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A synthetic multi-antigen approach targeting *Plasmodium falciparum* malaria

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P. falciparum (Pf) malaria remains a significant public health problem. Current evidence suggests a vaccine candidate that elicits humoral and cellular responses to multiple sporozoite and liver-stage antigens may be able to confer protection against Pf malaria. Here, we report the preclinical assessment of a DNA vaccine approach that targets four Pf antigens: CSP, LSA1, TRAP, and CelTOS (MAV4). Synthetic DNA sequences were designed and delivered using electroporation (EP). In mice, DNA+EP delivery induced robust cellular and humoral immune responses. Further, hepatic $CD8^+$ T cells produced antigen-specific IFNγ. A chimeric *Pf-Plasmodium berghei* (Pb) CSP sporozoite challenge model, a Pb sporozoite that contains Pf CSP in place of Pb CSP, was used to evaluate if immune responses induced by the Pf CSP component of MAV4 could decrease liver-stage parasite burden. Immunization with the synthetic pDNA Pf CSP resulted in a significant decrease in liver-stage levels. In Rhesus macaques, MAV4 elicited robust antibody and T cell responses to all antigens. Notably, the phenotype of the majority of antigen-specific $CD8^+$ T cells indicated potential for cytotoxic and effector functions. In conclusion, DNA+EP delivery elicits strong immune responses against multiple malaria antigens and merits further study in clinical trials.

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