

ZIKA MOUSE LETHAL MODEL

Zika Strain PRV ABC58 From Current Outbreak



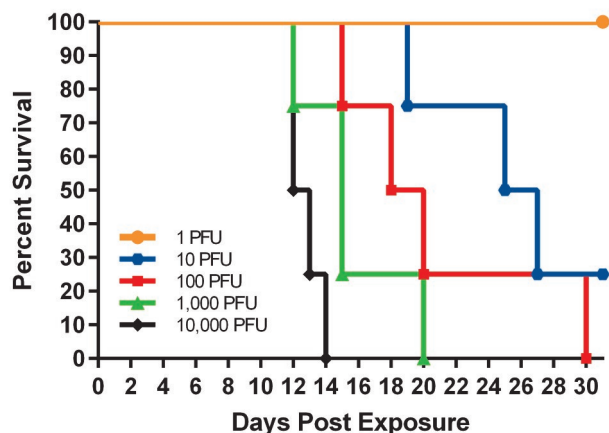
Description

IITRI has developed a mouse animal model using the PRV ABC59 strain, an isolate of Zika virus from the current outbreak. IFN α -KO mice, fully competent in humoral immune response, were inoculated with the PRV ABC59 Zika strain and were observed for signs of infection. The PRV ABC59 Zika strain used in the study is not mouse-adapted, and has a very low passage number. The mice demonstrated dose-dependent body weight loss and mortality. This mouse model is available immediately for the evaluation of vaccines and antivirals in development to combat the emerging Zika threat.

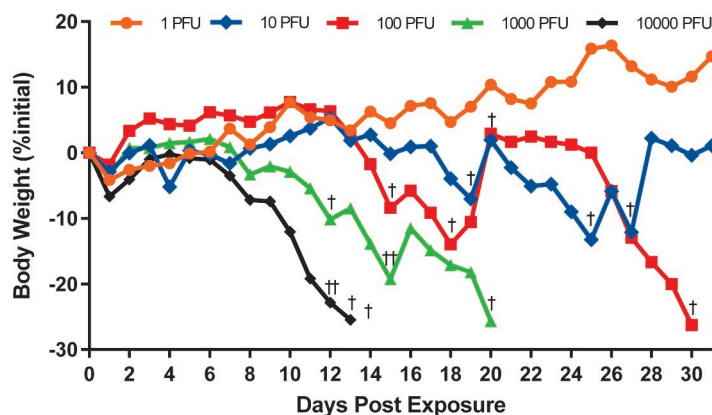
Experimental Design

A cohort of 30 male mice were divided into 6 groups and were inoculated subcutaneously with 10^0 - 10^4 PFU of Zika virus inoculum diluted in phosphate buffered saline (PBS). Following challenge, mice were monitored at least two times each day for clinical signs of disease for at least 28 days in this ongoing study. Necropsies were performed on day 3, 6, 9, and 12 to determine organ tissue titers. Samples are planned to be analyzed by qPCR and plaque assay to measure viral titers.

Survival Curve



Body Weights



A Kaplan–Meier survival curve with all experimental groups is shown above left. Median days of survival is as follows: day 12.5, 15.0, 19.0 and 25.5 post infection for mice inoculated with 1×10^4 , 1×10^3 , 1×10^2 and 1×10^1 PFU/mL, respectively. Changes in weight of mice inoculated with different challenge doses of PRV ABC59 Zika strain is shown above right. Loss or gain of weight was calculated for each mouse as the percentage change from baseline. Daggers represent days mice succumbed to infection.

Summary/Conclusions

A lethal mouse model for Zika infection and disease progression was established for the PRV ABC59 (Puerto Rico) strain. Mortality was inversely dose-dependent to initial challenge, as was change in body weight. This study is ongoing, with results pending for viremia and tissue viral titer analysis.

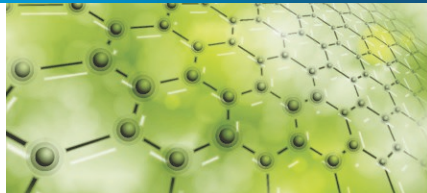
This mouse model is an important new tool for the evaluation of potential antivirals and vaccines to combat the emerging Zika outbreak.



CORE SERVICES

Infectious Disease and Biodefense

DISCOVERY & DEVELOPMENT



GLP SAFETY & TOXICOLOGY



CLINICAL TRIAL SUPPORT



In vitro efficacy studies

In vivo efficacy studies

- Vaccine and therapeutic models
- Animal models including ferrets, marmosets
- Bioaerosol models including select agents
- Wound models

Immunogenicity studies

- ELISA
- Hemagglutination inhibition assays
- Virus neutralization assays
- FACs analysis

Pharmacokinetics/ADME studies

Genetic toxicology

Repeat-dose toxicology studies

- All relevant routes of administration including inhalation
- All relevant animal models

Safety pharmacology

Immunogenicity and immunotoxicology

Bioanalytical services

- Bioanalytical method validation
- Sample analysis with TK modeling

Reproductive toxicology

Carcinogenicity studies

Bioanalytical method cross-validation

Bioanalytical sample analysis

Pharmacokinetics

Immunogenicity testing

- Neutralization assays
- Hemagglutination inhibition assays

Quantitation of cytokine expression

Assessment of biomarkers

Molecular biology analysis

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The IITRI Advantage

- Wide range of preclinical services available to evaluate the efficacy, potency and safety of vaccines, antitoxins, and therapeutics
- US Department of the Army Biological Surety Program
- Registered with the CDC and USDA for possession and use of select agents and toxins
- Highly experienced and integrated study team from a broad range of disciplines including virology, bacteriology, immunology, analytical chemistry, molecular biology and toxicology
- Hands-on study directors provide personalized attention and flexible study design
- Over 10,000 square feet of Biosafety Level ABSL/BSL-2/3⁺ facilities