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Pan-Flavivirus Vaccine that Protects Against Zika Virus and Dengue Virus

Researchers at the La Jolla Institute for Immunology are exploring ways to produce a pan-flavivirus vaccine against the four Dengue Virus (DENV) serotypes and Zika Virus (ZIKV) that elicits both robust antibody and T cell responses. The proposed hexavalent vaccine will be comprised of a combination of mRNA encoding a tandem sequence of two structural proteins from each DENV serotype and ZIKV as well as mRNA encoding a conserved non-structural protein region from all four DENV serotypes and ZIKV.

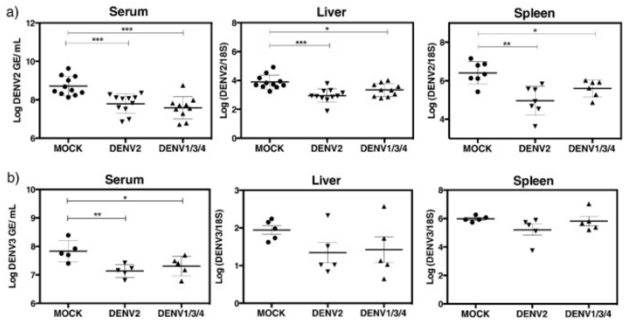
The DENV field has been focusing vaccine development efforts towards induction of humoral immunity as DENV-specific antibodies (Abs) are assumed to be the key mechanism of protection against natural infection. However, Abs can play a dual role in protection and pathogenesis. Studies of relevant mouse models have demonstrated a direct role for Abs in DENV pathogenesis by mediating Ab-dependent enhancement (ADE) of infection. Furthermore, epidemiologic studies and phase III clinical trial data on Dengvaxia®, the only licensed DENV vaccine, support a role for ADE in DENV pathogenesis.

In addition to Abs, LJI researchers' mouse model studies have demonstrated that both virus-specific and cross-reactive CD8 T cells can protect against DENV. Based on preliminary studies, they predict that effective immunity against flaviviruses is mediated by antigen-specific CD8 T cell responses with superior magnitude, breadth, and polyfunctional capacity in addition to a robust Ab response. As such, they plan to test various compositions and treatment strategies to develop a vaccine against DENV and ZIKV that generates both an optimal CD8 T cell response and Ab response.

ADVANTAGES:

- **Generates an optimal CD8 T cell response against DENV and ZIKV**
- **Prevents potential ADE of infection from subsequent exposure to other flaviviruses**

Hexavalent pan-flavivirus vaccine that protects against both ZIKV and DENV



DENV2 and DENV3 viral burden in peptide-immunized mice.

(a) DENV2 and (b) DENV3 RNA levels in serum, liver, and spleen are represented in log scale.

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