

Hybrid Immunity Elicits Cross-Reactive Memory B Cells and Protects Against SARS-CoV-2 Omicron BA.1 Replication in Rhesus Macaques

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INTRODUCTION

- A combination of COVID-19 infection and vaccination, termed hybrid immunity, elicits greater immune responses than either alone.

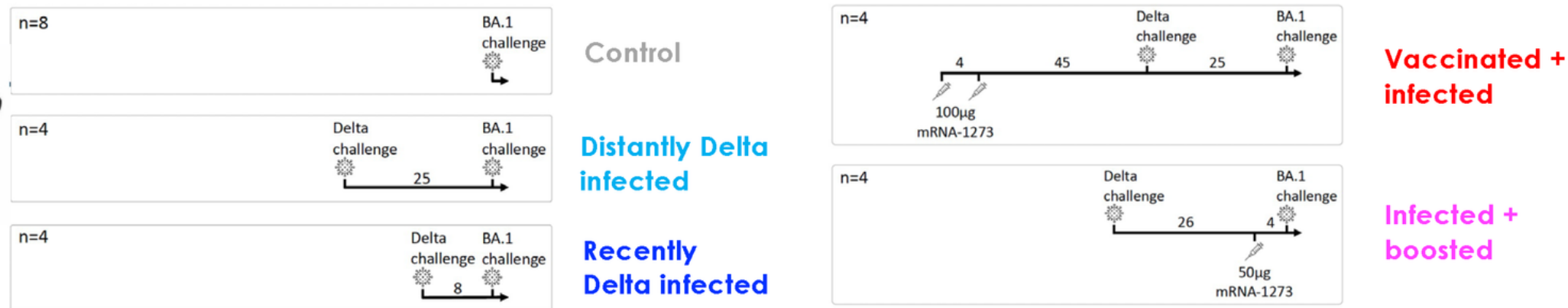
- Exposure to variant SARS-CoV-2 spikes after priming with ancestral spikes primarily elicits cross-reactive memory B cells, with limited *de novo* variant-specific B cell response.

- Therefore, the first SARS-CoV-2 antigens to which children are exposed are critical for determining their subsequent immune responses.

- Objective:** Determine immune responses to and protection from Omicron BA.1 virus replication in rhesus macaque nonhuman primates (NHP) with different antigenic exposure histories, including infection alone and a combination of vaccination and infection.



STUDY DESIGN

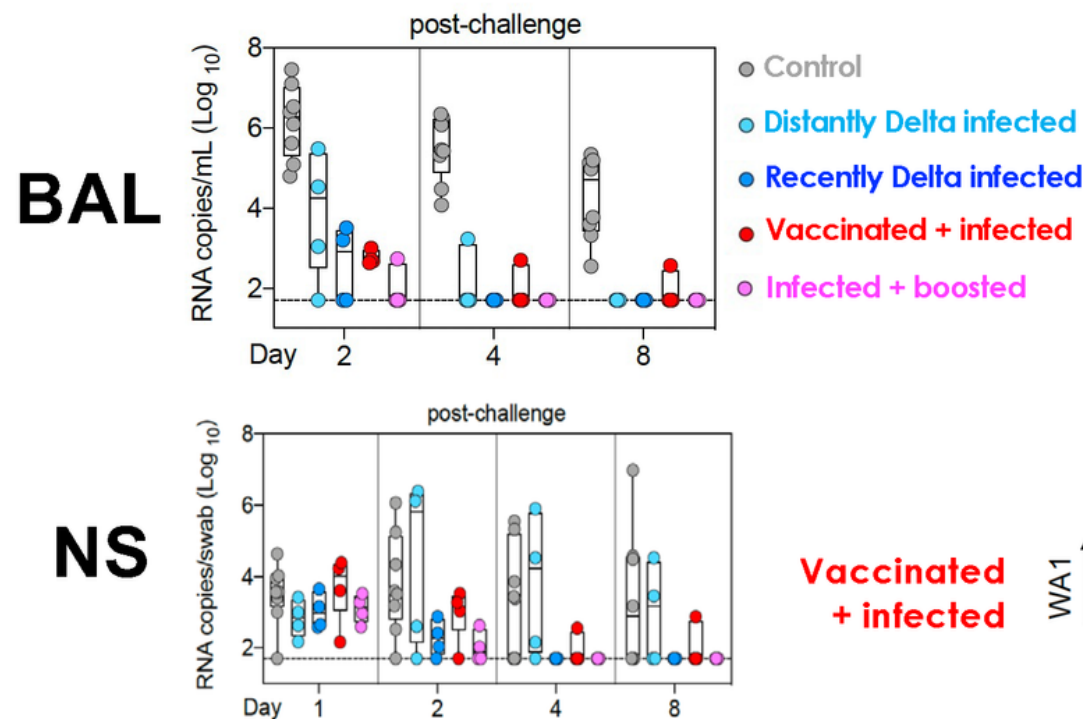


Numbers in diagram = weeks between antigenic exposures; n = number of NHP in each group.

CONCLUSIONS

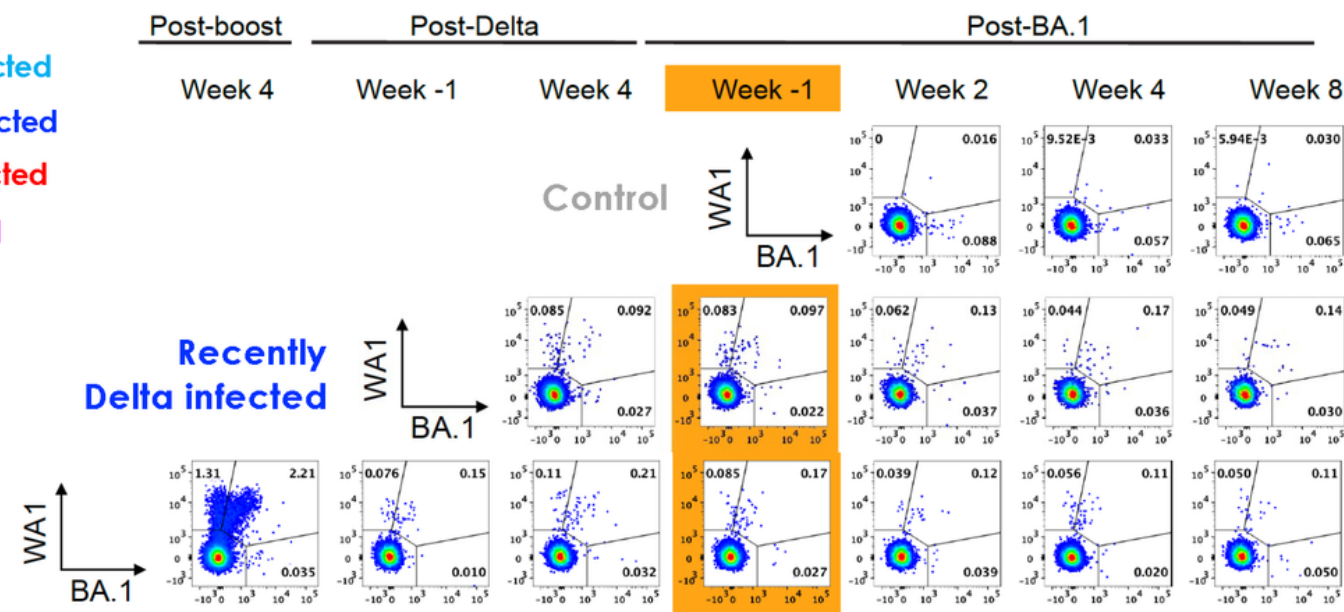
- Protection from virus replication elicited by infection alone wanes over time, indicated by lack of protection in nasal swabs (NS) in **distantly Delta infected** NHP.
- Forms of hybrid immunity (**vaccinated + infected** and **infected + boosted**) displayed superior protection than previous infection alone.
- BA.1 challenge in NHP with previous antigenic exposure (such as **recently infected** and **vaccinated + infected**) elicits primarily WA1 (ancestral SARS-CoV-2 Spike)-specific and WA1/BA.1 cross-reactive memory B cells. BA.1 challenge in previously naïve (**control**) animals elicits some BA.1-specific memory B cells.
- Superior protection from future Omicron sublineages may be achieved through the use of Omicron-specific or multivalent vaccines as a primary childhood immunization regimen. However, the future evolutionary path of the virus remains uncertain.

VIRUS REPLICATION



Hybrid immunity mediates protection from SARS-CoV-2 subgenomic RNA (sgRNA) in the lungs and nose of NHP. BAL = bronchoalveolar lavage; NS = nasal swabs.

MEMORY B CELL REACTIVITY



Memory B cell binding to WA1 (ancestral SARS-CoV-2) and BA.1 Spike S-2P probes.

