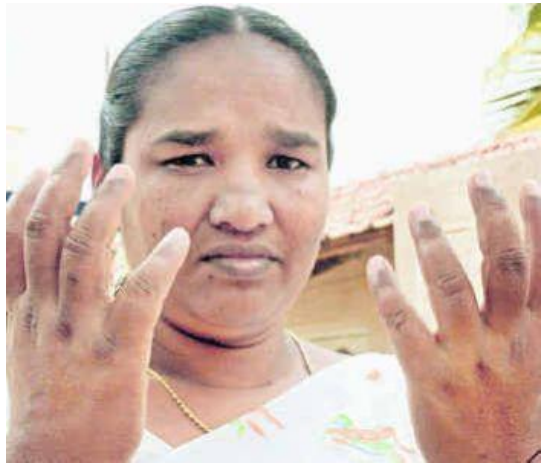
# Bioengineering for Health

*Andres Merits*

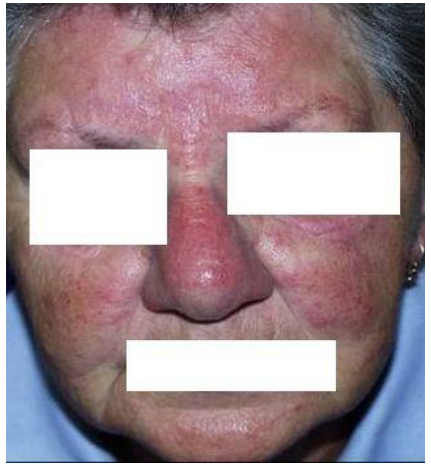
Institute of Bioengineering
University of Tartu
Estonia

October 10, 2024

# Viruses of current interest



chikungunya virus



Barmah Forest virus

Zika virus

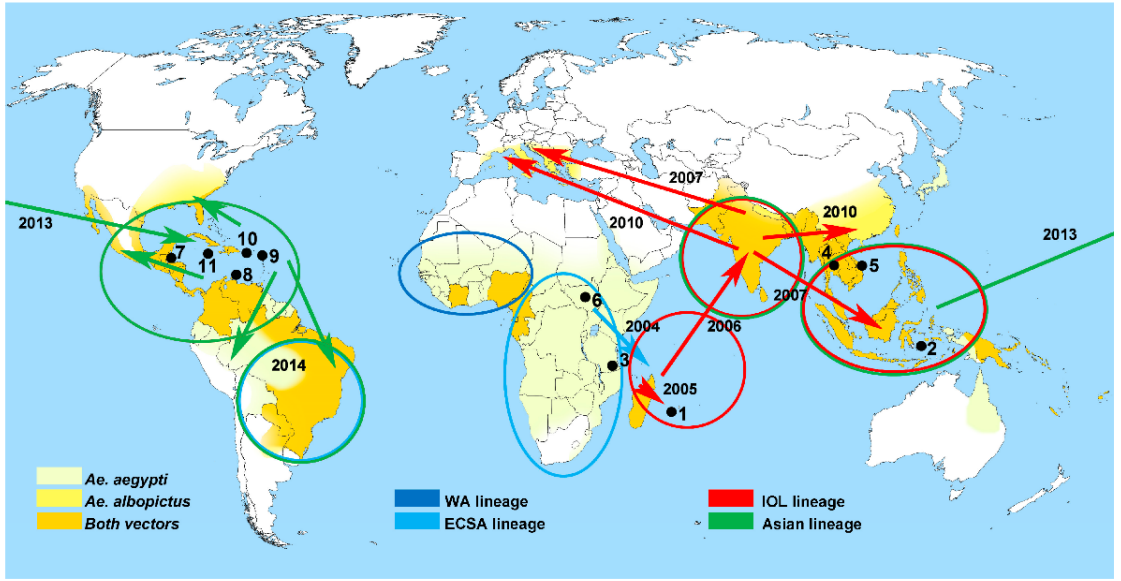
**Alphaviruses:**
chikungunya virus
Ross River virus
Mayaro virus
o'nyong-nyong virus
Eastern equine encephalitis virus
Barmah Forest virus
**Flaviviruses:**
Zika virus
Dengue virus 1-4
Tick born encephalitsis virus
Kyasanur Forest disease virus (AHFV variant)
**Coronaviruses:**
SARS-CoV-2

**Our approach: basic studies of the molecular- and infection biology and use of obtained results for:**

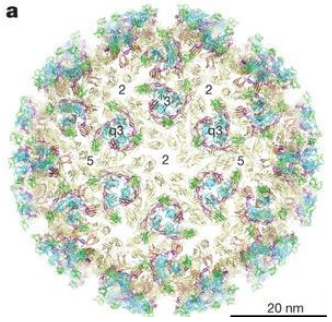
1. **Development of live attenuated vaccines**
2. **Development of RNA based biotechnologies**
3. **Development of approaches to break virus transmission cycle**

# Chikungunya virus (CHIKV)

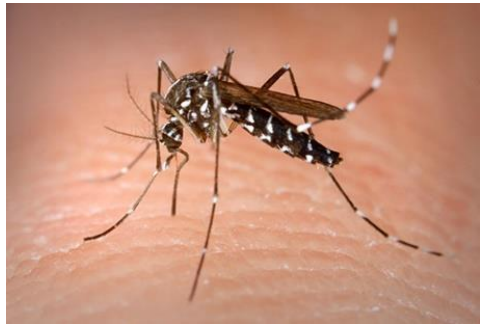
- Old World (arthritogenic) alphavirus
- Distributed around the world, including the Americas
- Symptoms in humans include rash, fever, joint pain
- High percentage of cases persist into chronic arthritis
- Mostly spread by *Aedes aegypty* or *Ae. albopictus* mosquitoes



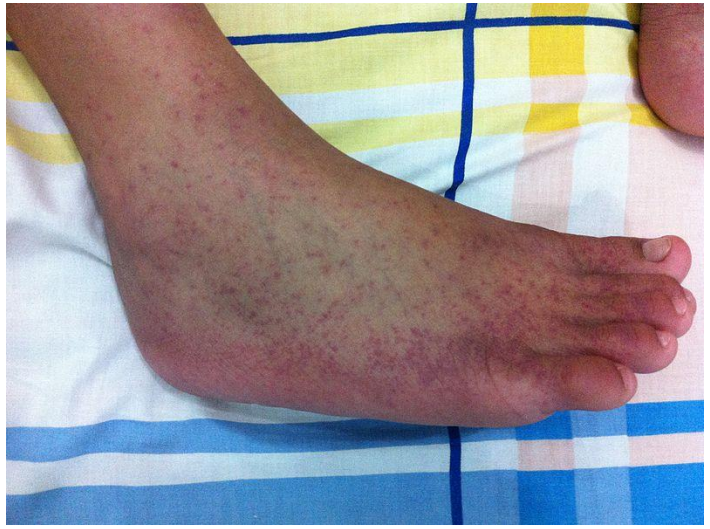

Kriekmann et al., 2019




Voss et al., 2010



CDC



Wikipedia

# Chikungunya vaccine IxChiq

JVI
Journals.ASM.org

## Novel Attenuated Chikungunya Vaccine Candidates Elicit Protective Immunity in C57BL/6 mice

David Hallengärd,[a] Maria Kakoulidou,[a] Aleksei Lulla,[b] Beate M. Kümmerer,[c] Daniel X. Johansson,[a] Margit Mutso,[b] Valeria Lulla,[b] John K. Fazakerley,[d] Pierre Roques,[e,f] Roger Le Grand,[e,f] Andres Merits,[b] Peter Liljeström[a]

Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden[a]; Institute of Technology, University of Tartu, Tartu, Estonia[b]; Institute of Virology, University of Bonn Medical Centre, Bonn, Germany[c]; The Pirbright Institute, Pirbright, United Kingdom[d]; Division of Immuno-Virology, iMETI, CEA, Paris, France[e]; UMR-E1, University Paris-Sud XI, Orsay, France[f]

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## Prime-Boost Immunization Strategies against Chikungunya Virus

David Hallengärd,[a] Fok-Moon Lum,[b,c] Beate M. Kümmerer,[d] Aleksei Lulla,[e] Valeria Lulla,[e] Juan García-Arriaza,[f] John K. Fazakerley,[g] Pierre Roques,[h,i] Roger Le Grand,[h] Andres Merits,[e] Lisa F. P. Ng,[b,c] Mariano Esteban,[f] Peter Liljeström[a]

Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden[a]; Singapore Immunology Network, Agency for Science, Technology and Research (A*STAR), Biopolis, Singapore[b]; Department of Biochemistry, Yong Loo Lin School of Medicine, National University of Singapore (NUS), Singapore[c]; University of Bonn Medical Centre, Bonn, Germany[d]; Institute of Technology, University of Tartu, Tartu, Estonia[e]; Department of Molecular and Cellular Biology, Centro Nacional de Biotecnología, Consejo Superior de Investigaciones Científicas, Madrid, Spain[f]; Institute of Virology, The Pirbright Institute, Pirbright, United Kingdom[g]; Division of Immuno-Virology, iMETI, CEA, Paris, France[h]; UMR-E1, University Paris-Sud XI, Orsay, France[i]

JCI insight

RESEARCH ARTICLE

## Attenuated and vectored vaccines protect nonhuman primates against Chikungunya virus

Pierre Roques,[1,2,3] Karl Ljungberg,[4] Beate M. Kümmerer,[5] Leslie Gosse,[1,2,3] Nathalie Dereuddre-Bosquet,[1,2,3] Nicolas Tchitchek,[1,2,3] David Hallengärd,[4] Juan García-Arriaza,[6] Andreas Meinke,[7] Mariano Esteban,[6] Andres Merits,[8] Roger Le Grand,[1,2,3] and Peter Liljeström[4]

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## Valneva Initiates Rolling Submission of FDA Biologics License Application for its Single-Shot Chikungunya Vaccine Candidate

August 18, 2022

**Saint-Herblain (France), August 18, 2022** – Valneva SE (Nasdaq: VALN; Euronext Paris: VLA), a specialty vaccine company, today announces that it has initiated rolling submission of the Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) seeking approval of the Company's single-shot chikungunya vaccine candidate in persons aged 18 years and above.

This BLA submission follows final pivotal Phase 3 data reported in March 2022[1] and final lot-to-lot consistency results reported in May 2022[2]. A clinical study of VLA1553 in adolescents is ongoing in Brazil[3], which may support future regulatory submissions in this group if VLA1553 is approved in adults.

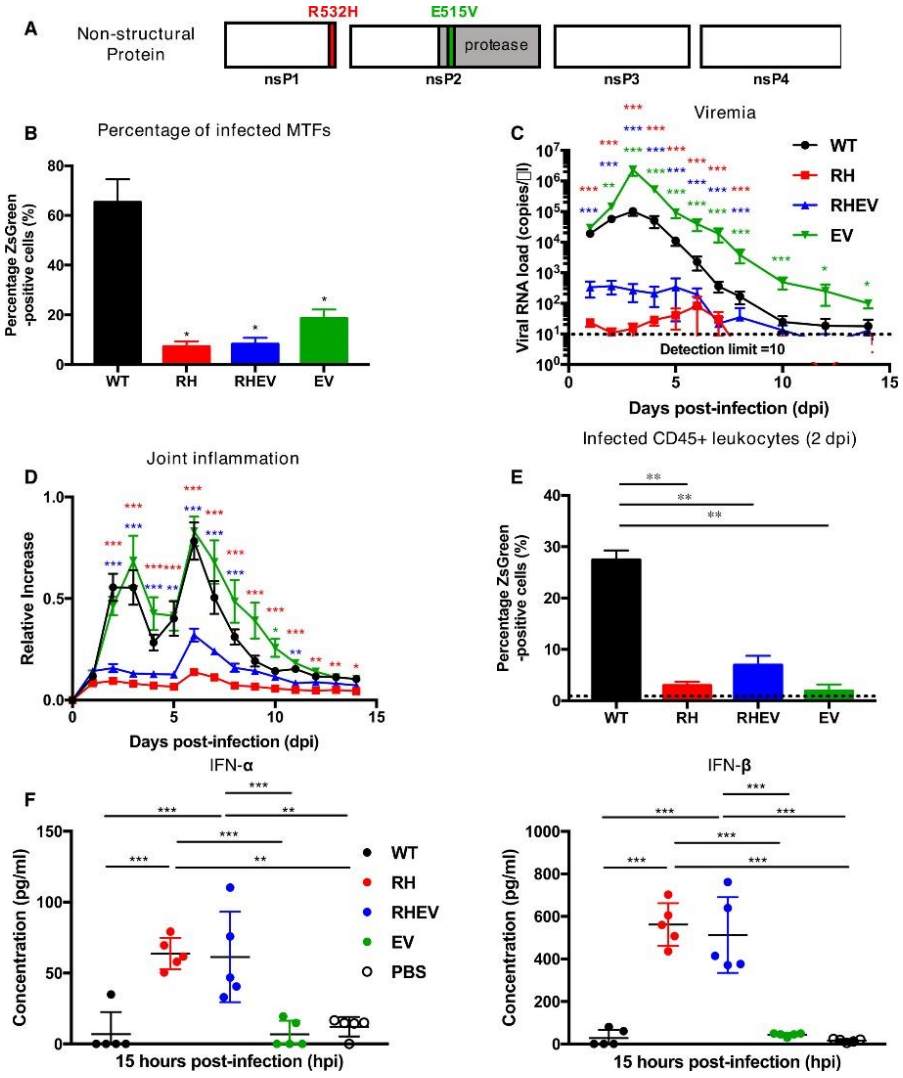
**Juan Carlos Jaramillo, MD, Chief Medical Officer of Valneva**, commented, "This is an extremely important milestone for our VLA1553 program and we are very proud to be the first company worldwide that has begun submission of a BLA for a chikungunya vaccine candidate. Chikungunya is a major public health threat that continues to grow, and no vaccine or specific treatments are currently available for this debilitating disease. We will continue to work assiduously to bring VLA1553 to market as soon as possible."

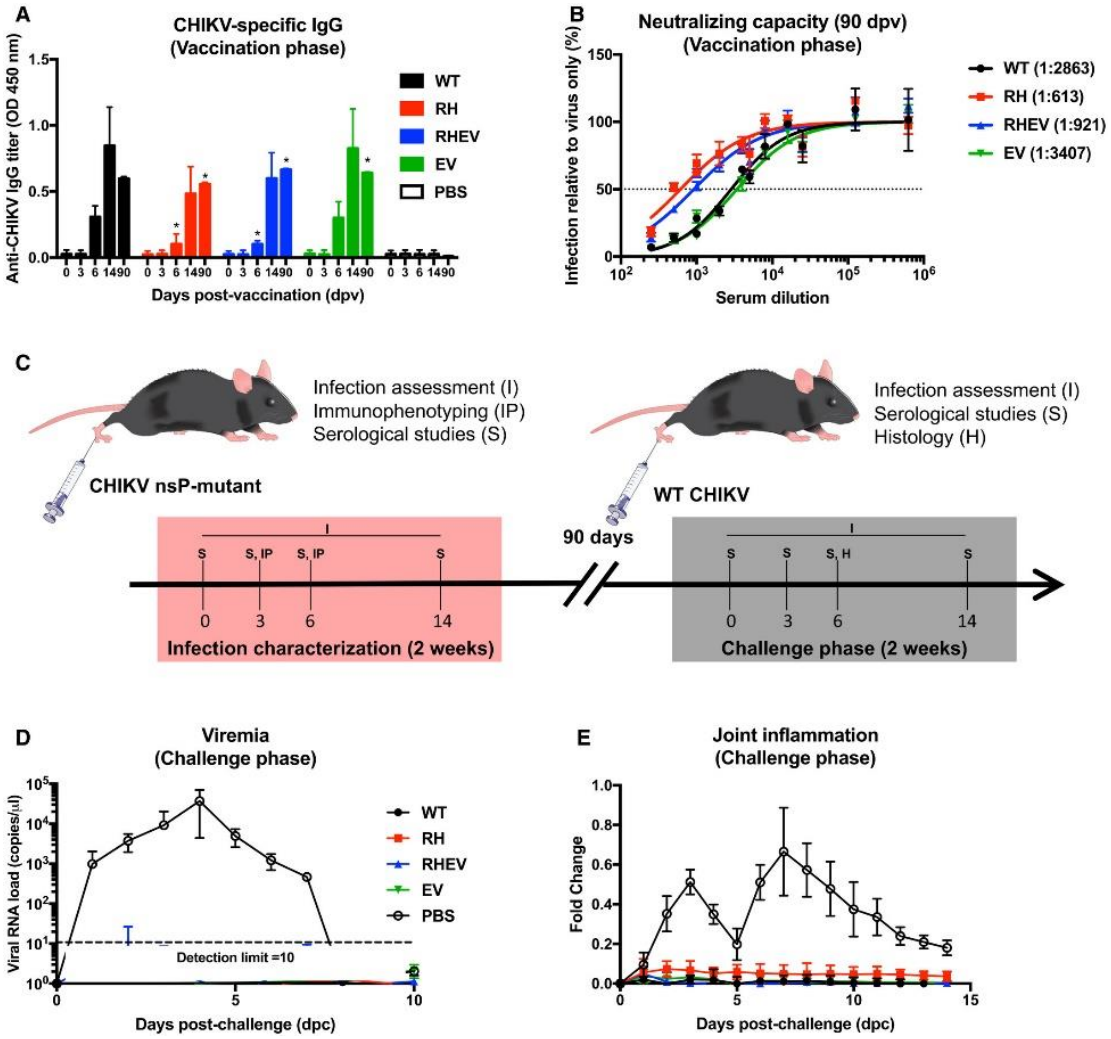
Valneva is currently targeting the end of 2022 for completion of the BLA submission. Once all portions of the application have been submitted and if the filing is accepted, the FDA will determine priority review eligibility and the action date which the FDA will target to complete its evaluation.

This rolling BLA submission is part of the accelerated approval pathway agreed upon with the FDA in 2020[4]. The program received FDA Fast Track and Breakthrough Therapy designations in 2018 and 2021, respectively. VLA1553 was also granted PRIority MEdicine (PRIME) designation by the European Medicines Agency (EMA) in 2020, and Valneva plans to make regulatory submissions for VLA1553 in Europe in the first half of 2023.

# FDA approval in November 2023

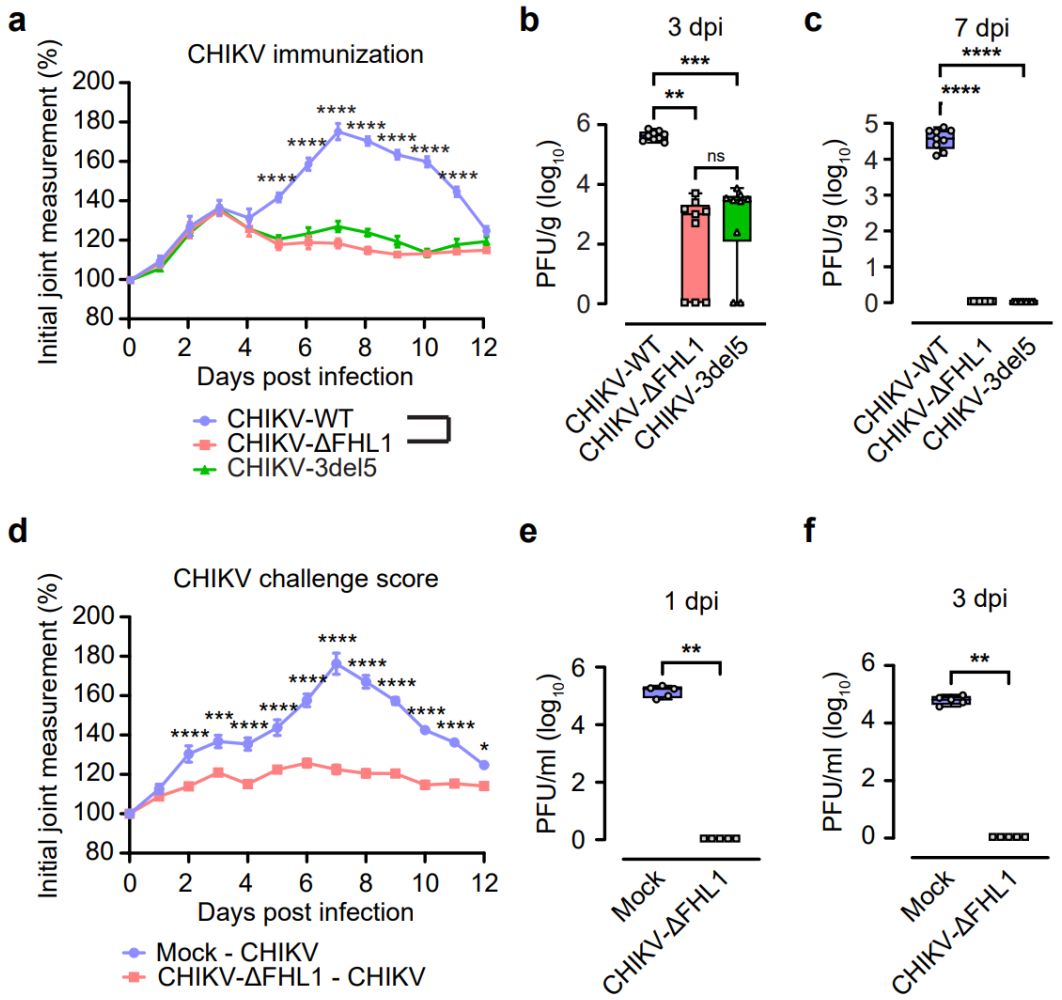
# The P4 Arg-to-His mutation has major impact on *in vivo* phenotype of chikungunya virus




Chan et al., 2019, EMBO Mol Med

# CHIKV-delFHL1 is attenuated and protects mice against wt CHIKV challenge

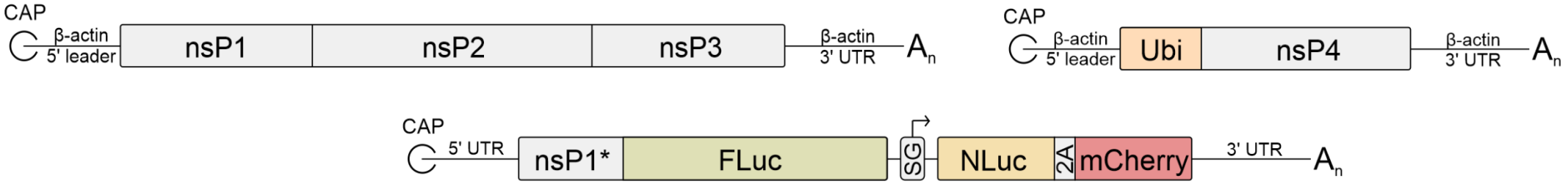


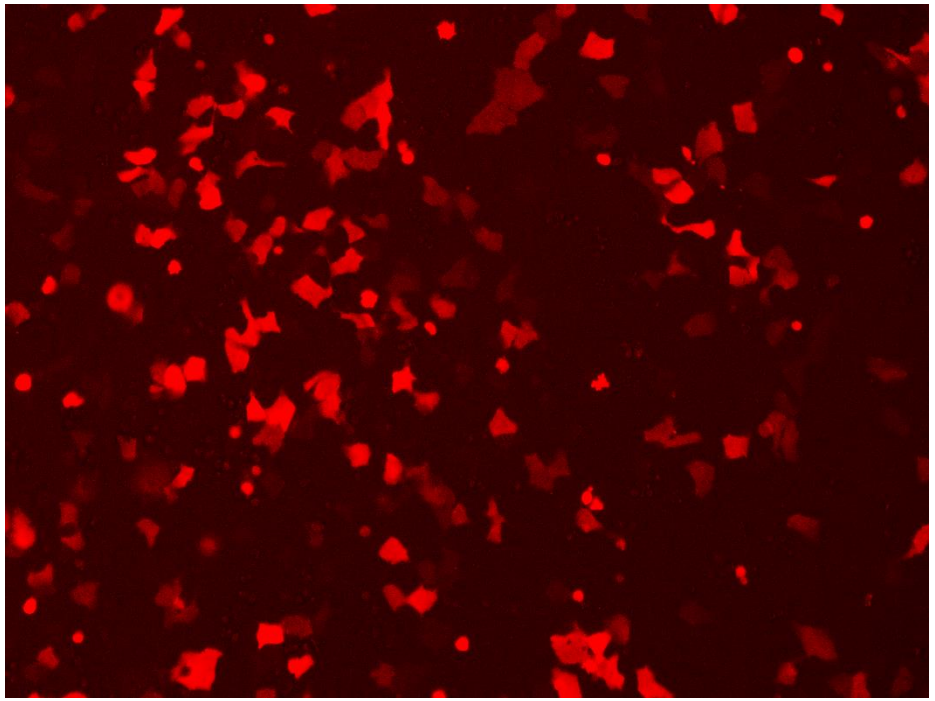

High level protection also against ONNV challenge.

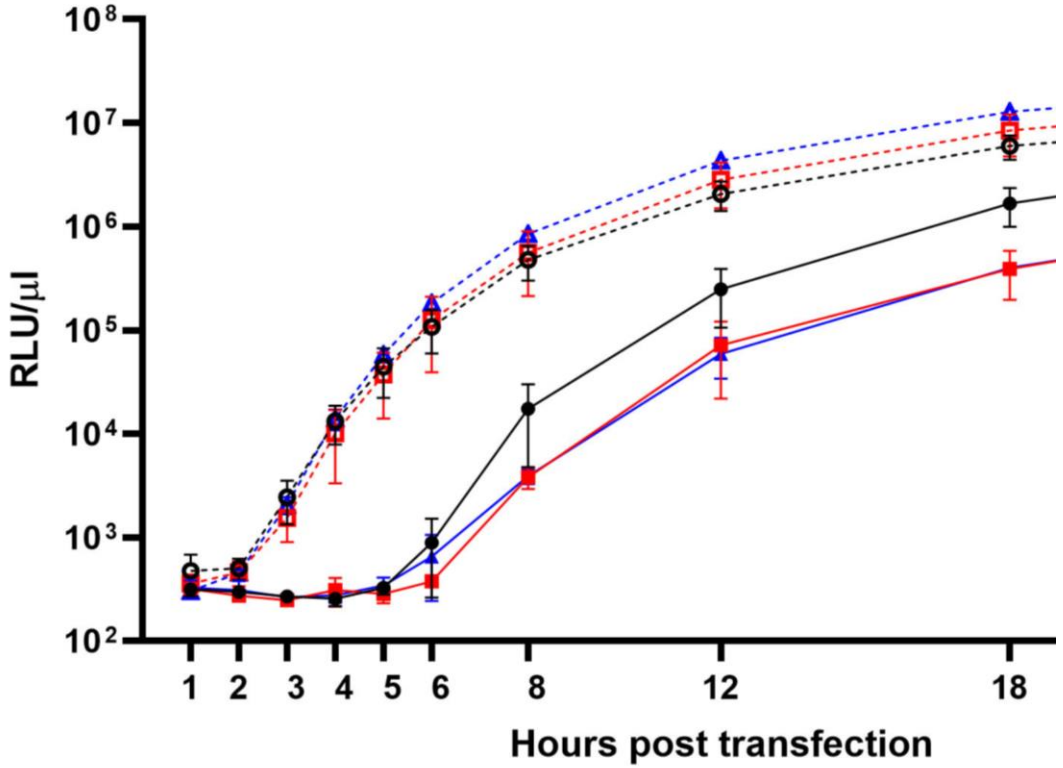
Less prominent protection against RRV or MAYV challenge.

Ng et al., Nature Communications, doi: 10.1038/s41467-023-42330-2.

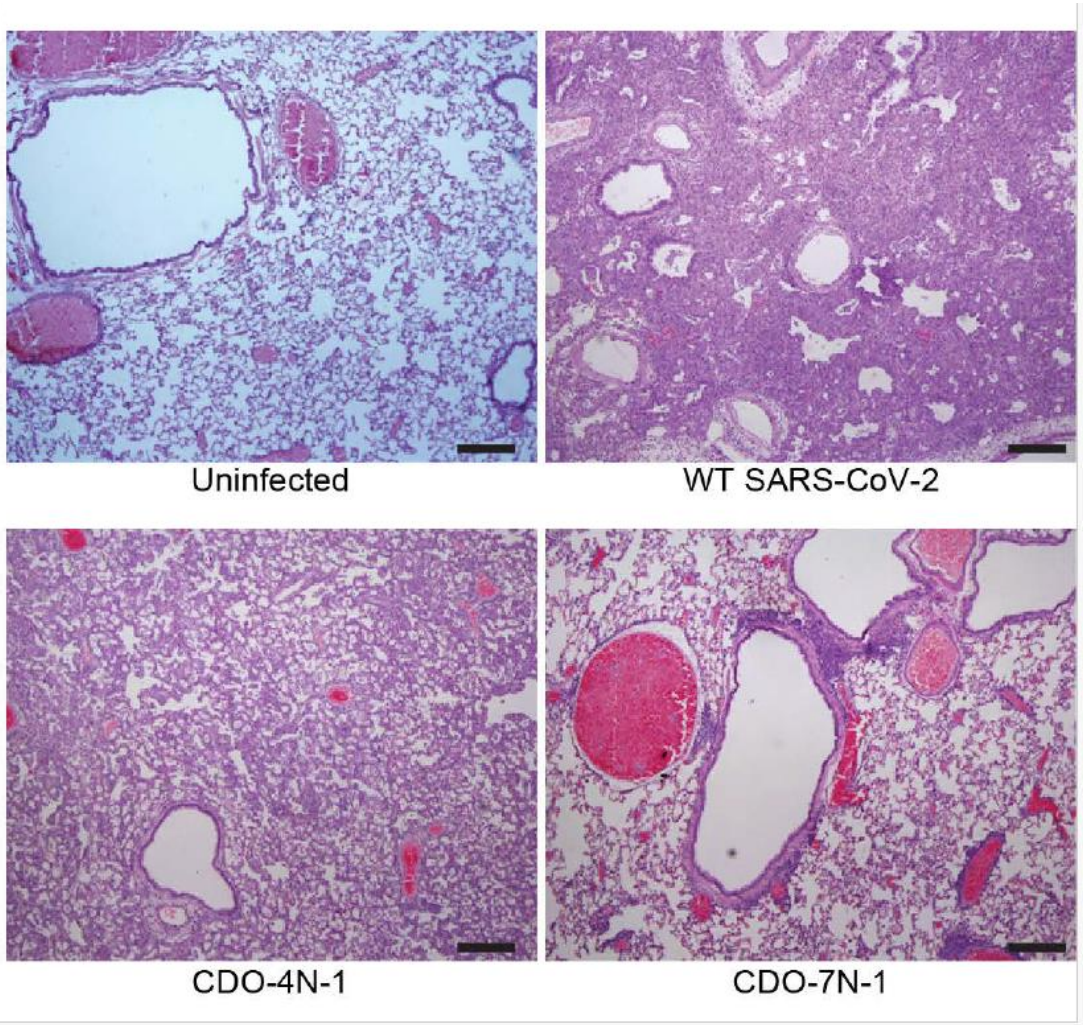
# Trans-amplifying mRNA technology is superior to modified mRNA technology

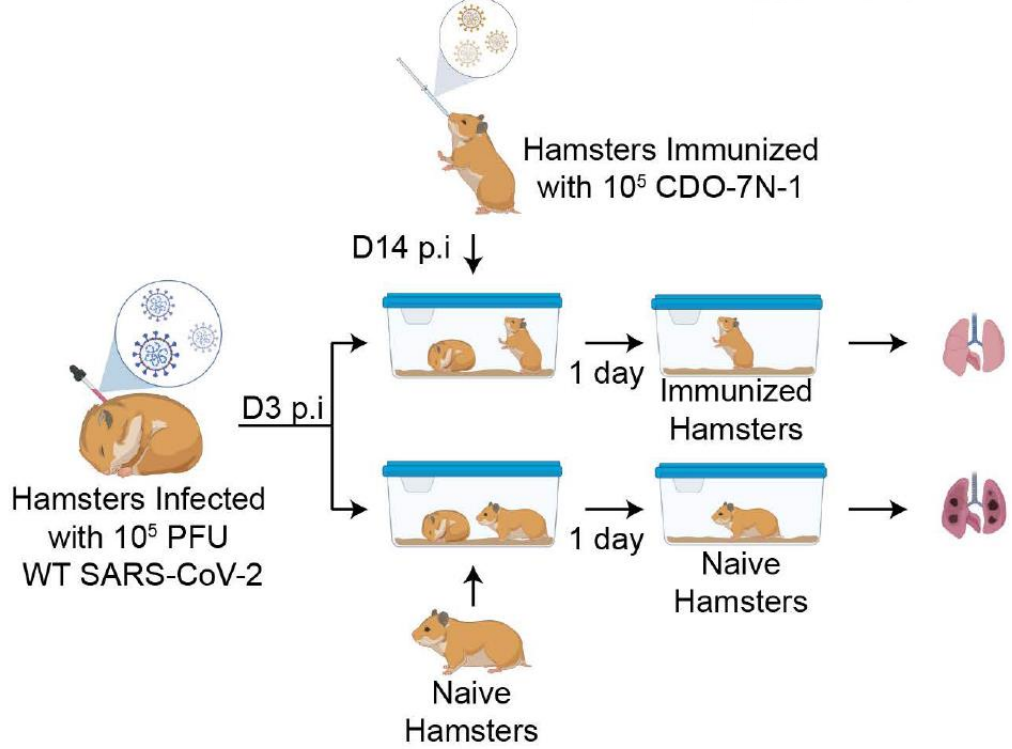


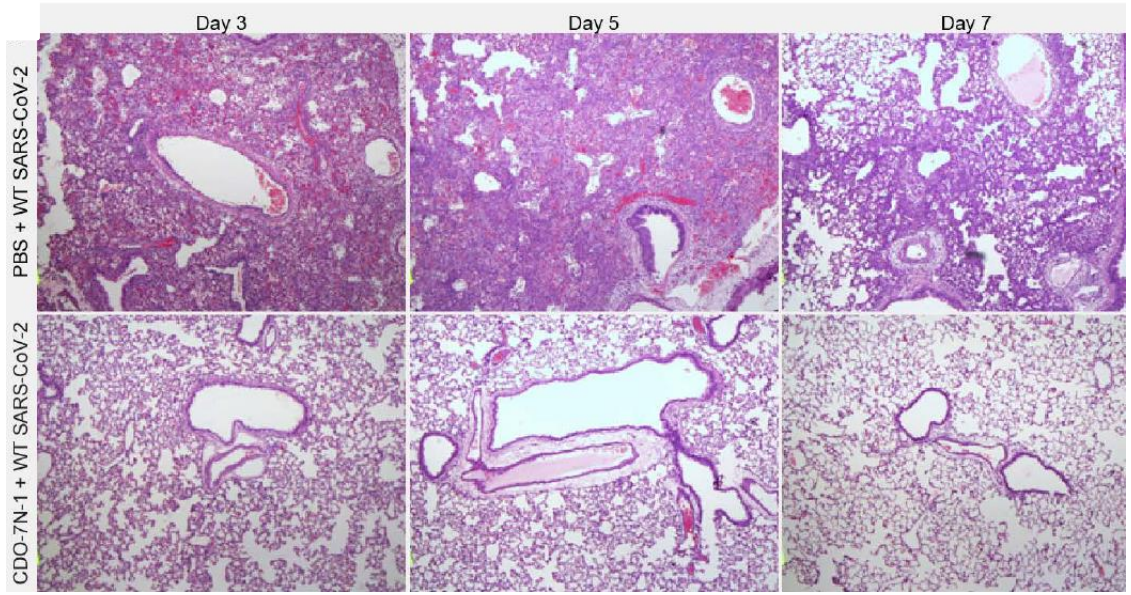





# Codon-altered variants of SARS-CoV-2 are attenuated in vivo and generate protective immunity

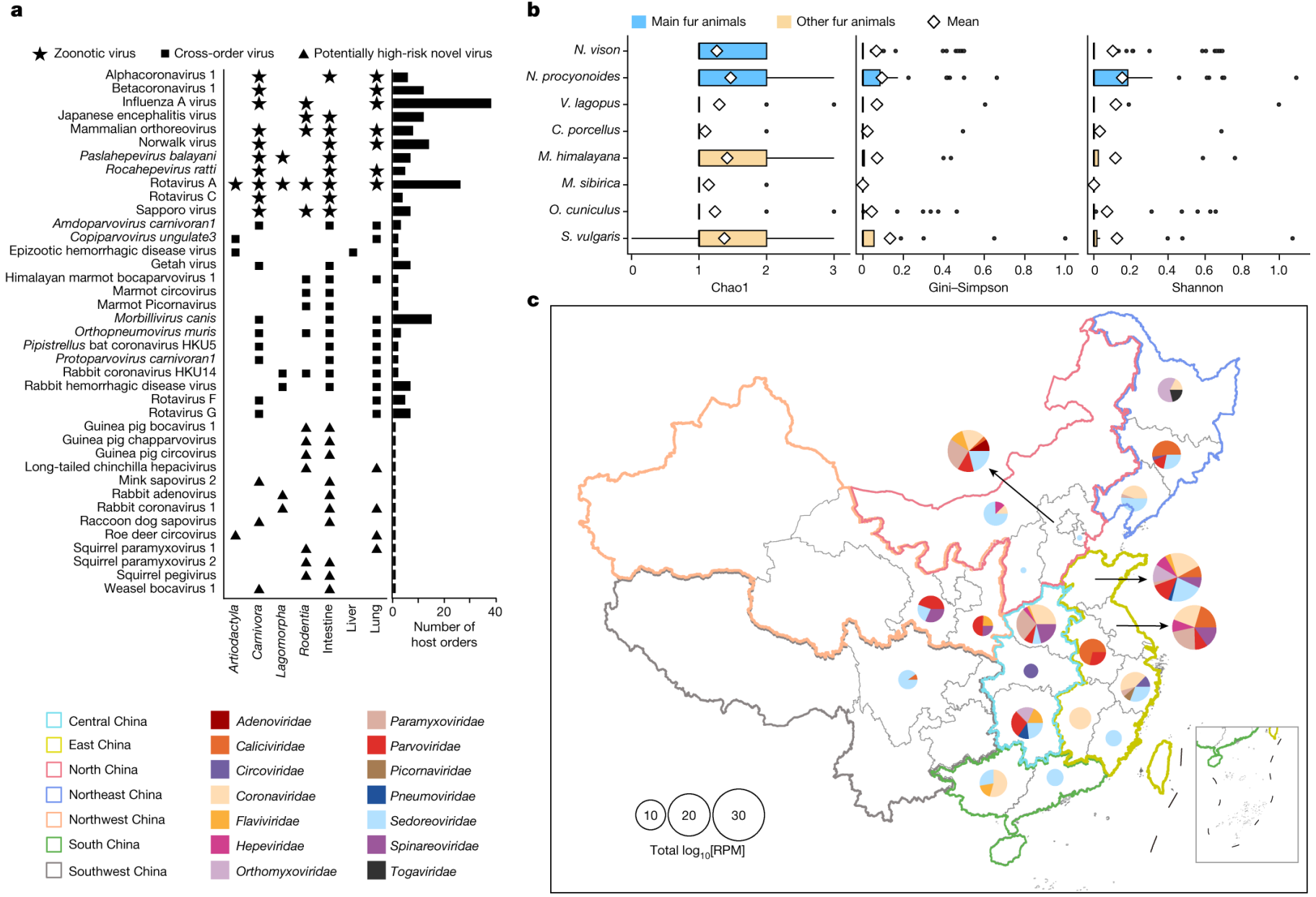



Ng et al, Nat. Commun. doi: 10.1038/s41467-023-42330-2.

# New players are emerging?




Zhao et al., Nature, August 2024. doi: 10.1038/s41586-024-07901-3.

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Suresh Mahalingam, Australia

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Eesti tuleviku heaks

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