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Rodent Models of Oropouche Virus Infection for Antiviral Screening

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INTRODUCTION

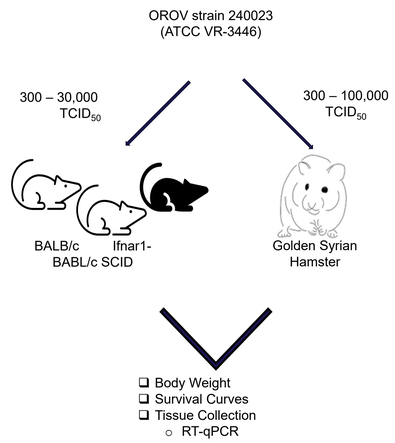
Oropouche virus (OROV) is an emerging public health threat due to its expanding global distribution. The surge in cases is associated with new symptoms, including congenital infection. Genetic analysis revealed this novel symptomology may be associated with emergence of a new natural reassortant. There are no antiviral therapies or vaccines available to treat OROV infection (1-2). Animal models to test the efficacy of antiviral therapies are urgently needed.

EXPERIMENTAL APPROACH

OBJECTIVE: To determine the susceptibility of mice and golden Syrian hamsters to OROV 240023 (ATCC® VR-3446™).

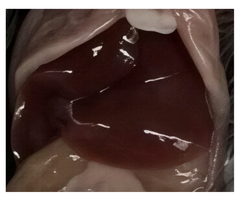
- BALB/c, BALB/c SCID and Ifnar1- mice were infected with 0 - 30,000 $TCID_{50}$ OROV (N=4/group).
- Golden Syrian hamsters were infected with 0 - 100,000 $TCID_{50}$ OROV (N=4/group).
- Body weight and clinical observations were performed daily.
- Euthanasia was performed when animals reached predefined terminal endpoints.
- Tissues, including liver, spleen, brain, and serum were collected for viral RNA extraction and RT-qPCR of viral RNA.

Fig. 1: OROV Infection in Mice and Hamsters

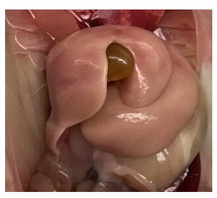


RESULTS

Fig. 2. Gross Liver Pathology in OROV Infected Mice



Normal Mouse Liver



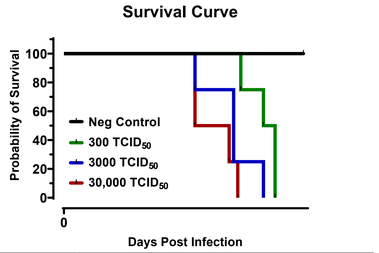
OROV Infected Mouse Liver

REFERENCES

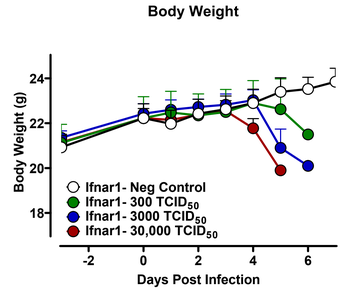
1. Gunter, K., et al. (2024). A reporter Oropouche virus expressing ZsGreen from the M segment enables pathogenesis studies in mice. Journal of virology, 98(9), e0089324. https://doi.org/10.1128/jvi.00893-24
2. Rodrigues, A. H., et al (2011). Oropouche virus experimental infection in the golden hamster (Mesocrisetus auratus). Virus research, 155(1), 35–41. https://doi.org/10.1016/j.virusres.2010.08.009

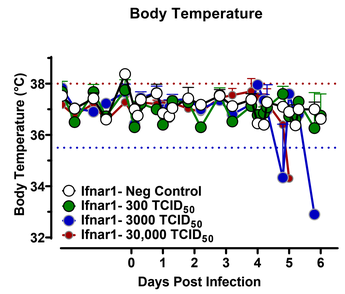
RESULTS

Fig. 3. Susceptibility of Ifnar1- Mice to OROV



	Neg Control	300 TCID50	3000 TCID50	30,000 TCID50
Median survival	Undefined	6	4.96	4.33





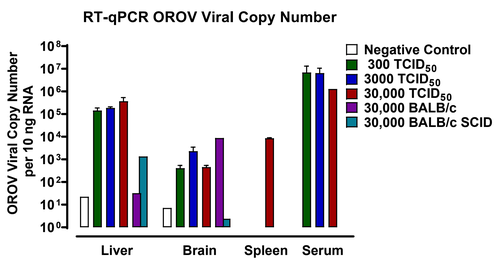
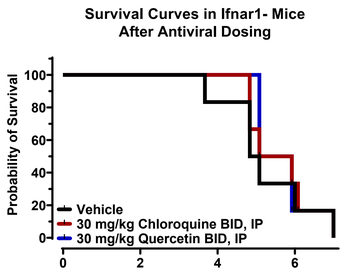
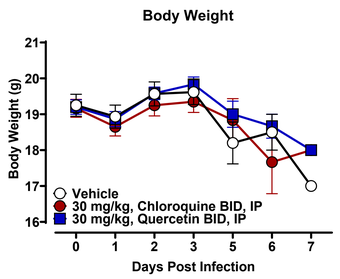


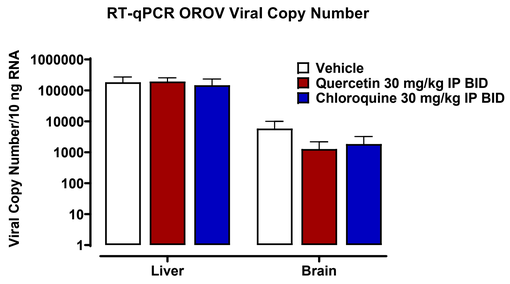
Fig. 4. Antiviral Treatment of OROV Infected Ifnar1- Mice

In a separate study, five-week-old male Ifnar1- mice were infected with 300 $TCID_{50}$ OROV for 4 h before intraperitoneal dosing of Chloroquine or Quercetin. Antiviral dosing was performed once per day.



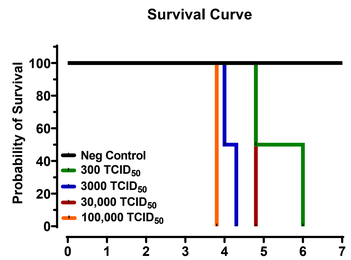
	Vehicle	Chloroquine	Quercetin
Median survival	4.9565	5.5	5.5



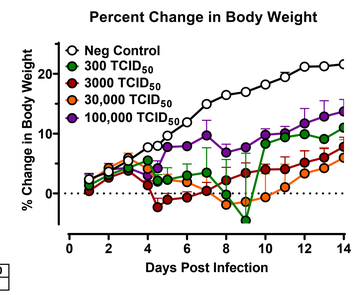


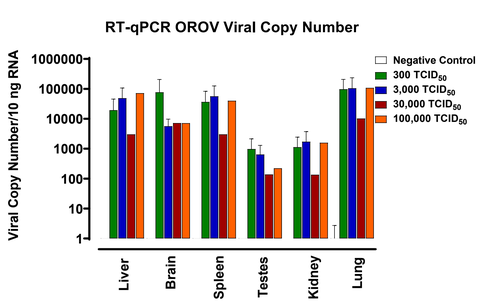
RESULTS

Fig. 5. Susceptibility of Golden Syrian Hamsters to OROV



	Neg Control	300 TCID50	3000 TCID50	30,000 TCID50	100,000 TCID50
Median survival	Undefined	5.4	4.15	4.8	3.8





SUMMARY

- OROV infection is 100% lethal in Ifnar1- mice and causes gross liver pathology.
  - OROV was rarely lethal in BALB/c (25% at 30,000 $TCID_{50}$) and BALB/c SCID (25% at 30,000 $TCID_{50}$) mice.
  - Quercetin and Chloroquine showed no antiviral activity against OROV infection in Ifnar1- mice.
- Evidence of OROV infection was detected in 87% of hamsters examined. Lethality was observed in 50% of infected animals. Six hamsters with nonlethal infection showed substantial transient weight loss.
- Of all tissue samples tested, the highest levels of viral RNA were found in the serum of infected mice. Measurable levels of viral RNA were detected in all tissues examined.
- The Ifnar1- mouse model can thus serve as a predictive model in evaluating potential therapies for this emerging disease.

ACKNOWLEDGEMENTS

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