Study proposes new bioinformatic approach to design better vaccines

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Credit: National Cancer Institute

A new paper in *Biology Methods & Protocols,* published by Oxford University Press, shows it may be possible to design vaccines that will induce a stronger immune response to infecting pathogens, such as the virus causing COVID-19. In this study, the authors proposed and tested a new bioinformatic approach and tool that allows researchers to select parts of proteins that will elicit a strong immune response. Vaccines

developed based on this approach would provide better protection from diseases.

The immune system of humans (and other vertebrates) discriminates between self and non-self structures to attack and destroy the latter. T cells are the part of the immune system responsible for this recognition. They accomplish this by identifying peptides, short chains of amino acids, that are present in non-self proteins, for example, in proteins of a virus or a bacterium, but absent in proteins of a host, such as humans.

To avoid recognition by a host's T cells, parasitic organisms eliminate all unnecessary peptides from their proteins. In particular, they mutate these peptides to mimic those present in the proteins of their host species.

In this study, the researchers tested a critical prediction of peptide mimicry theory: they investigated whether they could predict the ability of a parasite's proteins to provoke an immune response based on the content of peptides absent in their host's bodies. Building upon earlier detailed mapping of T-cell clones related to SARS-CoV-2, they explored the intersecting points between the list of actual T-cell response targets and a list of potential T-cell recognition targets, peptides present in SARS-CoV-2 but absent in the human body.

Computer simulations showed that the actual T-cell recognition targets had a significantly higher proportion of pentapeptides and hexapeptides (peptides consisting of five and six amino acids respectively) not found in human proteins. The new method, grounded in immunological theory, was four times more efficient in detecting the targets in the case of SARS-CoV-2 than currently used methods based on empirical observations.

The authors believe the method will allow researchers to develop more effective vaccines, specifically designed to recognize and target the parts

of proteins of parasites that trigger the strongest immune responses.

"Our peptide mimicry theory, which delves into how a parasite adapts its peptide vocabulary to that of its host, began primarily as a fundamental research endeavor," said the paper's lead author, Jaroslav Flegr.

"However, as we've explored this topic, we've discovered that it might also have extensive practical implications, such as in the field of vaccine construction. We hope our findings will deepen our understanding of disease evolution and pathogen transmission and provide valuable insights in the enhancement of vaccine design and the broader fight against infectious diseases."

More information: Jaroslav Flegr et al, Exposing and Exploiting Host-Parasite Arms Race Clues in SARS-CoV-2: A Principally New Method for Improved T-cell Immunogenicity Prediction, *Biology Methods & Protocols* (2023). DOI: 10.1093/biomethods/bpad011 , academic.oup.com/biomethods/ar … 3/biomethods/bpad011

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