

Molecular analysis of biological tissues of BALB/c mice experimentally infected with dengue virus serotype 4

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The Dengue virus (DENV) is an arbovirus of the *Flaviviridae* family, being responsible for the tropical disease known as the Dengue fever (DEN). DEN is an emerging disease, deemed endemic by the Center for Disease Control (CDC) in at least one hundred countries, with growing incidence in South America since 1981. DENV-4 has been recently reintroduced to Brazil, more than thirty years after it was first detected, in the northern region of the country, and this marks the simultaneous co-circulation of the four serotypes in the Brazilian territory. Tissue alterations originated from DENV can be observed in a wide array of organs, ranging from liver to spleen, with varying degrees of severity. Currently, one of the greatest hardships of conducting experiments related to DENV is the inexistence of a proper animal model that faithfully replicates this disease as it appears in human cases. The main goal of this study is to evaluate the potential of the BALB/c strain of mice as an adequate animal model for the experimental infection by DENV, and whether it accurately replicates the effects of the DENV infection in humans. To this end, adult immunocompetent BALB/c mice were inoculated via intravenous route with a non-neuroadapted strain of DENV-4, grown in C6/36 mosquito cell line. The mice were euthanized 72 hours post infection, and the biological tissues (liver, lung and heart) were harvested and stored in a -70°C freezer for molecular analysis. Subsequently the organs were macerated, centrifuged, and the RNA was extracted from the resulting supernatant. The quantification was performed via real time RT-PCR. Analysis of the results has shown that viral copies of DENV-4 were successfully detected via real time RT-PCR in the liver, lungs and heart. The results observed demonstrate that the BALB/c strain of mice is indeed susceptible to DENV-4 infection, and the detection of viral RNA in the analyzed tissues indicates that replication did occur.

Keywords: Dengue vírus serotype 4, Animal Model, BALB/c

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