VAC_02 - Immunogenicity and protection evaluation of a live attenuated chimeric vaccine for zika virus in mice model

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Introduction: Despite the substantial reduction in the number of zika cases in recent years, an efficacious vaccine is urgently necessary to limit the reemergence of zika and congenital zika syndrome.

Objectives: This work evaluated the immunogenicity and protection of a live attenuated chimeric yellow fever 17D/Zika virus that has been developed at Fiocruz.

Methodology: Two different mice strains were used: the immunocompetent C57BL/6, to assess immunogenicity, and the immunocompromised AG129 (IFN α/β/γ R−/−), to assess protection. Fifty animals of each mouse strain were distributed into five groups. Three groups were immunized with a single dose at 3 different concentrations (x, 10x, and 100x); the positive control group was inoculated with a wild type ZIKV, and the mock-immunized group received the vaccine excipient. Forty-two days after immunization, all mice lineages were challenged with a wild-type ZIKV strain. AG129 were observed 28 days for clinical signs, and sera samples were collected in days -1, 27, 41, 54 and 70 to analyze RNAemia and neutralizing antibody titer (NAb) by RT-qPCR and PRNT50 respectively. C57BL/6 were euthanized at days 2, 3 and 4 post challenge and subjected to the same tests. Spleen samples were collected at endpoint.

Results: Regarding the knockout mice, animals that received the highest doses of the antigen resulted in 100% survival after challenge, whereas the lowest concentration protected 70% of the animals. Furthermore, an increase of 100 times in NAb was observed in all vaccinated groups compared to pre-immunization titers. Viral RNA was detected in the spleen of both mice strains, however this finding did not seem to impact AG129 mice survival. No RNAemia was detected in all groups of C57BL/6 mice, and the level of NAb increased just after challenging, indicating that C57BL/6 strain poses limitations to evaluating the chimeric vaccine immunogenicity, due to its natural refractoriness to ZIKV infections.

Conclusion: The results obtained in this non-clinical study show that the attenuated chimeric virus was able to induce a robust humoral response and to protect the AG129 mice from death at the highest concentrations. These results will guide the selection of the vaccine formulations that will be tested in the non-human primate model.

Keywords: Zika virus, live -attenuated chimeric vaccine, non-clinical study