Spike plus Nucleocapsid Vaccine Protects against SARS-CoV-2 delta infection in rhesus macaques

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BACKGROUND

- Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2), emerged in late 2019 with subsequent rapid spread throughout the human population.
- There is a great need for the development of vaccines that induce broadly cross-reactive humoral and T cell responses especially in upper and lower airway mucosal tissue to fight against emerging SARS-CoV-2 variants of concern (VOCs) especially against the delta VOC that is most dominant in the world.
- Mucosal vaccination is most efficient at inducing mucosal antibody responses compared to systemic vaccination, however different routes of mucosal vaccination differ in their ability to induce mucosal immunity in different compartment.
- We previously evaluated MVA/S, an MVA-based SARS-CoV-2 vaccine expressing the full-length spike with two proline mutations (K986P/V937P, S-2P) to stabilize in its prefusion conformation. We showed that it was highly immunogenic in mice and was able to protect against WA-1/2020 infection in rhesus macaques (Routhu et al., 2021b).

OBJECTIVES

- Assessing immunogenicity and protective efficacy of MVA-based COVID-19 vaccine co-expressing prefusion-stabilized and furin cleavage inactivated spike and nucleocapsid (MVA/SdFCS-N) against SARS-CoV-2 B.617.2 (delta) in macaques.
- Investigating the oral (buccal- BU) or sublingual- SL) and systemic (intramuscular- IM) vaccination approaches for MVA-based COVID-19 vaccines in rhesus macaques.

Affiliations

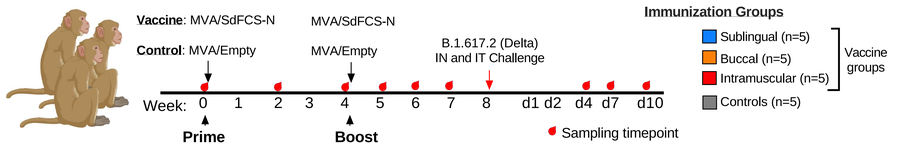
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Footnotes

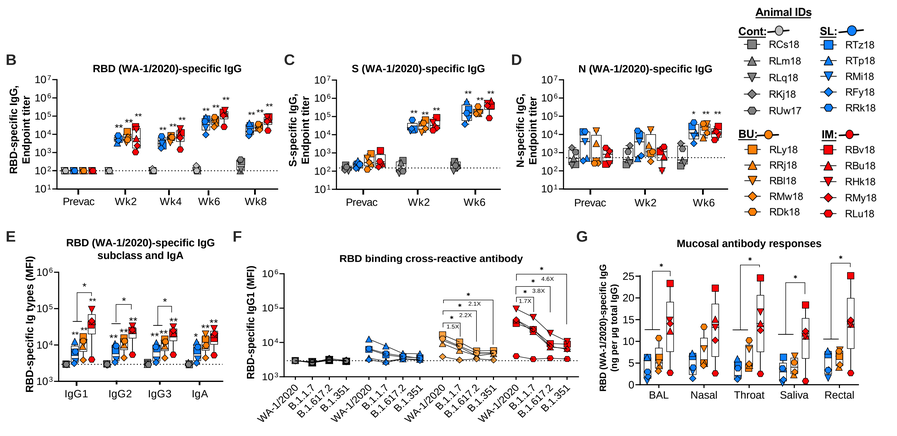
[†]Contributed equally to this work

Generated MVA-based COVID-19 vaccine co-expressing prefusion-stabilized and furin cleavage inactivated spike and nucleocapsid induces strong neutralizing antibody (nAb) responses and T cell responses in macaques protects macaques from heterologous SARS-CoV-2 (B.1.617.2) infection.

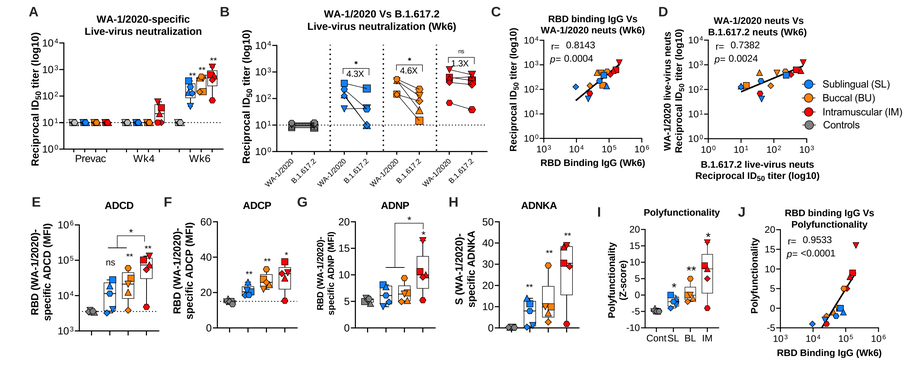
Schematic of immunizations and SARS-CoV-2 B.1.617.2 challenge in rhesus macaques



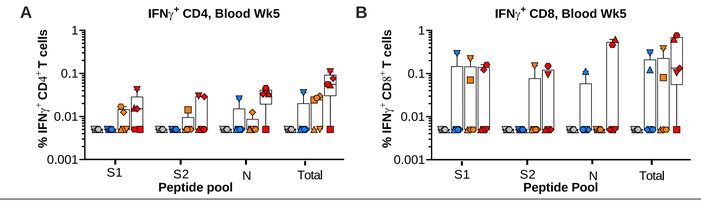
Intramuscular MVA/SdFCS-N vaccine induces strong and cross-reactive binding antibody responses in systemic and mucosal compartments of macaques



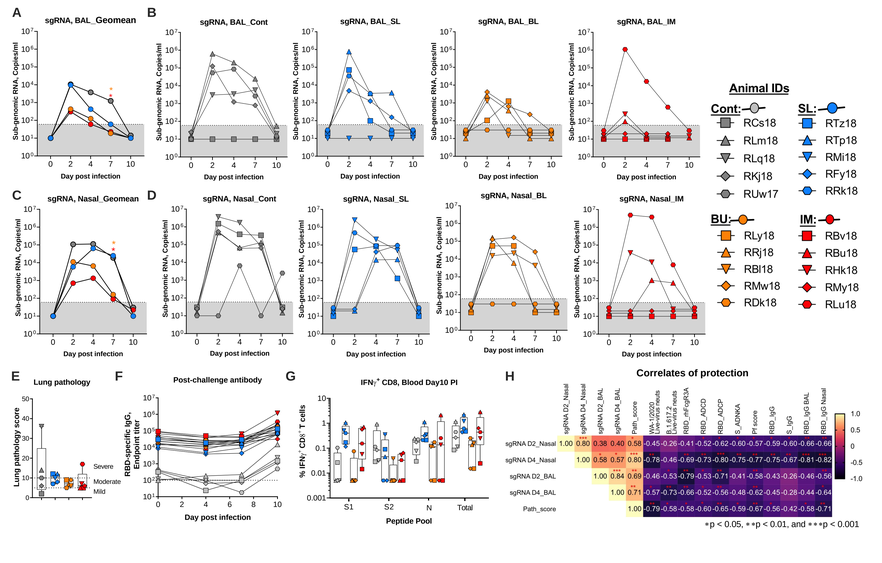
Intramuscular vaccination induces greater poly-functional antibodies in serum of macaques



MVA/SdFCS-N vaccine induced S and N-specific CD4 and CD8 T cell responses



MVA/SdFCS-N vaccination protects against B.1.617.2 infection in macaques



*p < 0.05, **p < 0.01, and ***p < 0.001

CONCLUSIONS

Our findings showed that IM vaccination with improved MVA-based SARS-CoV-2 vaccine elicits cross-reactive antibody and T cell responses and protect against heterologous SARS-CoV-2 Delta challenge in RMs. They also showed IM vaccinations are superior to oral vaccinations.

FUNDING

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