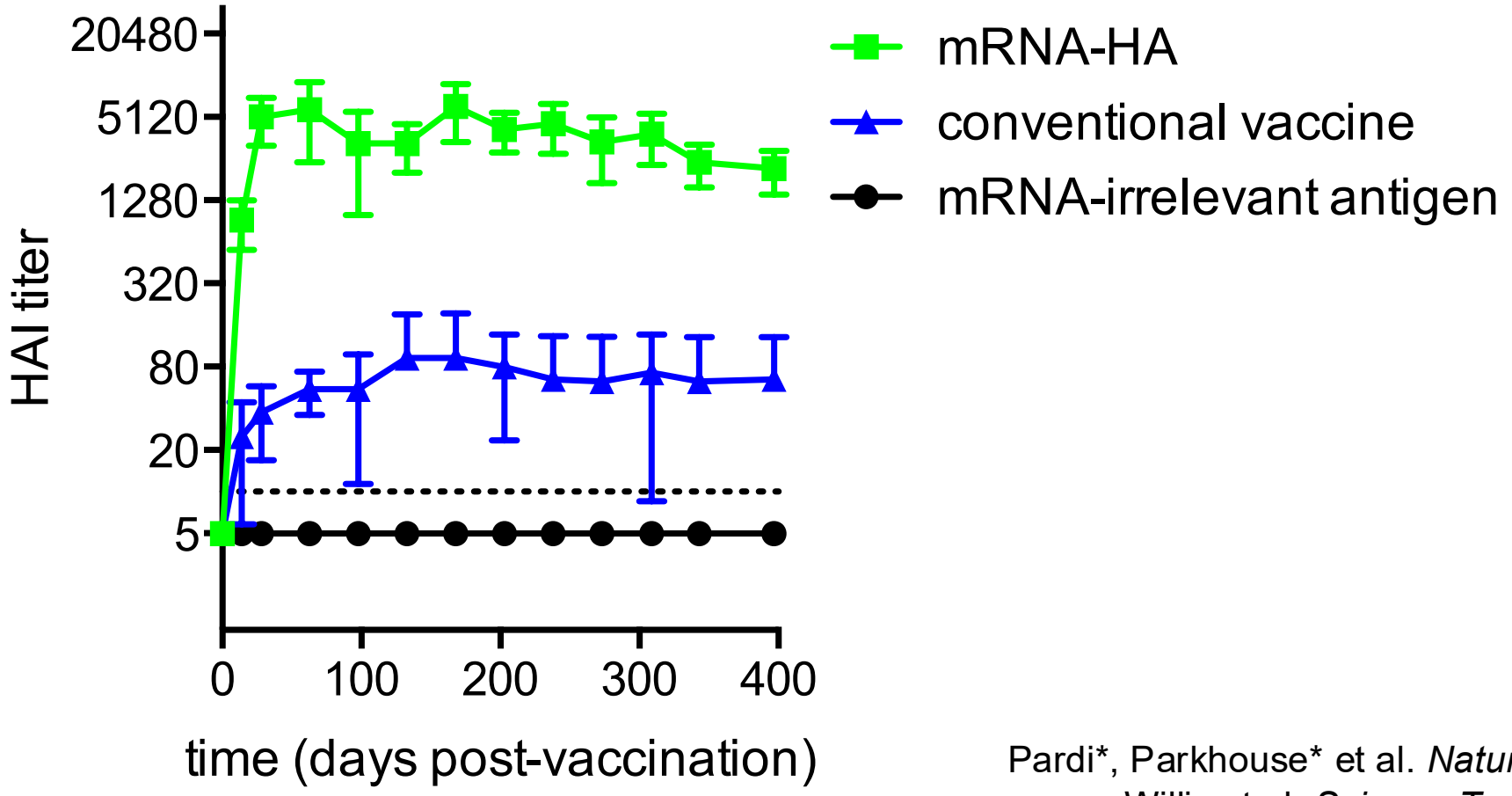
Evaluation of the immune response after vaccination

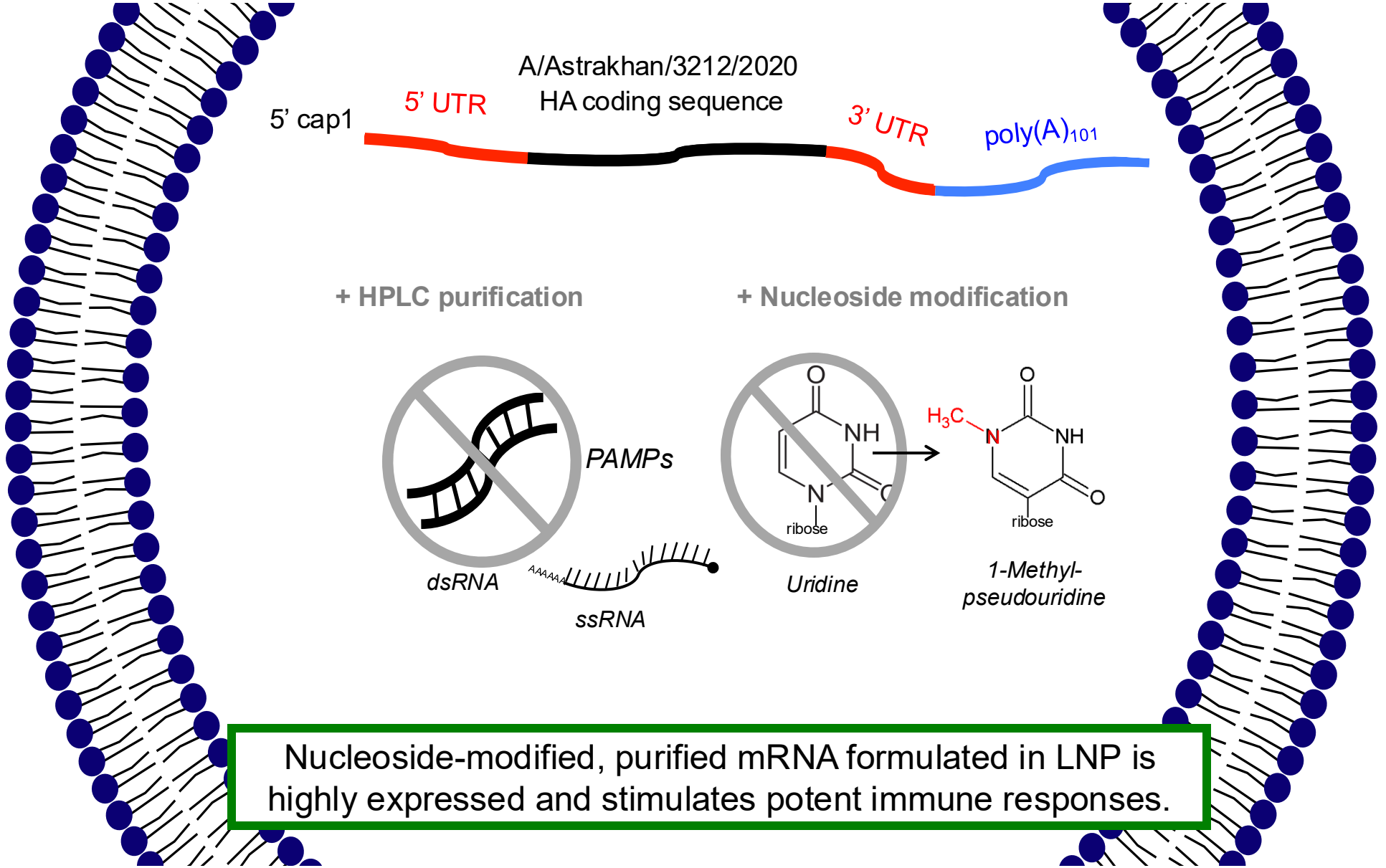
Scott E. Hensley, Ph.D.
Professor of Microbiology
Director, Penn-CEIRR

Influenza virus mRNA vaccines elicit strong antibody responses



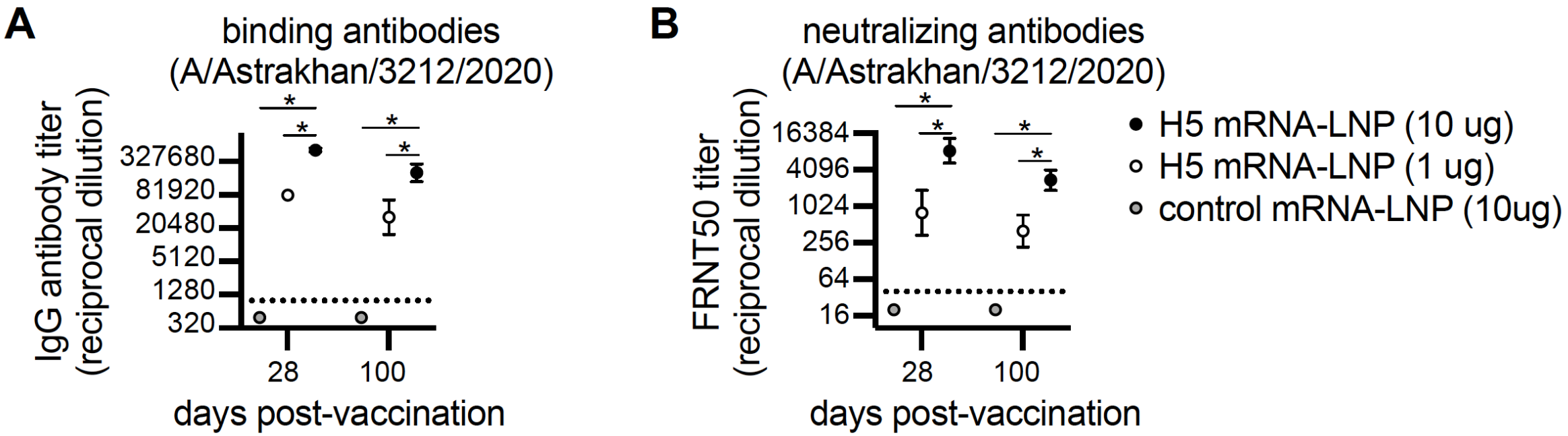
Pardi et al. *JEM (2018)*
Pardi*, Parkhouse* et al. *Nature Communications (2018)*
Willis et al. *Science Translational Medicine (2020)*
Arevalo et al. Science (2022)
Gouma et al. Journal of Virology (2023)

Clade 2.3.4.4b H5 mRNA-LNP vaccine



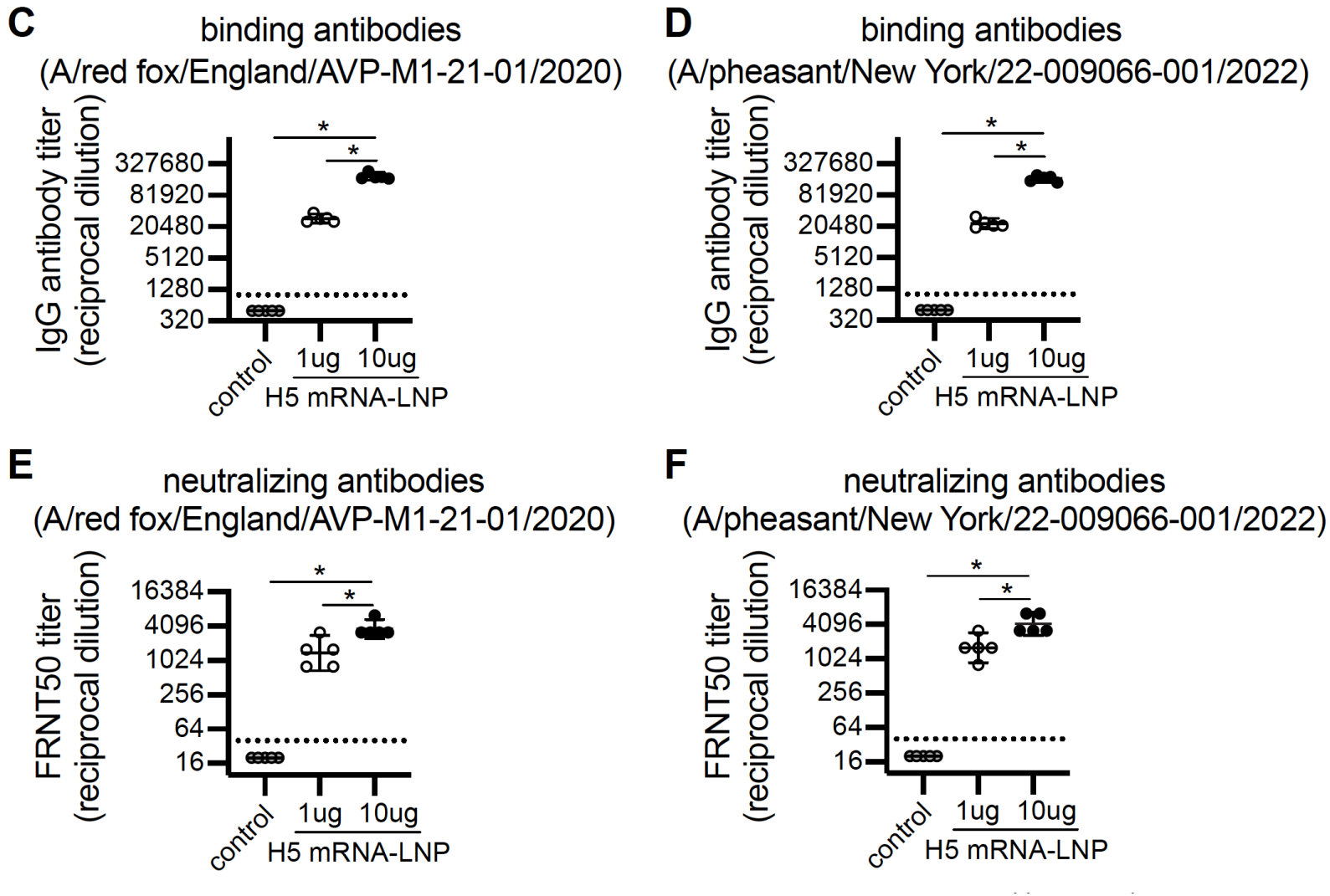
Nucleoside-modified, purified mRNA formulated in LNP is highly expressed and stimulates potent immune responses.

H5 clade 2.3.4.4b mRNA-LNP elicits antibodies in mice after single vaccination



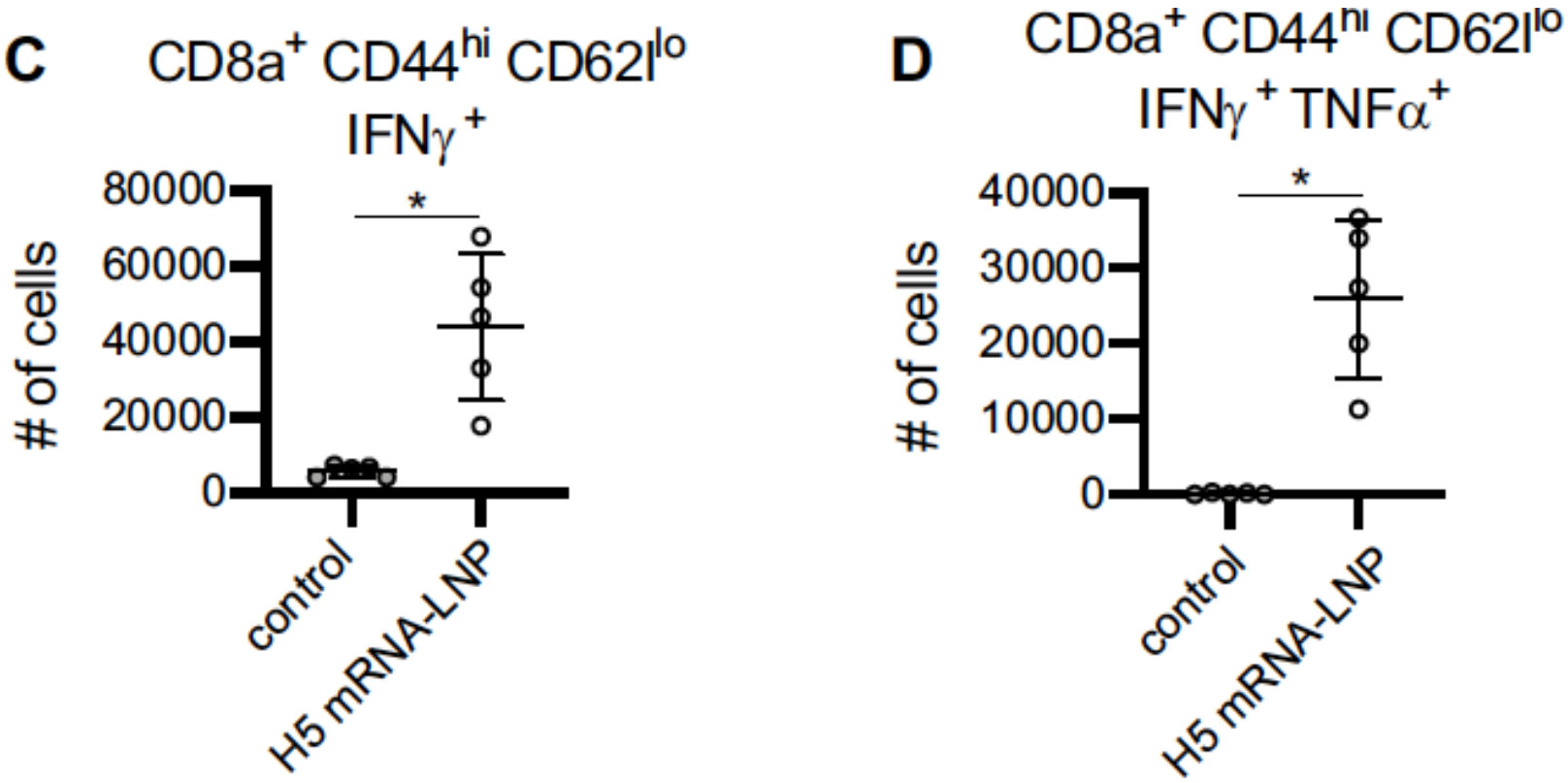
Furey et al. *Nature Communications* (2024)

Antibodies elicited by H5 mRNA-LNP vaccination can bind and neutralize different viral strains



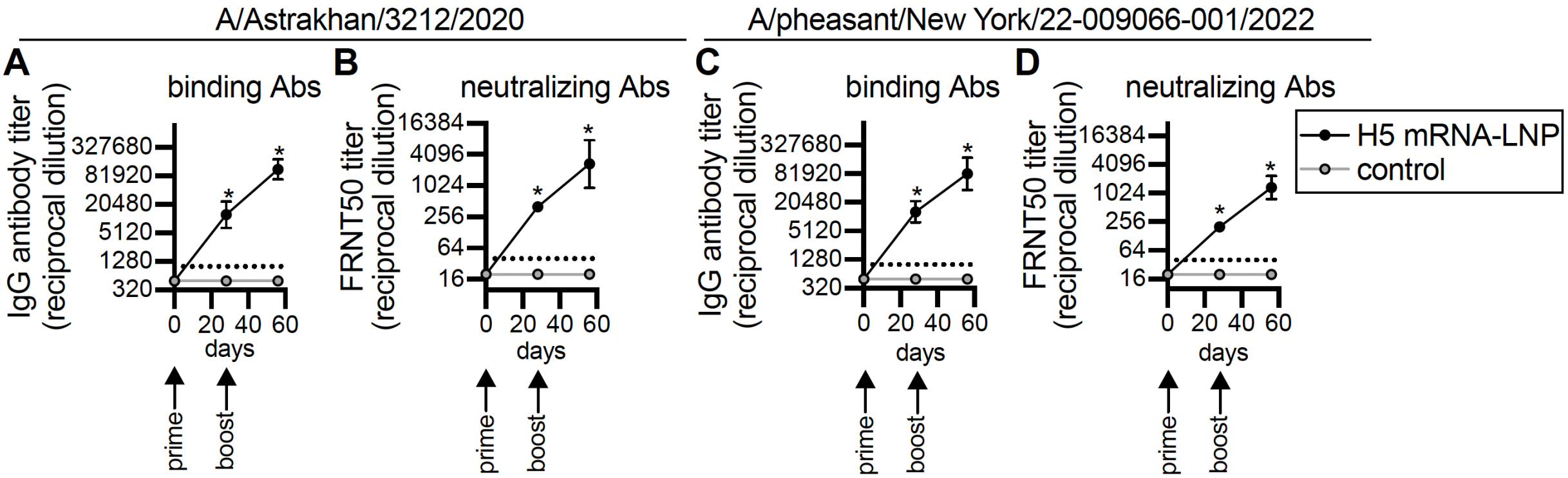
Furey et al. *Nature Communications* (2024)

H5 mRNA-LNP vaccine elicits CD8+ T cells in mice



Furey et al. *Nature Communications* (2024)

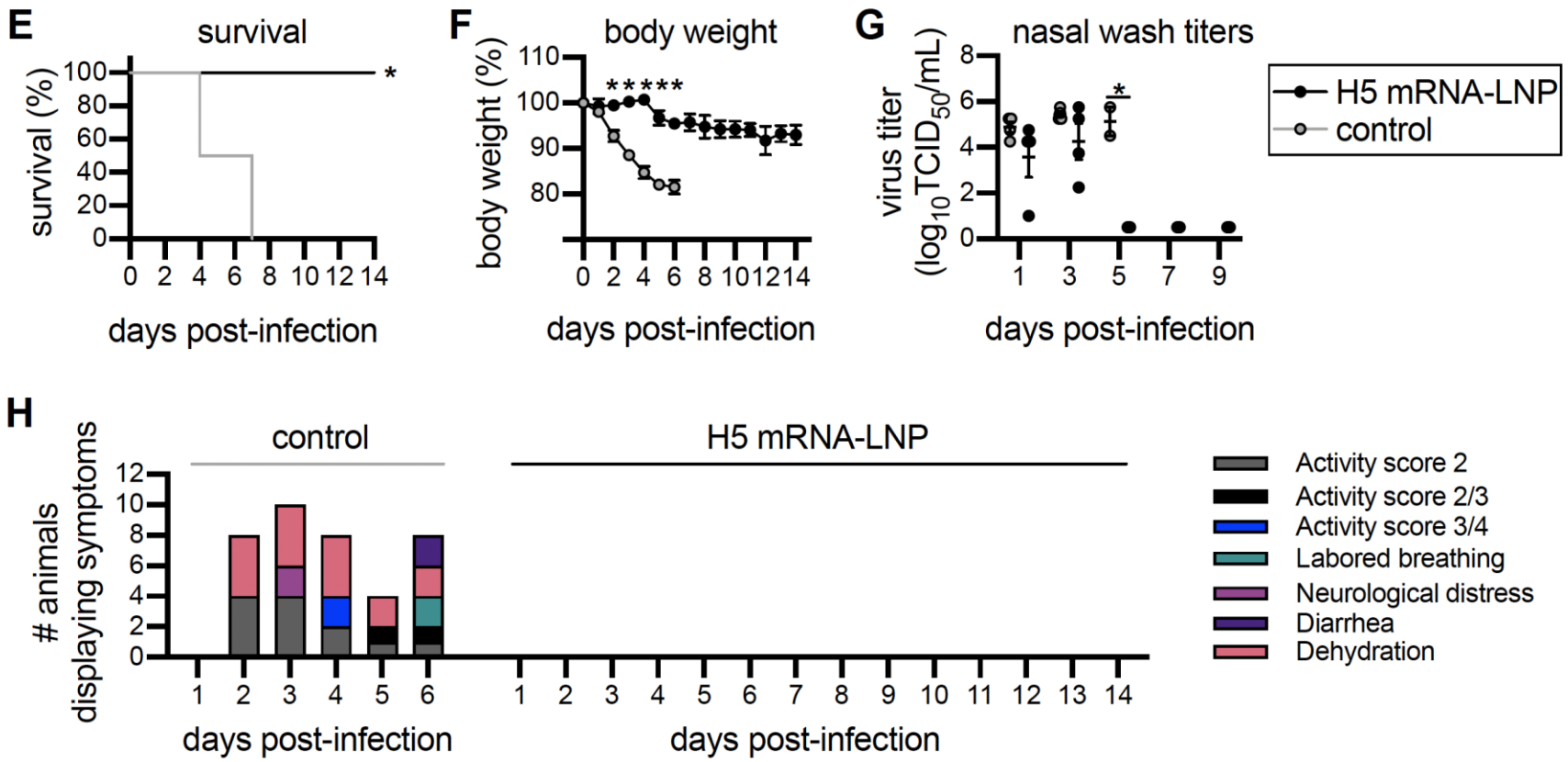
H5 clade 2.3.4.4b mRNA-LNP vaccine elicits antibodies in ferrets



ferret work: Richard Webby (St. Jude)

Furey et al. *Nature Communications* (2024)

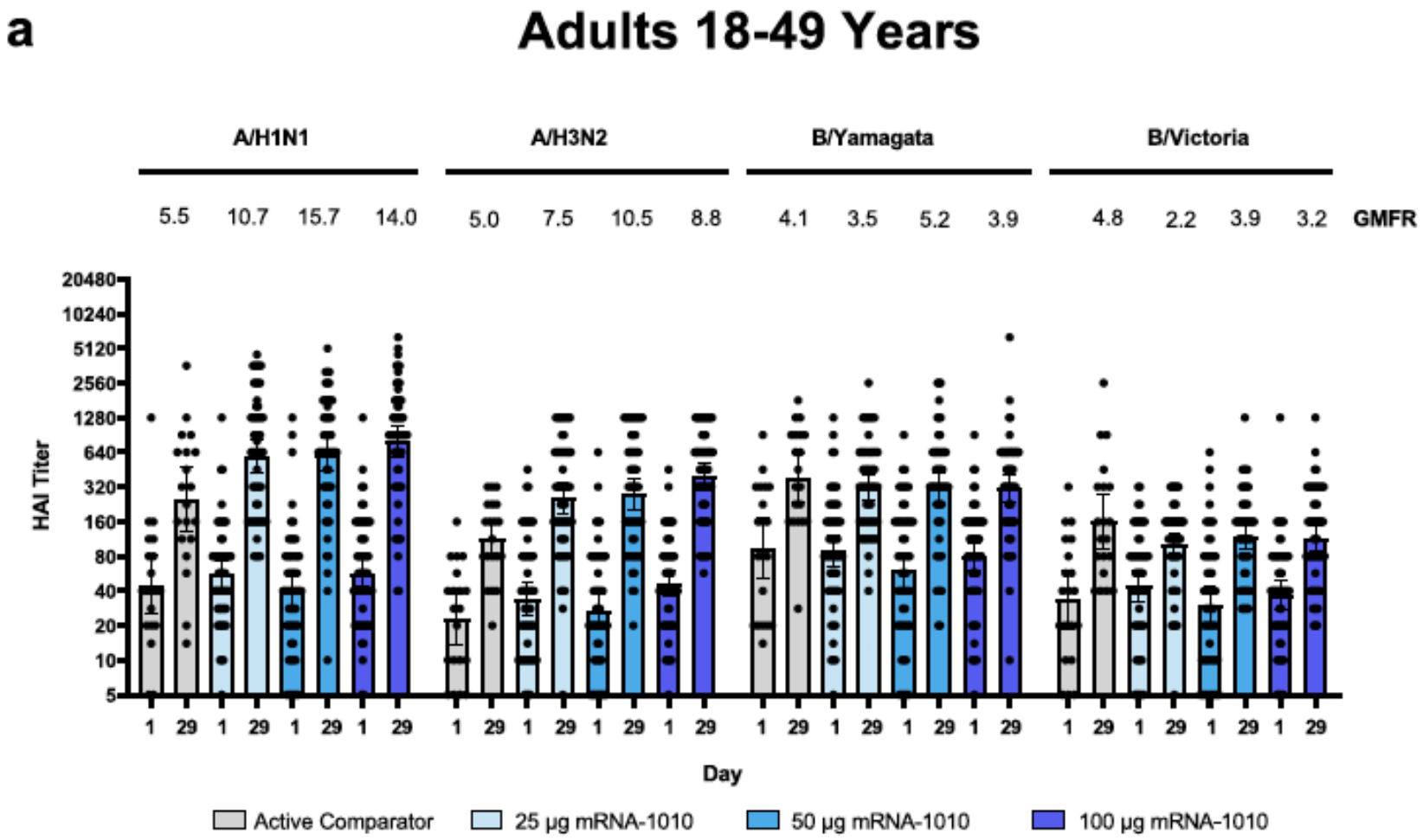
H5 clade 2.3.4.4b mRNA vaccine protects ferrets from lethal challenge



ferret work: Richard Webby (St. Jude)
challenge strain: A/Bald eagle/North Carolina/W22-140-2022

Furey et al. *Nature Communications* (2024)

Moderna and others are testing HA mRNA-LNPs in humans

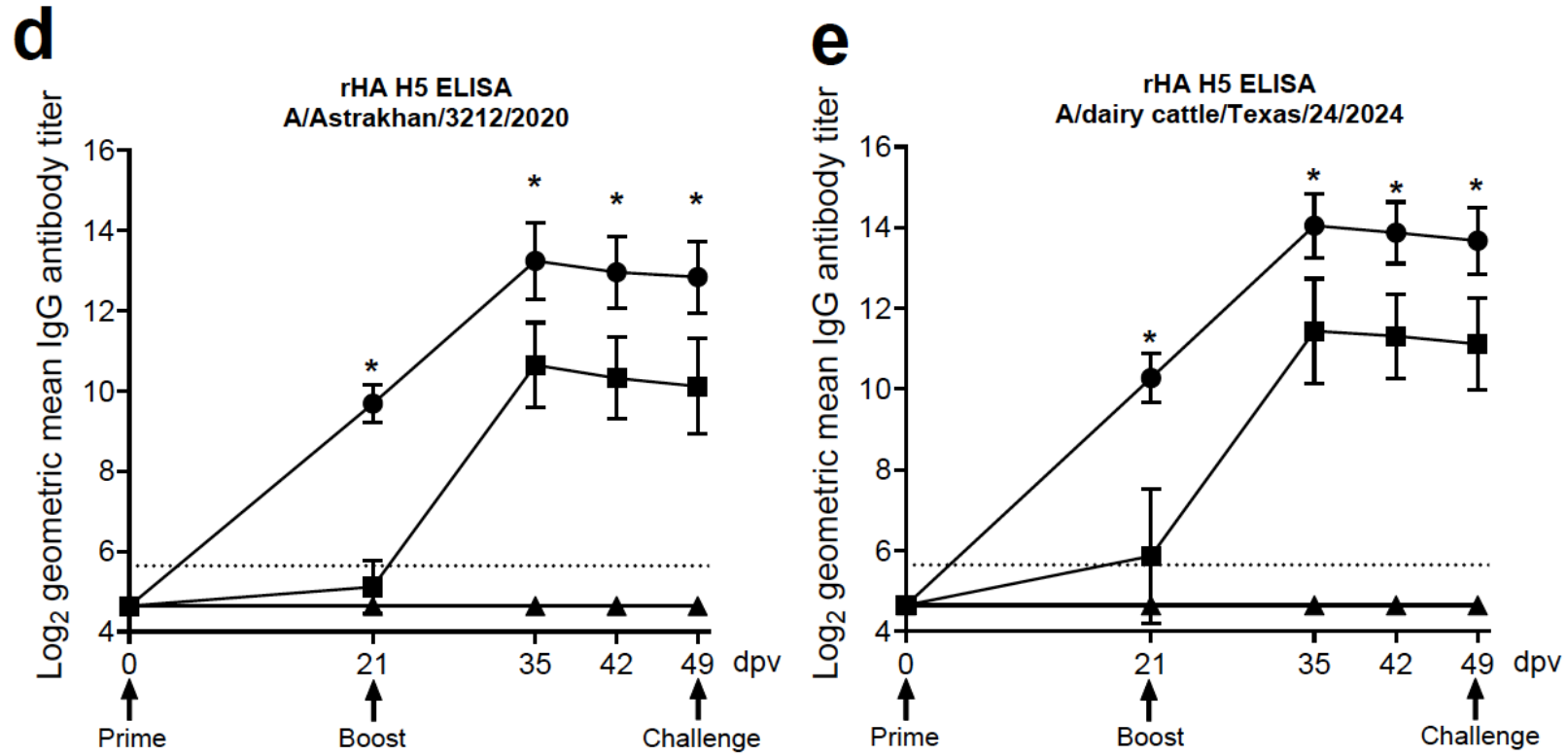


*seasonal influenza mRNA-LNP vaccine

Lee et al. *Nature Communications* (2023)

Can the monovalent clade 2.3.4.4b H5 mRNA-LNP vaccine reduce viral spread in livestock?

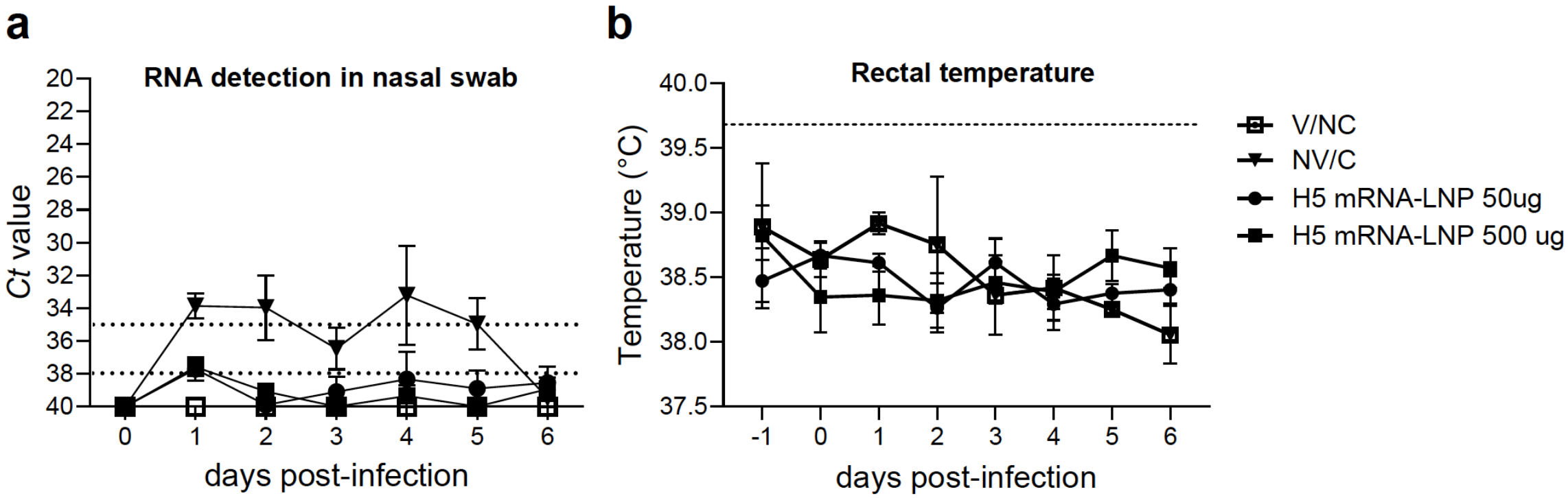
H5 clade 2.3.4.4b mRNA-LNP vaccine elicits antibodies in calves



Collaboration with Amy Baker at USDA

Manuscript in prep

H5 clade 2.3.4.4b mRNA-LNP vaccine protects calves from H5N1 infection

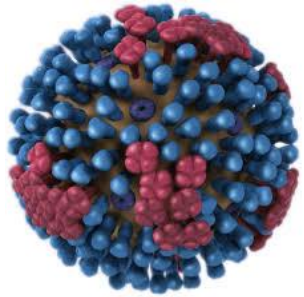


Collaboration with Amy Baker at USDA

Manuscript in prep

New mRNA-LNP experiments in lactating cattle just launched through collaboration with Dr. Gary Althouse

animals shipped to Iowa



@Penn
Vaccinate and obtain milk and blood
(BSL 1)

@USDA
H5N1 viral challenge via mammary gland injection
(BSL3)

Overall Summary

- Clade 2.3.4.4b H5N1 mRNA-LNP vaccine elicits strong antibody responses in mice, ferrets, and calves
- The vaccine protects ferrets and calves from H5N1 infection
- Ongoing experiments are evaluating the vaccine in lactating cattle, swine, and birds

- Clinical testing of H5N1 mRNA-LNP vaccines should be top priority
  - Phase 1, 2, 3 testing can be done **before** a pandemic
  - With early clinical testing, can updated vaccine antigens be considered a vaccine strain update?
  - Clinical testing is money well spent even if H5 doesn't cause a pandemic

Acknowledgements

HENSLEY LAB

Grace Li
Elizabeth Drapeau
Rachel Serafin
Lydia Mendoza
Ashley Sobel-Leonard
Ross England
Jiaojiao Liu
Gabby Scher
Jefferson Santos
Naiqing Ye
Reilly Atkinson
Tyler Garretson
Jordan Ort
Colleen Furey
Yan Zhao
Leanne Good
Tachianna Griffiths
Claudia Arevalo

Penn
Drew Weissman
Mohamad-Gabriel Alameh

USDA
Amy Baker
Carine Souza
Tavis Anderson

St. Jude
Richard Webby
Lisa Kercher
Jennifer DeBeauchamp
Jeri Carol Crumpton
Trushar Jeevan
Chris Patton
John Franks

BURROUGHS WELLCOME FUND

Penn | CEIRR
CENTER OF EXCELLENCE FOR INFLUENZA RESEARCH AND RESPONSE

National Institute of Allergy and Infectious Diseases

CIVICs
Collaborative Influenza Vaccine Innovation Centers