Replicating RNA platform enables rapid response to the SARS-CoV-2 Omicron variant and elicits enhanced protection in naïve hamsters compared to ancestral vaccine

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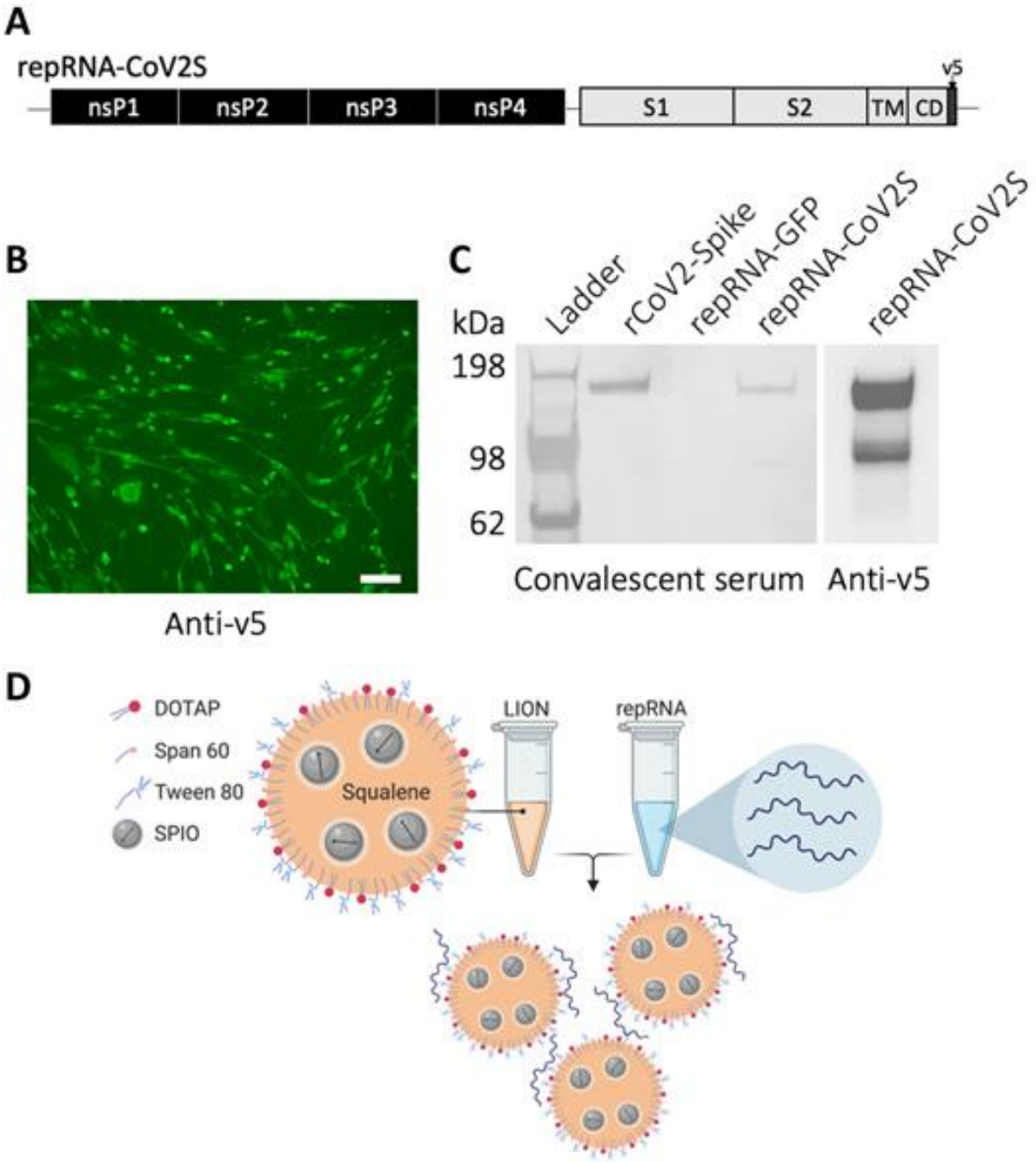
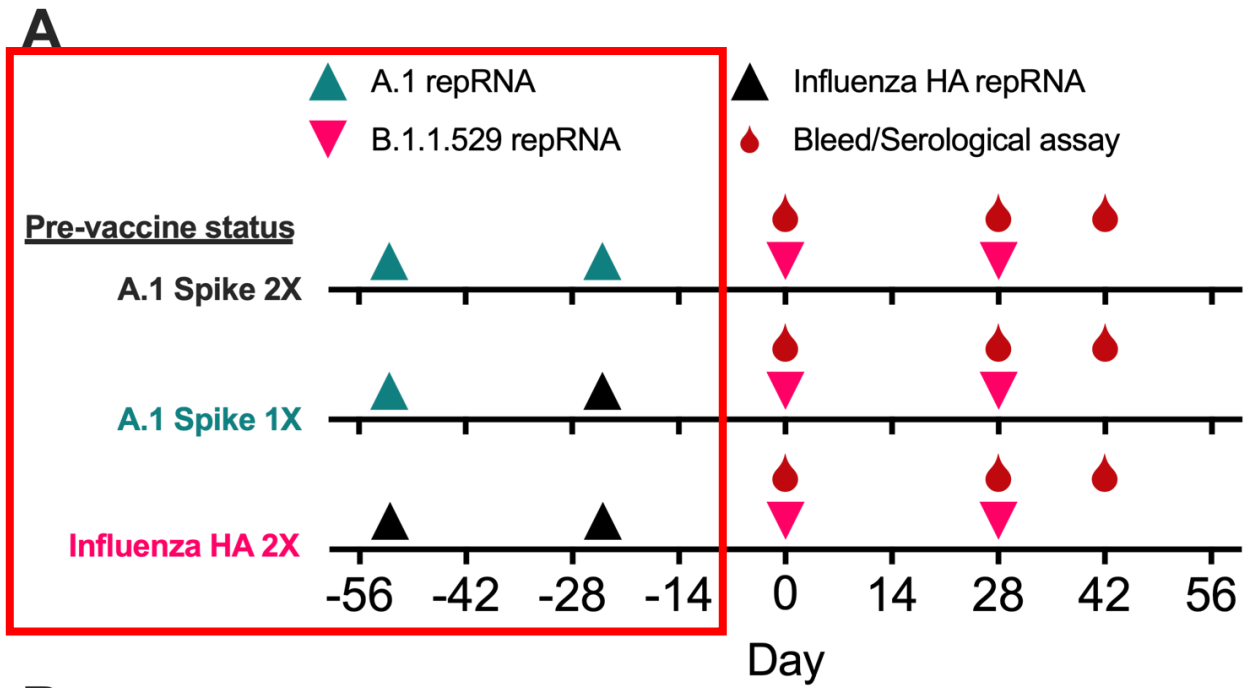
repRNA Platform

- RNA backbone: Replicon in which the structural proteins of Venezuelan Equine Encephalitis Virus are replaced with SARS-CoV-2 spike
  - Single-round of replication
  - Mimics authentic viral infection through production of dsRNA, CPE
  - High level GOI expression
- Delivered through a cationic nanocarrier
- Demonstrated immunogenicity in mice, hamsters and non-human primates
- In clinical trials in India, South Korea, Brazil and USA
- Pre-clinical grade B.1.1.529-specific vaccine synthesized and hamsters vaccinated within ~two-weeks of B.1.1.529 sequence availability



Erasmus et al. 2020. *Science Translational Medicine*

Does pre-existing A.1 immunity impact B.1.1529 boosting?



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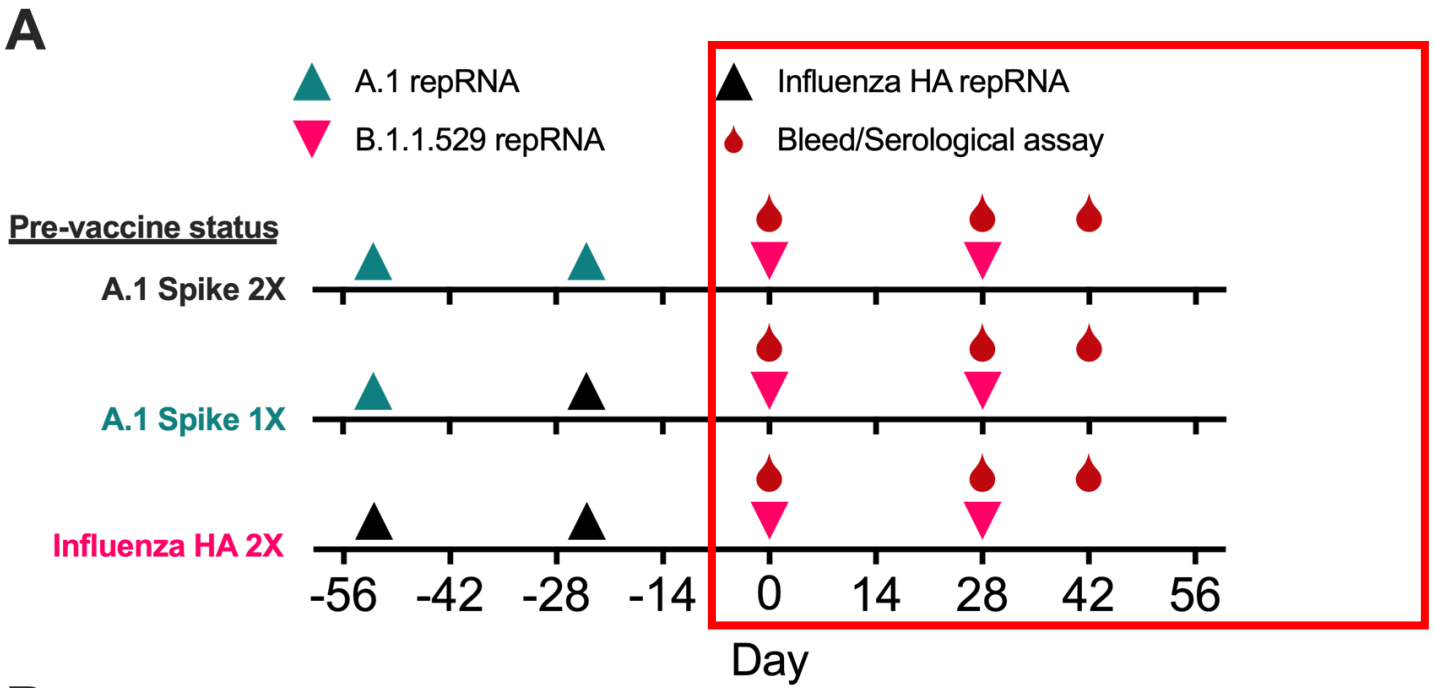

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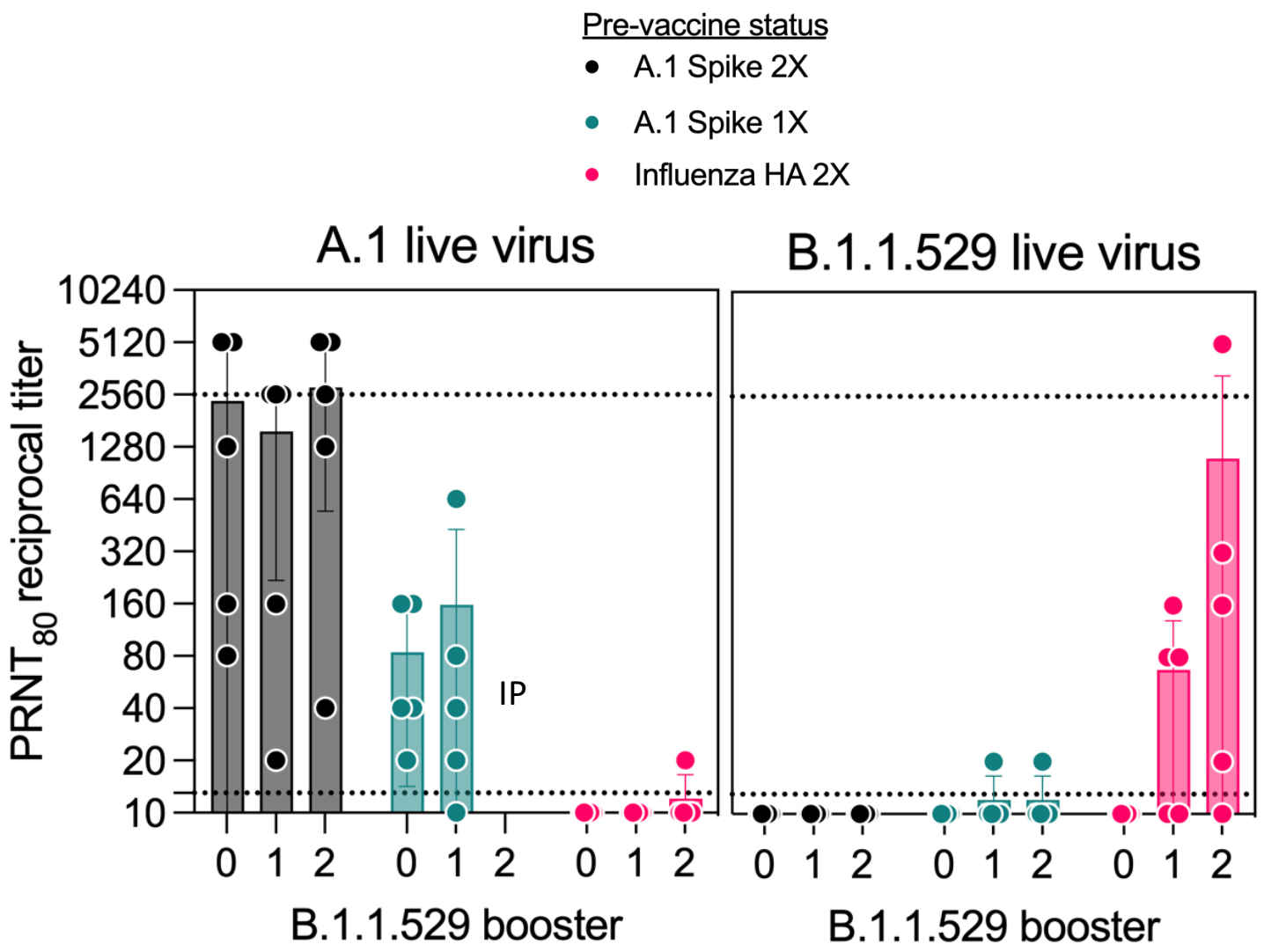


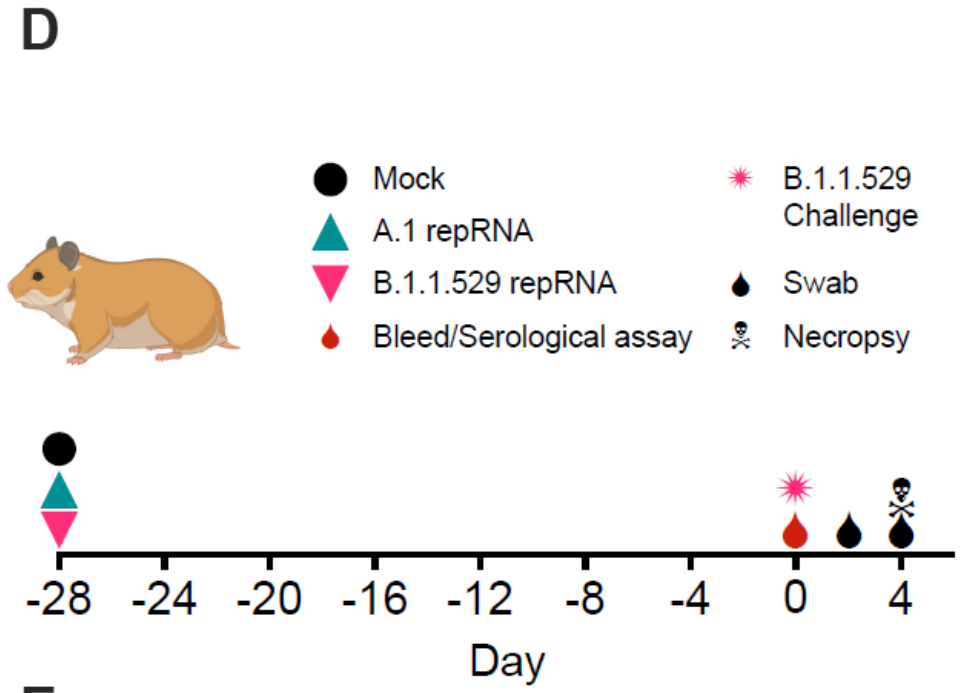
Hamster study

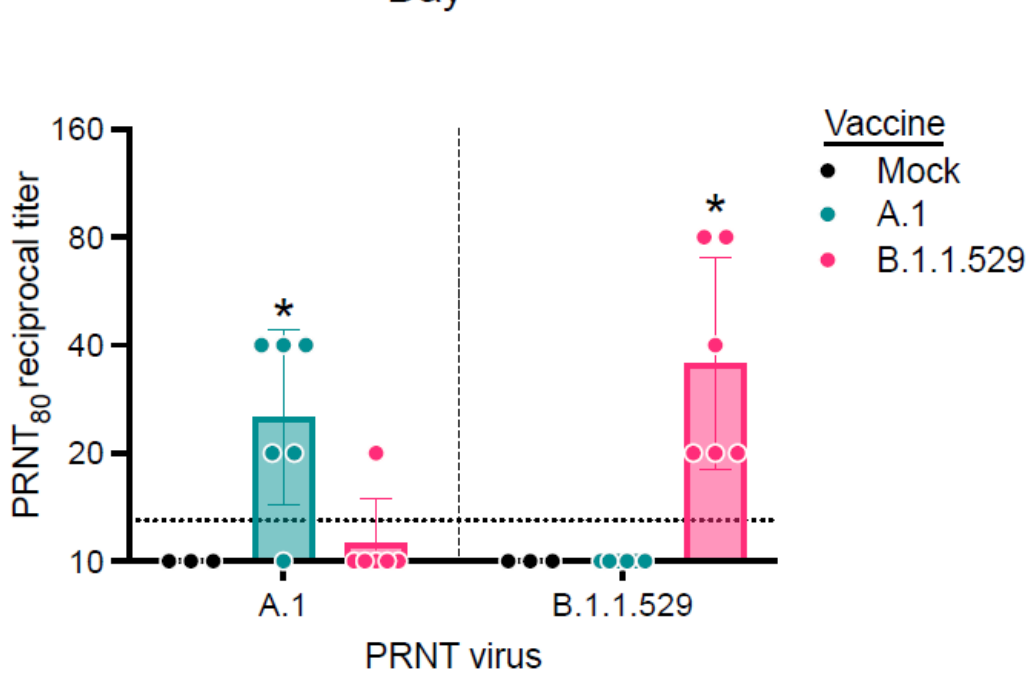
Single immunization with 20ug of repRNA

Four weeks post-vaccination challenged with 1000 TCID50 of B.1.1.529 via IN route

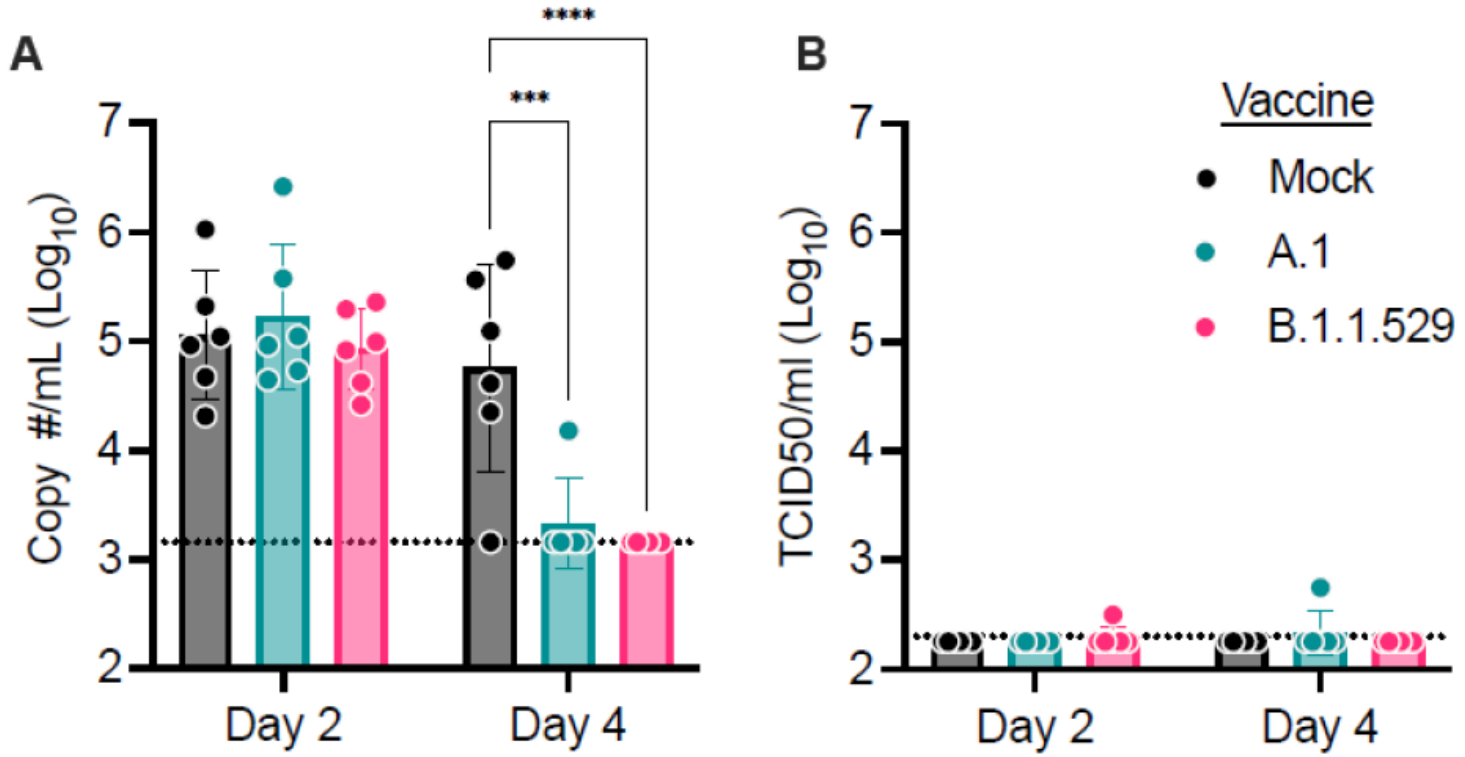
Oral swabs on day +2 and +4

Scheduled necropsy on day +4



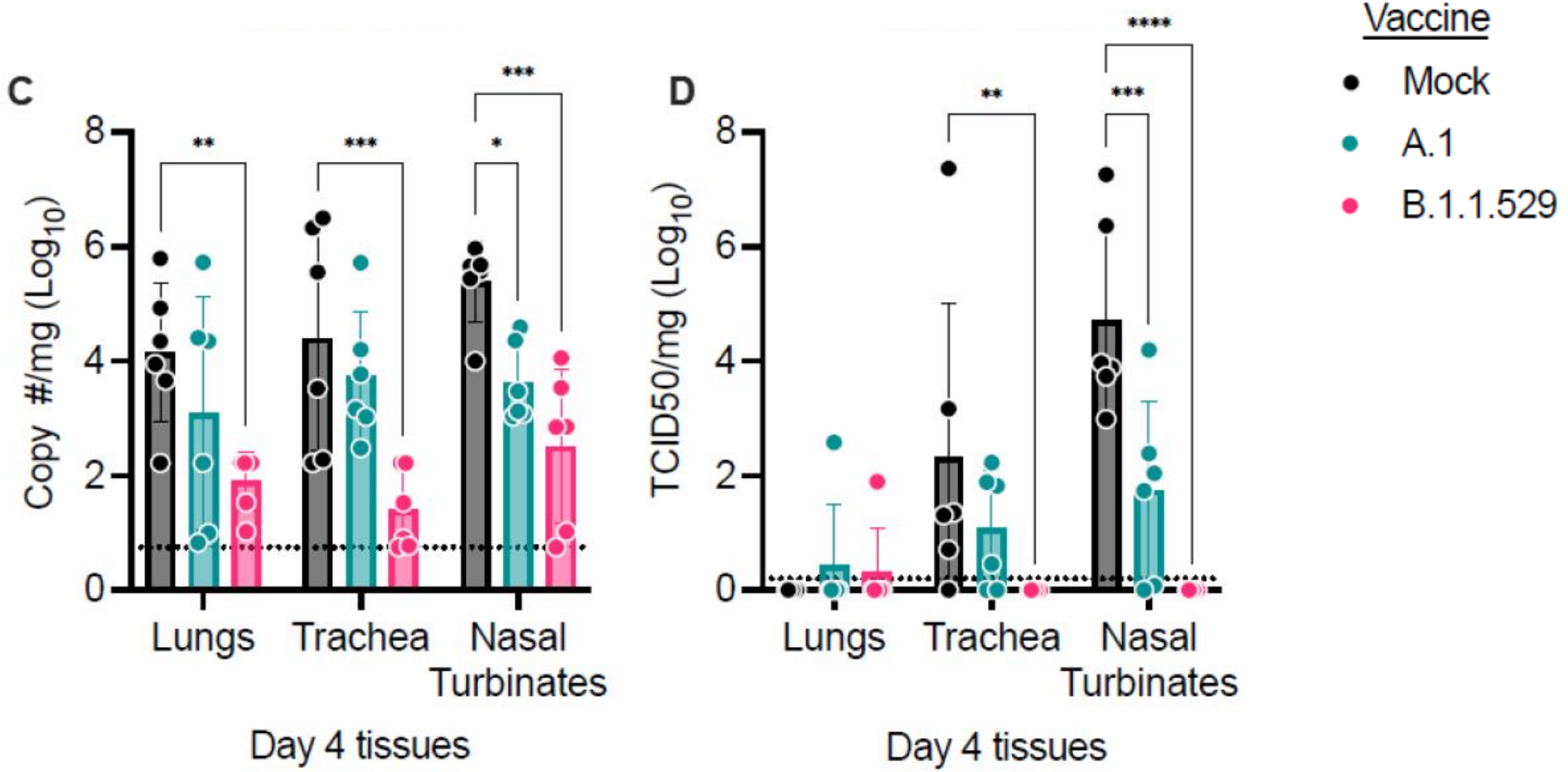


repRNA vaccination reduced viral shedding



Oral Swabs

repRNA vaccination reduced viral loads in upper respiratory tract



Nasal Turbinates

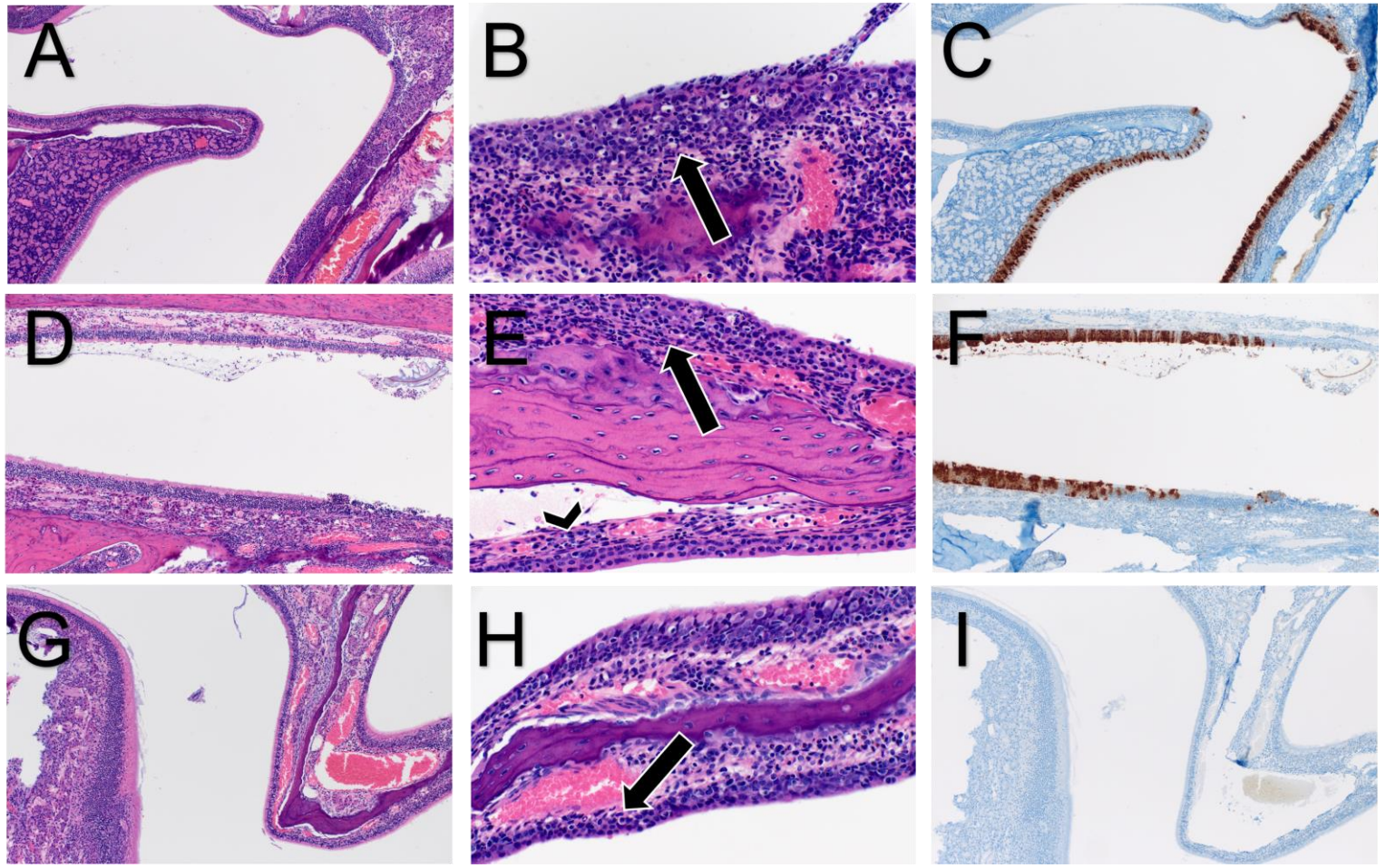
H&E

IHC

Mock

A.1-repRNA-CoV2S

B.1.1.529-repRNA-CoV2S



Conclusions

- repRNA platform can be rapidly updated to address VoCs
- Pre-existing immunity may influence efficacy of B.1.1.529-targeted boosters
  - Little-to-no cross-neutralization activity was seen between A.1 and B.1.1.529 immune animals
- B.1.1.529-targeted vaccine provided superior immunity to B.1.1.529 challenge than ancestral A.1 vaccine
- Our data support findings that B.1.1.529 appears milder possibly due to restriction in the lower respiratory tract

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