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

Christopher Cole Honeycutt, BS¹, Matthew Gagne, PhD¹, Lauren McCormick, BS¹, John-Paul M. Todd¹, BS, Shayne F. Andrew, BS¹, Kathryn E. Foulds, PhD¹, Robert A. Seder, MD¹, Daniel C. Douek, MD, PhD¹

¹Vaccine Research Center, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, 20892

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.

VIRUS REPLICATION

- BAL:
  - Control
  - Distantly Delta infected
  - Recently Delta infected
  - Vaccinated + infected
  - Infected + boosted

- NS:
  - Vaccinated + infected

MEMORY B CELL REACTIVITY

- 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.

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.

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