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

David W. Hawman, Staff Scientist, Laboratory of Virology, DIR/NIAID
Heinz Feldmann, Chief Laboratory of Virology, DIR/NIAID
Jesse Erasmus, Director-Virology, HDT Bio & Univ. Washington
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

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

Pre-vaccine status:
- A.1 Spike 2X
- A.1 Spike 1X
- Influenza HA 2X

Graph showing PRNT$_{80}$ reciprocal titer for A.1 live virus and B.1.1.529 live virus with different booster doses.
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

A. Mock
B. A.1-repRNA-CoV2S
C. B.1.1.529-repRNA-CoV2S

H&E

IHC
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
Acknowledgements

• Laboratory of Virology, NIAID
• HDT Bio
• University of Washington
• Rocky Mountain Veterinary Branch
• ABSL-4 facilities staff