An mRNA–lipid nanoparticle vaccine targeting the Plasmodium vivax E140 antigen

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Introduction: *Plasmodium vivax* is the leading cause of malaria outside Africa, yet no licensed vaccine is available. Identification of conserved antigens combined with next-generation vaccine platforms such as mRNA–lipid nanoparticles (mRNA-LNP) may accelerate the development of effective vaccines.

Objectives: To evaluate the immunogenicity and protective potential of the conserved multi-stage antigen E140 delivered using a nucleoside-modified mRNA-LNP vaccine platform.

Methods: BALB/c mice were immunized intramuscularly with mRNA-LNP encoding *P. berghei* E140 (PbE140) or *P. vivax* E140 (PvE140) using either a single 10 µg dose or a prime-boost regimen (2 x 5 µg). Antibody responses were assessed by ELISA and B-cell responses were characterized by flow cytometry. Protective efficacy was evaluated in mice challenged with *P. berghei*. Functional activity of PvE140-induced antibodies was assessed using *ex vivo* reticulocyte invasion assays with clinical *P. vivax* isolates.

Results: Vaccination induced strong and durable antigen-specific IgG responses that persisted for at least six months and displayed a balanced IgG subclass profile. Robust germinal center B cell and plasma cell responses were detected in spleen and bone marrow. Immunization with PbE140 mRNA-LNP reduced parasitemia and improved survival following parasite challenge. Importantly, sera from mice immunized with PvE140 mRNA-LNP inhibited *P. vivax* merozoite invasion of human reticulocytes by 56–78% in independent *ex vivo* assays.

Conclusion: These findings demonstrate that E140 delivered through the mRNA-LNP platform induces strong humoral and cellular immune responses and generates functional antibodies capable of inhibiting *P. vivax* erythrocyte invasion, supporting E140 as a promising candidate for next-generation malaria vaccines.

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