



Novel Common Marmoset Model for Arboviruses

Development and Implementation in an OCONUS Laboratory

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The experiments reported herein were conducted in compliance with the Animal Welfare Act and per the principles set forth in the "Guide for Care and Use of Laboratory Animals," Institute of Laboratory Animals Resources, National Research Council, National Academy Press, 1996.



Disclosure



- LTC Andrew Schrader, DVM has no conflicts to report.



Overview



1. Historical use of rhesus macaques in arbovirus research
2. Existing animal model gaps
3. Marmosets have potential
4. Adding a new animal to a care and use program
5. Outcomes and lessons learned



Historical Use of Rhesus Macaques

- Rhesus macaques serve as critical preclinical models for arbovirus research
 - Pathogenesis
 - Immune kinetics
 - Vertical transmission
 - Vaccine efficacy
- Genome is 93.45% homologous to humans¹
- Susceptible to natural infections to several arbovirus families
 - Flaviviruses, Alphaviruses, Bunyaviruses, Orthonaviruses
- Macaques serve as the most common non-human primate (NHP) model for dengue virus infection primarily used as a model of viral infection kinetics and immunogenicity





Limitations of the Rhesus Model



Practical

- Large animals that require intense husbandry care
- Occupational health risks to personnel
- Macaques are in short supply with high acquisition and per diem costs

Scientific

- Lack consistent, detectable physiological changes and severe disease pathology
- Viremia curves can be blunted compared to human infections



Advantages of the Marmoset

Journal of General Virology (2014), 95, 591–600

DOI 10.1099/vir.0.060384-0

Demonstration of marmosets (*Callithrix jacchus*) as a non-human primate model for secondary dengue

Journal of General Virology (2011), 92, 2272–2280

DOI 10.1099/vir.0.031229-0

Immunology Letters 158 (2014) 126–133

Contents lists available at ScienceDirect

Immunology Letters

Journal homepage: www.elsevier.com/locate/immlet

JOURNAL OF
GENERAL VIROLOGY

RESEARCH ARTICLE

Moi et al., Journal of General Virology 2017;98:2955–2967
DOI 10.1099/jgv.0.000913



Callithrix
infe

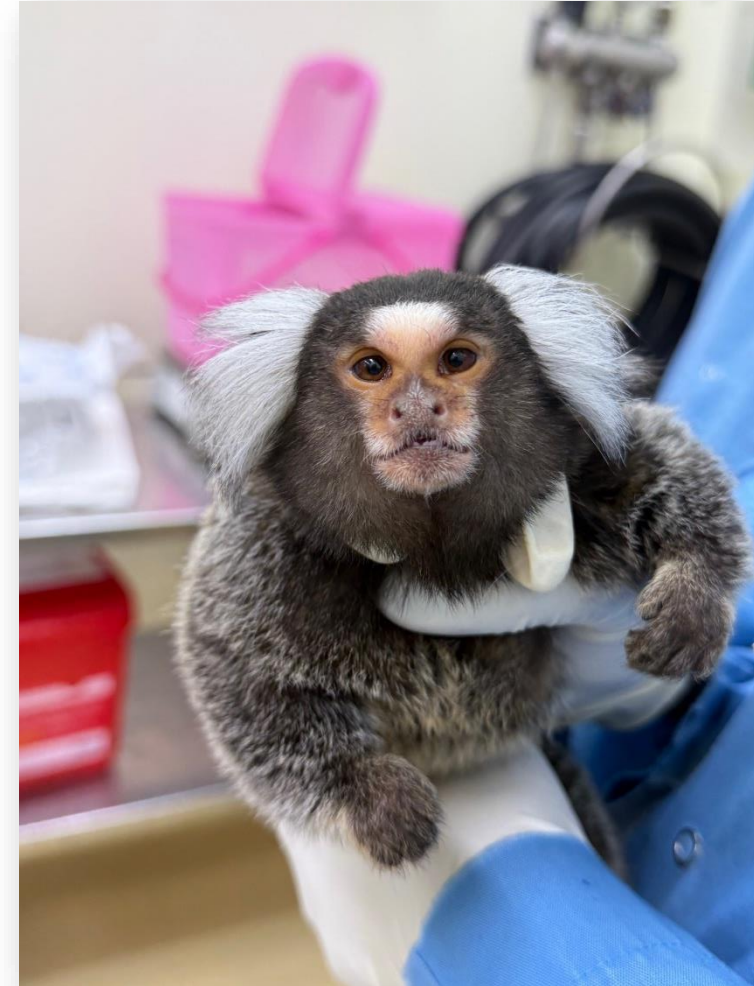
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Marmosets (*Callithrix jacchus*) as a non-human primate model for evaluation of candidate dengue vaccines: induction and maintenance of specific protective immunity against challenges with clinical isolates

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Abstract

Dengue virus (DENV) is one of the major infectious diseases in tropical regions and approximately half of the world population is at risk of infection. Vaccines would offer an effective control measure against this disease. We previously reported on the utility of marmosets as an animal model for studying primary and secondary dengue infections. Infected marmosets consistently develop viraemia and antibody kinetics that reflect those of patients with dengue. Thus, it is important to determine the utility of marmosets as an animal model for demonstrating vaccine efficacy. In this study, marmosets were inoculated with candidate vaccine and parent strains and challenged with a clinical DENV strain. The viraemia and antibody kinetics in these marmosets were determined. Marmosets consistently develop lower viraemia with an attenuated vaccine strain. During secondary challenge, the IgM response was delayed, whereas the IgG levels rose rapidly, indicating a secondary antibody response. The neutralizing activities against the homotypic serotype were high; all marmosets were protected against viraemia following secondary inoculation. The viraemia markers and antibody responses were consistent with those of human DENV infection and vaccinees. These results demonstrate the utility of marmosets as an animal model for the study of vaccine efficacy.





Advantages of the Marmoset



General

- Small size
- Housing requirements
- Restraint
- Acquisition and Per diem costs
- Occupational health concerns
- Personnel requirements

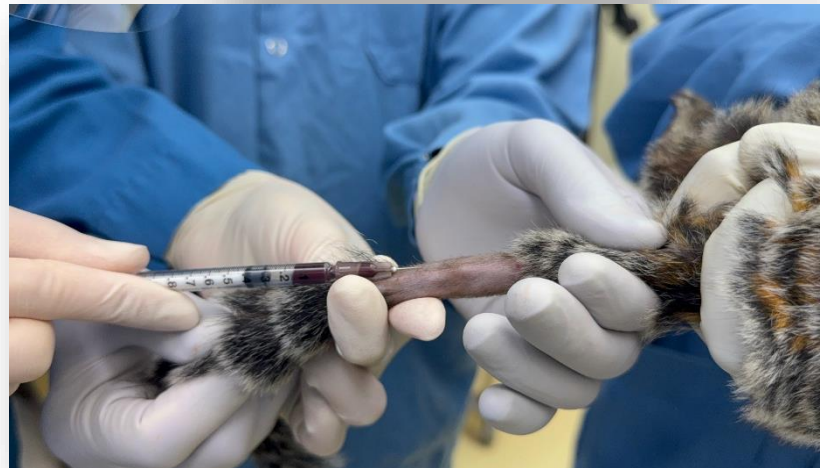
Dengue specific

- Robust IgG and IgM response
- Greater viremia levels
- Recapitulate physiological response



Factors for Adding Marmosets to the Animal Care and Use Program

- Sourcing and acquisition
- Facility
- Behavioral considerations
- Personnel/training
- Housing
- Biosafety/biosecurity
- Nutritional
- Enrichment
- SOPs





OCONUS Considerations





Training





Outcome



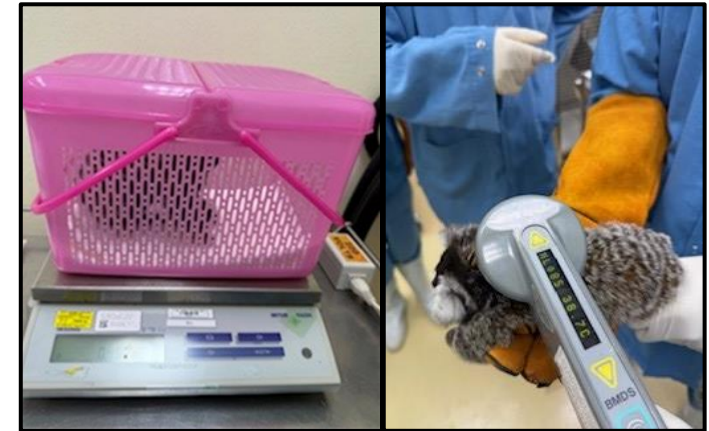
German-origin common marmoset confirmed to be flavivirus-naïve based on HAI assay results.



Subcutaneous (SC) inoculation of DENV-2 in common marmosets



Blood collection from the femoral vein (left) and tail vein (right) in common marmosets

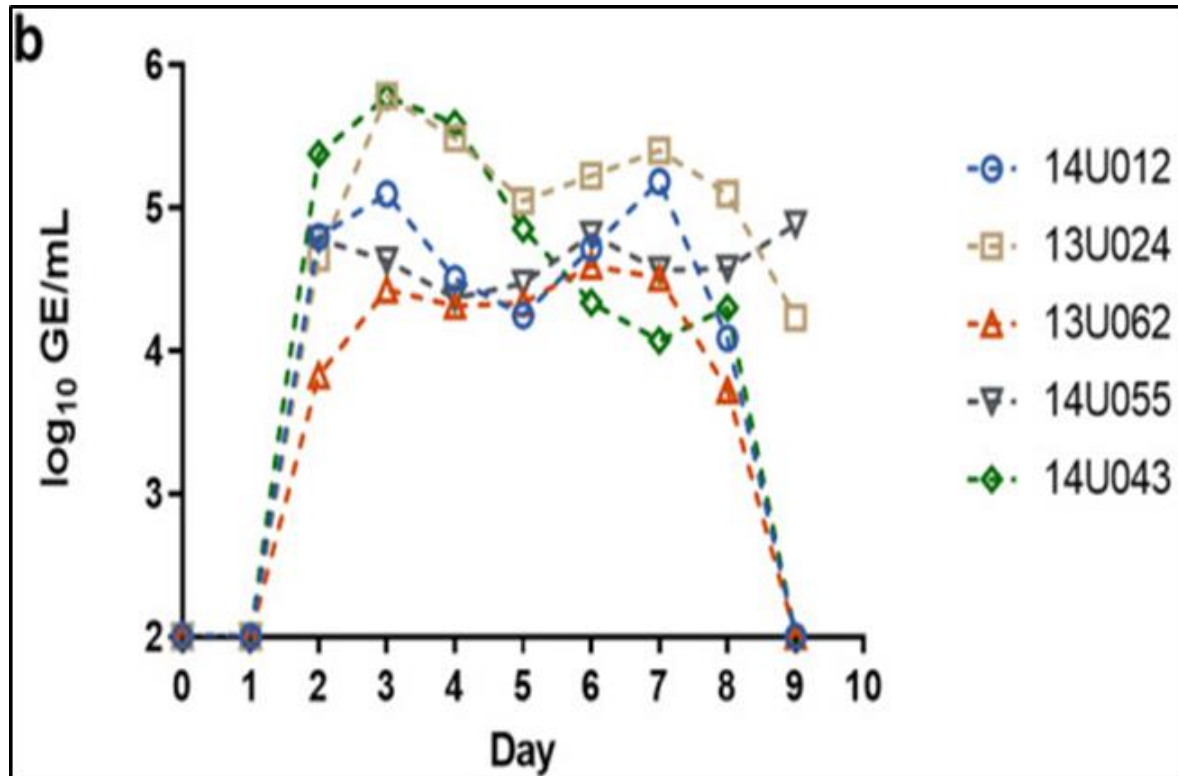


Measurement of animal weight and body temperature using a transponder.

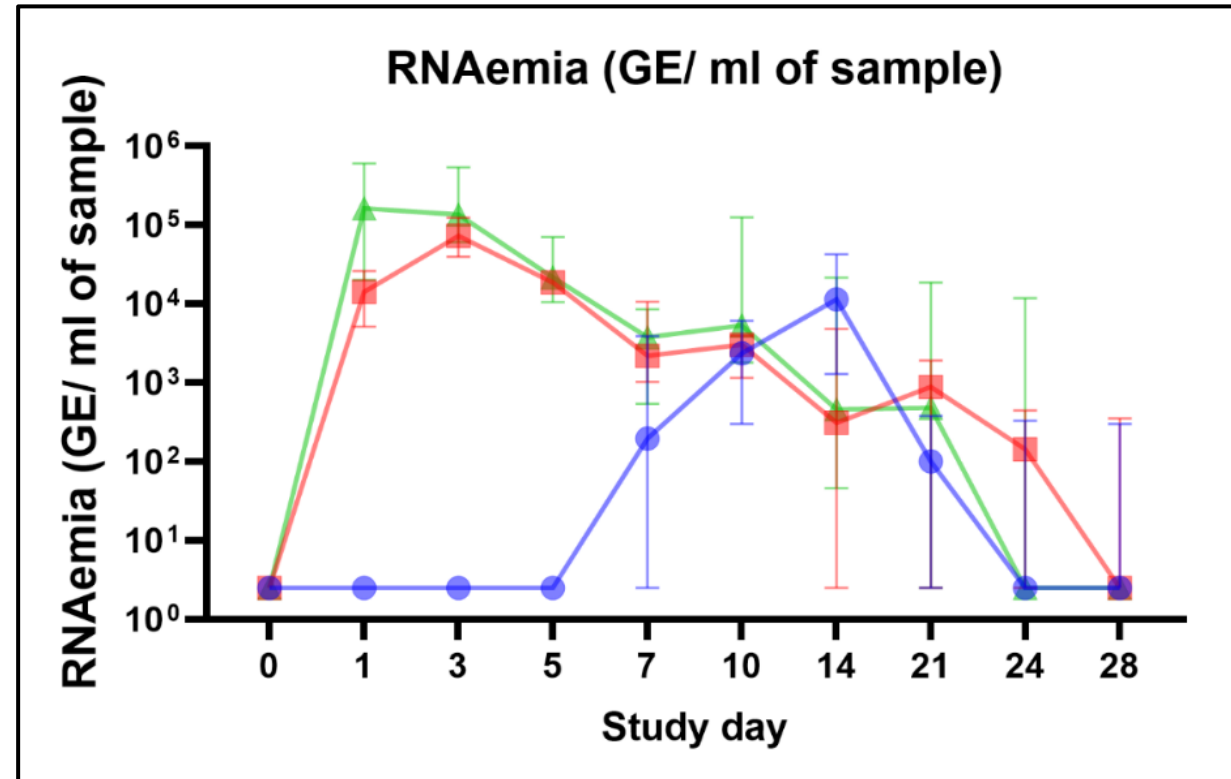


Outcome

Rhesus Macaque



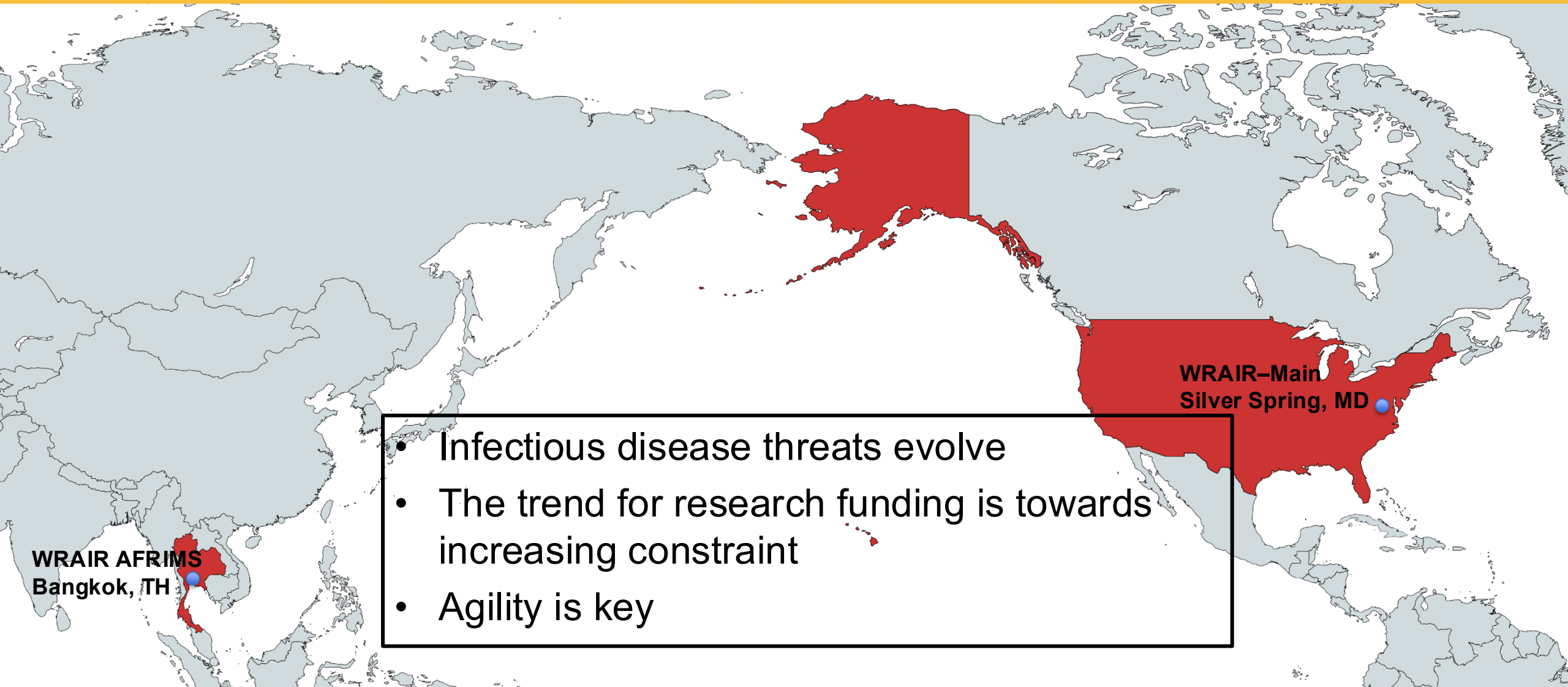
Marmoset



Data provided by McCracken et. al.



The Big Picture



- Infectious disease threats evolve
- The trend for research funding is towards increasing constraint
- Agility is key



Acknowledgements



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Questions



QUESTIONS?

