doi:10.20396/revpibic26201876

XXVI Congresso de Iniciação Científica Unicamp
17 a 19 de outubro Campinas | Brasil

Establishment and characterization of a model of Mayaro virus infection in immunocompromised mice.

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Abstract
Mayaro virus (MAYV) belongs to the Alphavirus genus along with other important viruses such as Chikungunya virus (CHIKV). The chronic disease caused by MAYV is described by a highly incapacitating joint pain which may endure for several weeks or months in at least 50% of the symptomatic patients. Recently, reports of sporadic outbreaks in humans has increased, however, the dynamic of the Mayaro infection is not completely understood and there is still no treatment or vaccine available. Herein, our goal was to develop an animal immunocompromised model ideal to understand the immunologic dynamic of the disease and perform antiviral tests.

Key words:
Mayaro virus, animal models, inflammation.

Introduction

Mayaro virus (MAYV) is an emerging mosquito-borne virus present in South and Central America, including Brazil. MAYV is the causative agent of Mayaro fever, an acute febrile illness characterized by pain, rash and polyarthralgia, which is often confused with Chikungunya. Mayaro fever patients may evolve to a chronic disease with incapacitating joint pain which may endure for months. Besides the increased risk posed by MAYV, infection is poorly understood and there is no treatment or vaccine available. Herein, our goal was to develop an animal model to study Mayaro fever development and test potentially protective compounds against the disease in vivo.

Results and Discussion

- We established a mouse model of infection in mice deficient for type I Interferon responses (ABR-/-) using the MAYV strain SJRP isolated in Brazil, which was highly pathogenic to mice. ABR-/- mice died after 4-5 days post infection regardless of the injection route and even when infected with the lowest inoculum tested (1 PFU). MAYV-induced disease includes weight loss, high viral loads in target tissues, viremia and morphological/histological changes in the inoculated paw. Edema, increased diapedesis and recruitment of granulocytes and mononuclear cells were observed in infected paws. Moreover, we developed a X-ray microtomography technique in collaboration with the National Synchrotron Light Laboratory that allow us to measure the total volume of MAYV-infected paws with µm3 precision. 3D reconstructions confirmed the development of edema in infected paws and indicated that paw bones may also be affected

Conclusions

We conclude that our MAYV infection model in ABR-/- mice recapitulates several features of the disease in humans, notably the viremia and inflammation in the limbs. Due to extensive MAYV replication and dissemination in ABR-/- mice, this model will should also be used for antiviral compound testing.

Acknowledgement

We would like to thanks FAPESP (Grant n° 2018/03917-6), CNPq and the Brazilian Center for Research in Energy and Materials (CNPEM)