking of demographic and clinical patient information, as well as strain information is indispensable to effectively combat COVID-19.

SARS-CoV-2, like all viruses, accumulates mutations – changes in its genetic code – over time as it replicates. This virus has inherent RNA repair mechanisms, and therefore accumulates mutations at a relatively slower rate than most other RNA viruses. On average, a genome from a virus collected in October 2020 has around 20 mutations compared to the first strain sequenced in January 2020 (Wuhan-Hu-1) ; the virus evolves at a rate of ~ 1.1×10^{-3} substitutions per site per year, corresponding to one substitution every ~11 days.

This compares to a rate of ~ 4×10^{-3} substitutions per site per year for the HIV virus . Across all virus genomes sequenced to date, thousands of mutations have emerged since the start of the pandemic, which in turn have given rise to thousands of different variants. The majority have had no perceivable impact on the virus or disease biology and can act as a useful genetic 'barcode' for tracking viral spread and evolution. However, more recently, several variants have been identified that appear to increase transmissibility, and potentially have an impact on disease severity. As a result, they have been labelled VOCs. Currently, four internationally confirmed VOCs have been identified − B.1.1.7, B.1.351, P.1 and Cluster 5 . These are the best characterized and studied so far, and there is supporting evidence of an impact on virus biology available from several countries. As the pandemic continues to unfold, it is likely that more VOCs will be identified, particularly in the presence of new selection pressures, such as vaccination

Genomic data is essential in supporting the identification of VOCs and having an effective genomic surveillance system in place can allow VOCs to be identified as rapidly as possible. Both the United Kingdom and South Africa, where VOCs have been identified, established genome sequencing initiatives early on in the pandemic: COG-UK and NGS-SA, respectively. Surveillance systems in Denmark, The Netherlands and Japan also contributed to the identification of VOCs. In the UK, the B.1.1.7 variant was first identified as a VOC by COG-UK in December 2020, as it was increasing in frequency during a nationwide lockdown, whilst other variants were decreasing in frequency. A retrospective examination of the data determined that the variant had been in circulation since September, but at that time there were insufficient data to suggest that it was a VOC. The B.1.1.7 variant is currently the most highly sequenced and well-characterized VOC, and has been shown to have increased levels of transmissibility at a rate of between 40 and 70% . In addition, a paper from the New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) and presented to the UK Government's Scientific Advisory Group for Emergencies (SAGE) outlined the results from several preliminary analyses of B.1.1.7, suggesting that there could be an increase in mortality rates as a result of the variant . The COG-UK mutation tracker outlines the spike protein mutations seen circulating in the UK .

It also details the scientific evidence to date on the impact of different mutations on immune evasion. In South Africa, the B.1.351 variant was identified after frontline clinicians alerted NGS-SA to a rapid increase in cases, which prompted genomic investigation. The B.1.351 variant is a concern as it has been shown to have increased transmissibility and to reduce the efficacy of some vaccines . For B.1.351, there may be some form of enhanced escape from immune pressure and onward transmission, generating a fitness advantage, but the evidence for this is still weak . In the case of the P.1 variant, Japan reported the variant via their surveillance system, after detection in four travellers who had returned from Brazil . The variant was flagged to be of concern due to the presence of spike mutations also found in the B.1.351 variant: N501Y (which increases virus binding affinity to the ACE2 receptor on human cells), E484K (which renders the virus less susceptible to some monoclonal antibodies) and K417N/T (suggested to increase binding affinity to ACE2, in combination with

N501Y). The set of mutations/deletions, especially N501Y, shared between the P.1, B.1.1.7 and the B.1.351 variants appear to have arisen independently.

P.1 and B.1.351 also appear to be associated with a rapid increase in cases in locations where COVID-19 disease rates were previously high. Therefore, it will be crucial to investigate whether there is an increased rate of recent re-infection, caused by these variants, in previously exposed healthy individuals. The fourth variant, Cluster 5, was a VOC identified on mink farms in Denmark and the Netherlands. Swift action from local public health authorities in these countries stopped the spread of this VOC, and it is now believed to be extinct. Ongoing monitoring of variants B.1.1.7, B.1.351 and P.1 is being carried out globally. However, B.1.617 had spread quickly in India. It was dominant strain in various states in 2nd wave. The "double mutant" is a bit of a misnomer, because it actually carries 13 mutations, 7 of which are in the spike protein. But the moniker comes from two notable mutations found in other variants that appeared together for the first time in this new strain: the L452R mutation and the E484Q mutation. The E484Q mutation is notable because it appears to be very similar to the E484K mutations found in the B.1.351 (South African) and P.1 (Brazilian) variants

Genomic surveillance has played an essential role in identifying and monitoring novel variants in SARS-CoV-2 that have had a direct impact on the control and spread of the virus. A range of public health measures have been implemented globally as a result of new information on variant transmissibility. In addition, the genetic data produced from surveillance has enabled further in-depth characterization of the variants to determine more precisely the roles of mutations, either individually or in combination, on virus biology. This information is, in turn, essential for informing future surveillance efforts, as well as identifying the impact mutations may have on vaccines, diagnostics, and therapeutics. Multiple countries around the world have invested in genomic sequencing infrastructure and resources, in recognition of the fact that genomic surveillance forms the basis of a robust national and international response to infectious disease. The surveillance systems established so far represent an important step towards global genomic surveillance, but there remain areas of the world with a paucity of genomic data, despite high numbers of cases. There are likely to be many more variants of SARS-CoV-2 circulating globally, but countries with robust and routine genomic surveillance strategies are more likely to detect them. Moreover, the identification of a variant in a particular jurisdiction does not necessarily mean that the variant arose there.

It is therefore essential that infrastructure and resources are developed in countries where currently little or no sequencing is being carried out, and efforts must continue to be made to share data as swiftly and openly as possible. Initiatives such as the recently announced 'New Variant Assessment Platform' launched by the UK, could help support countries with limited resources to detect SARS-CoV-2 variants. Genomic surveillance during the pandemic is an international effort and will be more effective if capabilities in this area are more evenly distributed globally. This will include ongoing support of data sharing through accessible international databases. While there is a general need to increase the number and representativeness of the viral samples that are being sequenced, well-planned methods for sample selection and production of high-quality genomic sequences can provide valuable insights in countries where there are limited sequencing capabilities. New SARS-CoV-2 variants will continue to arise as a result of the natural evolution of the virus, and potentially also in response to vaccination and other measures. Despite the increasing availability of vaccines, it will remain vital to ensure that the number of infections in populations are limited by ongoing public health measures, not least to reduce the likelihood of additional VOCs arising. The availability of viral genome sequencing data to understand ongoing changes in the viral genome will become increasingly important as SARS-CoV-2 vaccines and antivirals become more widely used

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