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T cells face off against variants to boost COVID-19 immunity, study finds

With the fight against COVID-19 beset with concerns around the efficacy of vaccines in the face of a mutating virus, University of Cape Town (UCT) virologists have shown that the body's T cells maintain 85% of their capacity to detect variants, continuing to mount a substantial defence to prevent severe illness, hospitalisation and death.

Although their work was focused on the Beta variant, the authors predict similar results in respect of Delta, which they are currently studying, and other future variants. Put simply, that's because the T cell response to infection with SARS-CoV-2 is far more multi-faceted than that of antibodies, providing a significant extra layer of protection against disease.

Growing fears around resistance of COVID-19 variants to antibody defences has sparked increased interest in the role of T cells, that other major part of the immune response. And it is here that lead authors Dr Catherine Riou and Associate Professor Wendy Burgers focused their attention for purposes of their study.

Burgers is an Associate Professor in the Division of Virology, in UCT's Institute of Infectious Disease and Molecular Medicine (IDM). She says the arrival of the Beta variant caused considerable alarm, especially at a time when the first vaccines were being administered on the back of favourable research results.

"We realised that SARS-CoV-2 can mutate, and the big question was how that might impact immunity, and affect vaccines. While vaccines provide us with a way out of the pandemic, we realised that there were still substantial obstacles ahead," Burgers recalls.

Riou, a senior research officer in the IDM, adds: "We knew that we needed to tackle this with major urgency, because Beta was the variant taking over in South Africa, and it was imperative for us to ascertain the implications for the immune response in people who had recovered from COVID-19, and what it meant for vaccines."

Still in revision, their paper, entitled *Loss of recognition of SARS-CoV-2 B.1.351 variant spike epitopes but overall preservation of T cell immunity*, determined two outcomes:

- That those who became infected with the Beta variant mounted as good a T cell response as those infected with the original version of SARS-CoV-2.
- While there was an average 15% reduction in the T cell response in those infected with the Beta variant, 85% of the cross-reactive response was retained.

T cells are the part of the body's immune response responsible for killing infected cells. So the T cells kick in following infection, complementing the antibody response – effectively offering a critical further layer of protection, including against the Beta variant, the research showed.

In COVID research globally, the T cell response has been less well examined than the antibody response, prompting IDM professorial director Professor Valerie Mizrahi to hail the study as a "real cross-disciplinary tour-de-force piece, led from UCT". The work also involved UCT Professors Ntobeko Ntusi, Robert Wilkinson and Carolyn Williamson, as well as collaborators from around the country.

Burgers says the complexity of the process required to measure the response of T cells in the blood, and because tests and analyses are both more complicated and more expensive, means that much less is known about what aspects of the T cell response actually provide protection.

But the uniqueness of South Africa's epidemic – with a first wave of ancestral, or original virus, followed by a second wave that was almost entirely Beta – gave the team the ideal opportunity to study immune responses in both the first and second wave.

Riou adds: "Our first focus was to ascertain whether people mounted the same T cell response to the mutated version of the virus as to the original. And we showed that they do, despite some loss of epitopes (small parts of the virus that infected cells 'present' to T cells so that they can recognise an infected cell, or provide 'help' to B cells to produce antibodies)."

On the likelihood of the result being similar for Delta and other variants, Burgers says this is the case because the mutations in the Beta and Delta variants are different; Delta is not a compound version of multiple variants. So while some of the epitopes in each variant may lose their ability to induce an immune response, the impact is not severe enough to compromise the ability of the T cell response to preserve overall immunity.

"This means that if a person becomes infected, or gets vaccinated against the original strain rather than any variant, we've shown that it's very likely that the vaccine will induce a similar response to Delta should that person encounter it."
Burgers and Riou are confident that existing vaccines will continue to protect populations from severe disease and hospitalisation, regardless of the COVID-19 variant involved.

"It's critical for people to understand that vaccines are still providing protection against severe COVID-19 disease, so they're doing their job against the variants, and likely will do so against future variants too," they stress.

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