Analysis of the impact of inoculation route on viremia, clinical parameters and immunogenicity in *Aotus nancymaae* non-human primate model of Dengue virus

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Introduction

Dengue virus (DENV) infects 100-400 million people word wide, resulting in 25,000 annual deaths and continues to have a major impact to military operational readiness [(1-2)].

Dengue vaccine development has been challenging, partly due to the unavailability of adequate animal models. Currently available mouse models require immunocompromised animals or genetic modifications to achieve susceptibility, and while some aspect of human clinical disease are achievable with rhesus monkeys, shortages can put rapid vaccine development at risk [3].

Aotus nancymaae monkeys are susceptible to DENV and other human pathogens of interest. The present study assesses the impact of intravenous (IV) versus intradermal (ID) delivery routes at physiologically relevant infectious doses on hematological, biochemical and immunological parameters that characterize human dengue infection, critical for evaluating novel prophylactics and vaccines against DENV infection.

Methods

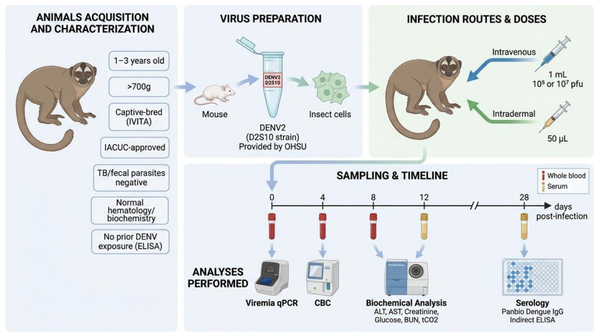


*Figure created with BioRender

Results

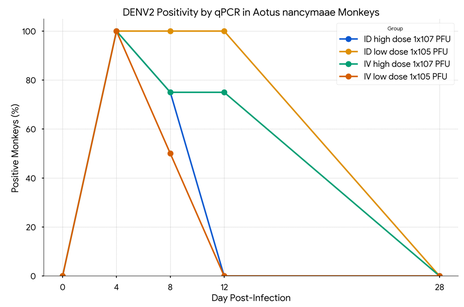


Figure 1. Prevalence of DENV2 infection detected by PCR. Animals from IV (higher or lower dose) and ID (higher or lower dose) were evaluated for detection of DENV2 by PCR at days 0, 4, 8, 12 and 28. Results are represented by (+) and (-) for positive or negative, respectively.

Results

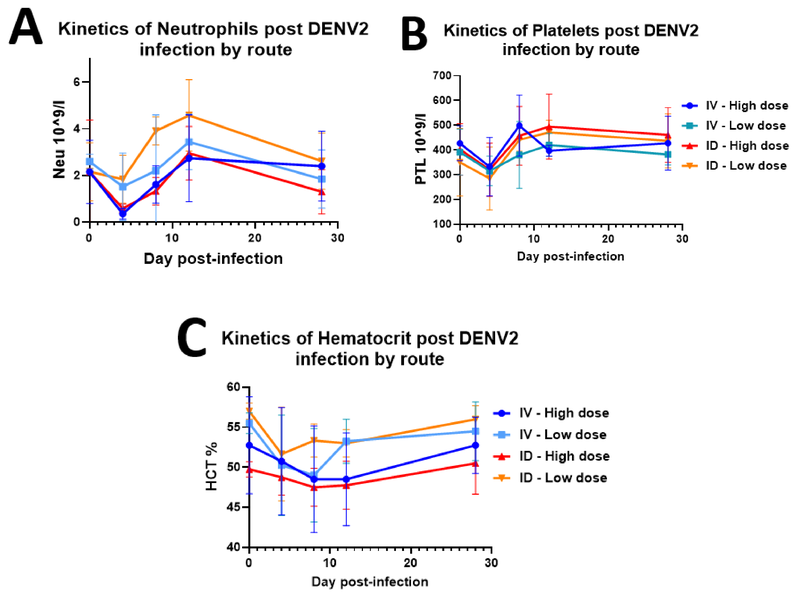


Figure 2. Kinetics of clinical parameters by CBC post DENV infection. Lines represent average values of neutrophils (A), platelets (B) and hematocrit (C) per group post DENV2 infection. Line colors represent IV-Higher dose (blue), IV-Lower dose (light blue), ID-Higher dose (red) and ID-Lower dose (orange).

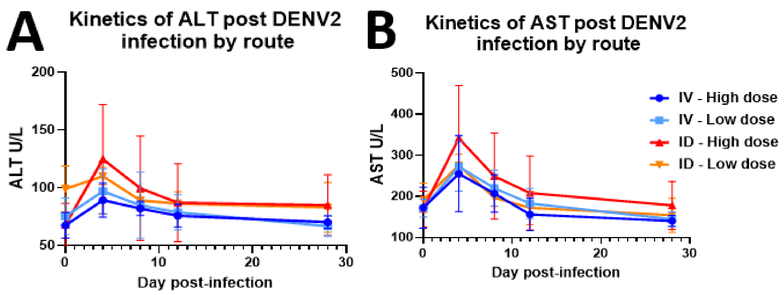
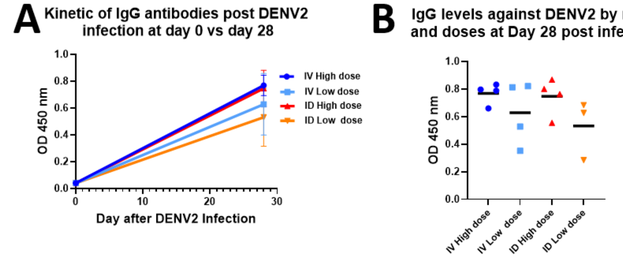


Figure 3. Kinetics of clinical parameters by biochemical analysis post DENV infection. Lines represent average values of ALT (A) and AST (B). Line colors represent IV-Higher dose (blue), IV-Lower dose (light blue), ID-Higher dose (red) and ID-Lower dose (orange).

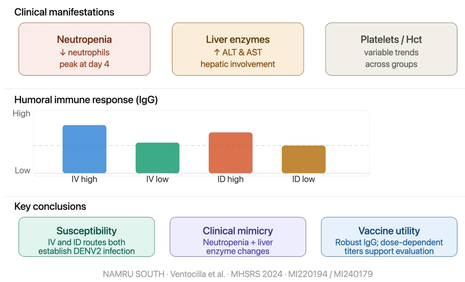
Results

Figure 4. Kinetics of IgG antibodies post DENV2 infection. (A) Lines represent OD average values of IgG antibodies between groups at day 0 vs day 28 post-infection. (B) Dot plot represent individuals values of IgG antibodies per group at Day 28.



Conclusion

- *Aotus nancymaae* is susceptible to DENV2 infection by IV or ID route, with all animals developing detectable viremia by day 4 post-infection across all groups.
- Clinical manifestations during infection that include neutropenia at 4 days post infection and increases in ALT and AST liver enzymes.
- All groups were seropositive for DENV-specific IgG with higher doses trending with higher titers.



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Partners/Collaborators

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Animal research protections: The experiments reported herein were performed in compliance with the Animal Welfare Act and in accordance with principles set forth in the "Guide for the Care and Use of Laboratory Animals", Institute of Laboratory Animals Resources, National Research Council, National Academy Press, 2011. All animals were bred in captivity and included in NAMRU SOUTH Institutional Animal Care and Use Committee (IACUC)-approved protocols. In addition, these animal studies were approved by the Peruvian government agency of "Servicio Nacional Forestal y de Fauna Silvestre" (SERFOR). This study was approved by the Directorate of Wild Forest and Fauna Management, Peruvian Ministry of Agriculture, with approval code: N° AUT-IFS-2024-054.