MVA-vectored multi-antigen COVID-19 vaccines induce protective immunity against SARS-CoV-2 variants spanning Alpha to Omicron in preclinical animal models

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Outline

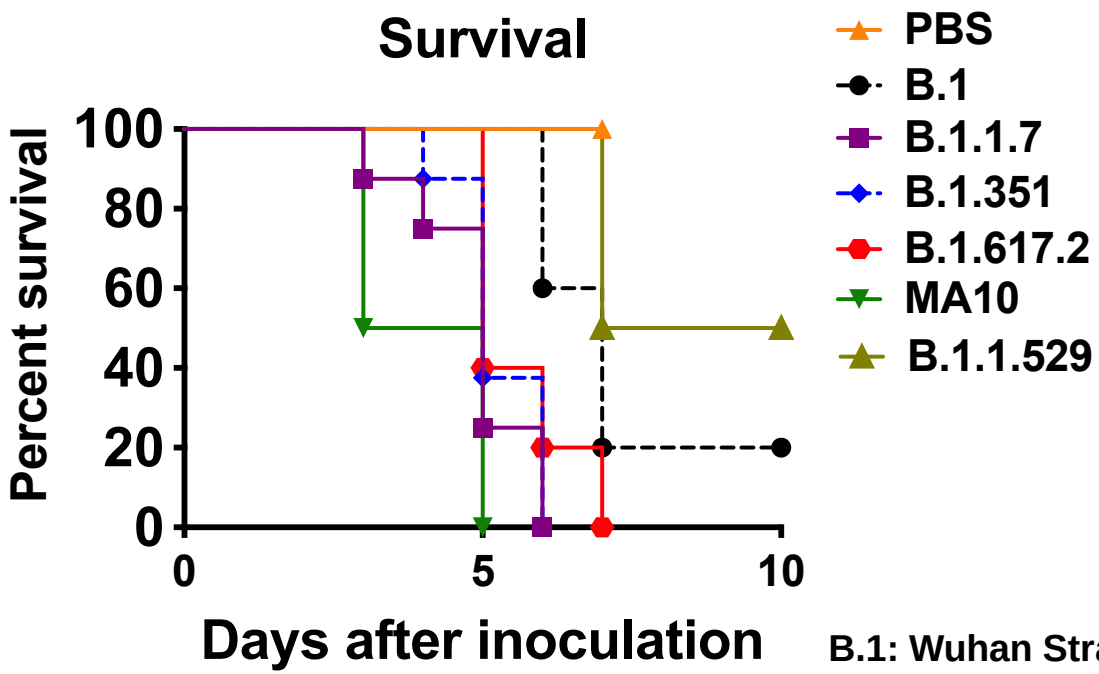
- **K18-hACE2 mouse model of SARS-CoV-2 infection**

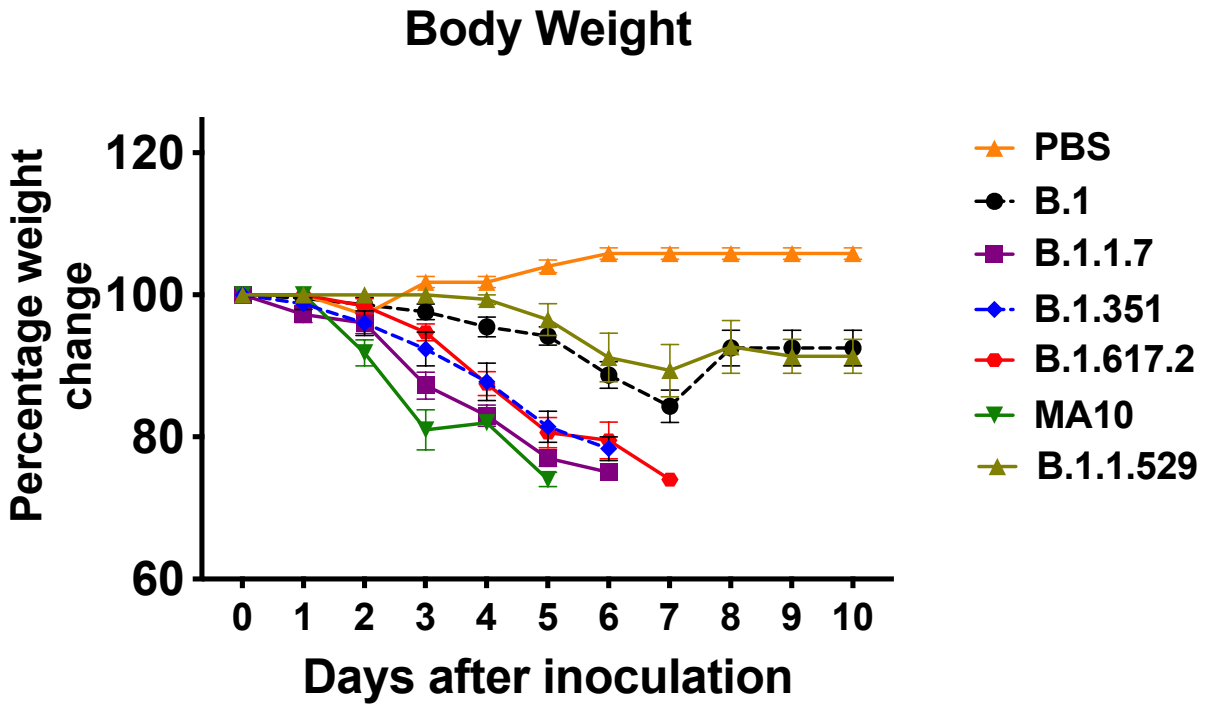
- **Evaluation of GeoVax GEO-CM02 vaccines efficacy against SARS-CoV-2 in a lethal K18-hACE2 transgenic mouse model**
  - **Wuhan challenge**
  - **South Africa challenge**
  - **Omicron challenge**

- **Evaluation of GeoVax GEO-CM04S1 vaccines efficacy against SARS-CoV-2 in a lethal K18-hACE2 transgenic mouse model**
  - **Wuhan challenge**
  - **Omicron challenge**

K18-hACE2 mouse model of SARS-CoV-2 infection

Six to eight weeks old Hemizygous K18-hACE2 mice were infected with 10^4 PFU of SARS-CoV-2 via the intranasal route. **These mice express human ACE2, receptor for SARS-CoV-2.**

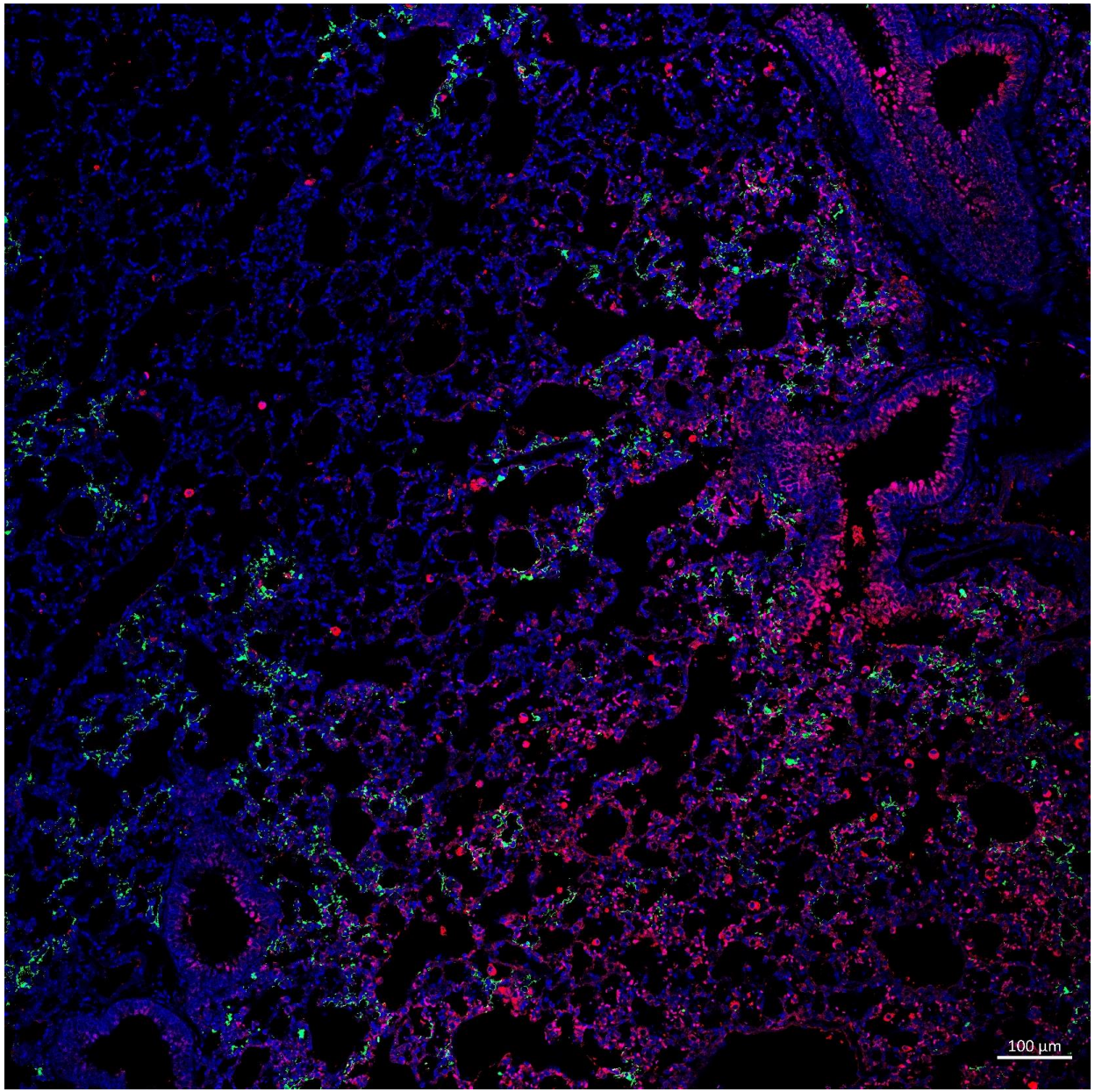




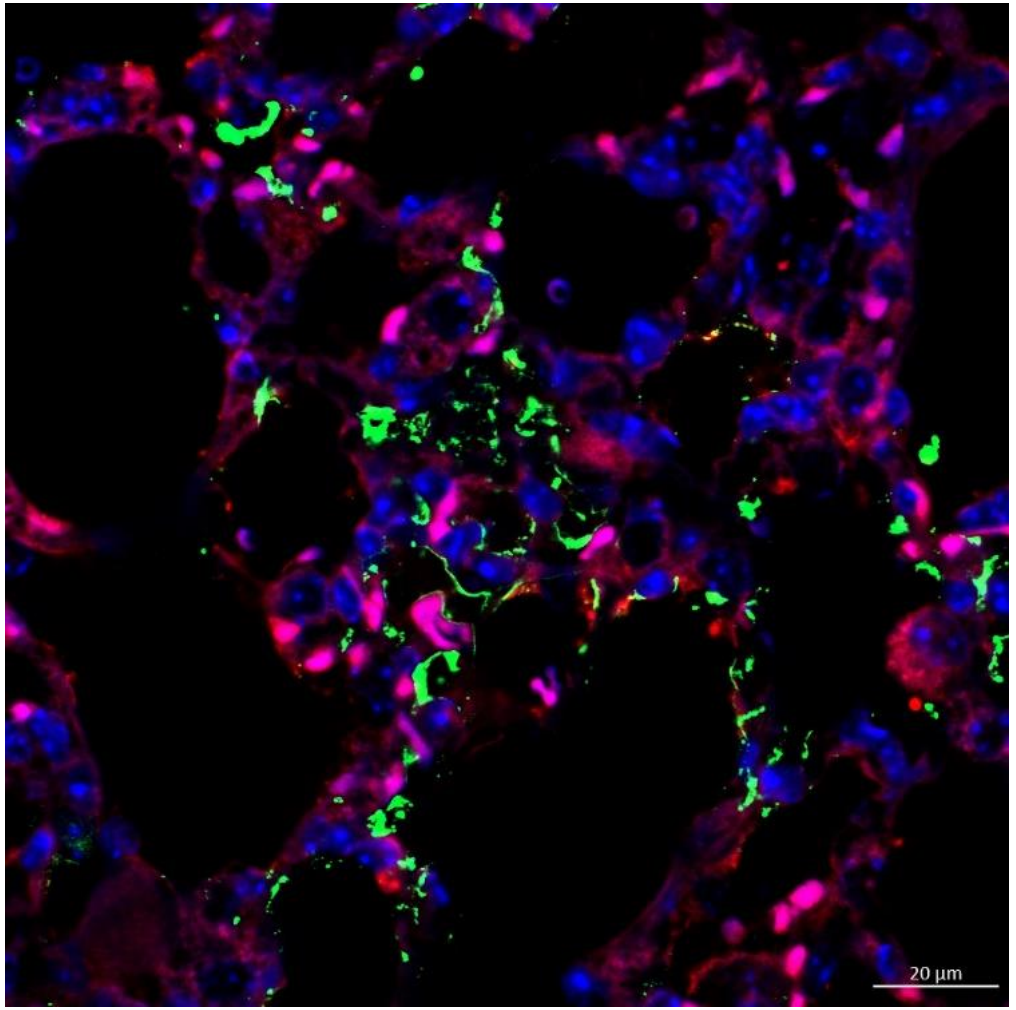
B.1: Wuhan Strain
MA10: Mouse-adapted virus
B.1.1.7: UK Variant
B.1.351: South Africa Variant
B.167.2: Delta Variant
B.1.1.529: Omicron Variant

Kumari et. al., 2021
Natekar et. al., 2022
Rothan et. al., 2022

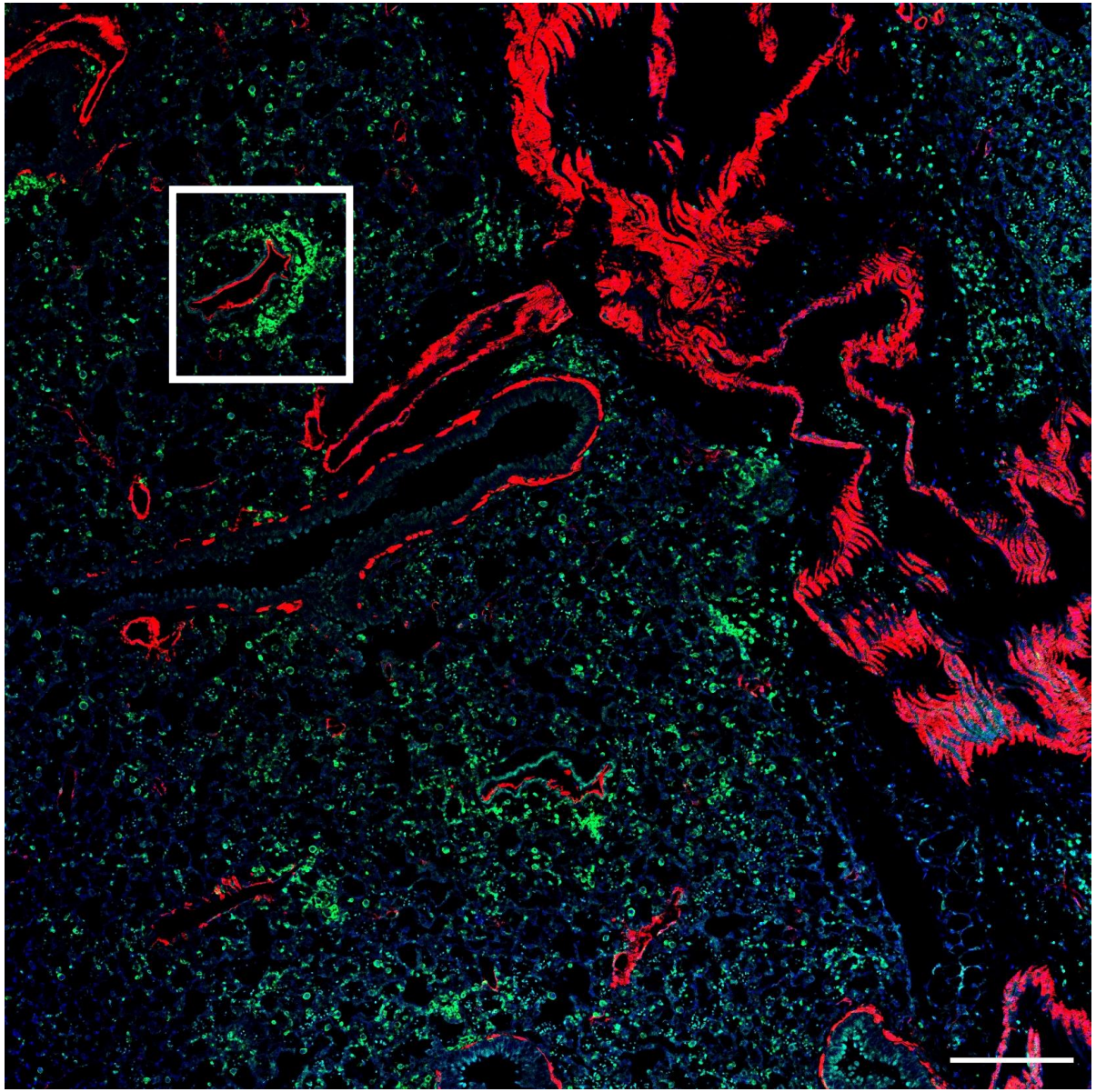
SARS-CoV-2 infection in the lungs of K18-hACE2 mice



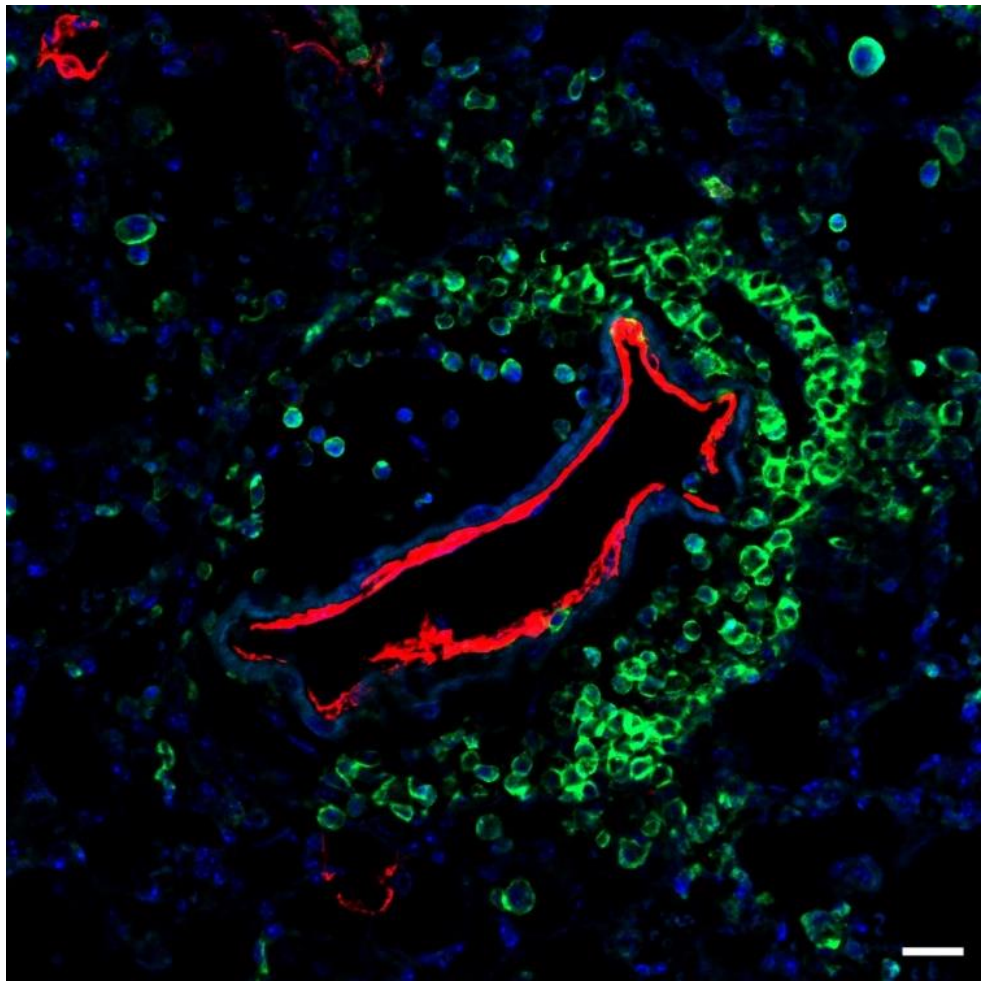
Red - **SARS Nucleocapsid**
Green- **dsRNA**
Blue- **Dapi**



Leukocytes infiltration in the lungs of K18-hACE2 mice

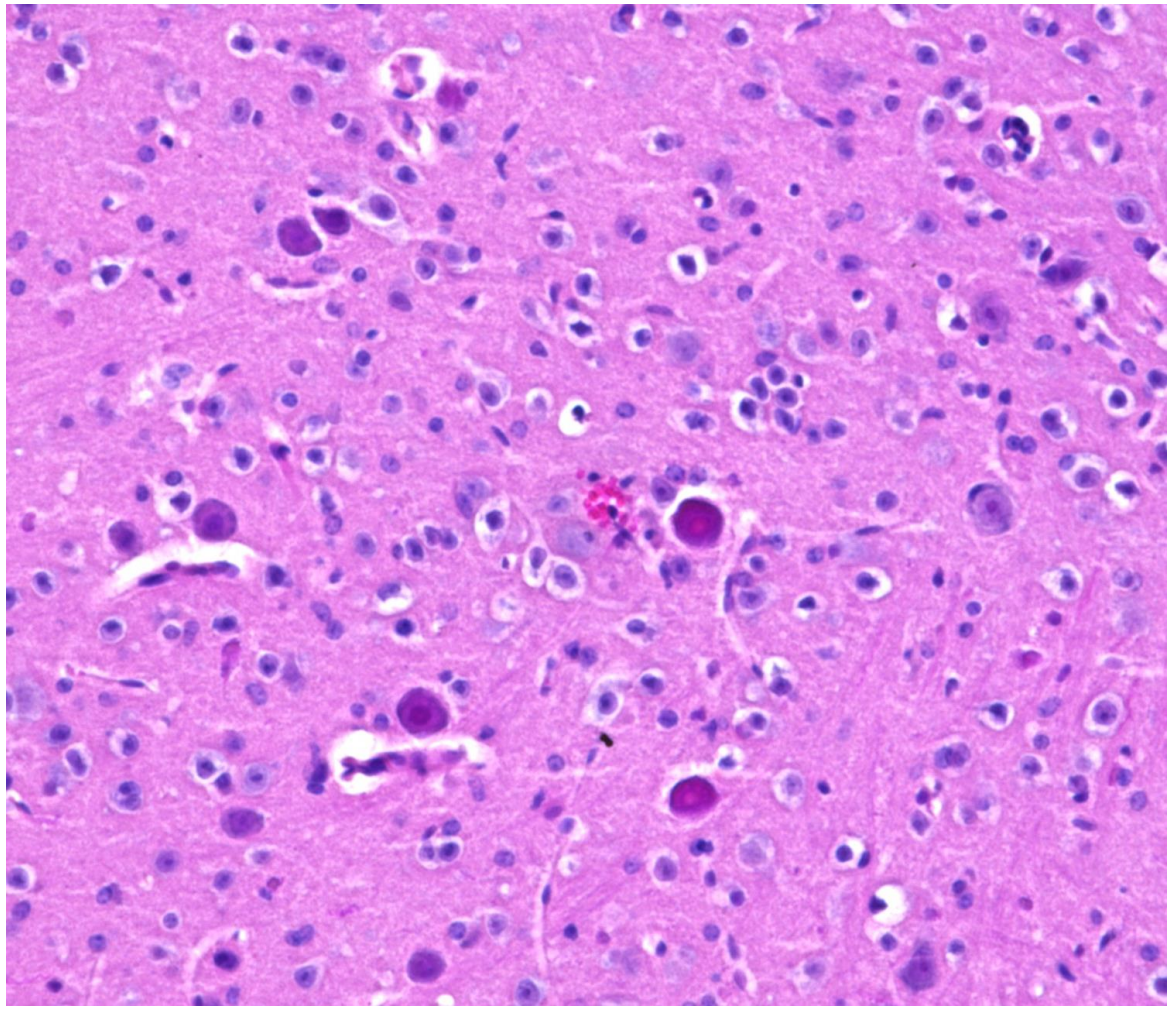


Red - **SMA**
Green- **CD45**
Blue- **Dapi**

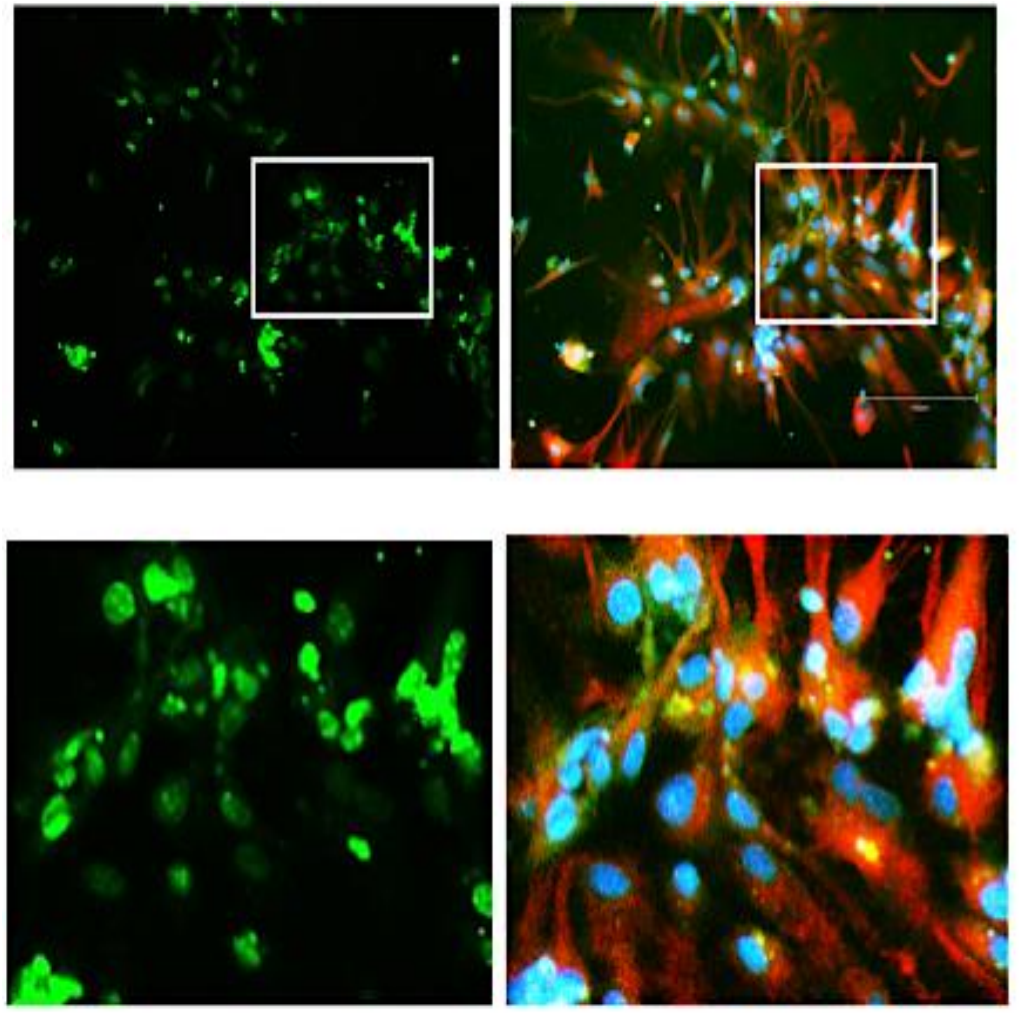


Encephalitis in SARS-CoV-2-infected mice

Pathology in the brain

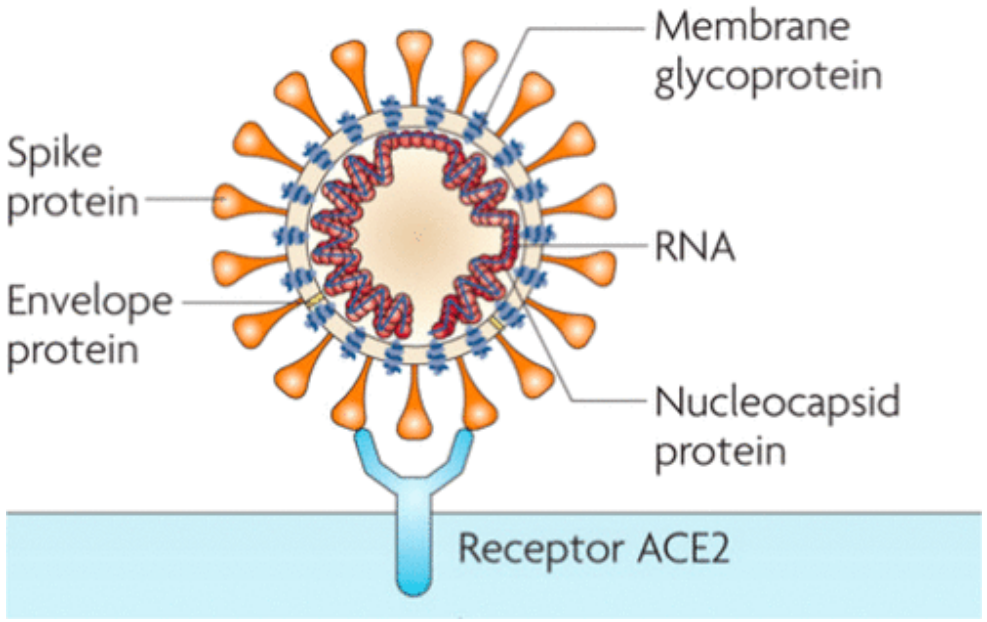


SARS-CoV-2 infected neurons



Evaluation of GeoVax GEO-CM02 vaccine efficacy against SARS-CoV-2

- GeoVax has developed GEO-CM02 vaccines, targeting SARS-CoV-2 based on proven safe MVA-VLP platform.
- **GEO-CM02a encodes Stabilized S (Wuhan variant), M, and E proteins of SARS-CoV-2.**
- The objective of this study was to evaluate protective efficacy of GEO-CM02 vaccines against lethal SARS-CoV-2 (Wuhan, South Africa, and Omicron) challenge in a K18-hACE2 mouse model.

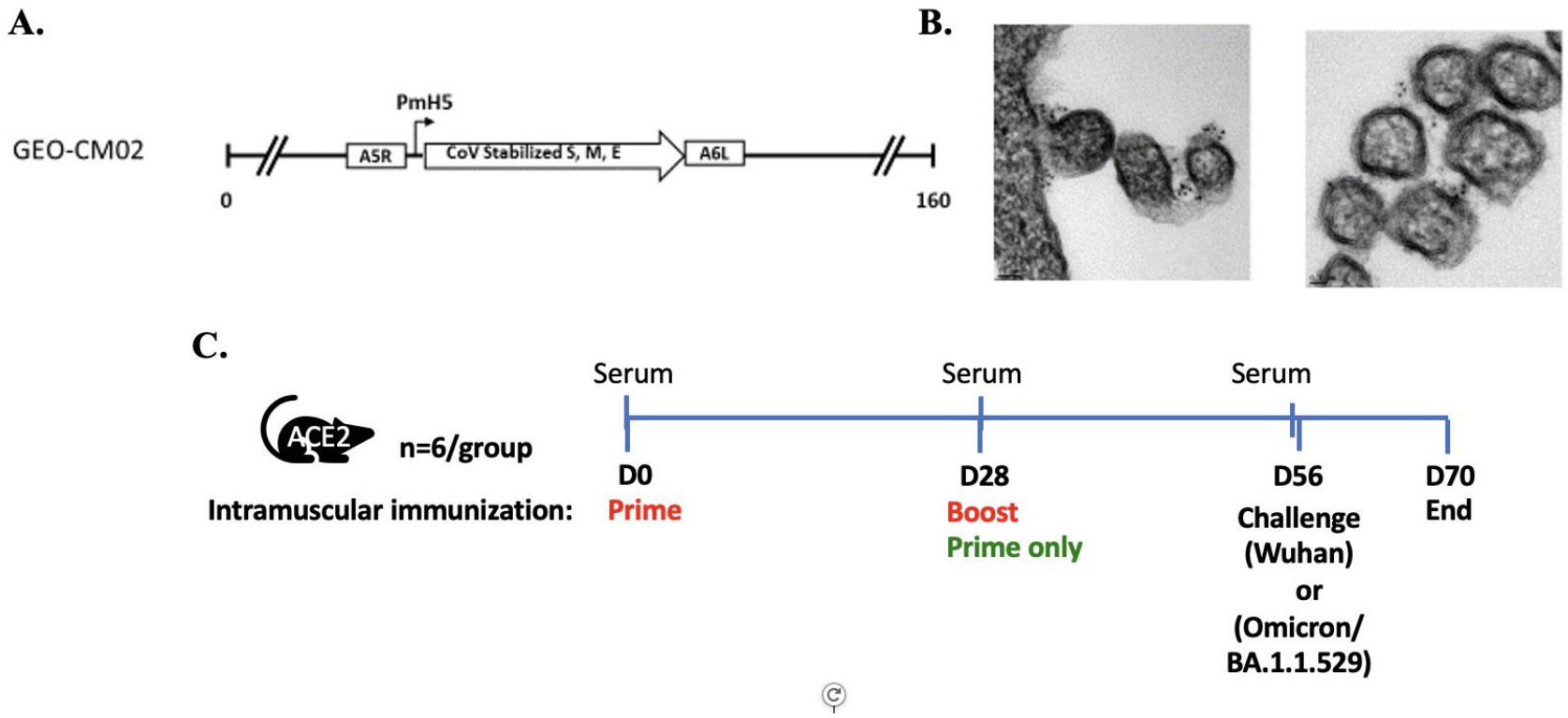


Complete construction and *in vitro* characterization of vaccine candidates

A) Vector construction map.

B) Electron microscopic analysis demonstrating VLP formation.

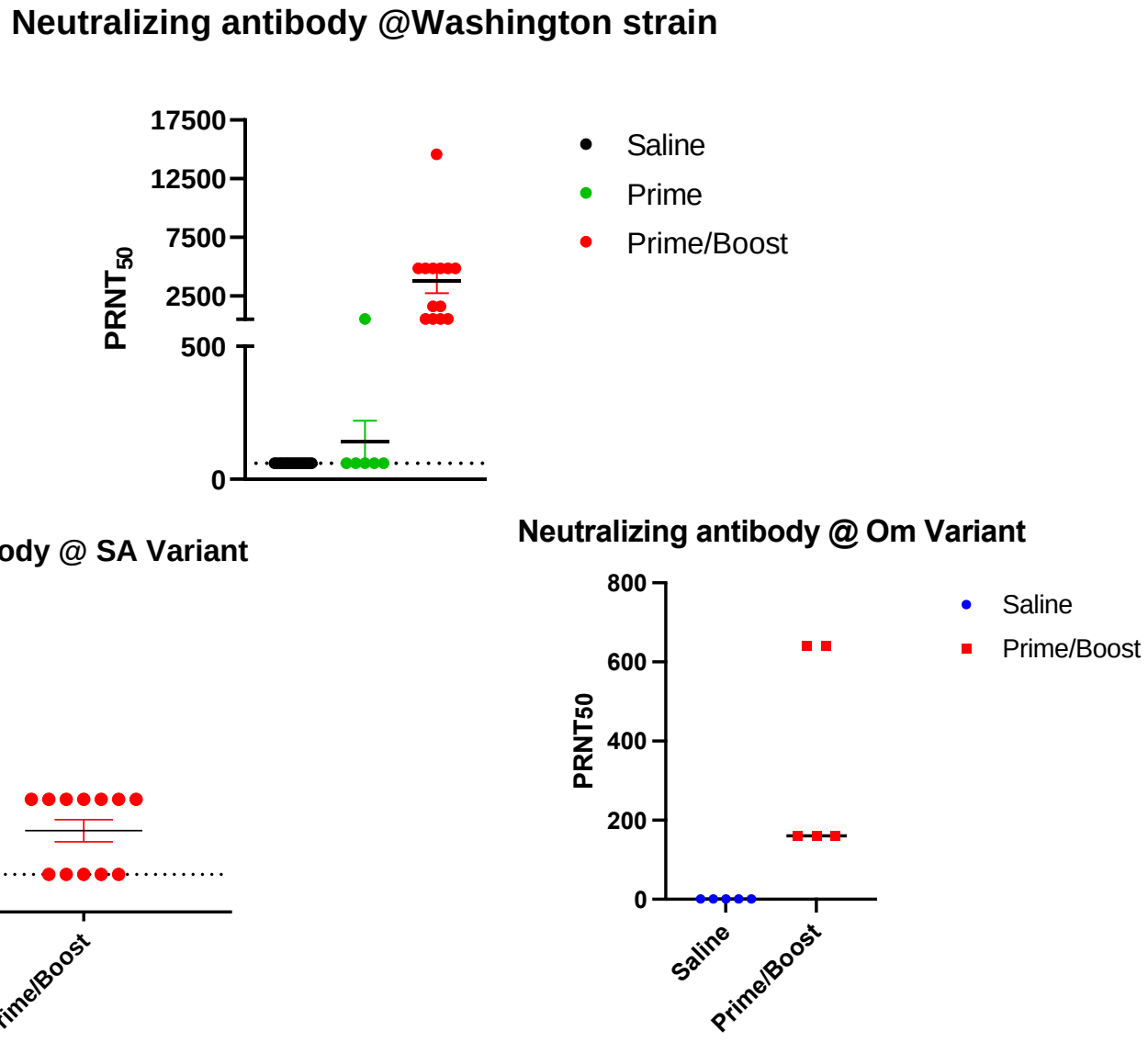
C) Flow of animal studies.



Humoral response following GEO-CM02 vaccination of K18-hACE2 mice

- Mice vaccinated with GEO-CM02 vaccine induced neutralizing antibodies against B.1, B.1.351 and BA.1.1.529 variants.

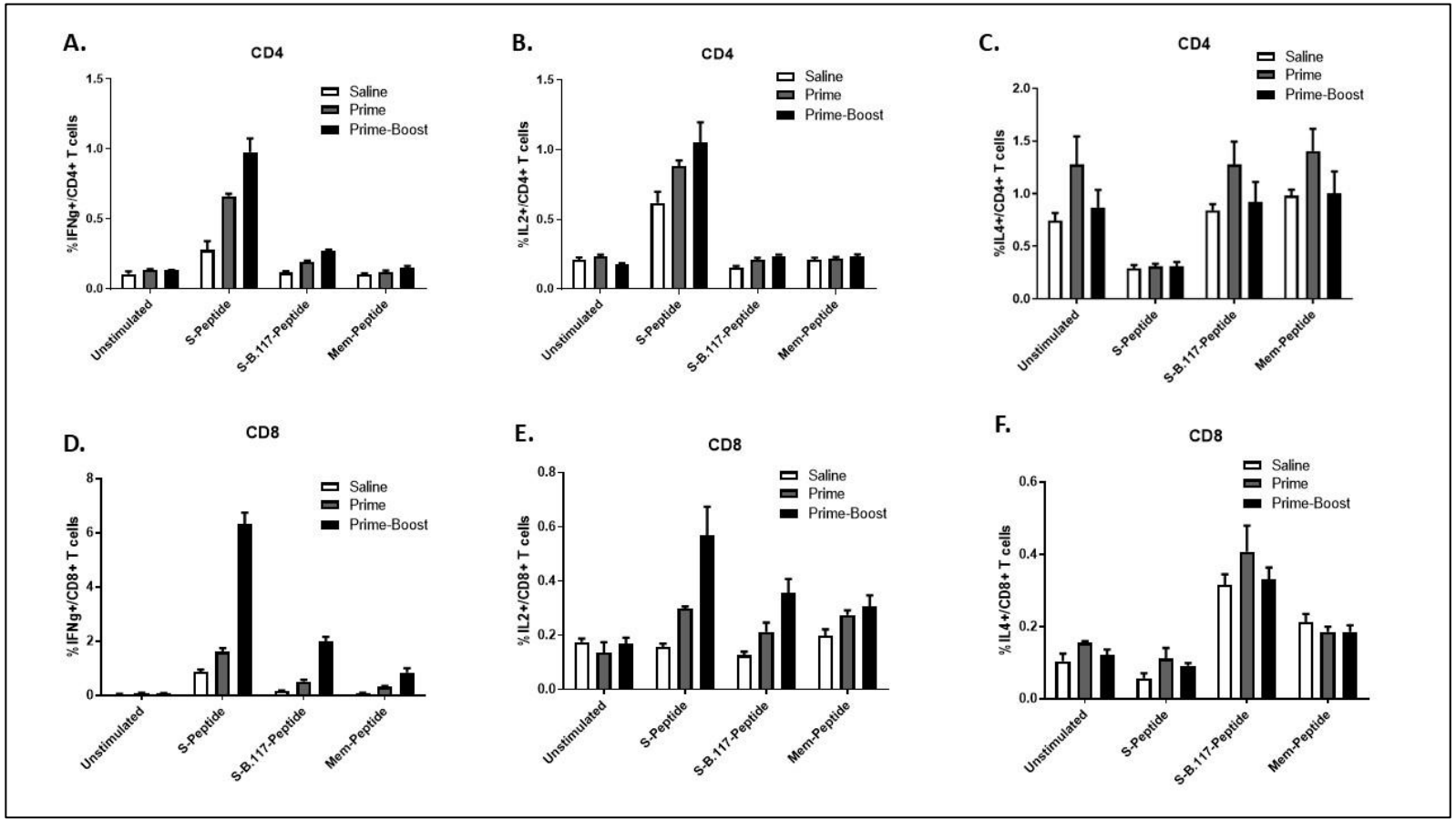
- Prime only vaccination resulted in little antibody production.



GEO-CM02 vaccine induce protective cellular immunity against VoC

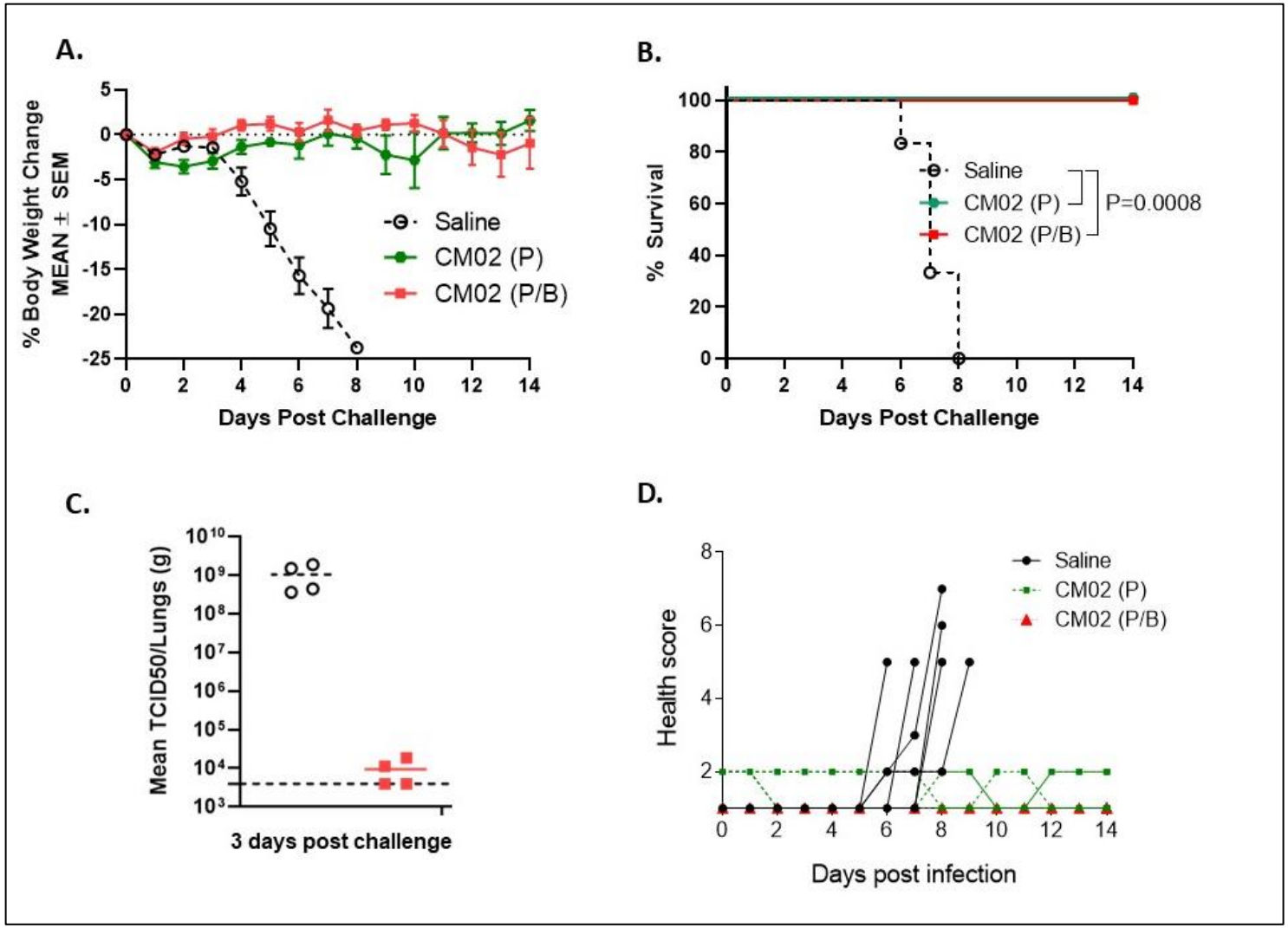
- GEO-CM02 vaccination produces functional CD4+ and CD8+ T cells while maintaining a Th1 rather than Th2 phenotype.

- Vaccination led to an increase in IFNγ and IL-2 producing CD4+ and CD8+ T cells specific for spike protein.



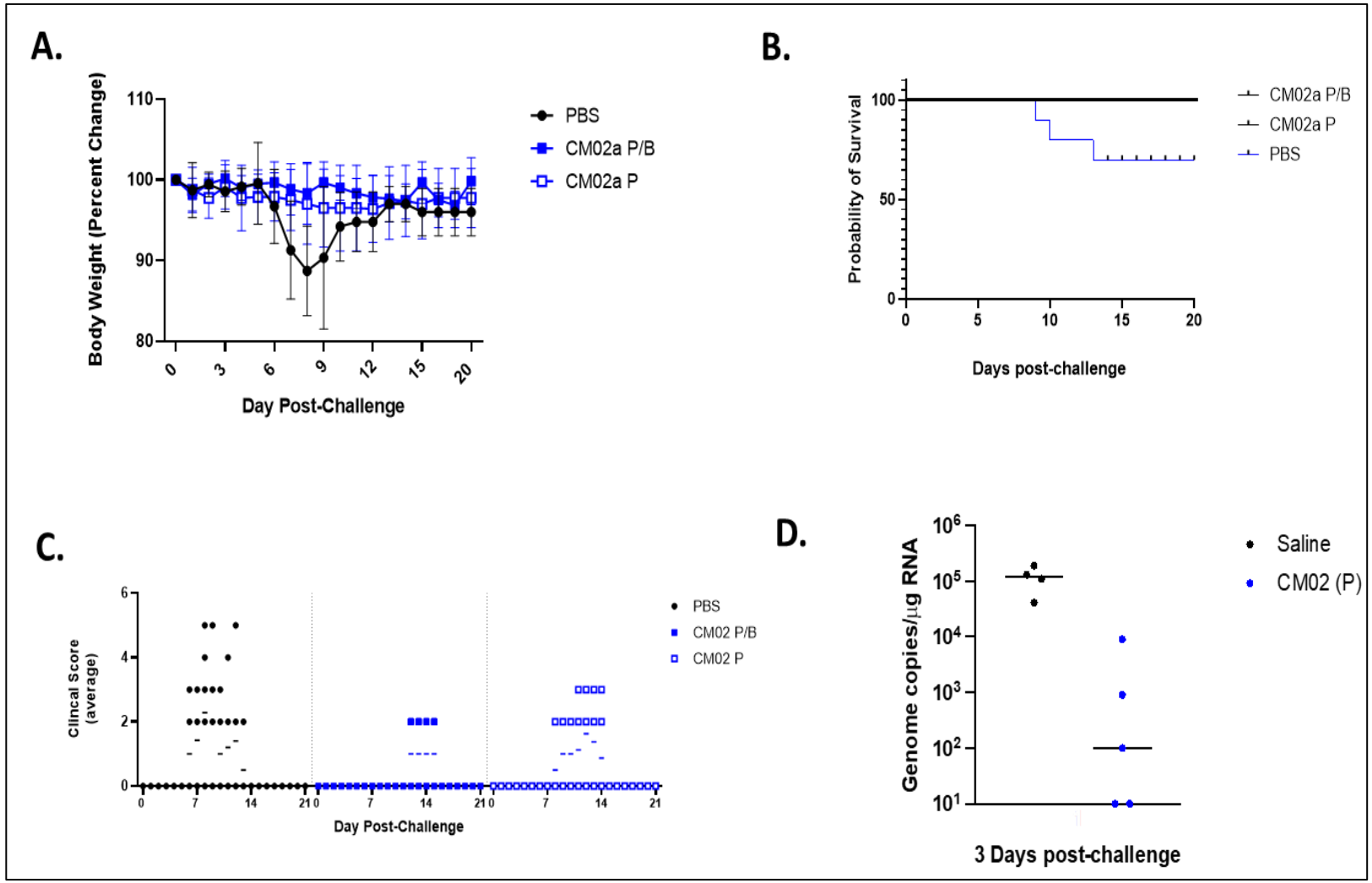
GEO-CM02 vaccine efficacy against SARS-CoV-2 (Wuhan) in a lethal hACE2 mouse model

- Control saline immunized animals succumb to infection between day 6-8.
- **Both GEO-CM02 prime only, and prime-boost immunized animals were fully protected.**
- Animals receiving two doses of GEO-CM02 exhibited no clinical disease.
- Control animals had very high viral loads, whereas viral loads in immunized animals remained low.

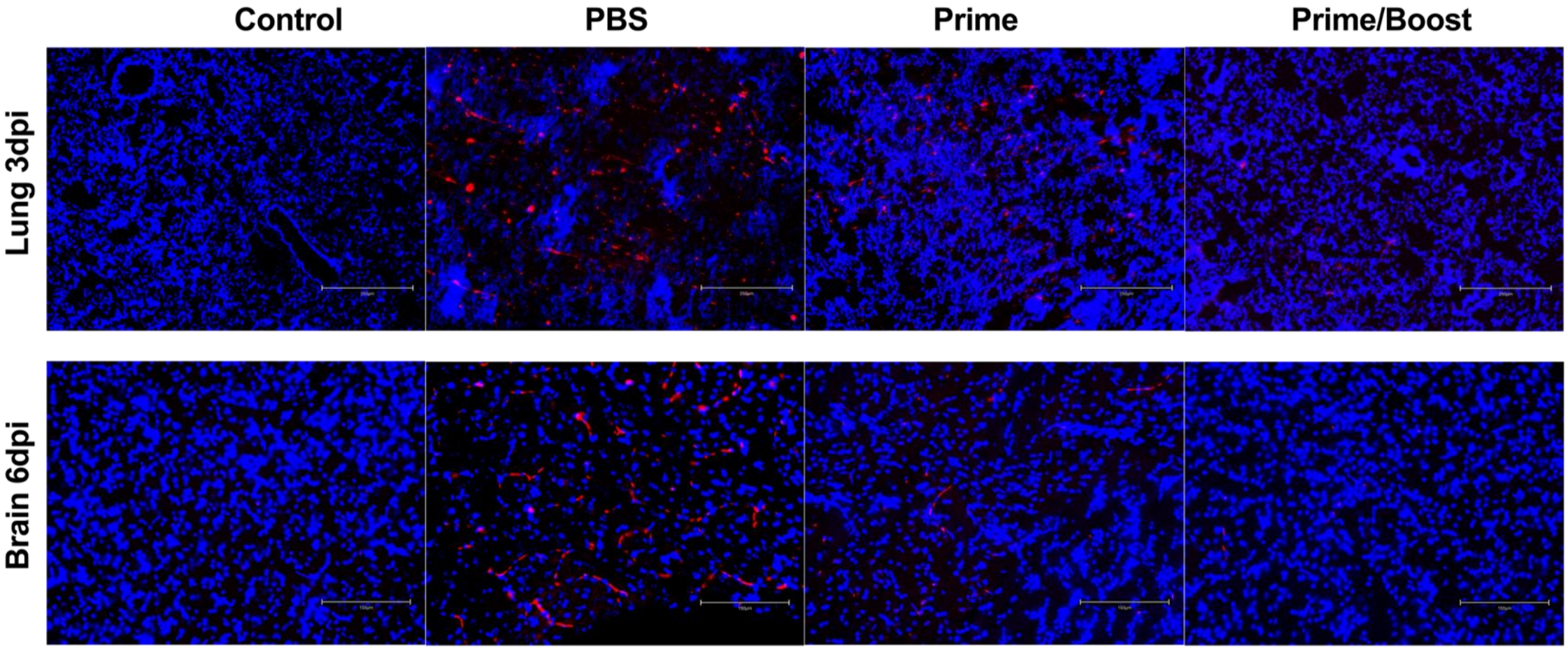


Characteristics of K18-hACE2 mice following CM02 vaccination and BA.1.1.529 SARS-CoV-2 challenge

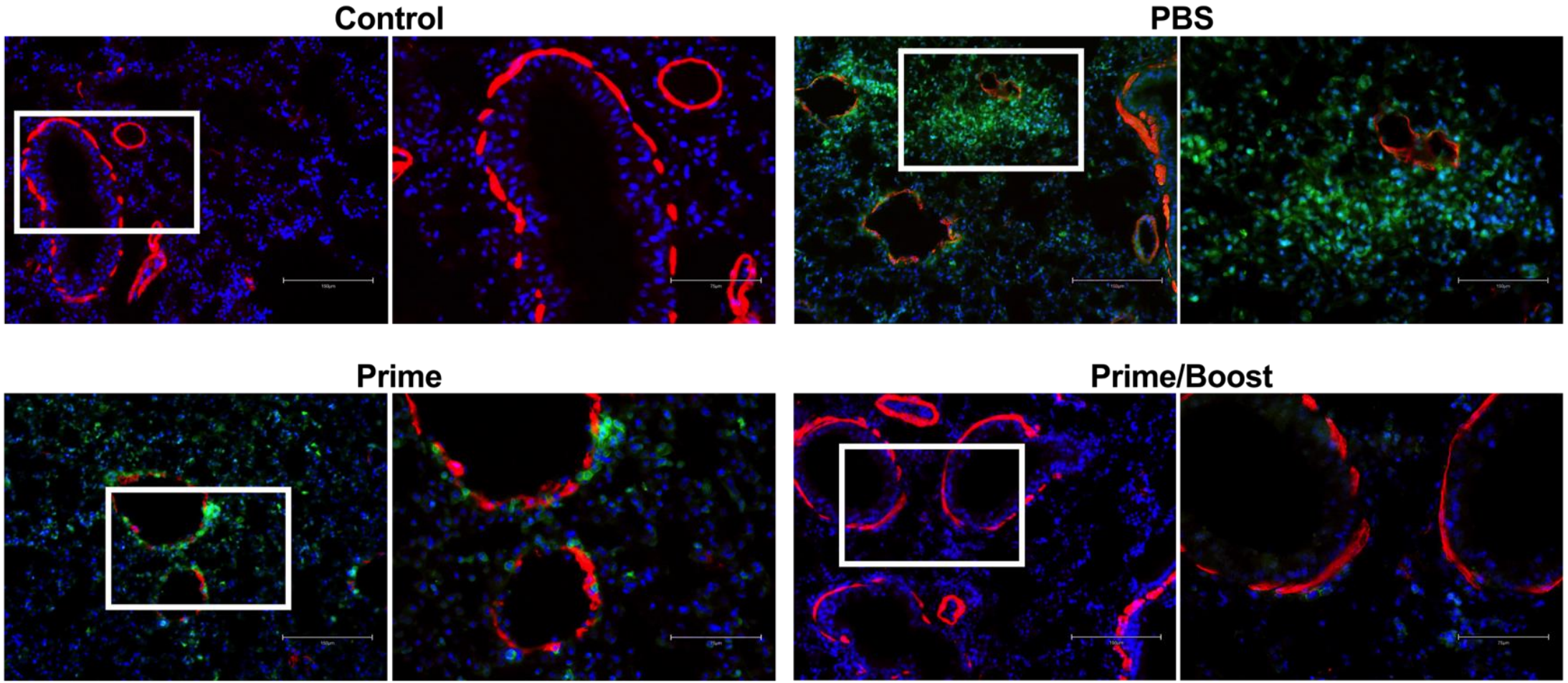
- GEO-CM02 immunized mice were fully protected from weight loss and death following Omicron challenge.
- GEO-CM02 immunized animals exhibited minimal clinical disease after challenge.
- Viral RNA levels were significantly lower in the vaccinated mice.



Decreased viral nucleocapsid protein expression in vaccinated mice following Omicron challenge



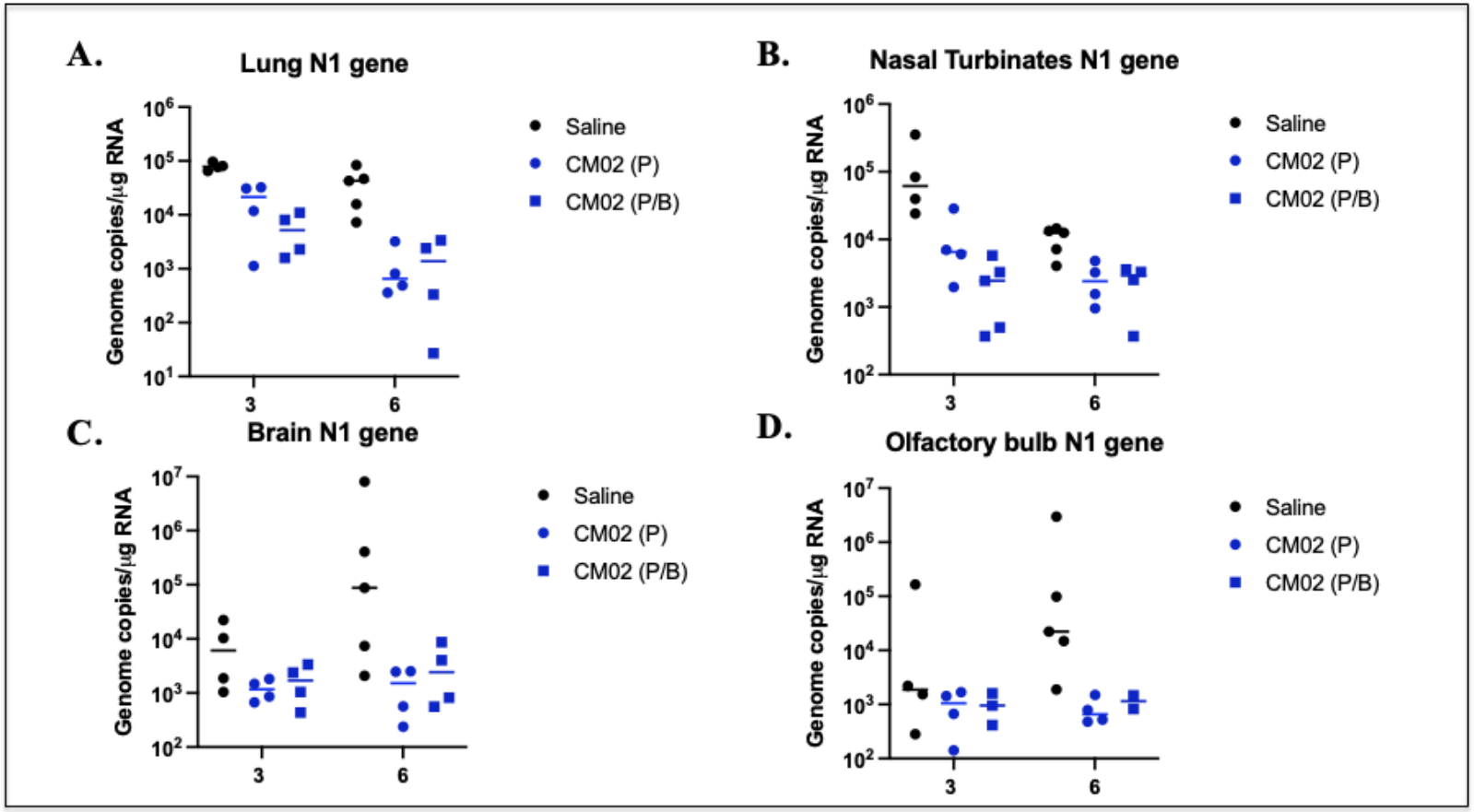
Reduced leukocytes infiltration in vaccinated mice following Omicron challenge



- Lungs at day 3 post infection

Reduced virus titers in vaccinated mice compared to saline mice

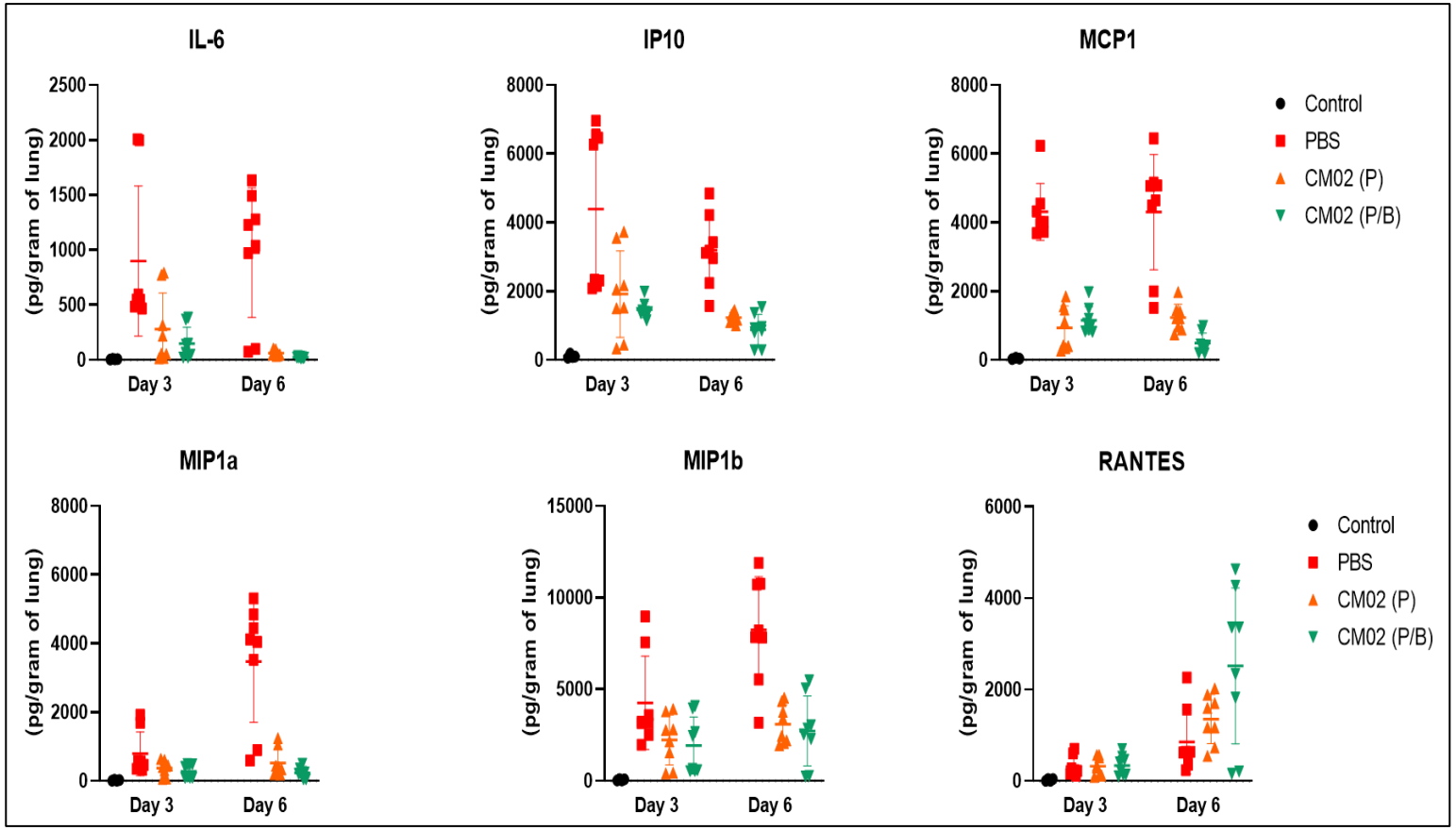
- Both GEO-CM02 prime only, and prime-boost immunized animals showed a decrease in the viral RNA levels at days 3 and 6 post challenge compared to the saline group.



Cytokine and chemokine levels in vaccinated mice following Omicron challenge

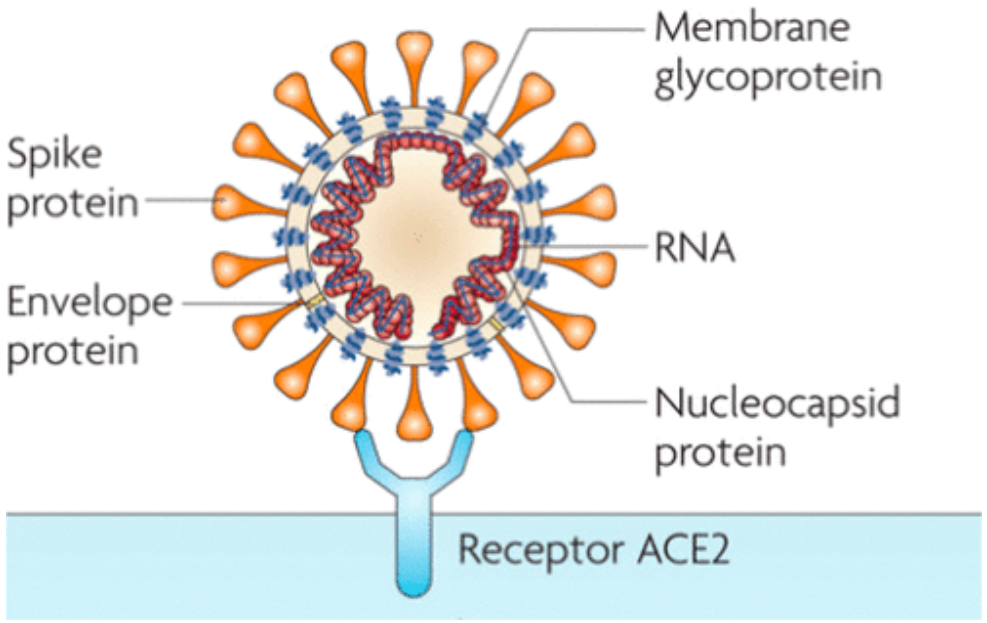
- Mice vaccinated with GEO-CM02 demonstrated significant reduced protein levels of inflammatory cytokines and chemokines compared to the saline mice.

- Interestingly, vaccination resulted in increased amounts of RANTES.



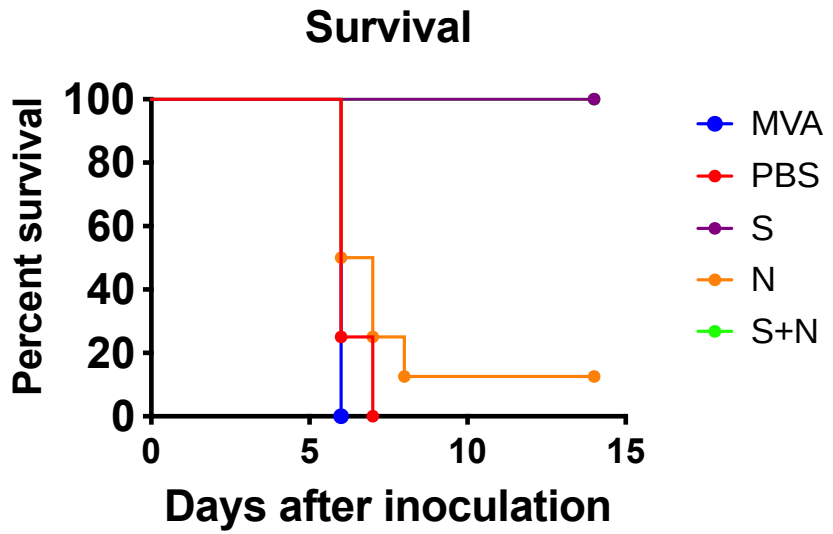
Evaluation of GeoVax GEO-CM04S1

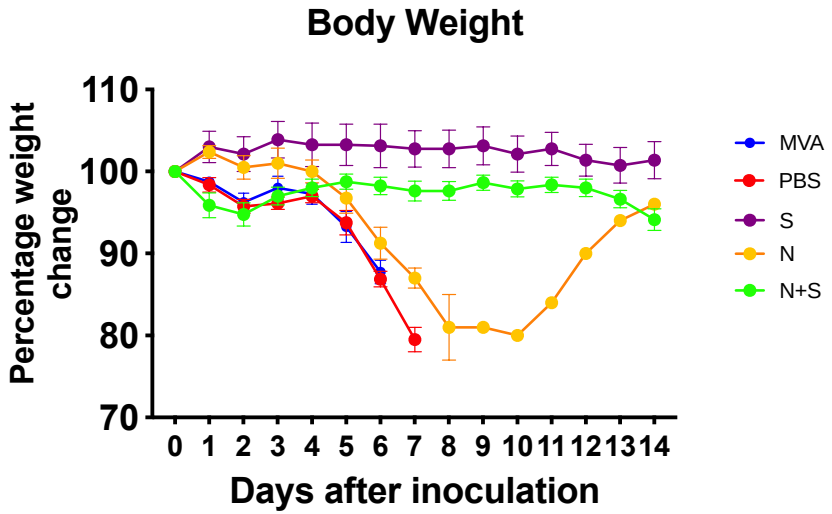
- GEO-CM04S1 is a clinical phase viral-vectored vaccine targeting SARS-CoV-2 based on our proven safe MVA platform.
- **GEO-CM04S1 encodes native Wuhan derived SARS-CoV-2 Spike and Nucleocapsid proteins.**
- **The objective of this study was to determine the relative contribution of individual antigens and cellular immunity to protective efficacy in a lethal SARS-CoV-2 challenge hACE2 mouse model.**



Characteristics of K18-hACE2 mice following CM04S1 vaccination and SARS-CoV-2 (Wuhan) challenge

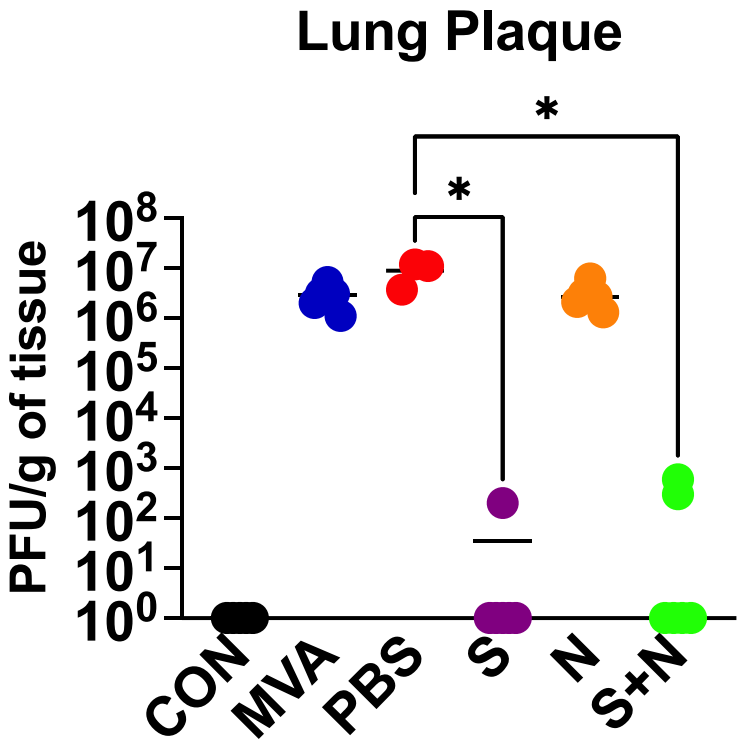
- Saline and MVA immunized animals succumb to infection between day 6-8.
- **GEO-CM04S1 (S and N+S) immunized animals were fully protected.**
- **Some protection was observed in mice immunized with N only.**





Reduced virus titers in CM04S1-vaccinated mice

- **Lung virus titers were significantly lower in GEO-CM04S1 (S and N+S) immunized animals.**



- **Lungs at day 3 post infection**

Summary

- Utilizing the MVA-VLP platform, we tested efficacy of multi-antigen vaccines expressing SARS-CoV-2 S, M and E in preclinical animal challenge models.
- Our data demonstrate that the MVA-based viral vaccine GEO-CM02 induces strong cellular and humoral immunity.
- GEO-CM02 vaccine-induced protective immunity protects mice from SARS-CoV-2 variants spanning Alpha to Omicron.
- Vaccinated mice remained healthy and expressed lower viral loads and an altered immune response compared to the saline mice.
- We also demonstrate that GEO-CM04S1 immunization provides excellent protection from morbidity and mortality following SARS-CoV-2 in a hACE2 transgenic mouse model.

Acknowledgements

Lab Members

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