Quantitative biological strategy helps upgrade vaccines against COVID-19

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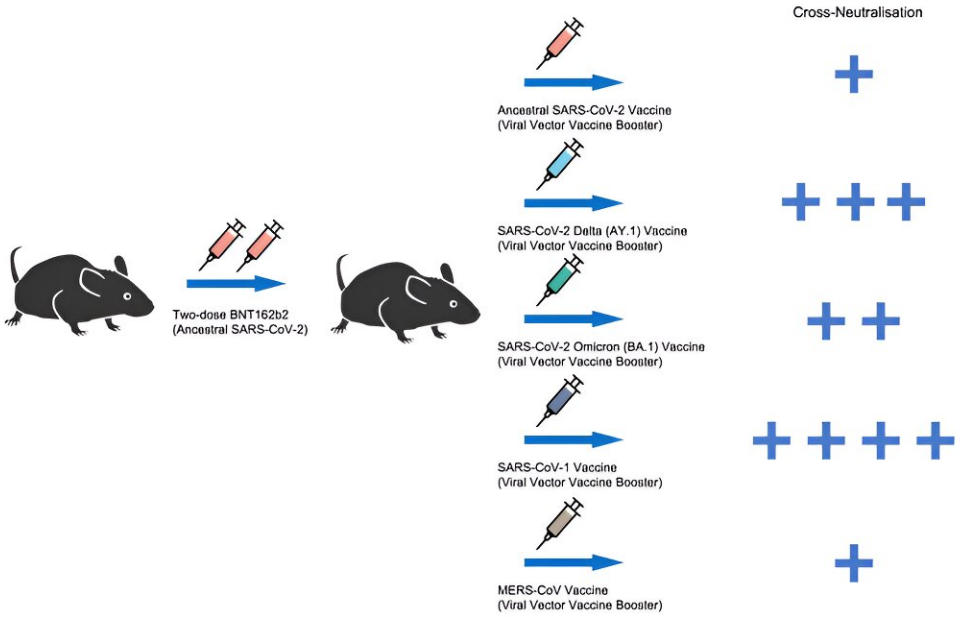

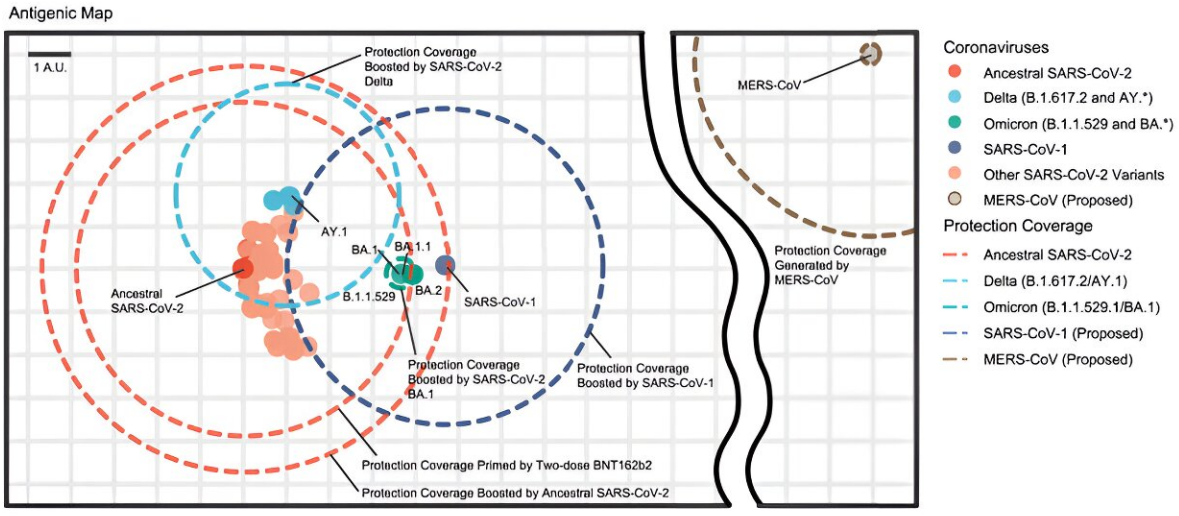

Credit: *Cell Host & Microbe* (2023). DOI: 10.1016/j.chom.2023.07.004

Researchers from the Shenzhen Institute of Advanced Technology (SIAT) of the Chinese Academy of Sciences (CAS) and the University of Hong Kong, along with their collaborators, have proposed a promising quantitative biological strategy for dynamic updates of vaccines against SARS-CoV-2 virus. They demonstrated that a vaccine based on the ancestral SARS-CoV-1 strain could offer more extended and broader protection than other options.

The study, titled "Rational design of a booster vaccine against COVID-19 based on antigenic distance," was published in *Cell Host & Microbe* on July 31.

Over the past three years, scientists around the world have developed vaccines against the virus. Initially, most vaccines demonstrated high effectiveness in preventing COVID-19, but the protection levels of all vaccines declined over time due to newly emerged variants. Thus, a COVID-19 booster shot is recommended to people who have already completed their initial vaccine series. Such a booster vaccine can increase immunity back to protective levels.

However, the process of developing and testing vaccines often lags behind the emergence of new variants. For example, the omicron strain (B.1.1.529/BA.1) surfaced in November 2021, but the second-phase clinical trial of the vaccine targeting the BA.1 strain began in February 2022. By April 2022, during the mid-term analysis, the strain had evolved into BA.2, and by September 2022, it had already become BA.5. The evolution of SARS-CoV-2 virus demands a new strategy for developing new vaccines to keep up.

Based on research and analysis of immune escape of SARS-CoV-2 virus, the researchers constructed an "antigen distance" model using existing neutralization and sequencing data. This model measured the degree of immune escape of different mutant strains based on the neutralizing abilities of human sera against various strains.

They plotted an antigen map of COVID-19 in terms of "antigenic distance" and explored the protection range of using different strains as booster vaccines, including the ancestral SARS-CoV-2 strain, the SARS-CoV-2 delta strain (B.1.617.2/AY.1), the SARS-CoV-2 omicron strain (B.1.1.529/BA.1), the SARS-CoV-1 strain, and the Middle East respiratory syndrome coronavirus (MERS-CoV) strain. The results demonstrated that a booster vaccine based on the SARS-CoV-1 strain might provide more extensive and durable protection against COVID-19 compared to the delta and omicron strains.

To validate their findings, the researchers conducted experiments using human serum samples, which confirmed the model's accuracy. Subsequently, they tested in a mouse model. The mice were given two doses of mRNA vaccine followed by booster shots based on different strains. The results showed that the SARS-CoV-1 booster shot outperformed other candidate vaccines in terms of specific antibody levels, neutralizing antibody levels, and protection durability. In live virus challenge tests, the SARS-CoV-1 booster also provided superior protection.

This study suggests that designing new COVID-19 booster shots based on "antigen distance" may be a valuable approach to tackle emerging SARS-CoV-2 variants.

More information: Ye-Fan Hu et al, Rational design of a booster vaccine against COVID-19 based on antigenic distance, *Cell Host & Microbe* (2023). DOI: 10.1016/j.chom.2023.07.004

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