Promising developments in pursuit to design pan-coronavirus vaccine

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Researchers at the Francis Crick Institute have shown that a specific area of the SARS-CoV-2 spike protein is a promising target for a pan-coronavirus vaccine that could offer some protection against new virus variants, common colds, and help prepare for future pandemics.

Developing a vaccine that provides protection against a number of different coronaviruses is a challenge because this family of viruses have many key differences, frequently mutate and generally induce incomplete protection against reinfection. This is why people can suffer repeatedly from common colds, and why it is possible to be infected multiple times with different variants of SARS-CoV-2.

A pan-coronavirus vaccine would need to trigger antibodies that recognize and neutralize a range of coronaviruses, stopping the virus from entering hosts cells and replicating.

In their study, published in *Science Translational Medicine* today, the researchers investigated whether antibodies that target the S2 subunit of SARS-CoV-2's spike protein also neutralize other coronaviruses. This specific area of the spike protein tethers it to the virus membrane and allows the virus to fuse with the membrane of a host cell.

The researchers found that after vaccinating mice with SARS-CoV-2 S2, the mice created antibodies that were able to neutralize a number of other animal and human coronaviruses, including the seasonal "common cold" coronavirus HCoV-OC43, the original strain of SARS-CoV-2, the D614G mutant that dominated in the first wave, alpha, beta, delta, the original omicron and two bat coronaviruses.

Kevin Ng, co-first author and Ph.D. student in the Retrovirus laboratory at the Crick says: "The S2 area of the spike protein is a promising target for a potential pan-coronavirus vaccine because this area is much more similar across different coronaviruses than the S1 area. It is less subject to mutations, and so a vaccine targeted at this area should be more robust."

George Kassiotis, corresponding author and principal group leader at the Crick, says: "The expectation for a vaccine that targets the S2 area is that it could offer some protection against all current, as well as future, coronaviruses. This differs from vaccines that target the more variable S1 area which, while effective against the matching variant they are designed against, are less able to target other variants or a broad range of coronaviruses.

"There's a lot of research still to do as we continue to test S2 antibodies against different coronaviruses and look for the most appropriate route to design and test a potential vaccine."

The S2 area of the spike protein has, until recently, been overlooked as providing a basis for vaccination. This is because certain critical targets in the S2 area are only revealed after the virus has

bound to a cell, a process mediated by the S1 area. As a result, there may be a narrower window of opportunity for S2 antibodies to neutralize the virus than for antibodies that target the S1 area.

Nikhil Faulkner, co-first author and Ph.D. student in the Retroviral Immunology Laboratory at the Crick adds: "While a potential S2 vaccine would not stop people being infected, the idea is it would prime their immune system to respond to a future coronavirus infection. This would hopefully provide enough protection to survive an initial infection during which they could develop further immunity specific to that particular virus."

The researchers will continue this work studying the potential of a pan-coronavirus that targets the S2 area of the spike protein and how it could be integrated with currently licensed vaccines.

More information: Kevin Ng et al, SARS-CoV-2 S2-targeted vaccination elicits broadly neutralizing antibodies, *Science Translational Medicine* (2022). DOI: 10.1126/scitranslmed.abn3715. www.science.org/doi/10.1126/scitranslmed.abn3715

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