

An evaluation of dengue type-2 inactivated, recombinant subunit, and live-attenuated vaccine candidates in the rhesus macaque model[†]

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Abstract

The safety, immunogenicity, and protective efficacy of two non-replicating antigen-based vaccines and one live-attenuated virus (LAV) vaccine for dengue type-2 (dengue-2) virus were evaluated in the rhesus macaque model. The non-replicating vaccines consisted of whole, purified inactivated virus (PIV) and a recombinant subunit protein containing the amino-(N)-terminal 80% of envelope protein (r80E), each formulated with one of five different adjuvants. Each formulation was administered to three animals on a 0, 3-month schedule. Following the primary immunizations, 37 of 39 animals demonstrated dengue-2 virus neutralizing antibodies. After the booster immunizations all animals had dengue neutralizing antibodies with peak titers ranging from 1:100 to 1:9700. The highest neutralizing antibody titers were observed in the groups that received r80E antigen formulated with AS04, AS05, or AS08 adjuvant, and PIV formulated with AS05 or AS08 adjuvant. These newer adjuvants are based on alum, fraction QS-21 of saponin, and monophosphoryl lipid A (MPL). Protection was evaluated by dengue-2 virus challenge 2 months after the booster by the measurement of circulating virus (viremia) and post-challenge immune responses. Several groups exhibited nearly complete protection against viremia by bioassay, although there was evidence for challenge virus replication by Taqman™ and immunological assays. None of the vaccines conferred sterile immunity.

The views expressed herein are those of the authors and should not be construed as official or to reflect the views of the Department of Defense or the U.S. Government.

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