

Mini Review

Variant Found in Brazil can Reinfect Sars-Cov-2 Survivors and could Evade Immune System from Past Infection: A Mini Review

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Introduction

The world has been the stage for a new coronavirus, officially named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing the coronavirus disease 2019 (COVID-19) [1]. The result of the rapid and uncontrolled epidemic, countries healthcare systems have shown different reactions in surveillance, diagnosis, and treatment. In the First Year of Global Pandemia, more than 121 million cases have been confirmed by the World Health Organization, with more than 2.6 million deaths registered worldwide [2]. Since the emergence of coronavirus disease 2019 (COVID-19) pandemic, efforts are continuously being made to sequence the SARS-CoV-2 genome and examine potential viral mutations. Some potential spike mutations have been identified in recently emerged variants of SARS-CoV-2 (the UK, South African, and Brazilian variants) that can significantly increase viral infectivity. A growing pool of evidence also indicates that some of these variants can evade host cell humoral immune responses induced by natural infection or vaccination. In the context of COVID-19, it has been observed that, unlike relatively short-lived anti-SARS-CoV-2 antibody responses, T cell-mediated adaptive immune responses provide robust and long-lasting protection against SARS-CoV-2. This suggests the need for developing new COVID-19 vaccines with specific peptides that can induce appropriate T cell responses against SARS-CoV-2. The purpose of the present review is to summarize our understanding of Brazilian Variant of Sars-Cov-2, bringing current evidence of the potential mechanisms of evade immunity from past infection.

Keywords: Evade immunity; Reinfection Sars-Cov-2; Variant found Brazil

The P.1 Lineage of the SARS-CoV-2 Variant First Observed in Brazil has Driven a Second Wave of Infections Even in a Region Hit Hard by the First Wave

The findings, which may point to risk of re-infection

or increased transmissibility, come from researchers at the University of São Paulo in collaboration with Imperial College London and the University of Oxford [3].

P.1 Lineage Around the World

Despite very high infection rates in the Amazon region, a second wave of infection hit in Manaus, Brazil between December 2020 and January 2021. Genomic sequencing of clinical samples from Manaus found that this second wave was associated with the emergence and rapid spread of a new Variant of Concern (VOC), the P.1 lineage. Statistical analysis of genome data suggests that the P.1 lineage has likely been circulating in Manaus since early November 2020. This lineage has been identified in over 20 countries worldwide and continues to spread, including several recently confirmed cases in the UK.

P.1 Background

Global collaborative efforts on rapid virus genome sequencing are allowing us to identify SARS-CoV-2 lineages of concerns in near real-time. Several genetic changes - substitutions and deletions - in this new P.1 lineage may have immunological significance. The team identified 17 mutations for this VOC, including a trio in the spike protein (K417T, E484K and N501Y) have been evidenced in previous studies to promote antibody resistance, and the N501Y mutation is thought to increase binding affinity to the angiotensin-converting enzyme 2 (ACE2), which is how SARS-CoV-2 enters and infects host cells. Both the South African and UK variants have this N501Y mutation, but the former also contains a K417N and E484K mutation. Using analysis of genome sequence data, researchers were able to date back the emergence of the P.1 VOC to early November 2020.

The research team tested the effectiveness of convalescent blood sera against the P.1 variant, as well as the effectiveness of the Oxford-AstraZeneca and Pfizer-BioNTech vaccines. Immune evasion responses to these were also compared to that of the

original Wuhan strain, and the South African and UK strains of SARS-CoV-2.

The team observed that P.1 could fully escape neutralization from a large number of common antibodies found in convalescent plasma that are effective against the ancestral virus. A similar reduction in effectiveness was also observed in the B.1.1.7 and B.1.351 variants, although the latter showed greater immunity than the former two.

The researchers also demonstrated that P.1 had greater ACE2-RBD binding efficacy than the ancestral model, but describe how one monoclonal antibody, mAb 222, was especially potent against the variant. mAb 222 contacts both the K417 and N501 regions of the virus, and resists the mutations found in the P.1 and B.1.351 viruses in that region (501Y and 417T/N, respectively). The team found that this is possible due to the light chain of the antibody. Antibodies are comprised of two immunoglobulin heavy chains and a single light chain. The two heavy chains define the class of the antibody, and act as the binders to antigens. The light chain subunit connects the two heavy chains. The research team restored the neutralizing ability of certain antibodies by swapping the light chain with the one present on mAb 222.

What are the Implications?

The researchers [4] report that P.1 resists many antibodies associated with ancestral SARS-CoV-2 immunity, although it has a lower degree of resistance than B.1.351. Monoclonal antibody 222 neutralizes all three variants of concern, and the light chain of 222 can restore the neutralizing ability of SARS-CoV-2 antibodies for mutated strains of the virus. The restoration of antibody effectiveness has broad implications for current vaccine programs; it may allow for effective vaccine boosters for all three variants mentioned here, and potentially any future variants that may arise in the future with antibody-resistant mutations. The authors caution that their investigation fails to account for the effectiveness of antibody-dependent cell-mediated cytotoxicity, which may affect neutralization of the virus in vivo – this experiment was all performed in vitro [4,5]. However, the team encourages further investigation of cross-protective measures against multiple COVID strains.

How Transmissible and Resistant is the SARS-CoV-2 Brazilian Variant to Antibodies?

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What is Unique About the P.1 Lineage?

The P.1 lineage has an unusually large number of mutations in comparison with previously circulating variants, including three mutations of interest located in a region of the spike protein that interacts with the receptor the virus uses to enter human cells.

For how Long has the P.1 Lineage Circulated Undetected?

The first confirmed infection was on 6 Dec 2020. However, based on statistical analysis of genome data, the researchers estimate that the P.1 lineage has likely been circulating in Manaus since early November 2020.

Is the P.1 Lineage More Transmissible Compared to Others?

Based on what is known so far, the researchers estimate the P.1 lineage is 1.4 to 2.2 times more transmissible. This might change over time.

Is the P.1 Lineage Better at Escaping Immunity Compared to other Lineages?

Partial immune escape is likely. It is not possible to provide an exact figure but it is estimated that P.1 evades between 25 and 61% of immunity conferred from prior infection with previously circulating strains. What this means is that 100 people previously infected with non-P.1 SARS-CoV-2 lineages that circulated in Manaus, between 25 to 61 of them could be re-infected if they are exposed to P.1 in Manaus.

Is the P.1 Lineage More Deadly Compared to Other Lineages?

The study found P.1 is associated with a 1.1-1.8 times increase in risk of mortality compared to previously circulating variants in Manaus. However, the health system in Manaus collapsed during this second wave and so it is unclear whether the increased risk of mortality is due to P.1 or the strain on the health system imposed by the large second wave. Uncertainty surrounding this effect and how it generalises outside the context of Manaus is therefore considerable.

How Quickly Does the Virus Change?

At the moment we find it acquires one or two new mutations a month. The speed of change of virus mutations is related to the number of cases in the world - the more we bring down the case numbers, the slower the virus will mutate.

Will Vaccines Still Protect Us From Infection with the P.1 Lineage?

Vaccines can protect from infection and protect from disease or death. This study shows evidence that the virus may cause more severe disease. However, this study only considered

acquired immunity and did not study vaccine effectiveness. There is no evidence that the current vaccines are less effective against the P.1 lineage.

Conclusion

SARS-CoV-2 has continued to spread across the world, infecting millions of individuals in the process. Global collaborative efforts on rapid virus genome sequencing are allowing us to identify SARS-CoV-2 lineages of concerns in near real-time. Yet, uncertainty in the ways SARS-CoV-2 is changing and implications for vaccine design calls for much more sequencing and analysis of virus genomes globally.

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