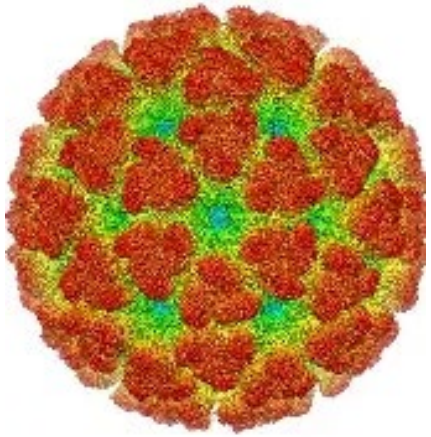


Overview of Chikungunya Virus Infection, Pathogenesis and Clinical Outcome

ศาสตราจารย์(เกียรติคุณ) ดร.ศุขธิดา อุบล

มหาวิทยาลัยมหิดล

Cumulative impact during the last decade

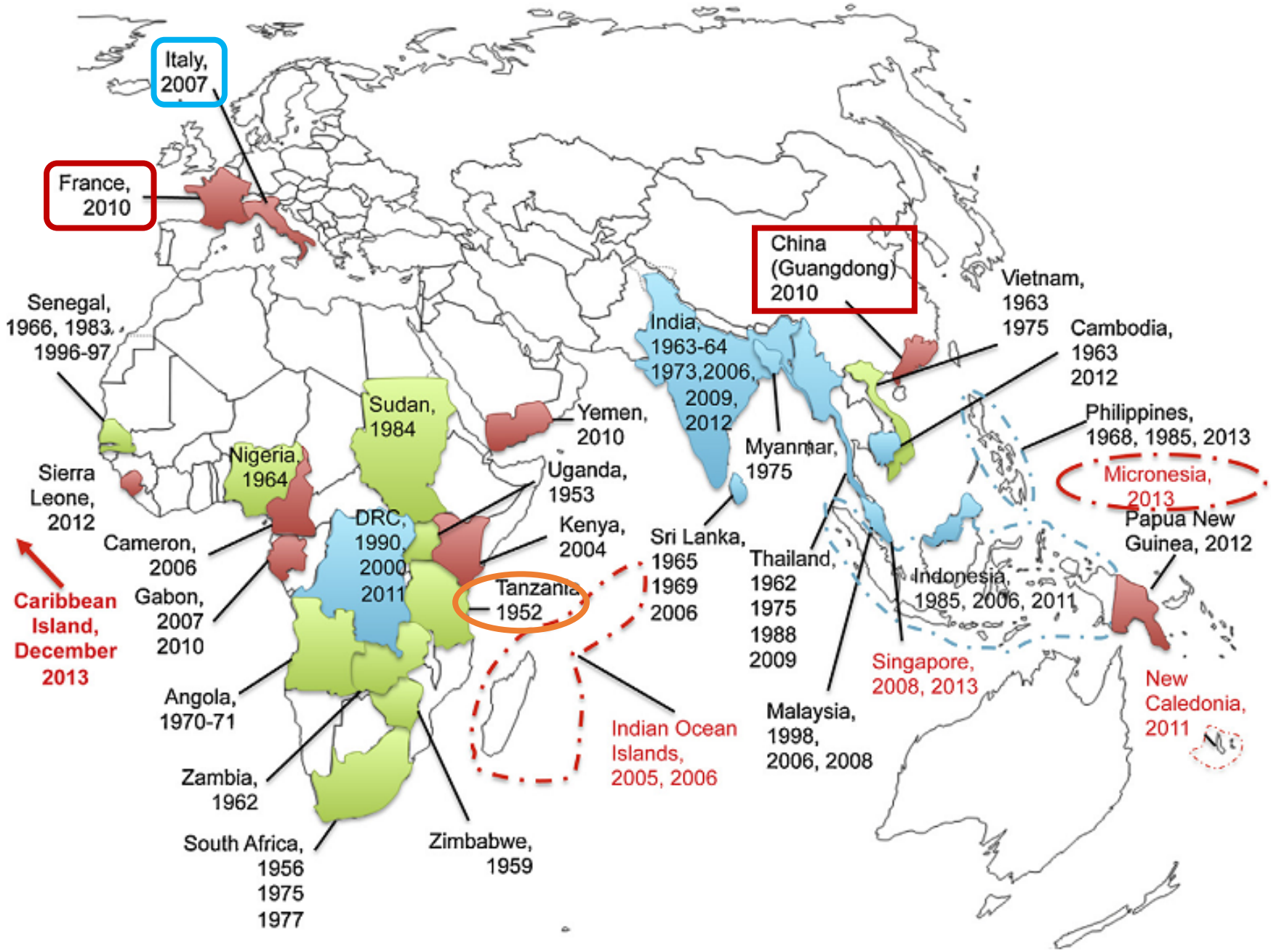
CHIKV-rheumatic disease in > 110 countries

An estimated annual loss of over 106,000 DALYs (disability-adjusted life years)

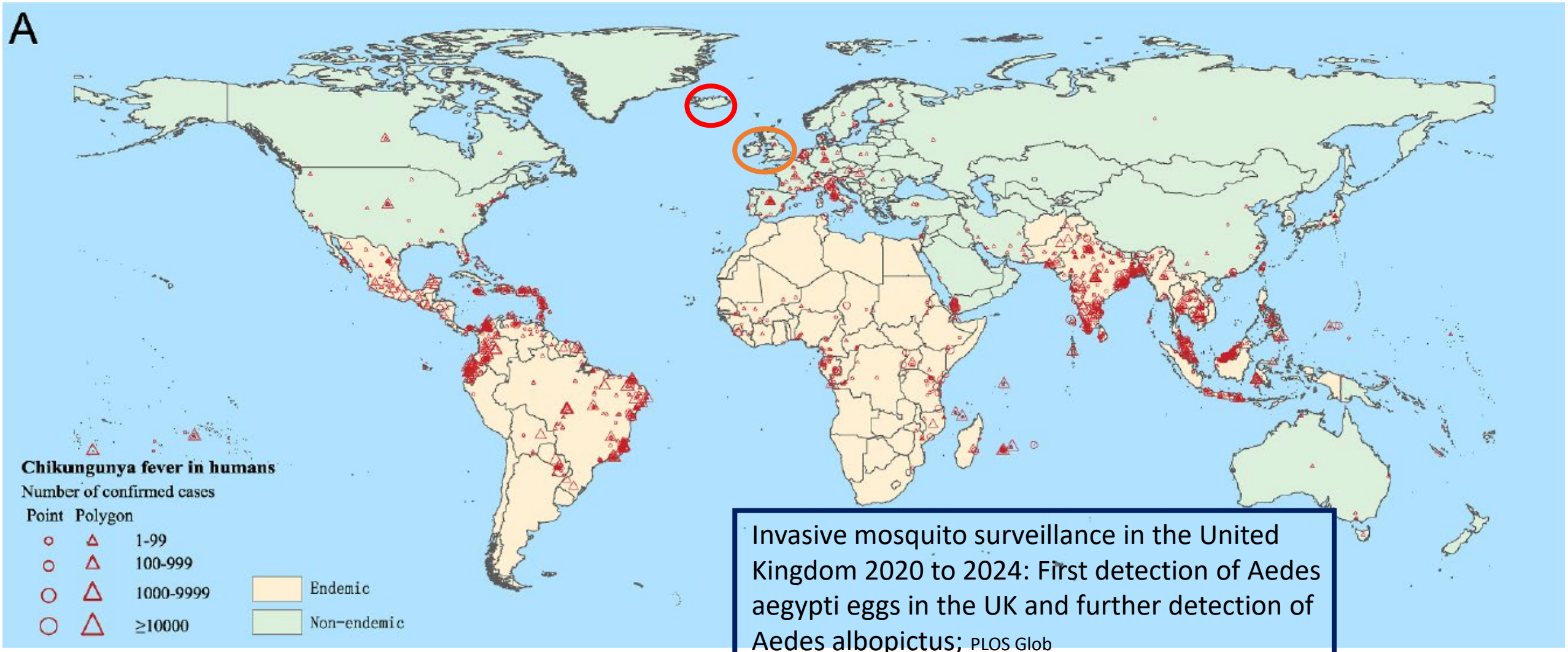
Reported total direct costs associated with Chikungunya Fever ranged from US$ 3.5 million (US Virgin Islands, 2014-2015) to US$ 83.6 billion (Region of the Americas, 2013-2015)

Trop Med Int Health. 2025 Sep;30(9):865-892.

Will it become a global health problem?


Italy, 2007
France, 2010
Senegal, 1966, 1983, 1996-97
Sierra Leone, 2012
Caribbean Island, December 2013
Cameron, 2006
Gabon, 2007 2010
Nigeria, 1964
Sudan, 1984
DRC, 1990 2000 2011
Angola, 1970-71
Zambia, 1962
South Africa, 1956 1975 1977
Zimbabwe, 1959
Tanzania 1952
Uganda, 1953
Kenya, 2004
Yemen, 2010
Indian Ocean Islands, 2005, 2006
Sri Lanka, 1965 1969 2006
India, 1963-64 1973,2006, 2009, 2012
Myanmar, 1975
China (Guangdong) 2010
Thailand, 1962 1975 1988 2009
Malaysia, 1998, 2006, 2008
Vietnam, 1963 1975
Cambodia, 1963 2012
Philippines, 1968, 1985, 2013
Micronesia, 2013
Papua New Guinea, 2012
Indonesia, 1985, 2006, 2011
Singapore, 2008, 2013
New Caledonia, 2011

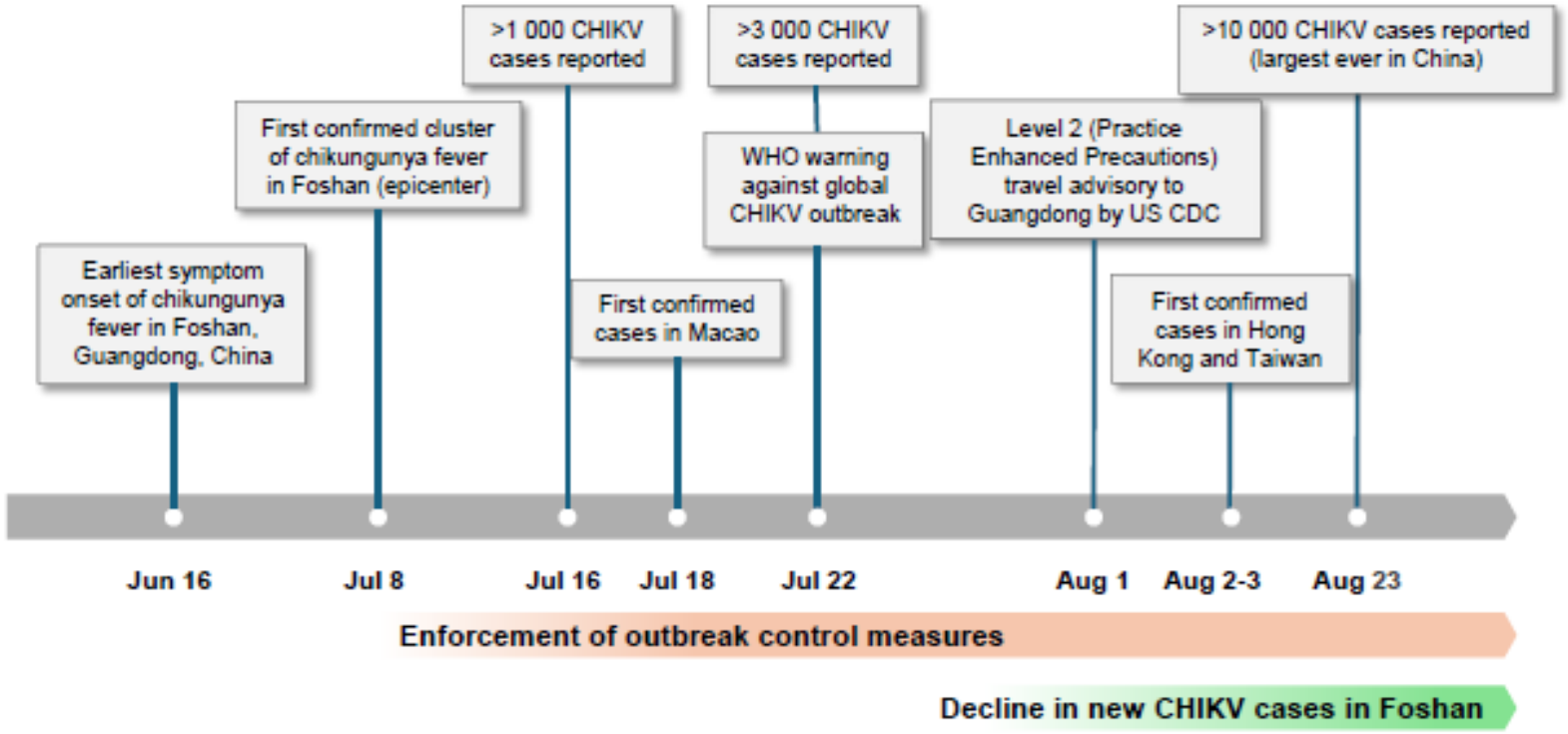
Italy (2007) 200 cases, (2017) >400 cases, (2025) 1st autochthonous cases (local transmission)



Invasive mosquito surveillance in the United Kingdom 2020 to 2024: First detection of Aedes aegypti eggs in the UK and further detection of Aedes albopictus; PLOS Glob Public Health 5(10): e0004968. https://doi.org/10.1371/journal.pgph.0004968

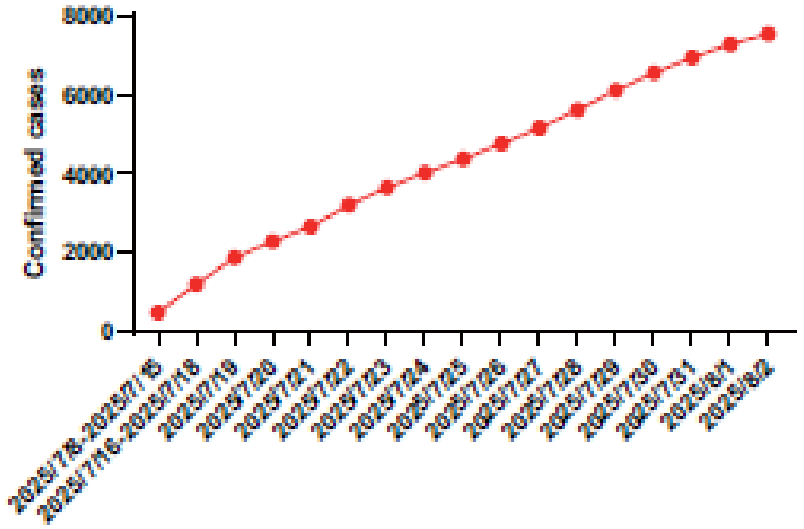
France (2010, 2014) ; 2025(799 imported cases; 30 autochthonous cases) 12 clusters of CHIKV transmission

Recent epidemic in China

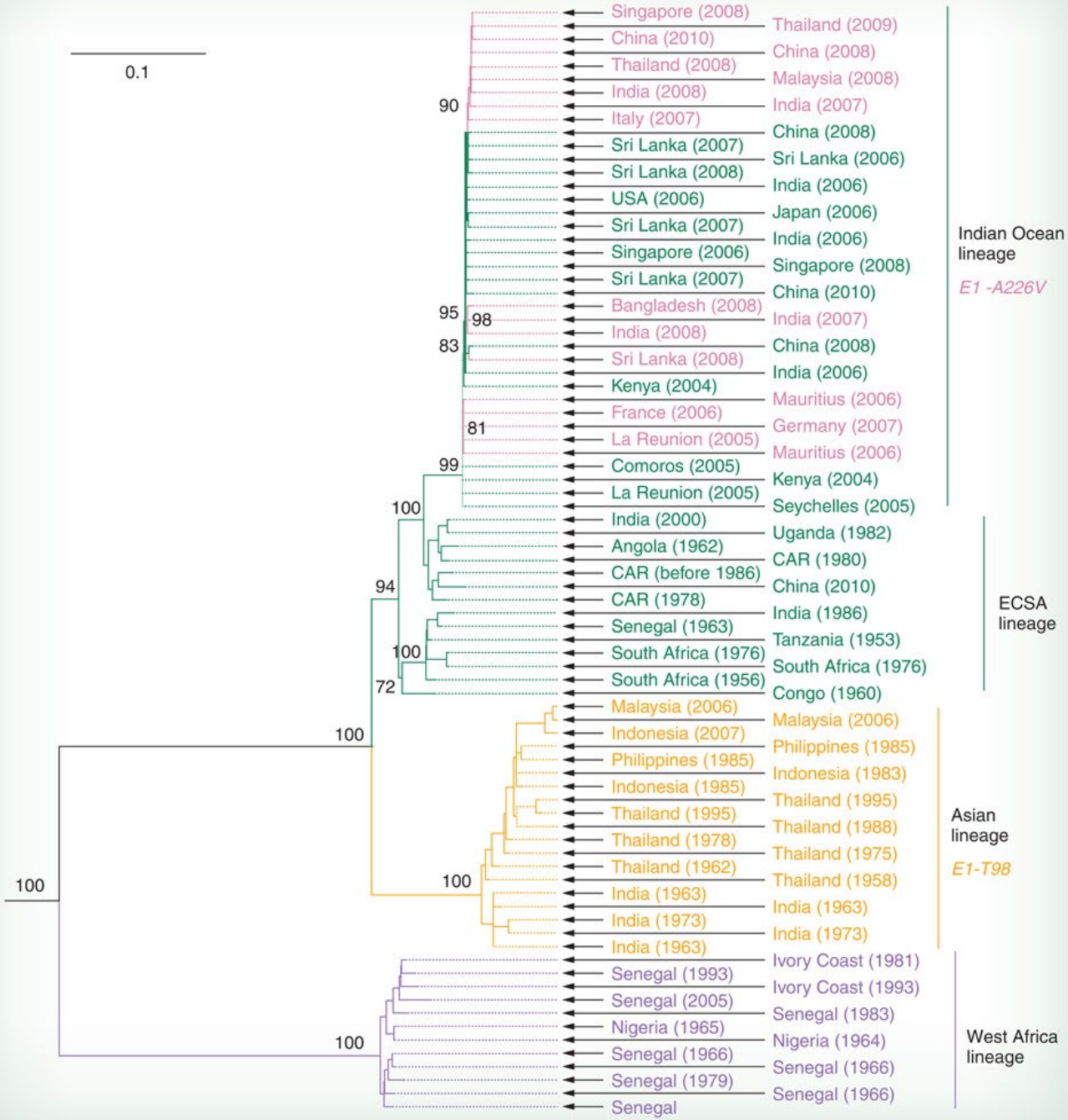


Timeline of the 2025 chikungunya outbreak in China.

International Journal of Infectious Diseases (2025),
doi:https://doi.org/10.1016/j.ijid.2025.108089



Journal of Infection, (2025)
doi:https://doi.org/10.1016/j.jinf.2025.106591



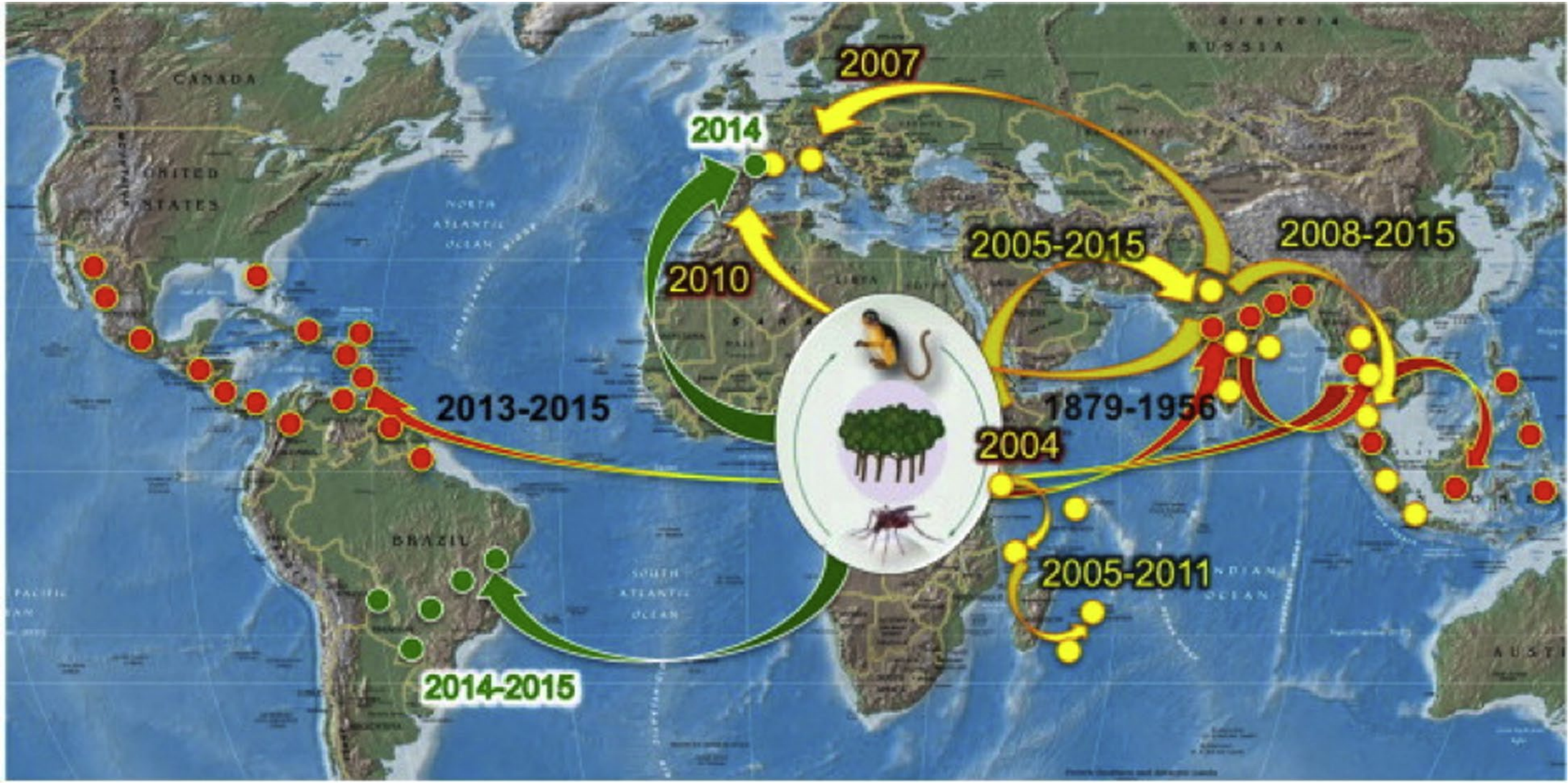
The CHIKV strain circulating in Foshan is ECSA linage with a fixed E1-226V mutation.

Indian Ocean-Southeast Asia
E2- 211 T, nsP3-259 P

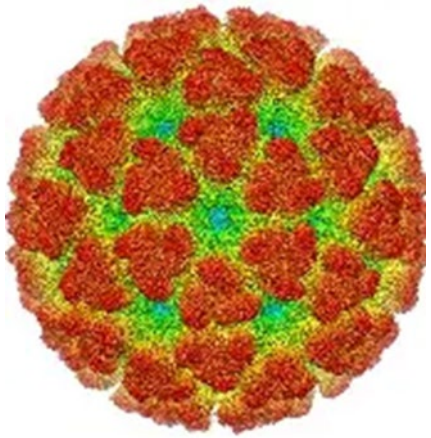
International Journal of Infectious Diseases (2025), doi:https://doi.org/10.1016/j.ijid.2025.108089

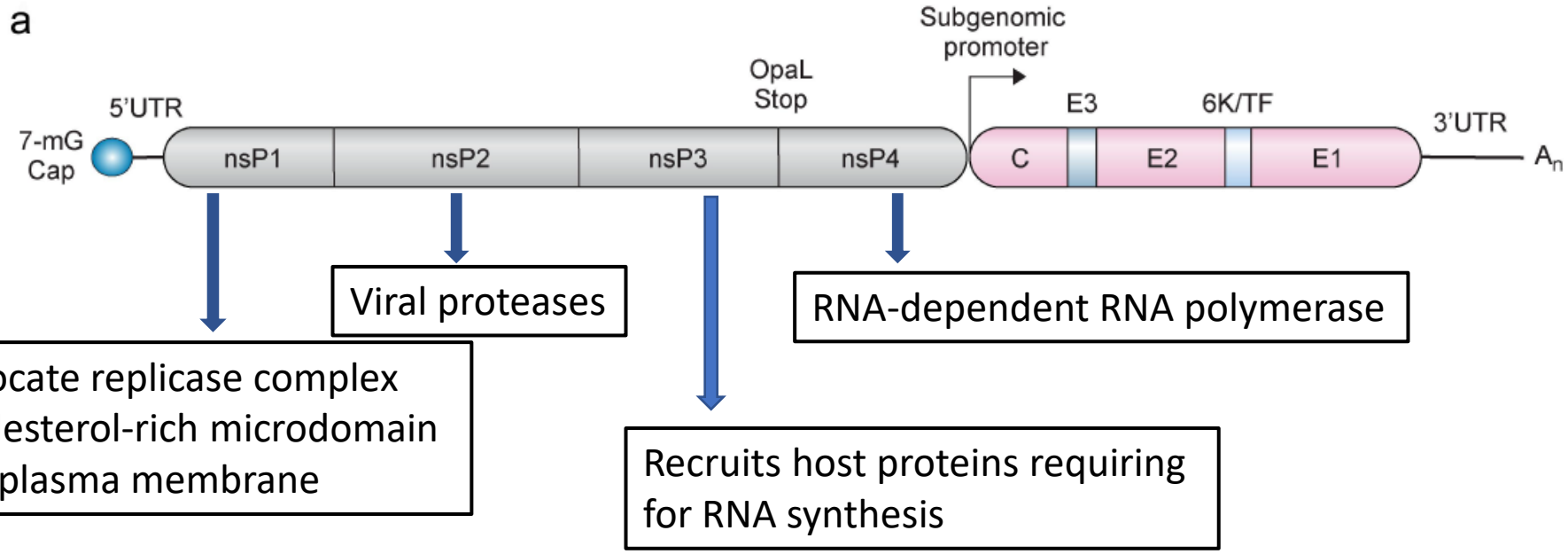
Journal of Infection, (2025) doi:https://doi.org/10.1016/j.jinf.2025.106591

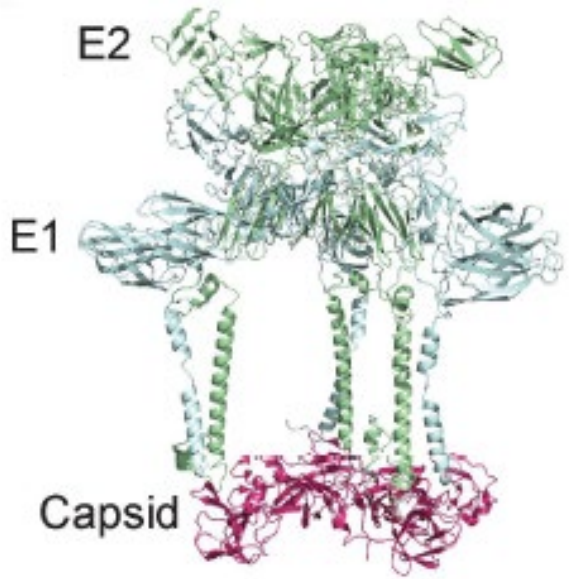
Brazil (January 1, 2025 - July 26, 2025), Mauritius (January 1, 2025 - July 18, 2025),
Bolivia (January 1, 2025 - July 5, 2025), Argentina (January 1, 2025 - July 19, 2025),
Peru (January 1, 2025 - July 5, 2025), Guatemala (January 1, 2025 - July 5, 2025),
Singapore (January 1, 2025 - July 5, 2025), Paraguay (January 1, 2025 - July 19, 2025),



ECSA lineage, Asian lineage, Indian Ocean Lineage

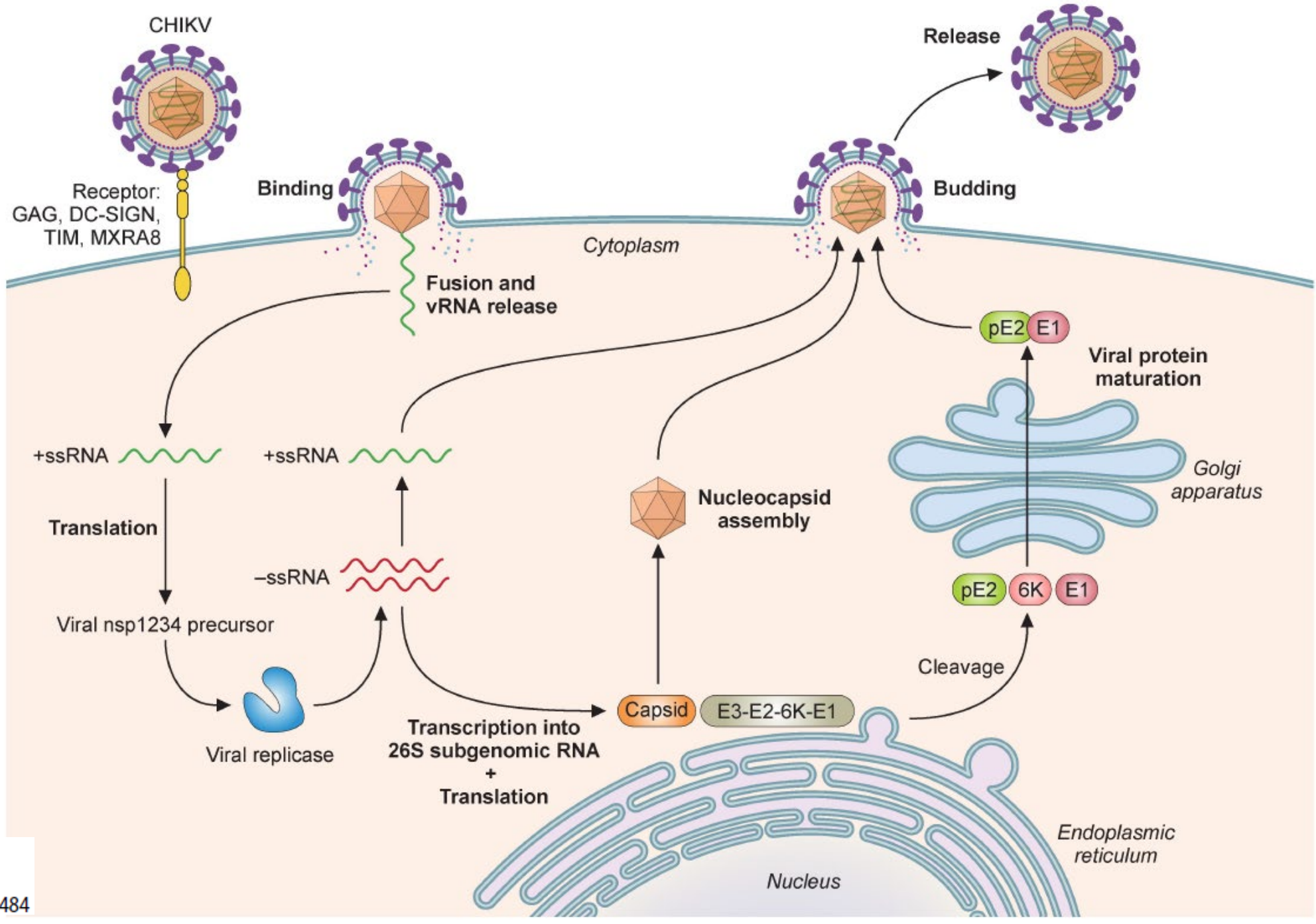






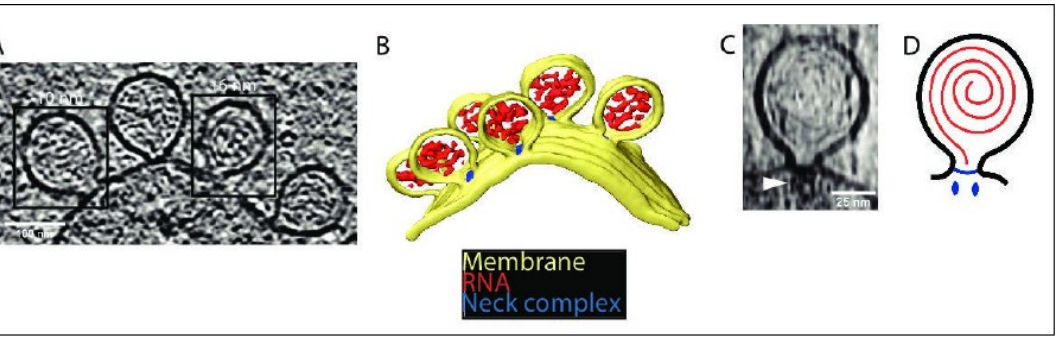
VIRULENCE
2024, VOL. 15, NO. 1, 2396484
https://doi.org/10.1080/21505594.2024.2396484

Replication cycle

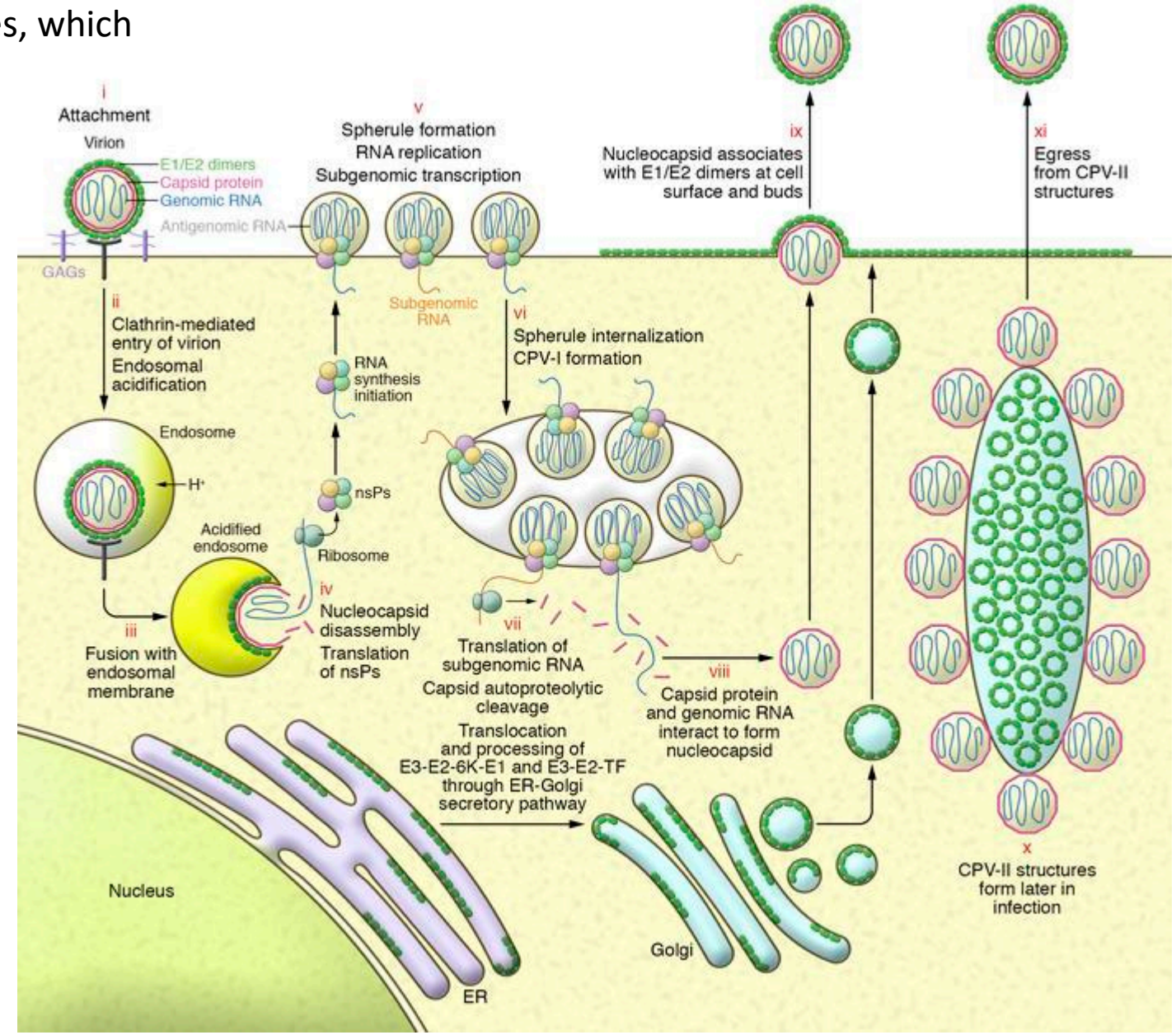


VIRULENCE
2024, VOL. 15, NO. 1, 2396484
https://doi.org/10.1080/21505594.2024.2396484

Replication of the viral RNA genome occurs in specialized membranous replication organelles (ROs) or spherules, which contain the viral replication complex.



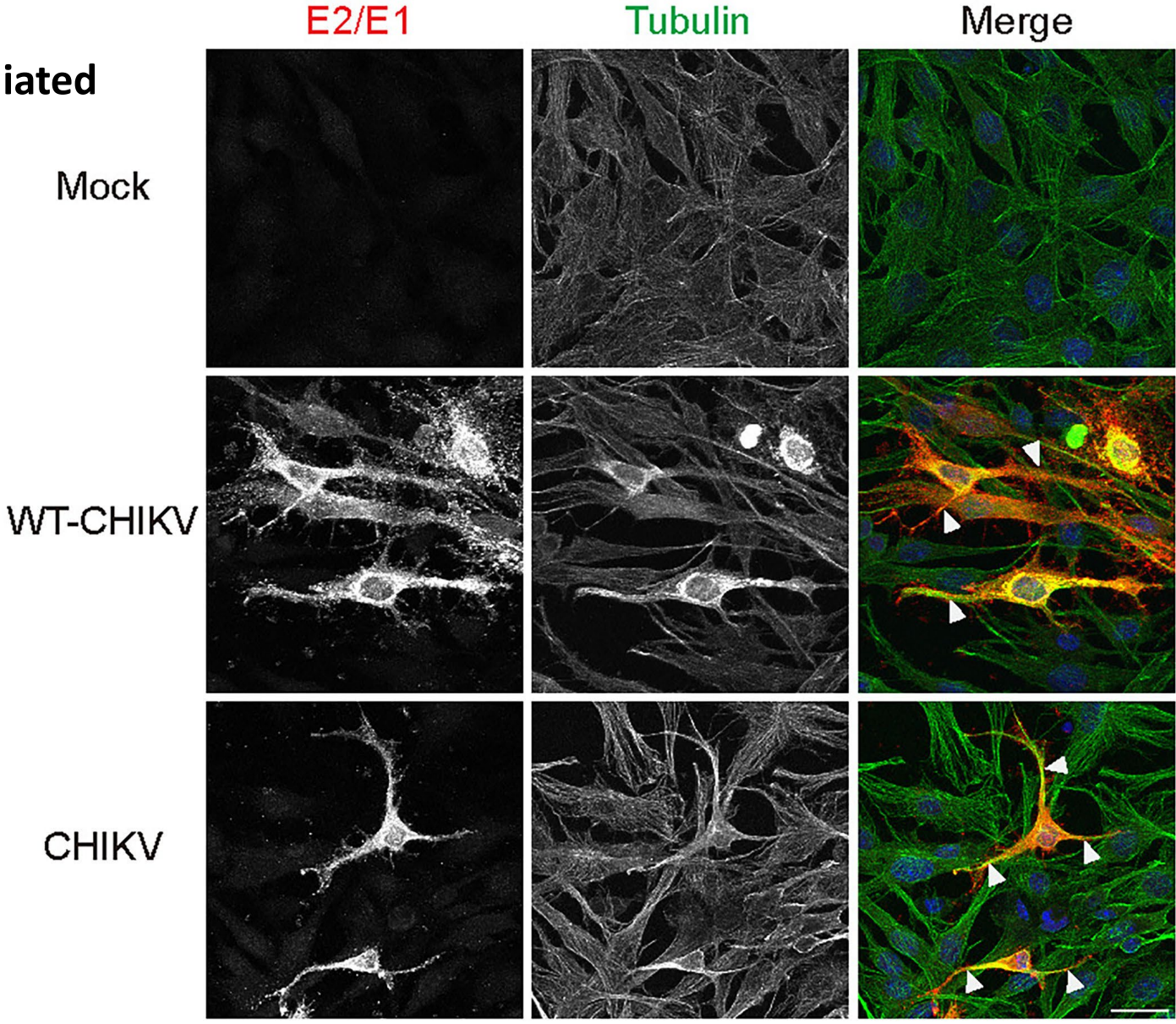
Laurent *et al*. eLife 2022;11:e83042.



J Clin Invest. 2017;127(3):737-749

Chikungunya virus cell-to-cell transmission is mediated by intercellular extensions in vitro and in vivo

Nat Microbiol. 2023 September ; 8(9): 1653–1667.
doi:10.1038/s41564-023-01449-0.



CHIKV cell-to-cell transmission exploits the target cell endocytic pathway including dynamin-dependent uptake, Rab5-mediated delivery to early endosomes, and exposure to endosomal low pH.

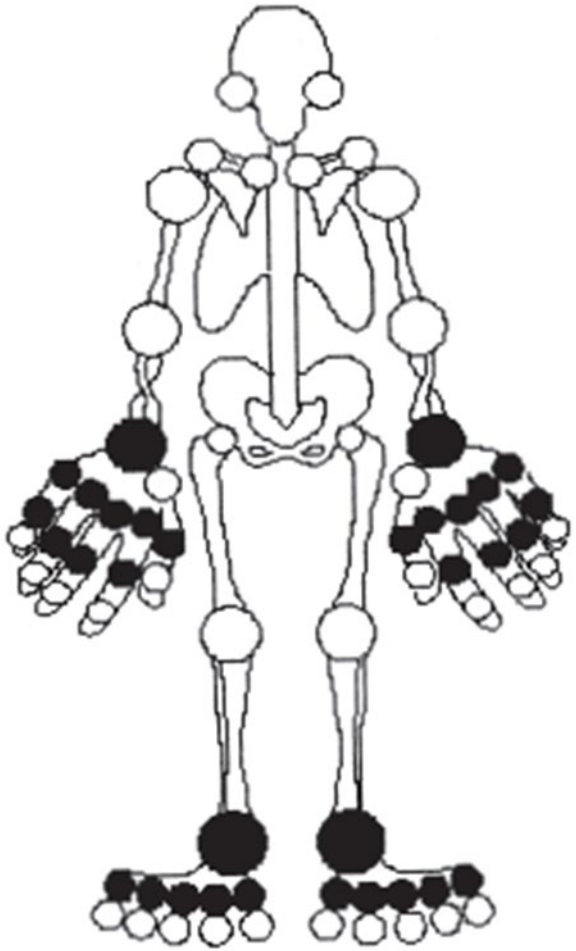
CHIKV infection and PATHOGENESIS

FEVER (>90%)

Myalgia(>90%)

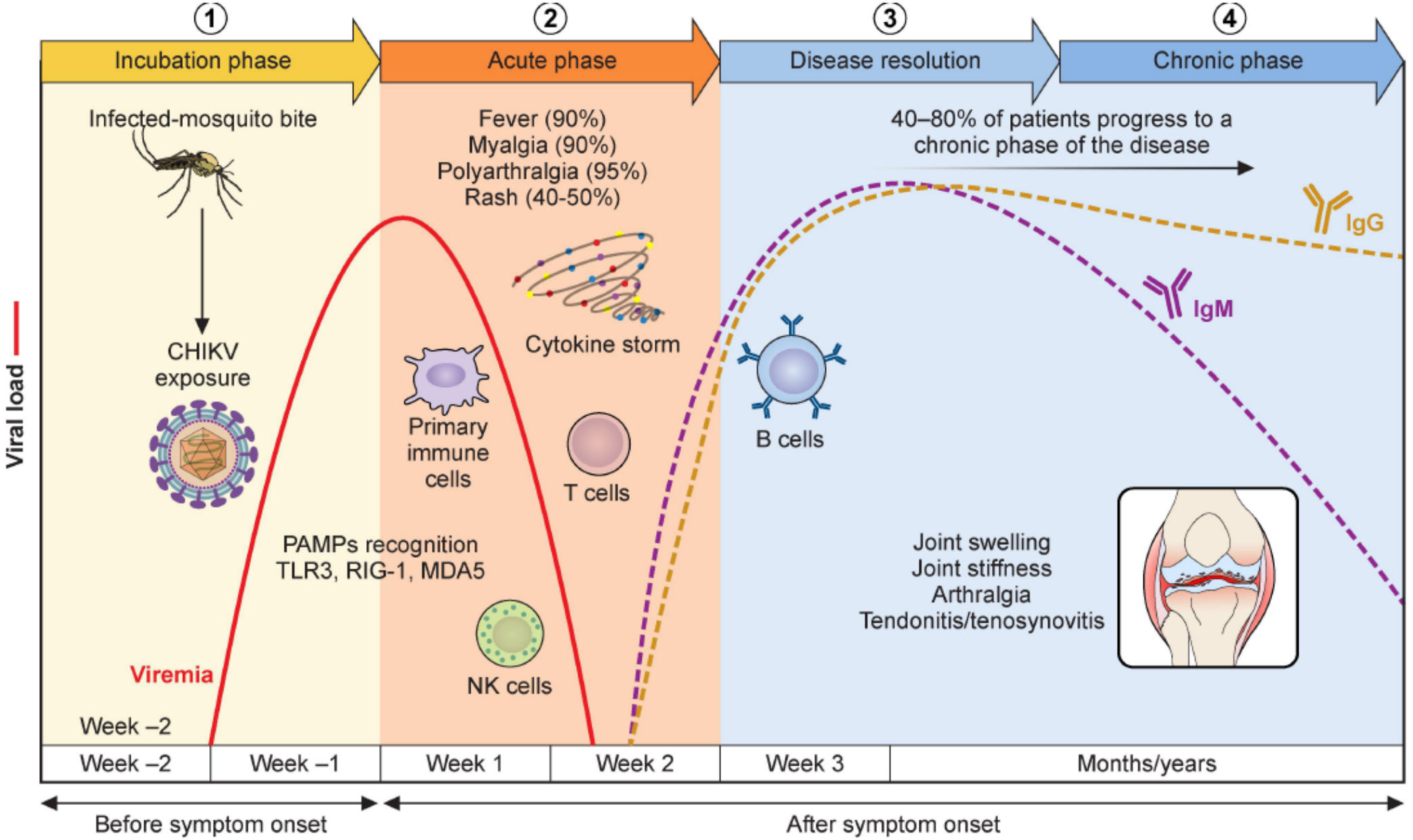
Polyarthralgia(95->95%)

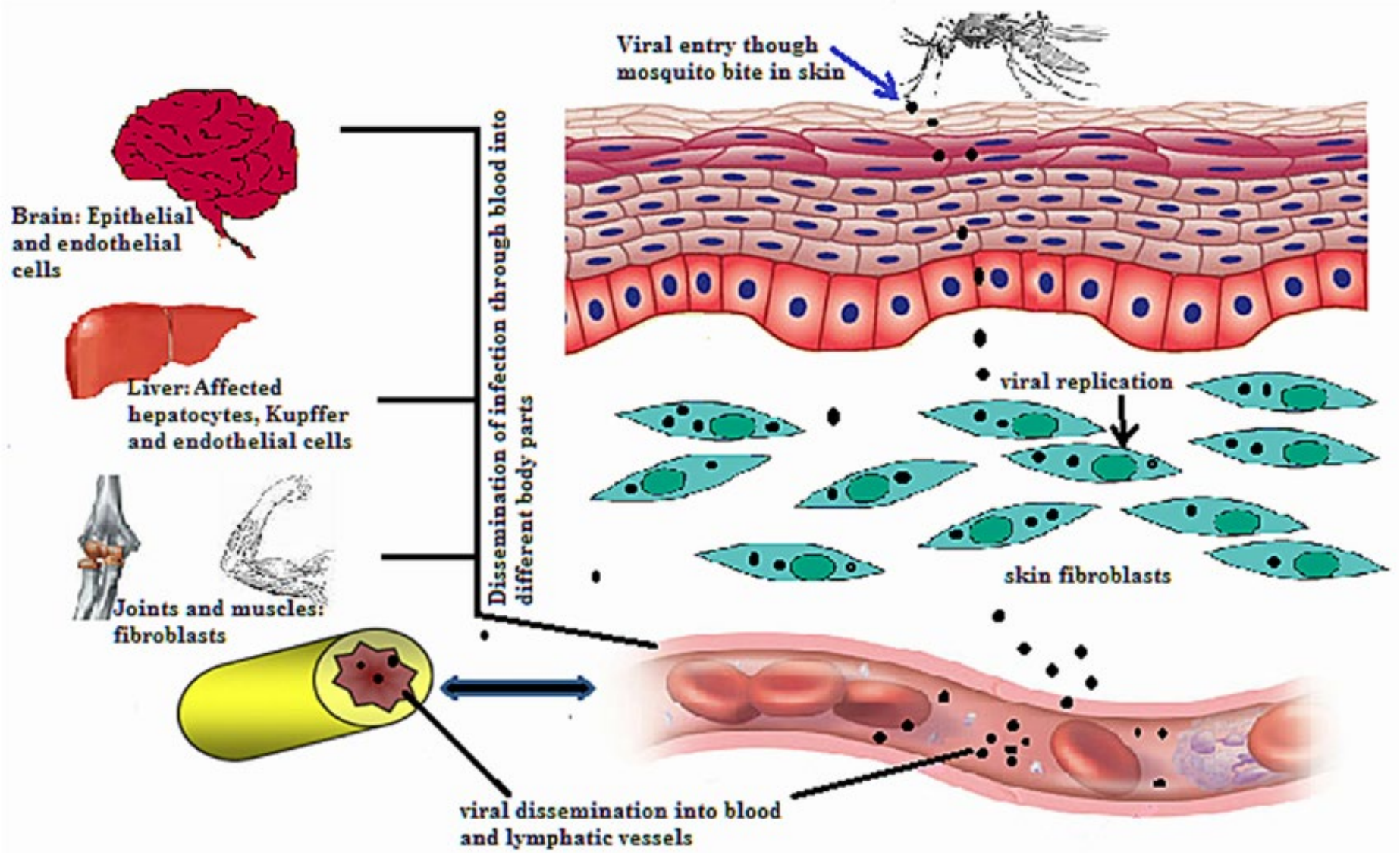
Rash (40-50%)



Timeline of CHIKV pathogenesis

VIRULENCE
2024, VOL. 15, NO. 1, 2396484
https://doi.org/10.1080/21505594.2024.2396484





Pathogens and Disease, 2016, Vol. 74, No. 3

Acute CHIKD

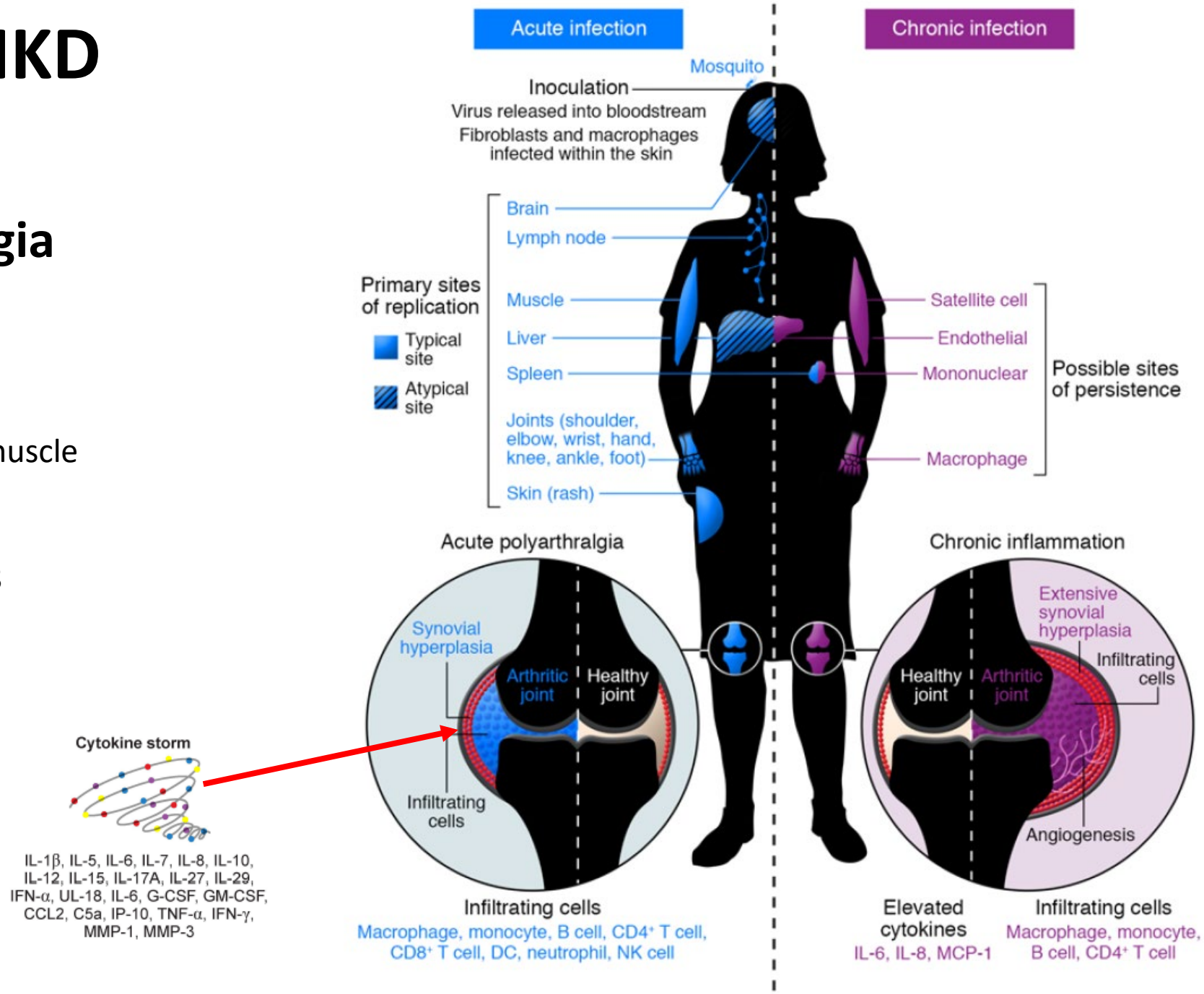
Polyarthralgia

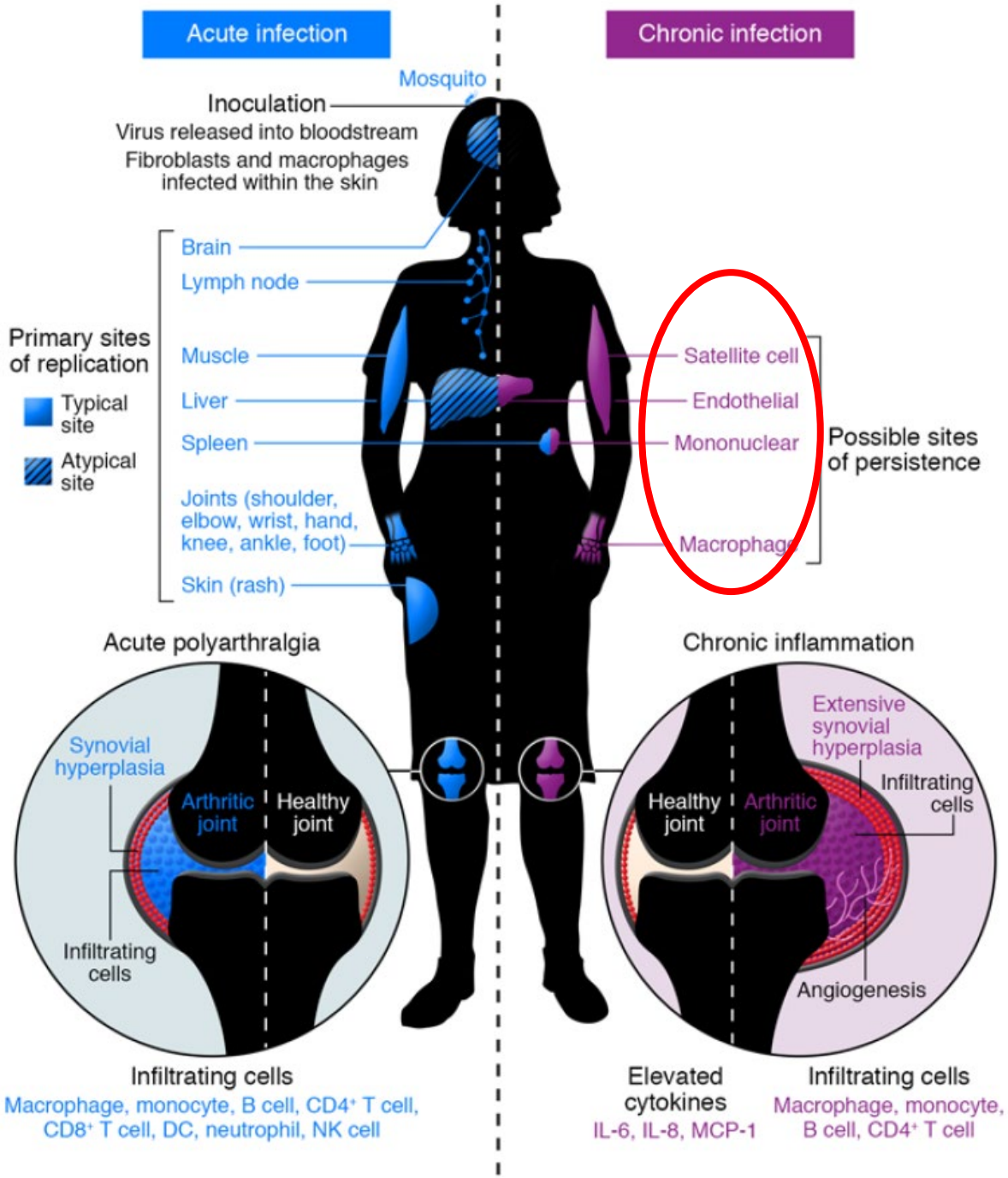
Myalgia

Myoblast, skeleton muscle

↓ CHIKV

IP-10, MIP-1a, IL-8





Chronic Chick Disease

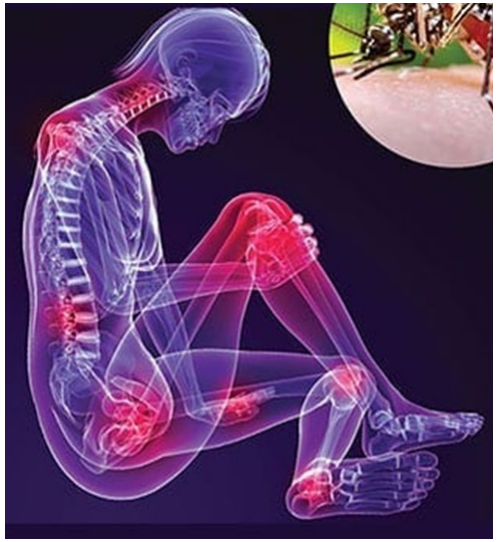
Synovial fluid : dsRNA but not viral RNA

Severe and prolong inflammation :

IL-1b, IL-6, IL-8, MCP-1/CCl2, MMp-1, MMp3, GMCSF, IL-17A, IL-27 and IL-29

Damage of connective tissues :

bone erosion, periostitis, enthesopathies



Chronic chikungunya disease

3 major mechanisms of connective tissue damage

1. CHIKV directly infects synovial fibroblast, chondrocytes, myocytes leading to inflammation and damage.

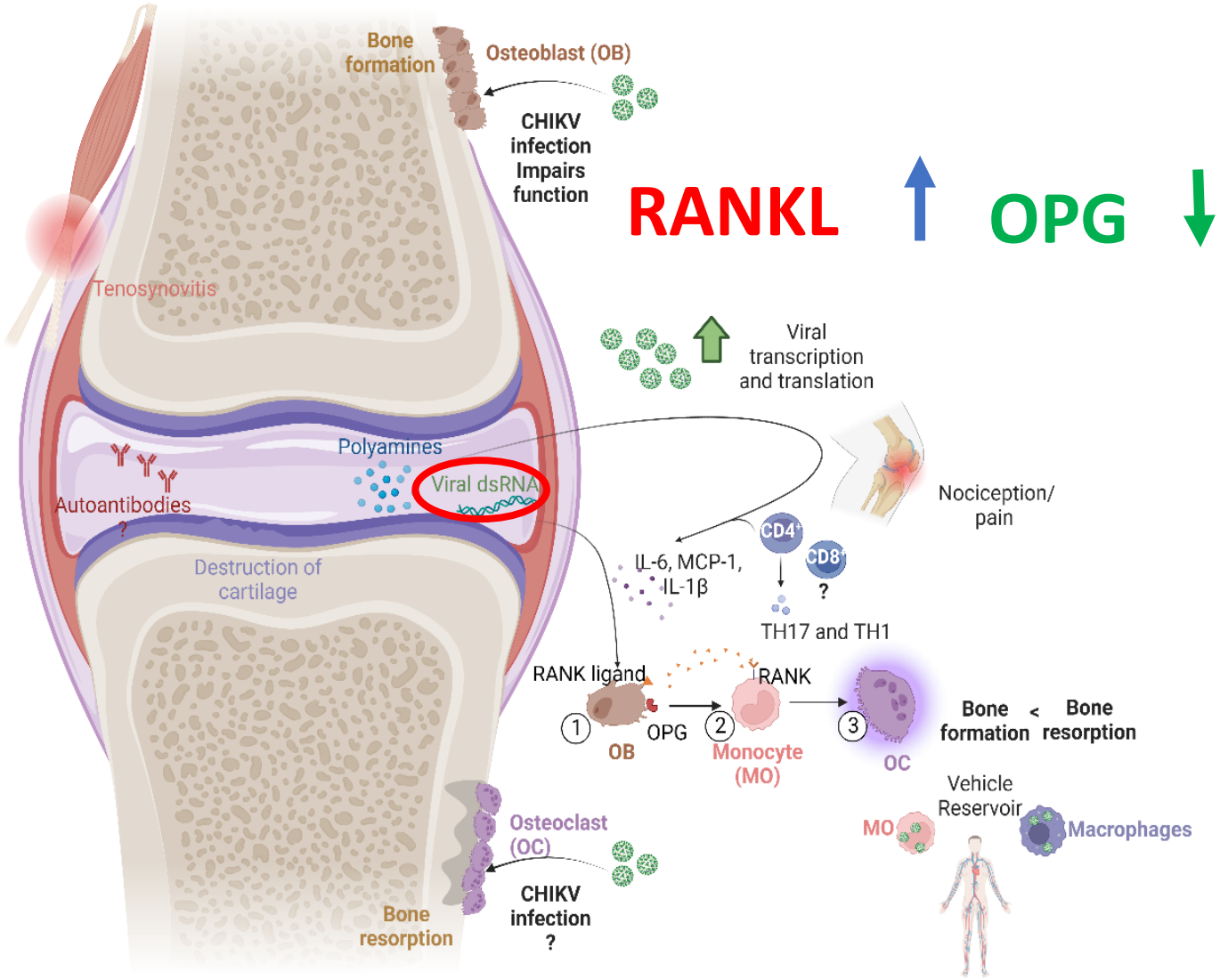
2. CHIKV infection is found to alter the RANKL/OPG ratio resulting in bone loss.

3. CHIKV infection results in a loss of proteoglycans in the cartilage matrix, resulting in bone loss.

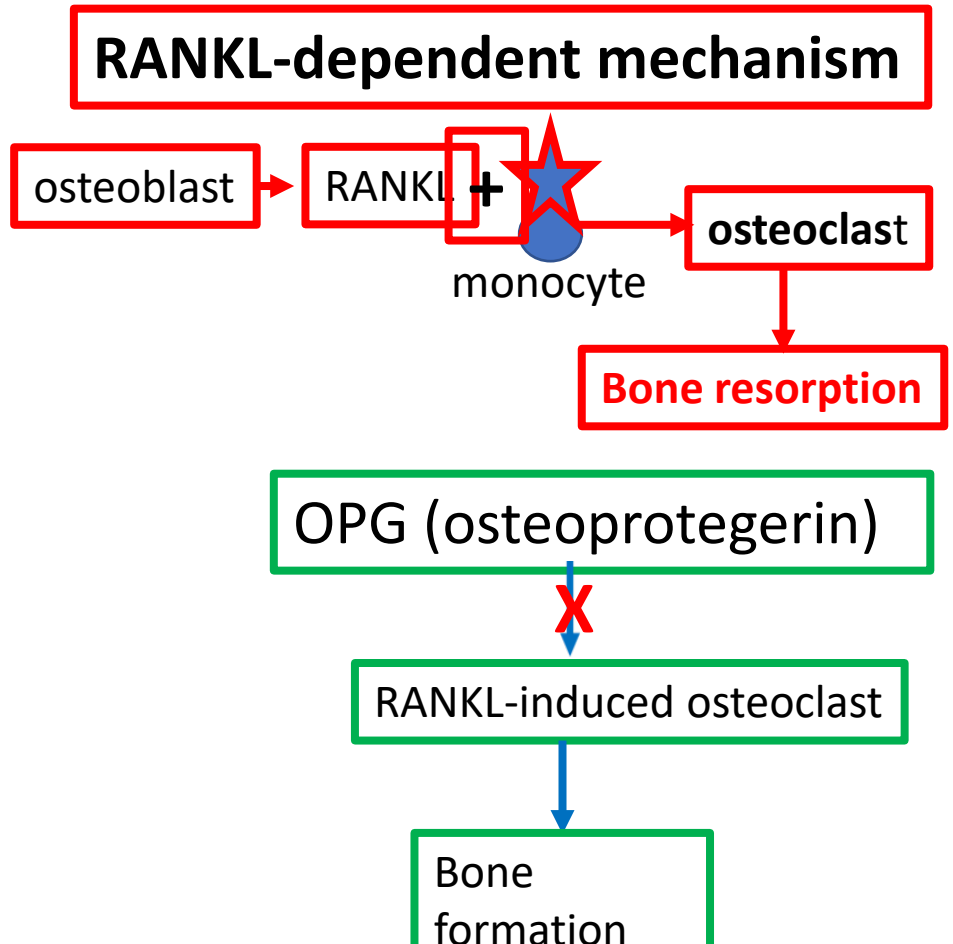
Noval MG, Nat Commun 2023; Pott F, Emerg Microbes Infect, 2021; Noret M, JID 2021, RuddPA, PLOS ONE 2021

Bone damage in chronic CHIKD

Levels of dsRNA in serum and synovial fluid corelates with bone erosion.
dsRNA induced PAMP activation in joints, thus, causes persistent inflammation.



RANKL ↑ **OPG** ↓



Determinants for disease severity

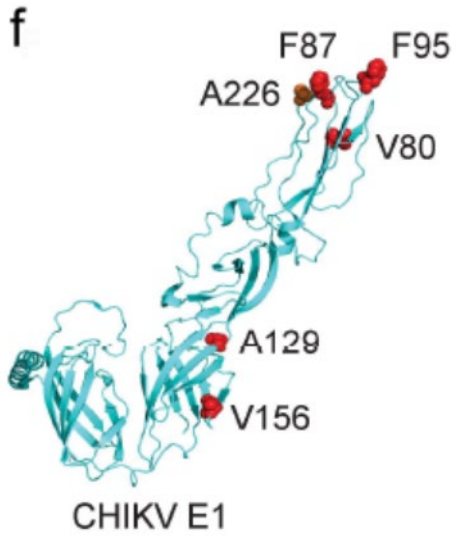
Viral factor

Virus strain and mutation : effect on transmission and immune evasion

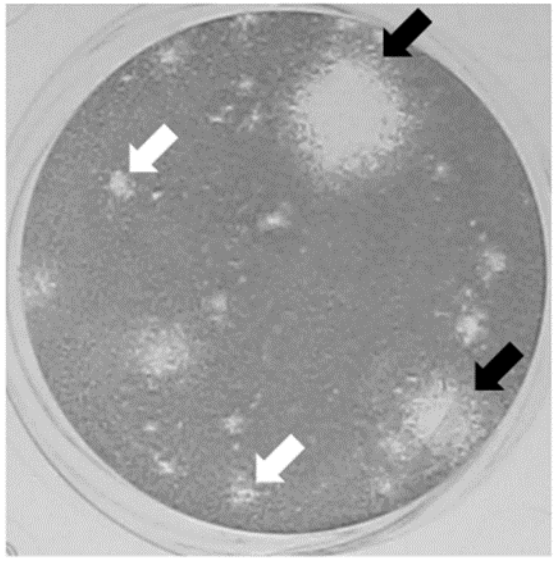
1. Mutations in nonstructural genes:

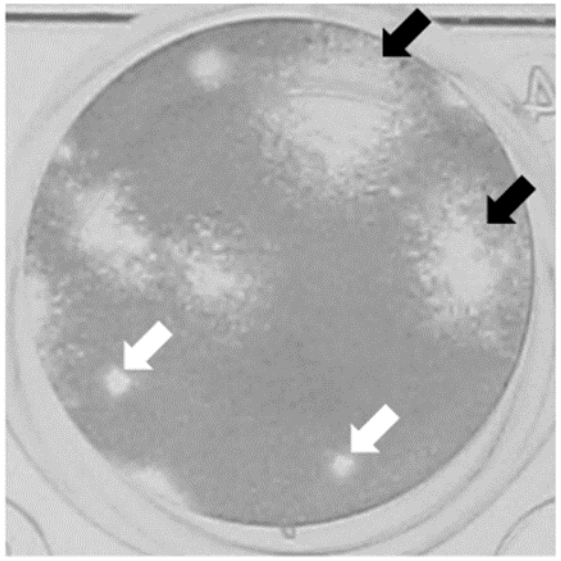
nsP1(R532H)
nsP2(E515V)
} Increased type 1 interferon production

E1 (A226V) → Increase transmission by A. albopictus



Heterogeneity of clinical isolates





Plague purification and in vitro model

- Large plaque CHIKVs
- Small plaque CHIKVs

> IL-6, IL8, MCP-1

> Promoting monocyte/macrophage migration

Reverse genetics

- Cloned-large plaque CHIKV
- Cloned-small plaque CHIKV

Small-plaque CHIKV caused more severe disease in mouse model

Determinants for disease severity (continue)

Human genetics

HLA-DRB1X04-HLA-DQB1X03 haplotype → **Susceptible to CHIKV infection**

HLA-DRB1X11, HLA-DQB1X03 haplotype → **Resistance to CHIKV infection**

Co-infection

1. Daniela Polania, et al. : Columbia, CHIKV epidemic 2015 (PLOS Neglc Trop Dis. 2025)

Caron, MI. study in South Africa,

No evidence that co-infection between DENV and CHIKV were associated with a worse clinical outcomes.

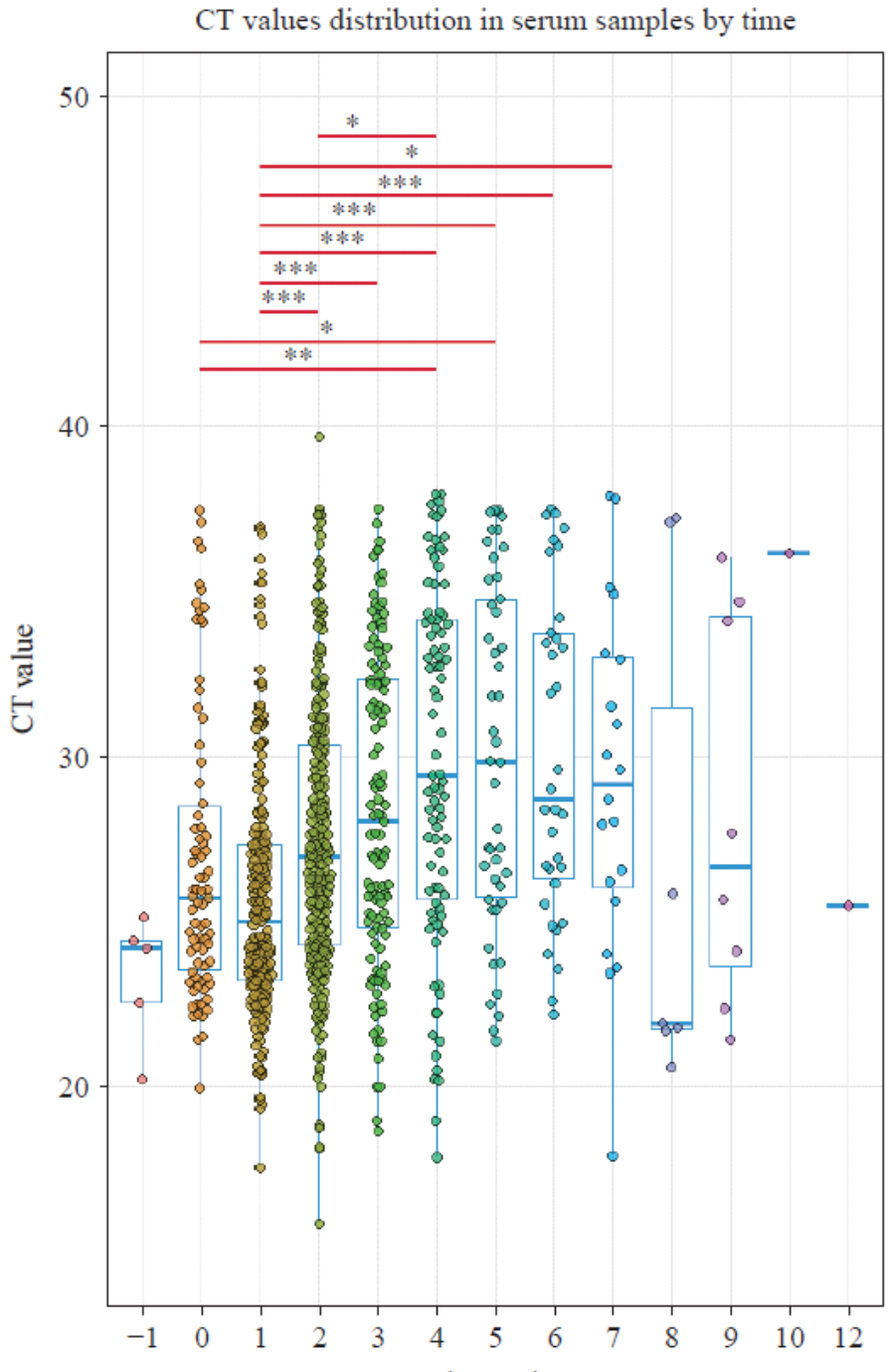
2. Gandhi, et. al. (Int. J. Health. Biomed. Res. 2015)

Mortality rate in co-infection = 12%
Mortality rate in monoinfection = 2%

Diagnosis

1. RT-PCR (China CDC Weekly, Vol7, N0. 33)

Blood = 90%
Saliva = 68%
Throat swabs =15%
Urine = 11%



Diagnosis

2. Antibody detection

TABLE 2 | Commercially available Chikungunya Virus (CHIKV) diagnostic assays in South Asia with principle of functions (Gaibani et al., 2016; Centers for Disease Control and Prevention (CDC), 2021; World Health and Organization (WHO), 2021).

Manufacturer	Country of origin	Principle	IgM	IgG
Abcam	Germany	IgM human ELISA kit	+	/
CTK Biotech	United States	CHIK IgM combo rapid test	+	/
CTK Biotech	United States	RecombiLISA CHIK IgM	+	
DRG*	Germany	CHIK IgM micro-capture ELISA	+	/
DRG	Germany	ELISA	/	+
Euroimmun	Germany	Anti-CHIKV IIFT	+	+
Euroimmun	Germany	Anti-CHIKV ELISA	+	+
GenWay	Germany	IgM-capture ELISA	+	/
GenWay	Germany	ELISA	/	+
IBL international	Germany	IgM micro-capture ELISA	+	/
IBL international	Germany	IgG-capture ELISA	/	+
InBios	United States	CHIKjj-MAC-ELISA	+	+
Novatec	Germany	IgM-capture ELISA	+	/
Novatec	Germany	ELISA	/	+
SD Diagnostics	South Korea	CHIKa IgM ELISA	+	/
SD Diagnostics	South Korea	SD BIOLINE Chikungunya IgM	+	/

*Only for research purposes.

Front. Microbiol. 12:689979.
doi: 10.3389/fmicb.2021.689979

Prevention and treatment

Treatment

There is no anti-CHIKV drug available at this moment.

As of Friday, August 22, 2025, FDA suspended the US license for IXCHIQ.

Prevention

The first FDA (USA) approved vaccine is a live-attenuated vaccine, Ixchiq. 2023

CHIKV(LR2006-OPY), deletion in nsP3, 1 dose IM, >18-65 years, not recommended for pregnancy women.

One dose can stimulate > 98% seroconversion.

Adverse effect : CHIKV-like syndrome , may cause serious in fetus.

Prevention (continue)

The only licensed vaccine available is **VIMKUNYA.**

VIMKUNYA is a VLP platform containing E1, E2, and C.

1 dose IM, >12 years,
I dose can induced NT Ab in 98.7% of vaccinees.

Adverse effect: no report

Table 1. *Cont.*

Vaccine	Technology	Virus Strain	CHIKV Immunogen	Number of Doses	Development Stage	Developer	Reference
CHIKV TSI-GSD-218	Live attenuated	Southeast Asian strain/AF15561	Whole Virus	Single-dose	Phase II	US Army Medical Research Institute of Infectious Diseases and University of Maryland	[114,115]
VAL-181388	mRNA-based	-	mRNA encoding C, E3, E2, 6k, E1	Two doses	Phase I	ModernaTX, Inc	NCT03325075
CHIKV001 (ChAdOx1-Chik)	Adenoviral vector	Multiple	C, E3, E2, 6k, E1	Single-dose	Phase I	Jenner Institute, University of Oxford	[116]
mRNA-1944	mLNP-mRNA-based	-	mRNA encoding CHKV-24 IgG (monoclonal)	One or Two doses	Phase I	ModernaTX, Inc	[117]

Abbreviations: MV measles virus; VLP virus-like particle; Δ5nsP3 five viruses with deletions in the nsP3 protein region (Δ5nsP3 mutants); LNP lipid nanoparticle encapsulated.

Thank you for your attention.