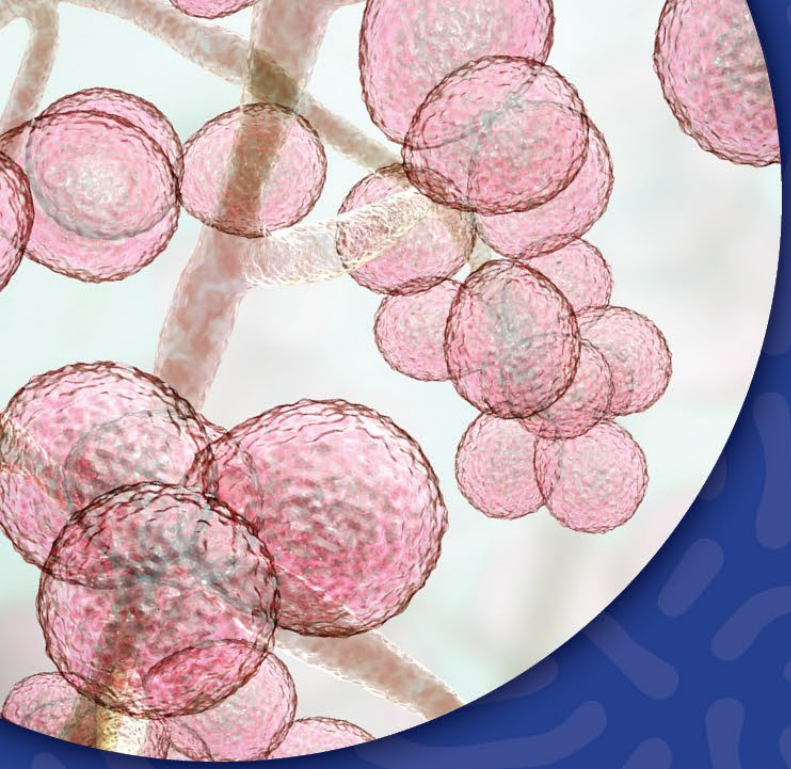
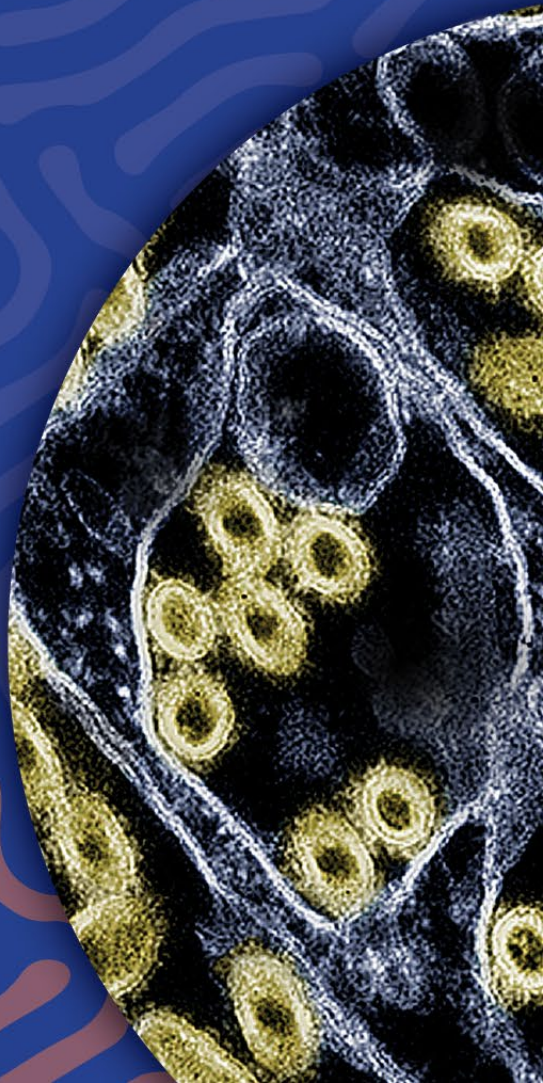


ID LAB CON

APHL

2025

#IDLabCon



Literature review:
vector-borne diseases (viruses)

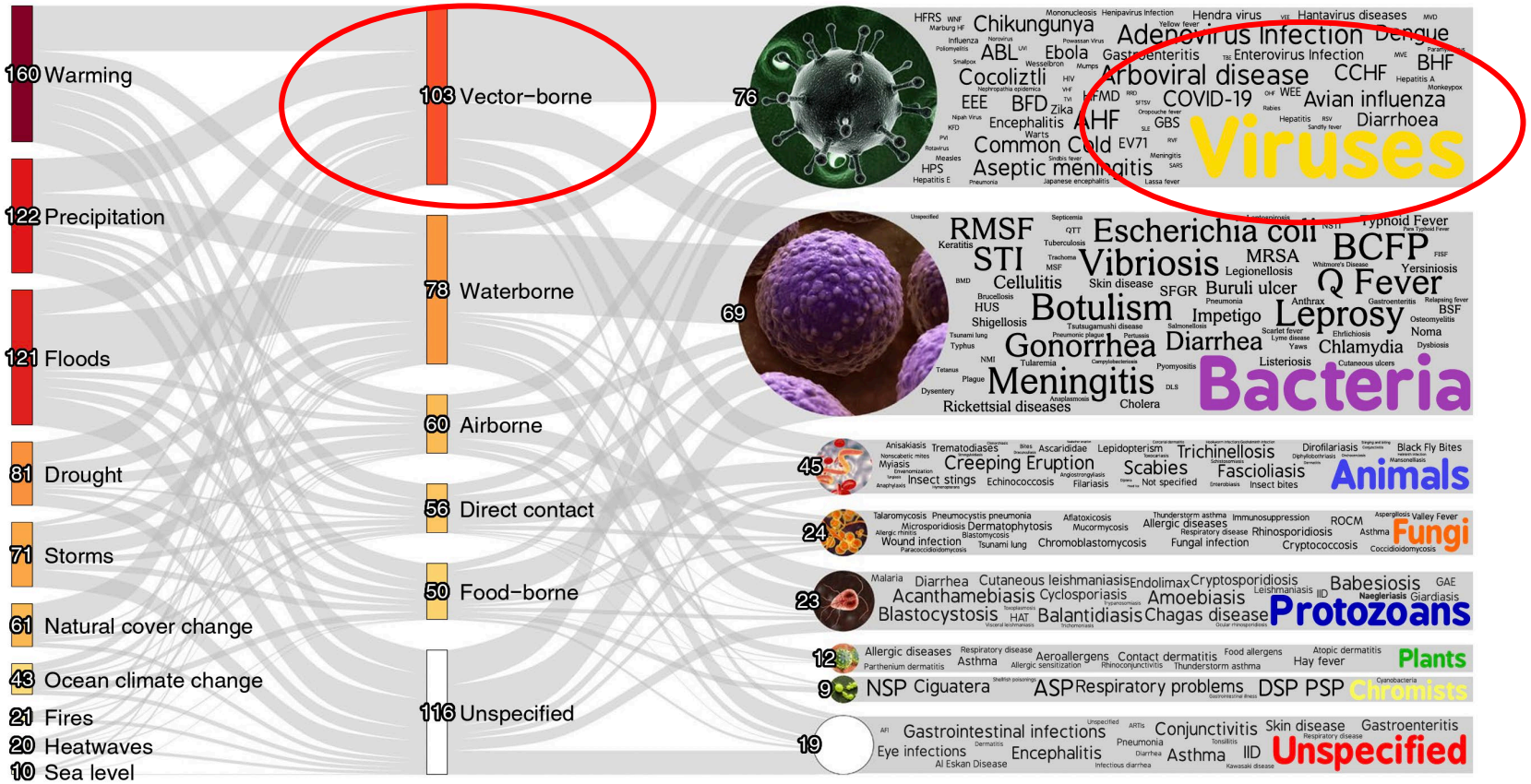
Natasha Louise Tilston, Ph.D
Assistant Professor
Department of Microbiology and Immunology
INDIANA UNIVERSITY SCHOOL OF MEDICINE

Analysis | Published: 08 August 2022

Over half of known human pathogenic diseases can be aggravated by climate change

Camilo Mora ✉, Tristan McKenzie, Isabella M. Gaw, Jacqueline M. Dean, Hannah von Hammerstein, Tabatha A. Knudson, Renee O. Setter, Charlotte Z. Smith, Kira M. Webster, Jonathan A. Patz & Erik C. Franklin

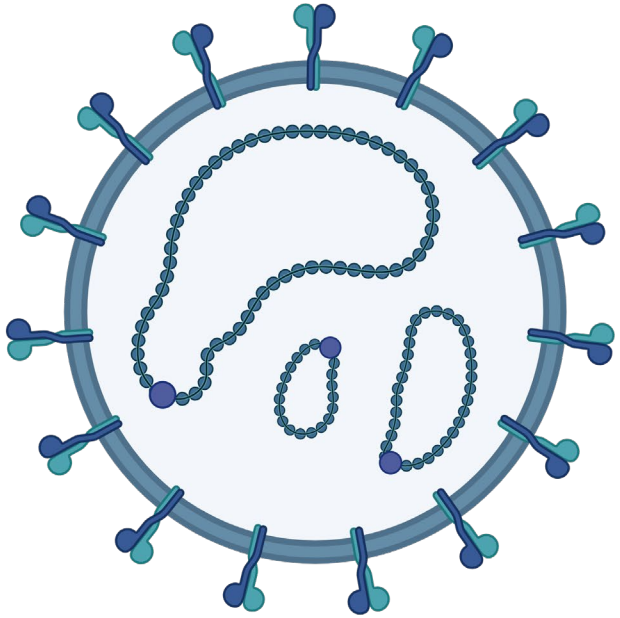
Nature Climate Change **12**, 869–875 (2022) | Cite this article



Papers for today

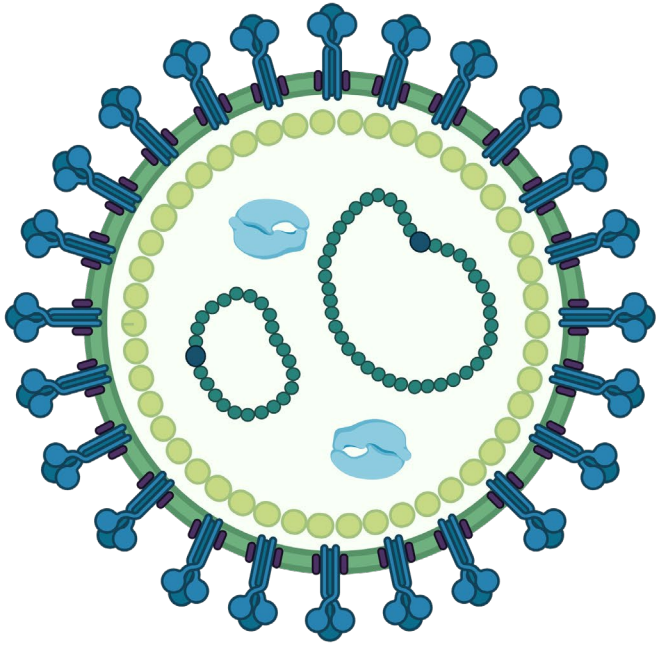
1. Detection: Human case of Potasi and Lone Star viruses (bunyaviruses)
2. Transmission: Mother to fetus of Oropouche virus (bunyavirus)
3. Treatment: Antiviral treatment of arenaviruses

Bunyaviruses and arenaviruses are negative-sense RNA viruses



bunyaviruses

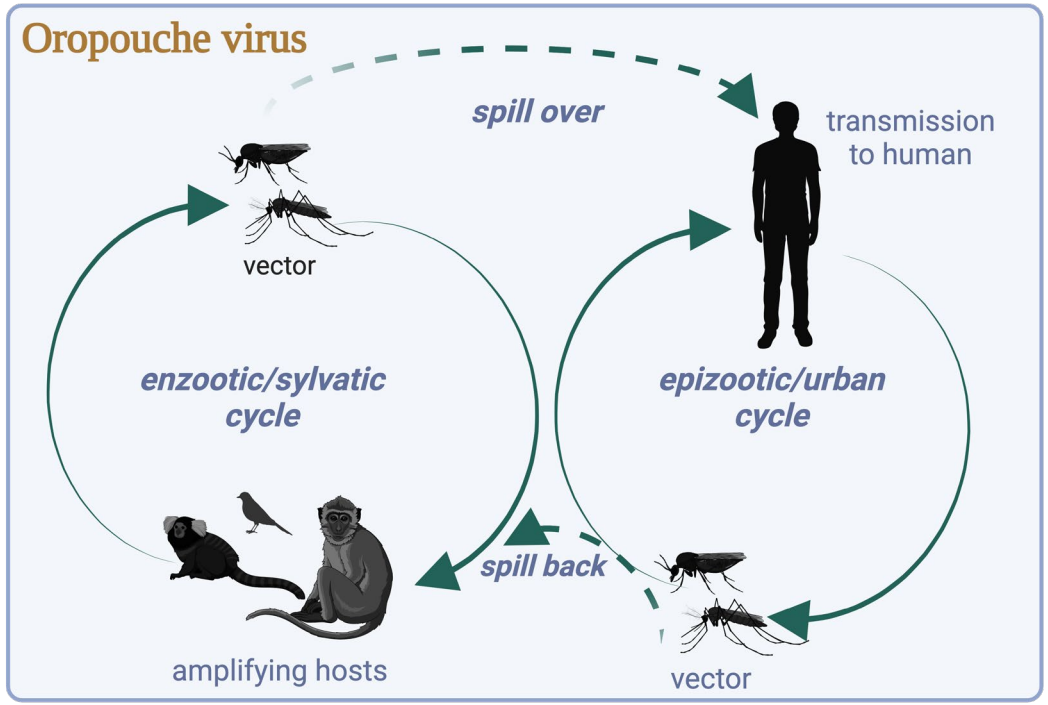
(tri-segmented, -ve RNA genome)



arenaviruses

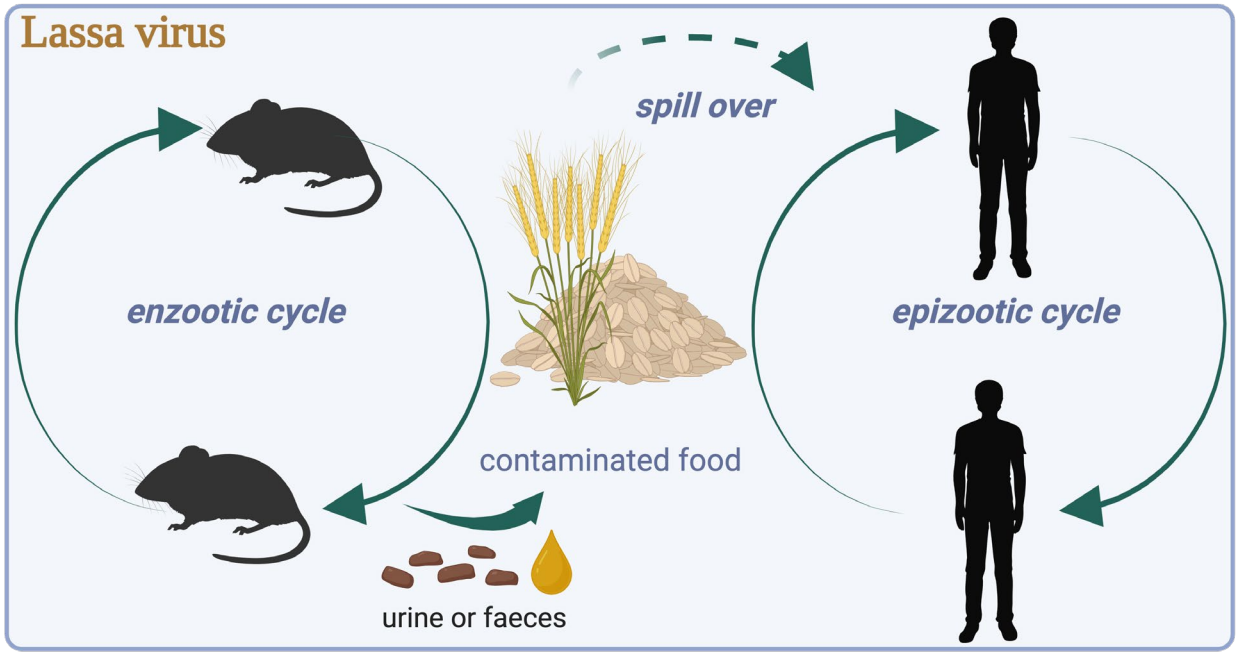
(two-segmented, -ve RNA genome)

Transmission cycles of bunya- and arena- viruses



bunyaviruses

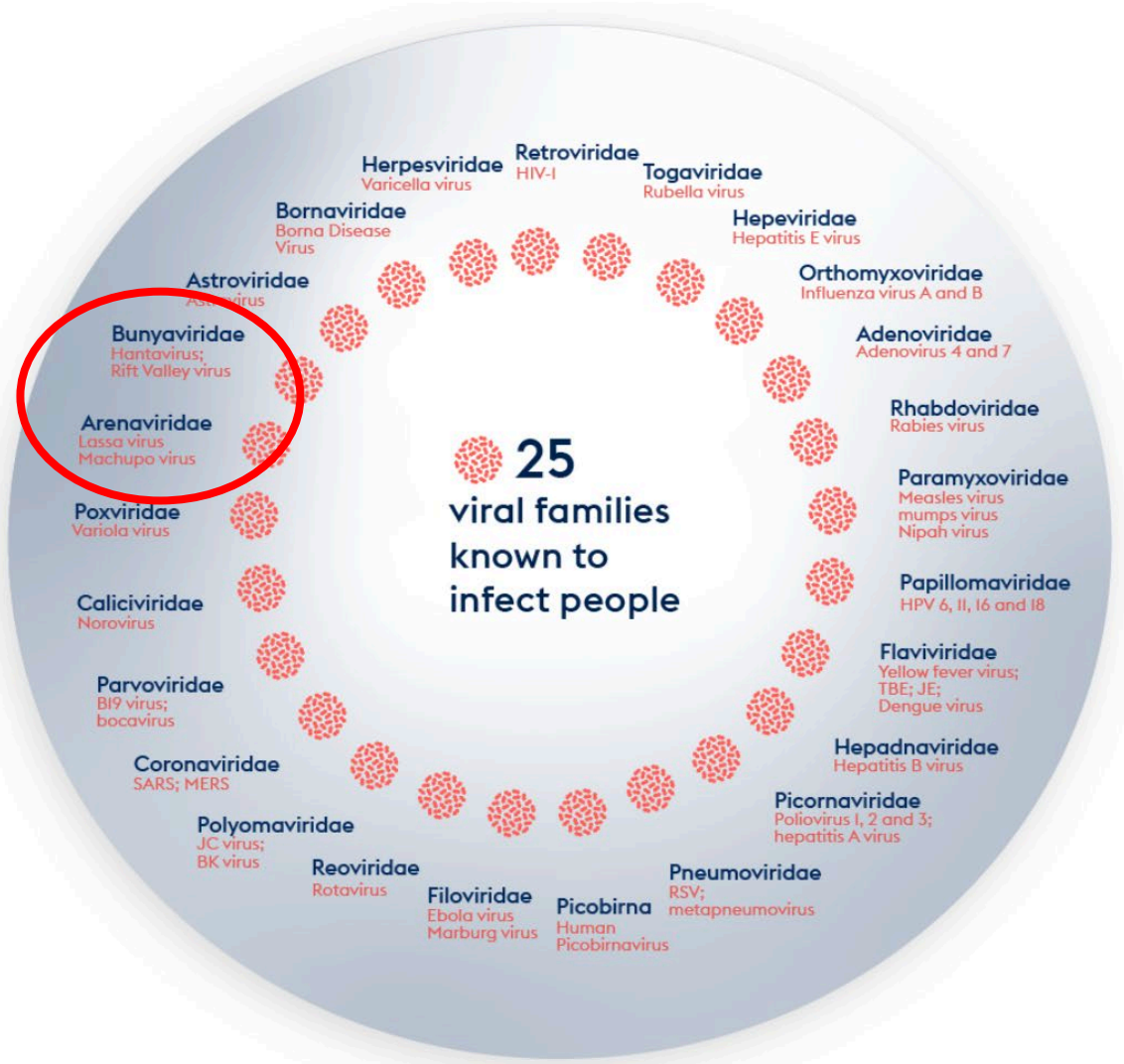
(arthropod-borne viruses)



arenaviruses

(rodent-borne viruses)

Bunyaviruses and arenaviruses



Graphic © CEPI *(Coalition for Epidemic Preparedness Innovations)*

Paper 1:

EMERGING INFECTIOUS DISEASES®

ISSN: 1080-6059

Volume 31, Number 2—February 2025

Synopsis

Two Human Cases of Fatal Meningoencephalitis Associated with Potosi and Lone Star Virus Infections, United States, 2020–2023

Charles Y. Chiu✉, Raja Rama Godasi, Holly R. Hughes, Venice Servellita, Kafaya Foresythe, Asritha Tubati, Kelsey Zorn, Sukhman Sidhu, Michael R. Wilson, Sai Varun Bethina, Daniel Abenroth, Yee Cheng, Raymond Grams, Camilla Reese, Carlos Isada, and Neeharika Thottempudi

Author affiliation: Chan–Zuckerberg Biohub, San Francisco, California, USA (C.Y. Chiu); Abbott Pandemic Defense Coalition, Abbott Park, Illinois, USA (C.Y. Chiu, V. Servellita, K. Foresythe); University of California, San Francisco (C.Y. Chiu, V. Servellita, K. Foresythe, A. Tubati, K. Zorn, S. Sidhu, M.R. Wilson); St. Luke's Boise Medical Center, Boise, Idaho, USA (R. Rama Godasi, D. Abenroth, Y. Cheng, R. Grams, C. Reese); Centers for Disease Control and Prevention, Fort Collins, Colorado, USA (H.R. Hughes); Wake Forest Baptist Medical Center, Winston-Salem, North Carolina, USA (S. Varun Bethina); Cleveland Clinic, Cleveland, Ohio, USA (C. Isada); University of Nevada, Reno, Nevada, USA (N. Thottempudi)

Cite This Article

On This Page

Figures

Hypothesis and Objectives

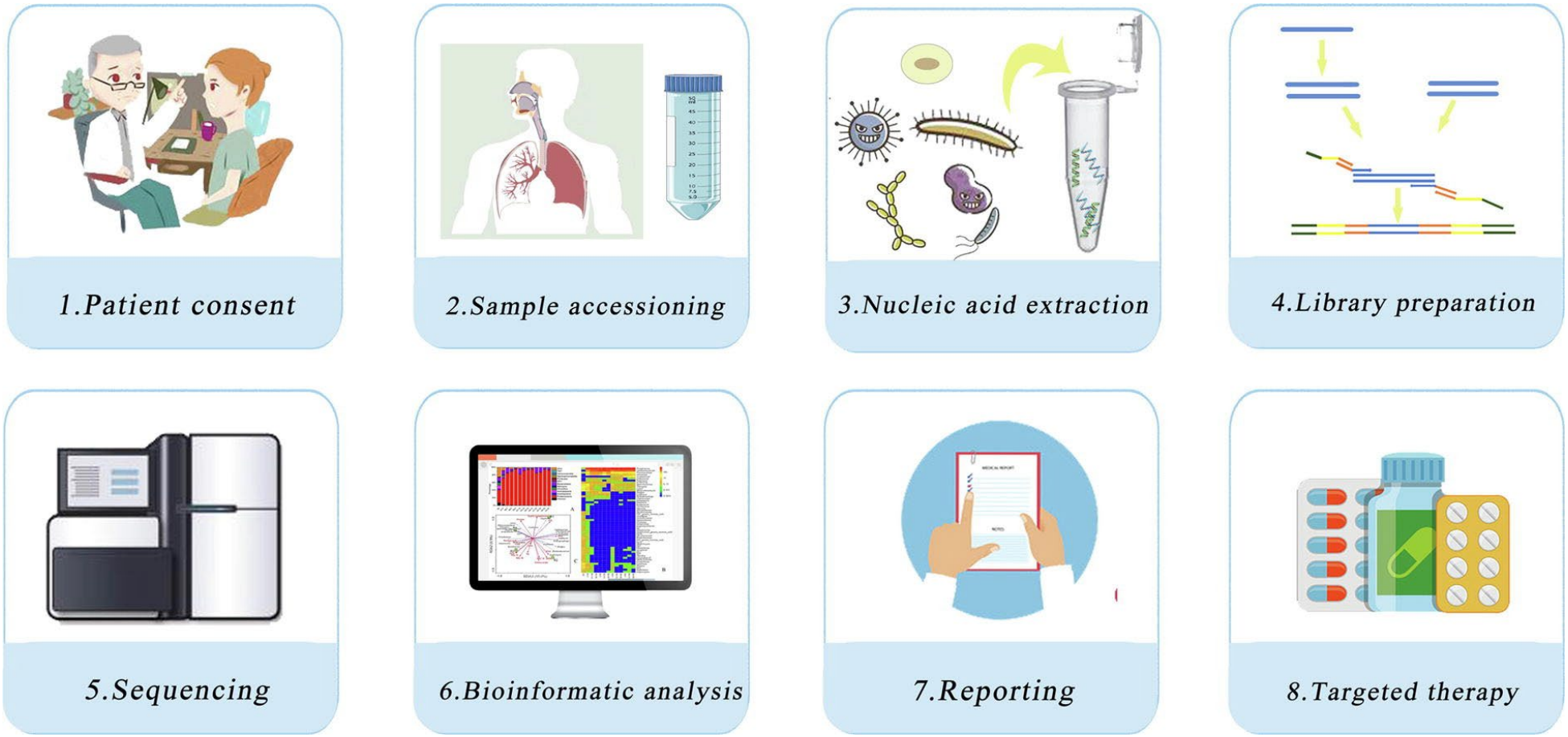
Unbiased clinical metagenomic next-generation sequencing (mNGS) enables the detection of viral pathogens missed by targeted diagnostics, offering a powerful tool for patient diagnosis.

Investigate two unexplained cases of fatal meningoencephalitis in immunocompromised patients.

Metagenomics next-generation sequencing tests take the stage in the diagnosis of lower respiratory tract infections

Zhenli Diao [a,b,c,1], Dongsheng Han [d,1], Rui Zhang [a,c,*], Jinming Li [a,b,c,*]

[a] National Center for Clinical Laboratories, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing Hospital/ National Center of Gerontology, PR China
[b] Peking University Fifth School of Clinical Medicine, Beijing Hospital, Beijing, PR China
[c] Beijing Engineering Research Center of Laboratory Medicine, Beijing, PR China
[d] Key Laboratory of Clinical In Vitro Diagnostic Techniques of Zhejiang Province, Department of Clinical Laboratory, First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, Zhejiang, PR China



Case 1 (2020)

Patient:

60-year-old male from Ohio with stage IV non-Hodgkin lymphoma.

Symptoms:

Cognitive decline, headache, fatigue, ataxia, fever, conjunctivitis.

Diagnostics:

- Conventional tests (PCR, serology) negative.
- **Clinical metagenomic next-generation sequencing (mNGS) detected Potasi virus (POTV).**

Outcome:

Progressive neurologic deterioration, died 37 days after admission.

Case 2 (2023)

Patient:

60-year-old male from Idaho with common variable immunodeficiency.

Symptoms:

Headache, memory difficulties, altered behavior, fever, confusion.

Diagnostics:

- Standard tests negative.
- **mNGS detected Lone Star virus (LSV).**

Outcome:

Neurologic deterioration, died 26 days after admission.

Methods and Results

- Sample Type:

  Cerebrospinal fluid (CSF)

- Sequencing Approach:

  Clinical mNGS performed at UCSF Clinical Microbiology Laboratory.

- Bioinformatics pipeline:

  SURPI+ for taxonomic classification and pathogen detection.

  GenBank database

  Potasi virus: 72 reads mapped (~5.1% genome coverage).

  Lone Star virus: 2,460 reads mapped (~13.6% genome coverage).

  Multiple sequence alignment (MAFFT) and maximum-likelihood phylogenetic trees (PHYML) to confirm virus identity.

Significance

- First report of fatal CNS infections caused by POTV and LSV in humans. Both viruses have previously only been isolated from mosquitoes (POTV) and ticks (LSV).
- Demonstrates diagnostic challenges for detecting emerging or neglected viral pathogens.
- Highlights the power of agnostic mNGS for detecting emerging or neglected viral pathogens.
- Underscores the need for continued arbovirus surveillance.

Paper 2:

EMERGING INFECTIOUS DISEASES®

ISSN: 1080-6059

Volume 31, Number 4—April 2025

Synopsis

Maternal and Fetal Implications of Oropouche Fever, Espírito Santo State, Brazil, 2024

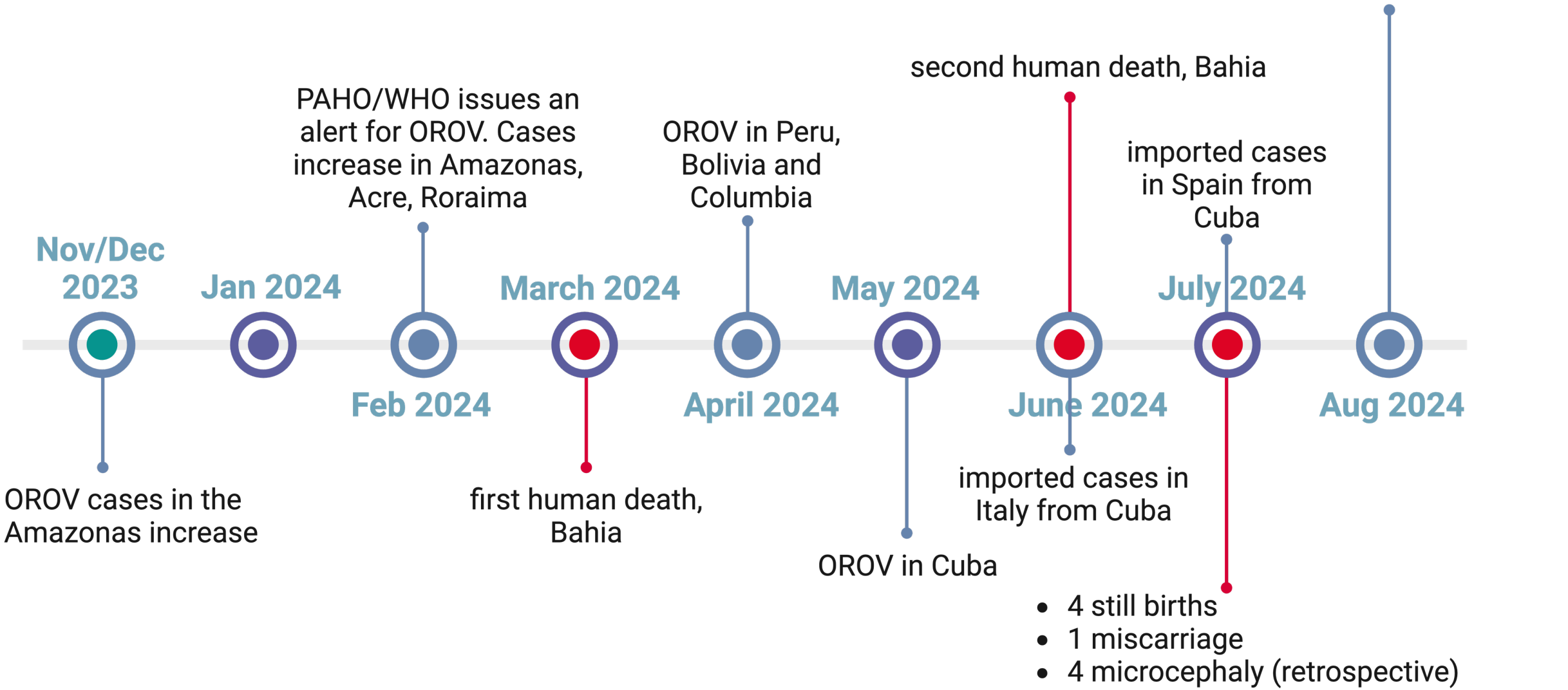
João Paulo Cola[1], Ana Paula Brioschi dos Santos[1], Raphael Lubiana Zanotti, Adriana Endlich da Silva Dela Costa, Karina Bertazo Del Carro, Lesliane de Amorim Lacerda Coelho, Angelica Espinosa Miranda[2], and Creuza Rachel Vicente[2]

Author affiliation: Secretaria de Estado da Saúde do Espírito Santo, Vitória, Brazil (J.P. Cola, A.P. Brioschi dos Santos, R. Lubiana Zanotti, A. Endlich da Silva Dela Costa, K. Bertazo Del Carro, L. de Amorim Lacerda Coelho); Universidade Federal do Espírito Santo, Programa de Pós-Graduação em Doenças Infecciosas, Vitória, Brazil (A.E. Miranda, C.R. Vicente)

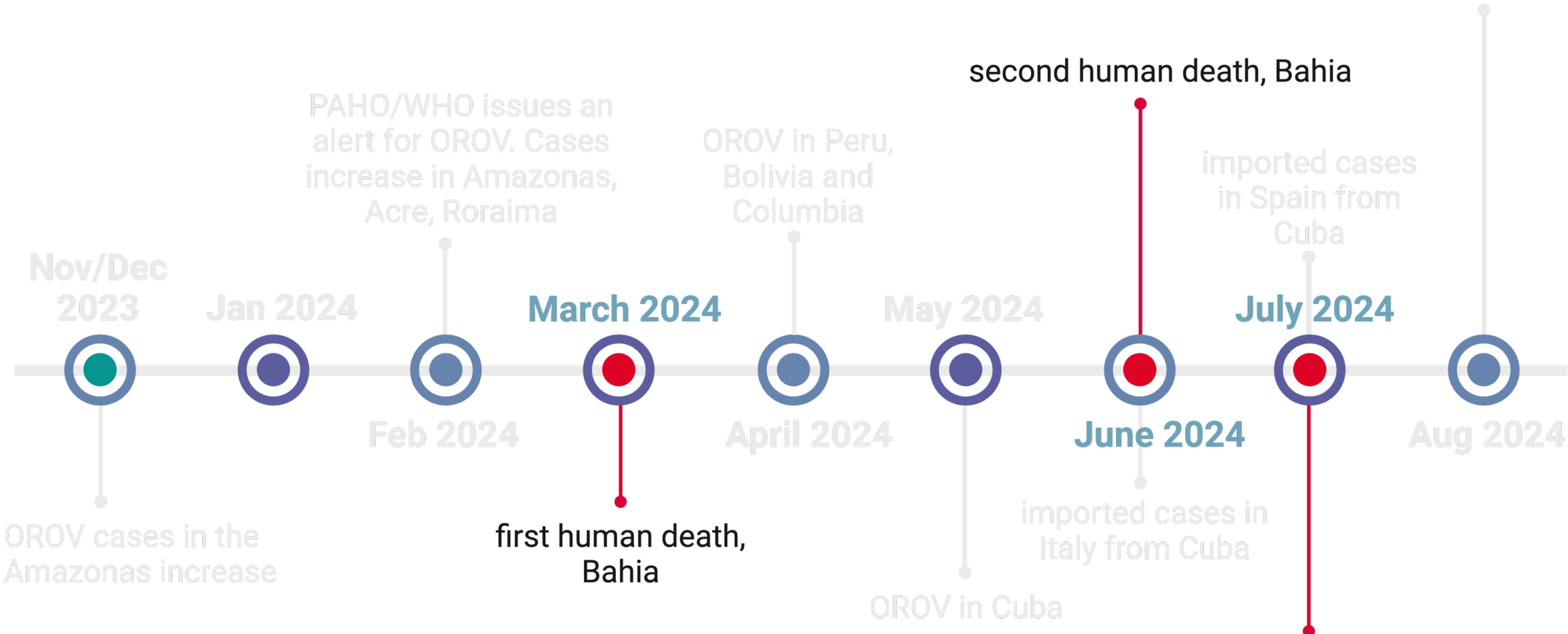
Suggested citation for this article

On This Page

Timeline of OROV outbreak in 2024



Timeline of OROV outbreak in 2024



Hypothesis and Objectives

Oropouche virus (OROV) infection during pregnancy may lead to adverse maternal and fetal outcomes, including spontaneous abortion, and fetal malformations.

1. Describe clinical and epidemiologic characteristics of OROV infection in pregnant women.
2. Evaluate maternal and neonatal outcomes, including potential vertical transmission.
3. Identify potential adverse pregnancy outcomes associated with OROV infection.

Study site: Espírito Santo State (March – December 2024)

Findings

- OROV-positive by RT-PCR.
- 4,062 OROV cases reported. 73 in pregnant women.
- 15 concluded pregnancies at time of the study:
  - 14 live births (10 cesarean sections, all full-term).
  - 1 spontaneous abortion (first trimester).
  - 5 placentas tested positive for OROV RNA (third-trimester infections).
  - 2 cases of possible vertical transmission were identified.
    - 1 neonate presented with corpus callosum dysgenesis.
    - 1 neonate showed symptomatic intrapartum transmission (symptoms at one-day of life, progressed healthy).

Significance

- First large case series linking OROV infection to maternal-fetal health outcomes.
- Provides evidence of possible vertical and intrapartum transmission.
- Highlights potential link between first-trimester infections and adverse outcomes (e.g., spontaneous abortion, fetal malformation).
- Underscores need for:
    - Enhanced surveillance in pregnant populations.
    - Strengthened diagnostics and public health measures.
    - Further research on teratogenicity and placental transmission.

Paper 3:

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

VIRAL INFECTIONS

Delayed low-dose oral administration of 4′-fluorouridine inhibits pathogenic arenaviruses in animal models of lethal disease

Stephen R. Welch[1]†, Jessica R. Spengler[1]†, Jonna B. Westover[2]†, Kevin W. Bailey[2], Katherine A. Davies[1,3], Virginia Aida-Ficken[1,4], Gregory R. Bluemling[5], Kirsten M. Boardma Samantha R. Wasson[2], Shuli Mao[5], Damien L. Kuiper[5], Michael W. Hager[5], Manohar T. Sain Meghan K. Andrews[5], Rebecca E. Krueger[5], Zachary M. Sticher[5], Kie Hoon Jung[2], Payel Cha Punya Shrivastava-Ranjan[1], Michael K. Lo[1], JoAnn D. Coleman-McCray[1], Teresa E. Sorvillo Sarah C. Genzer[1], Florine E. M. Scholte[1], Jamie A. Kelly[1], M. Harley Jenks[1], Laura K. McMul César G. Albariño[1], Joel M. Montgomery[1], George R. Painter[5], Michael G. Natchus[5], Alexander A. Kolykhalov[5]*, Brian B. Gowen[2]*, Christina F. Spiropoulou[1], Mike Flint[1]*

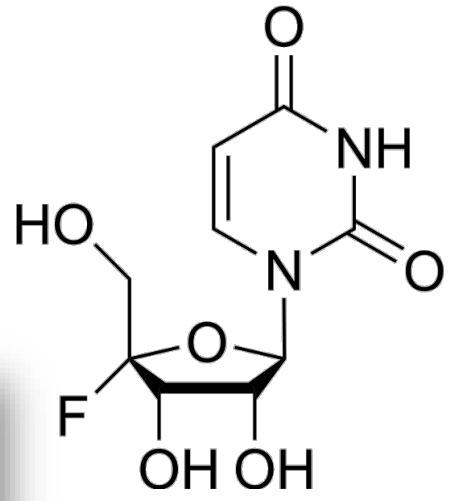
20 Nov 2024
Vol 16, Issue 774

Hypothesis and Objectives

4'-fluorouridine (4'-FIU) is a potent, orally bioavailable ribonucleoside analog that can inhibit pathogenic arenaviruses, reducing disease severity and mortality even when administered at low doses or after delayed treatment.

1. Assess the antiviral efficacy of 4′-FIU against Old World and New World arenaviruses *in vitro*.
2. Evaluate the protective efficacy of oral 4′-FIU in guinea pig models of Lassa virus (LASV) and Junín virus (JUNV) infection.
3. Determine the pharmacokinetic properties and safety profile of 4′-FIU.

4′-fluorouridine (4′-FIU)



DNA and Cell Biology > Vol. 41, No. 8

Research Article | NO ACCESS | Published Online: 4 August 2022

4'-Fluorouridine Is a Broad-Spectrum Orally Available First-Line Antiviral That May Improve Pandemic Preparedness

Authors: Carolin M. Lieber and Richard K. Plemper | AUTHORS INFO & AFFILIATIONS

Publication: DNA and Cell Biology • https://doi.org/10.1089/dna.2022.0312

4'-Fluorouridine is an oral antiviral that blocks respiratory syncytial virus and SARS-CoV-2 replication

JULIEN SOURIMANT, CAROLIN M. LIEBER, MEGHA AGGARWAL, ROBERT M. COX, JOSEF D. WOLF, JEONG-JOONG YOON, MART TOOTS, CHENGIN YE, ZACHARY STICHER, ALEXANDER A. KOLYKHALOV, LUIS MARTINEZ-SOBRIDO, GREGORY R. BLUEMLING, MICHAEL G. NATCHUS, GEORGE R. PAINTER, AND RICHARD K. PLEMPER fewer Authors Info & Affiliations

SCIENCE • 2 Dec 2021 • Vol 375, Issue 6577 • pp. 161-167 • DOI: 10.1126/science.abj5508

Virology | Research Article | 3 May 2024

4′-Fluorouridine inhibits alphavirus replication and infection *in vitro* and *in vivo*

Authors: Peiqi Yin, Nicholas A. May, Laura Sandra Lello, Atef Fayed, M. Guston Parks, Adam M. Drobish, Sainan Wang, Meghan Andrews, Zachary Sticher, Alexander A. Kolykhalov, Michael G. Natchus, George R. Painter, Andres Merits, Margaret Kielian, Thomas E. Morrison SHOW FEWER | AUTHORS INFO & AFFILIATIONS

PLOS Pathogens

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

Influenza A virus resistance to 4′-fluorouridine coincides with viral attenuation *in vitro* and *in vivo*

Carolin M. Lieber, Hae-Ji Kang, Megha Aggarwal, Nicole A. Lieberman, Elizabeth B. Sobolik, Jeong-Joong Yoon, Michael G. Natchus, Robert M. Cox, Alexander L. Greninger, Richard K. Plemper

Version 2 Published: February 1, 2024 • https://doi.org/10.1371/journal.ppat.1011993

PLOS Pathogens Browse Publish About

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

4′-Fluorouridine mitigates lethal infection with pandemic human and highly pathogenic avian influenza viruses

Carolin M. Lieber, Megha Aggarwal, Jeong-Joong Yoon, Robert M. Cox, Hae-Ji Kang, Julien Sourimant, Mart Toots, Scott K. Johnson, Cheryl A. Jones, Zachary M. Sticher, Alexander A. Kolykhalov, Manohar T. Saindane, Stephen M. Tompkins, Oliver Planz, George R. Painter, Michael G. Natchus, Kaori Sakamoto, Richard K. Plemper [view less]

Methods

- *In vitro*

  model: Huh7, HeLa, and Vero E6 cell lines

  viruses: LASV, LUJV, JUNV, MACV, ANDV, HeV, SNV

  output: infectious virus yield reduction and cytotoxicity

  EC_{50} (50% effective concentration, *low* EC_{50} = *potent compound*)

  CC_{50} (50% cytotoxic concentration, *high* CC_{50} = *low toxicity*)

- *In vivo*

  model: guinea pig, lethal, oral, doses: 0.15 – 5 mg/kg

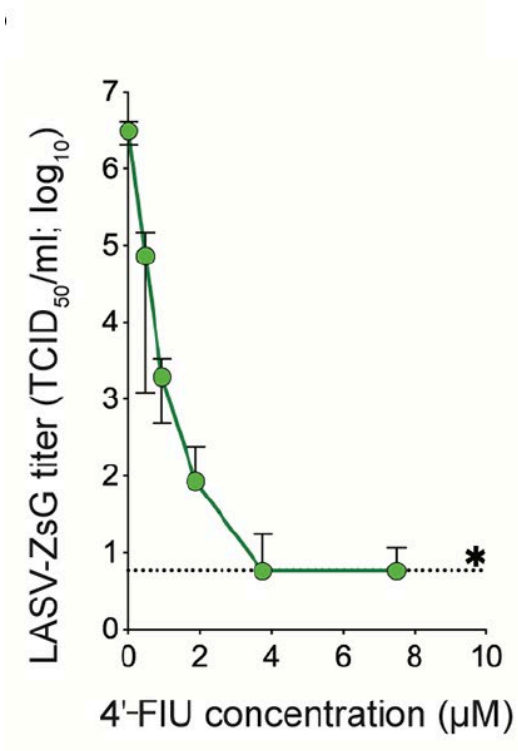
  viruses: LASV, JUNV

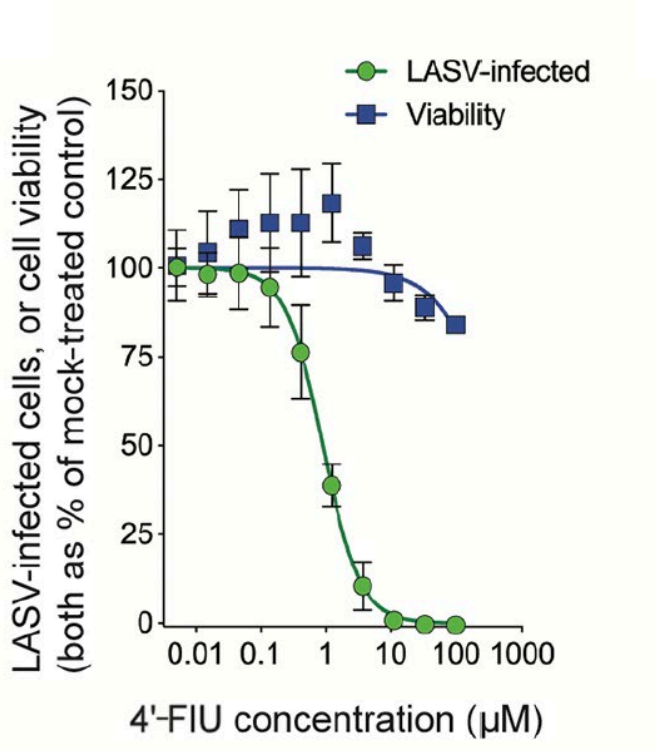
  output: pharmacokinetics, survival, and viral tissue load

Results: 4’-FIU inhibits LASV and JUNV in cell culture

- Huh7 cells, pre-treatment for 1-2 hours, MOI=0.1, measured infectious virus at 72 h.p.i.

Lassa virus (LASV)





Junín virus (JUNV)

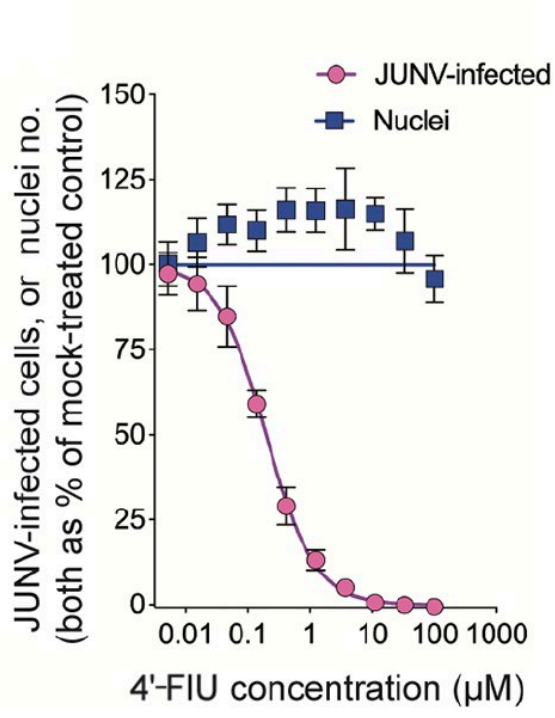
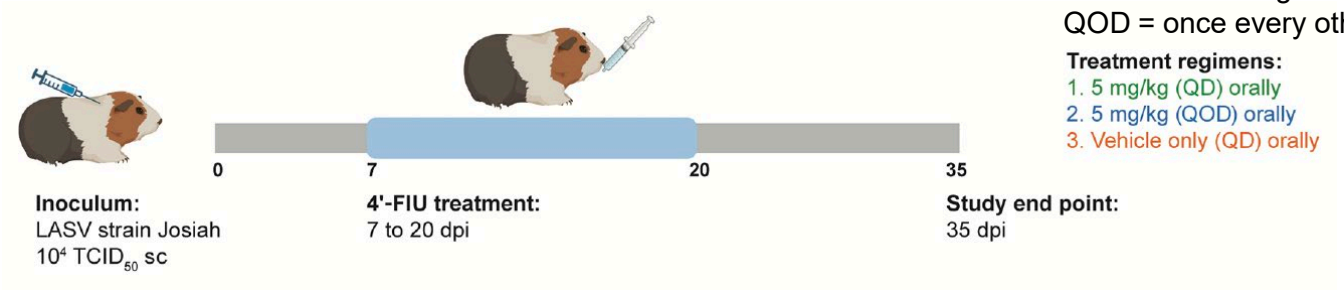


Table 1. 4′-FlU activity against Old and New World arenaviruses. EC_{50}, means ± SD, from *n* independent determinations; CC_{50} (assessed by nuclei number), means ± SD, from *n* independent determinations; SI, defined as CC_{50}/EC_{50}.

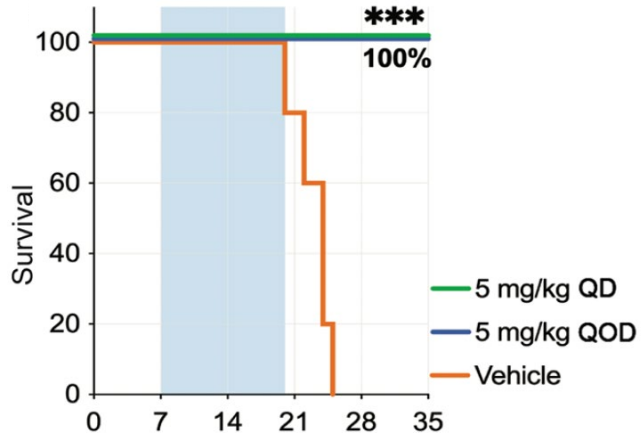
Virus	Details	Cell line	EC_{50} (μM)	CC_{50} (μM)	SI
LASV-ZsG	Recombinant reporter Old World arenavirus, clade IV (strain Josiah)	Huh7	1.47 ± 1.03 ($n = 3$)	>100 ($n = 5$)	>68
LASV	Old World arenavirus, clade IV (strain Josiah)	HeLa	1.00 ± 0.61 ($n = 3$)	>77 ($n = 3$)	>77
LASV	Old World arenavirus, clade I (strain Pinneo)	HeLa	2.03 ± 1.33 ($n = 3$)	>77 ($n = 3$)	>38
LASV	Old World arenavirus, clade II (strain Nigeria-322)	HeLa	2.14 ± 0.20 ($n = 3$)	>77 ($n = 3$)	>36
LASV	Old World arenavirus, clade II (strain Sauerwald)	HeLa	4.40 ± 1.46 ($n = 3$)	>77 ($n = 3$)	>18
LASV	Old World arenavirus, clade III (strain Nigeria-383)	HeLa	7.97 ± 2.00 ($n = 3$)	>77 ($n = 3$)	>10
LASV	Old World arenavirus, clade III (strainNigeria-231)	HeLa	8.43 ± 1.02 ($n = 3$)	>77 ($n = 3$)	>9
LASV	Old World arenavirus, clade IV (strain NJ-2015)	HeLa	2.09 ± 0.21 ($n = 3$)	>77 ($n = 3$)	>37
LASV	Old World arenavirus, clade IV (strain Ouoma R-123)	HeLa	2.58 ± 1.02 ($n = 3$)	>77 ($n = 3$)	>30
LASV	Old World arenavirus, clade VI (strain Togo)	HeLa	10.08 ± 3.06 ($n = 3$)	>77 ($n = 3$)	>8
LUJV	Old World arenavirus (strain 200809232 Zambia)	HeLa	0.29 ± 0.19 ($n = 3$)	>77 ($n = 3$)	>266
JUNV	New World arenavirus (strain Romero)	HeLa	0.11 ± 0.09 ($n = 3$)	>77 ($n = 3$)	>700
MACV	New World arenavirus (strain Carvallo)	HeLa	0.28 ± 0.24 ($n = 3$)	>77 ($n = 3$)	>275

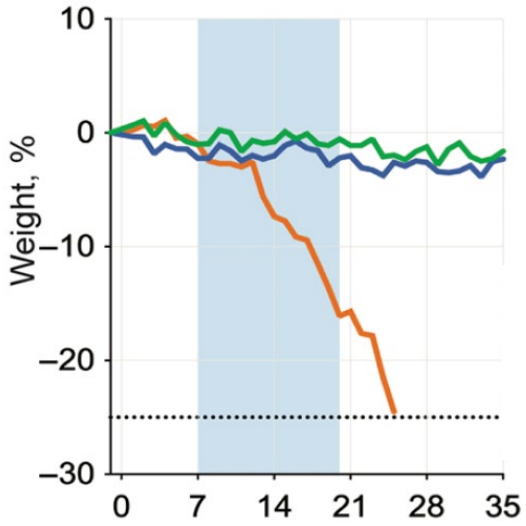
Results: Therapeutic efficacy in LASV

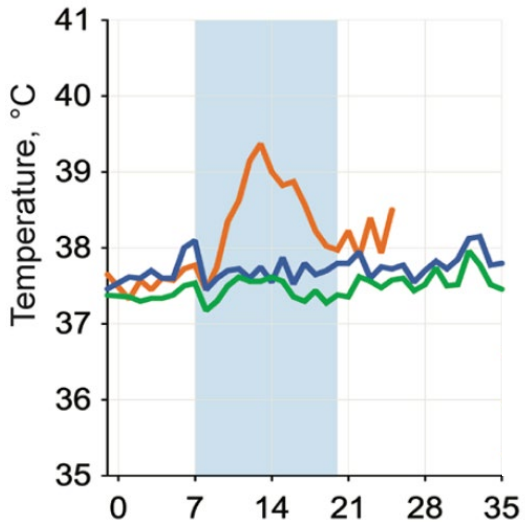


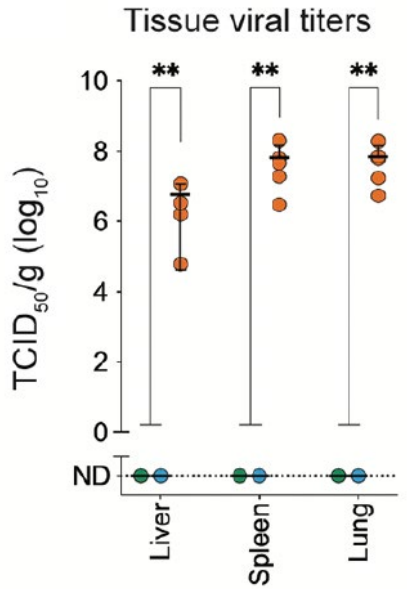
QD = oral dosing
QOD = once every other day

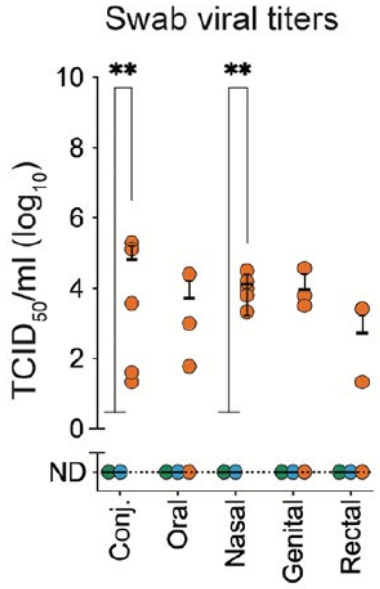
Treatment regimens:
1. 5 mg/kg (QD) orally
2. 5 mg/kg (QOD) orally
3. Vehicle only (QD) orally



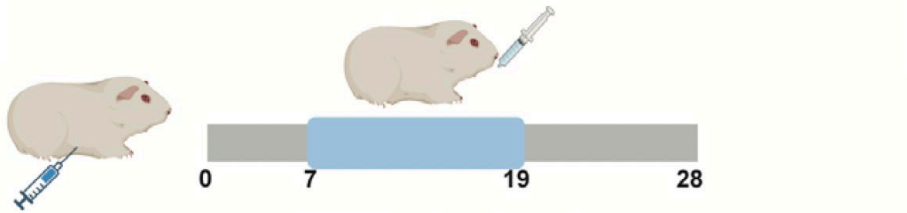








Results: Therapeutic efficacy in JUNV



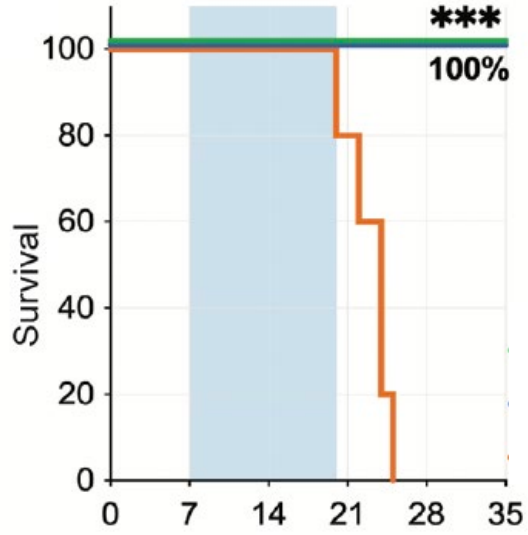
Inoculum:
JUNV strain Romero
10^4 $CCID_{50}$ ip

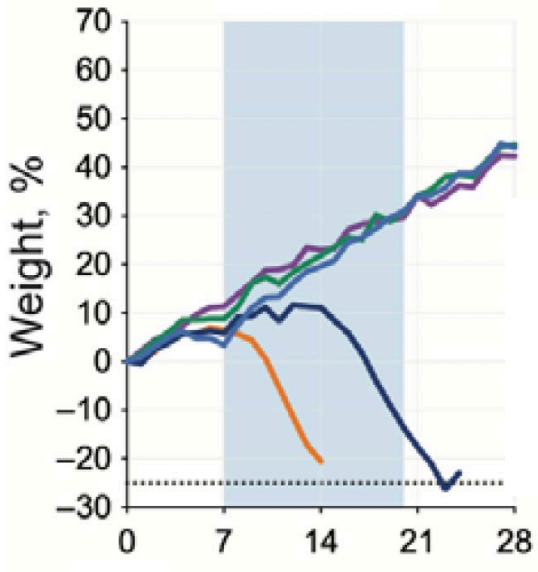
4′-FIU treatment:
7 to 19 dpi

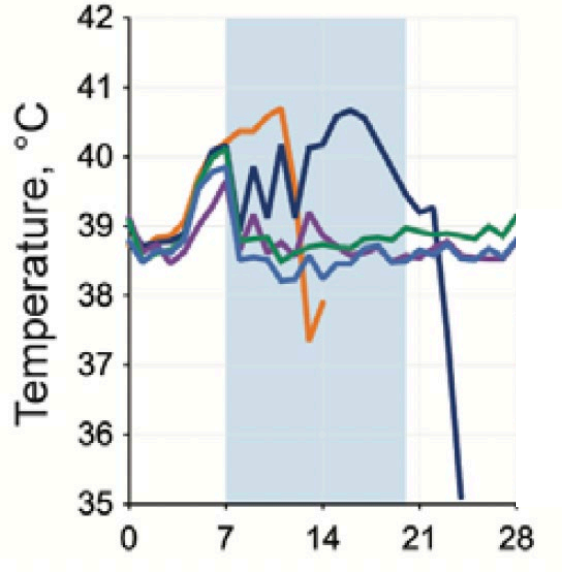
Study end point:
28 dpi

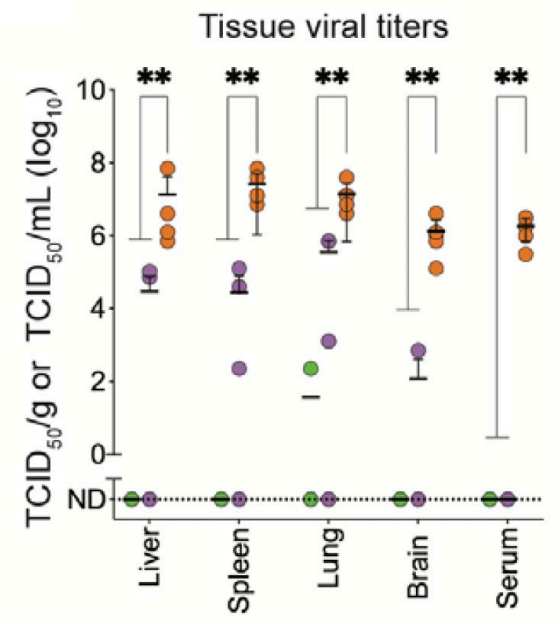
Treatment regimens:
1. 5 mg/kg (QOD) orally
2. 1.5 mg/kg (QOD) orally
3. 0.5 mg/kg (QOD) orally
4. 0.15 mg/kg (QOD) orally
5. Vehicle only (QOD) orally

QD = oral dosing
QOD = once every other day

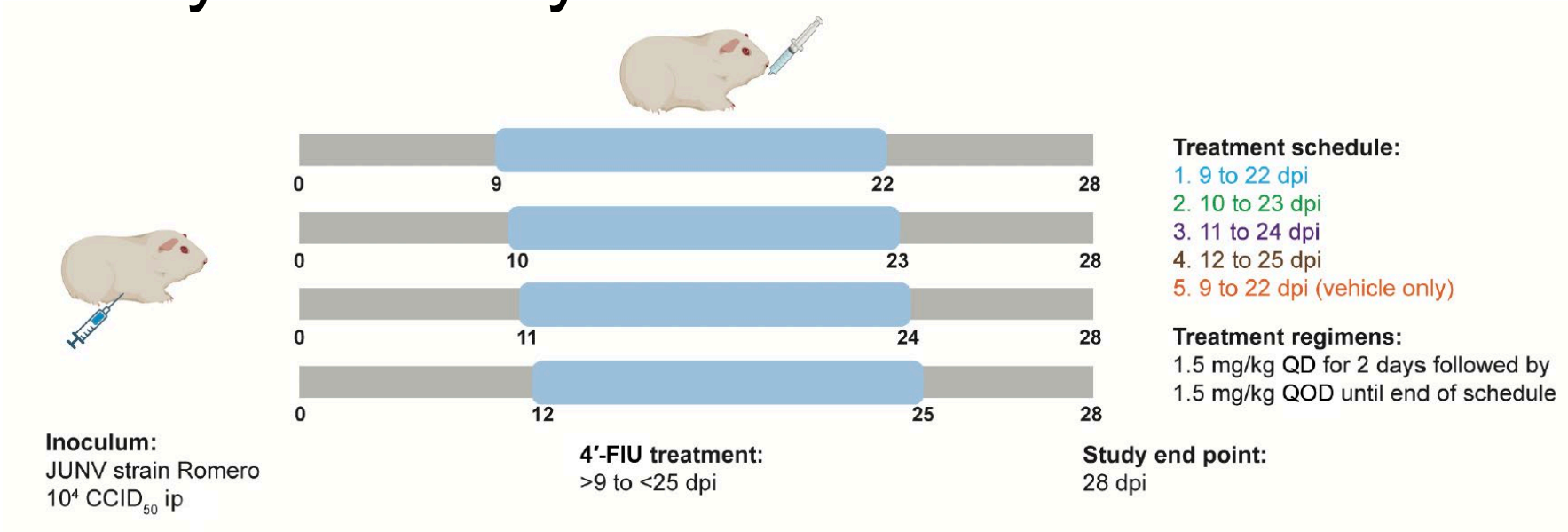


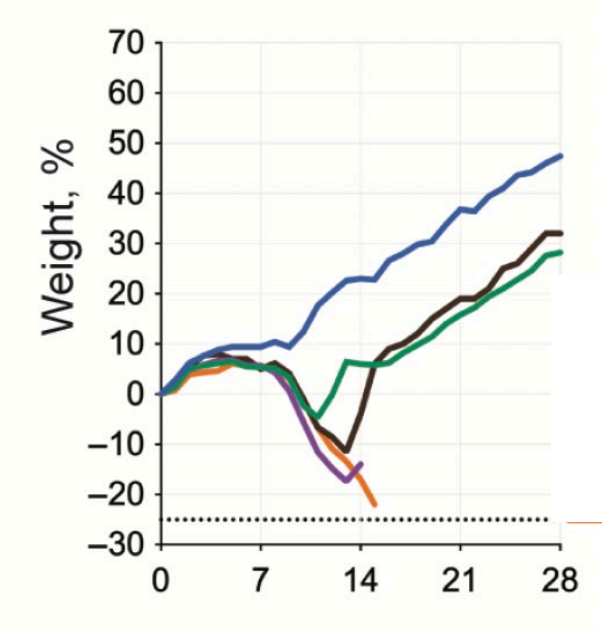


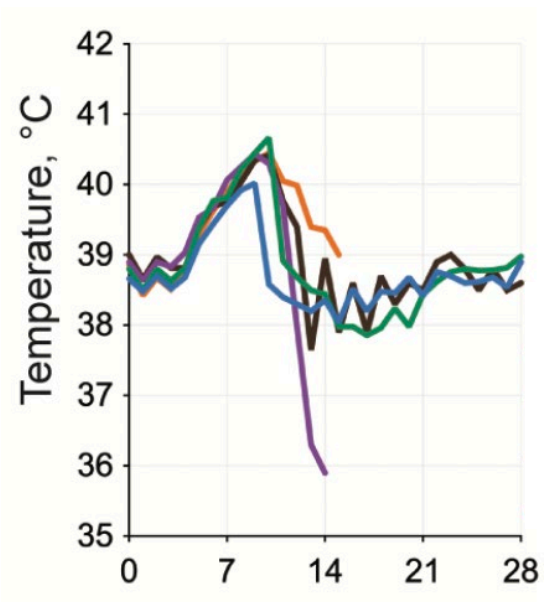


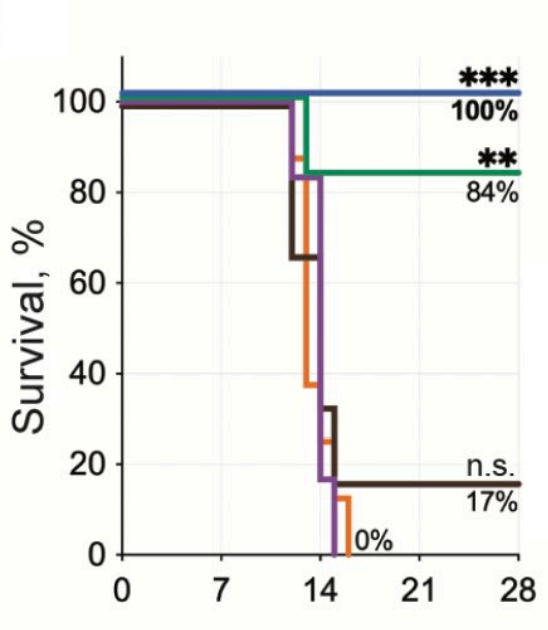


Results: Delayed efficacy in JUNV









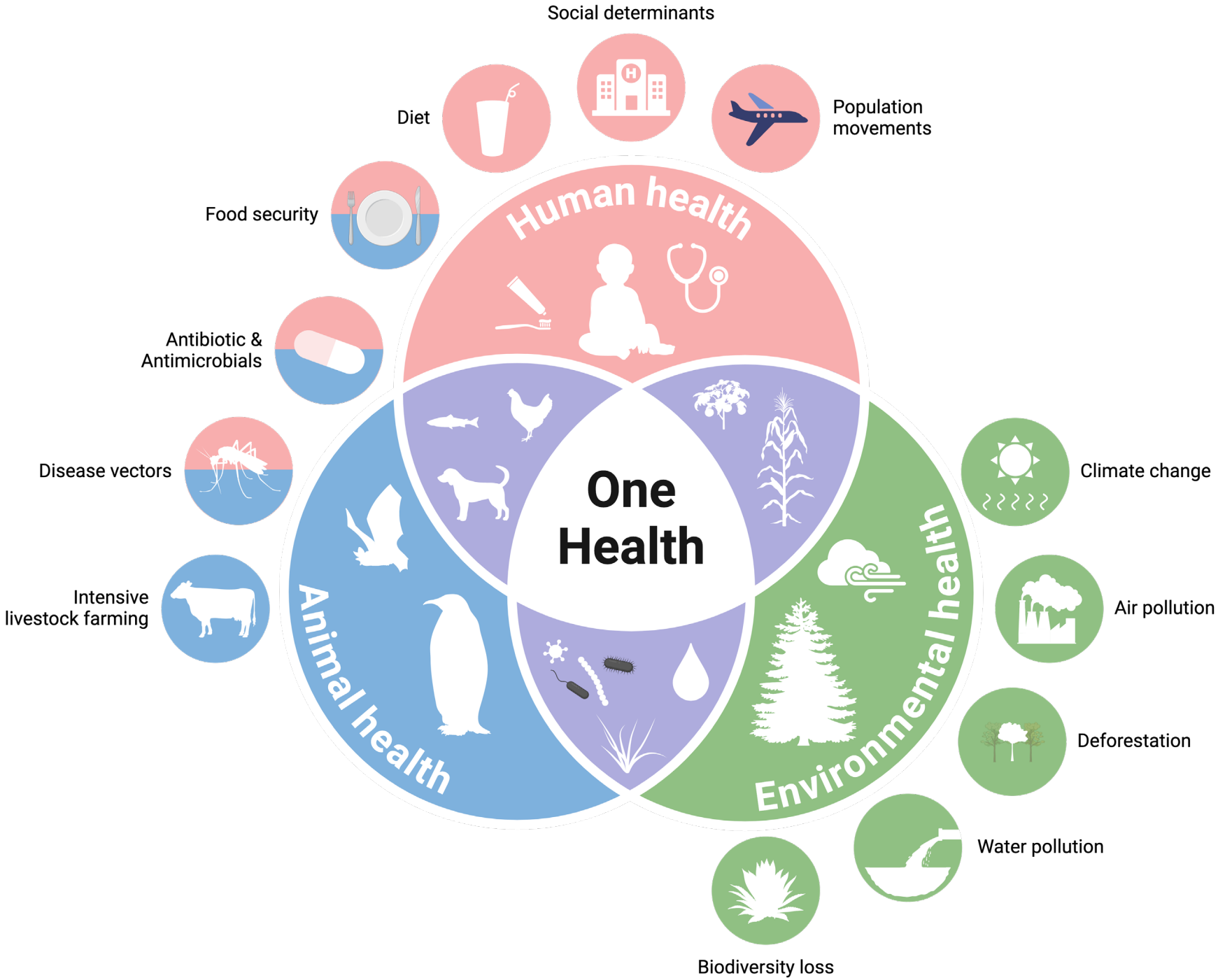
Significance

- No approved antivirals are available for highly pathogenic arenaviruses
- LASV causes 300,000 infections and 5,000 deaths in West Africa annually
- In guinea pigs, 4’-FIU access several tissues at concentrations high enough for an antiviral effect
- The first preclinical study to demonstrate that 4’-FIU is a promising candidate for the treatment of several arenaviruses

Take home message from the three papers

- Advanced sequencing technologies (mNGS) can be critical in pathogen surveillance and diagnostics.
- Emerging and neglected arboviruses and arenaviruses pose significant threats to immunocompromised individuals, pregnant populations, and public health at large.
- Development of broad-spectrum antiviral therapies are critical for outbreak and pandemic preparedness against emerging and reemerging viruses.

These studies highlight the urgency of integrating genomic diagnostics, public health monitoring, and antiviral drug development to mitigate viral threats in high-risk populations.


Social determinants
Diet
Population movements
Food security
Human health
Antibiotic & Antimicrobials
Disease vectors
Intensive livestock farming
One Health
Animal health
Environmental health
Climate change
Air pollution
Deforestation
Water pollution
Biodiversity loss

Questions?

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