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New Candidate Vaccines against Blood-Stage *Plasmodium falciparum* Malaria: Prime-Boost Immunization Regimens Incorporating Human and Simian Adenoviral Vectors and Poxviral Vectors Expressing an Optimized Antigen Based on Merozoite Surface Protein 1 †

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ABSTRACT

Although merozoite surface protein 1 (MSP-1) is a leading candidate vaccine antigen for blood-stage malaria, its efficacy in clinical trials has been limited in part by antigenic polymorphism and potentially by the inability of protein-in-adjuvant vaccines to induce strong cellular immunity. Here we report the design of novel vectored *Plasmodium falciparum* vaccines capable of overcoming such limitations. We

optimized an antigenic insert comprising the four conserved blocks of MSP-1 fused to tandemly arranged sequences that represent both allelic forms of the dimorphic 42-kDa C-terminal region. Inserts were expressed by adenoviral and poxviral vectors and employed in heterologous prime-boost regimens. Simian adenoviral vectors were used in an effort to circumvent preexisting immunity to human adenoviruses. In preclinical studies these vaccines induced potent cellular immune responses and high-titer antibodies directed against MSP-1. The antibodies induced were found to have growth-inhibitory activity against dimorphic allelic families of *P. falciparum*. These vectored vaccines should allow assessment in humans of the safety and efficacy of inducing strong cellular as well as cross-strain humoral immunity to *P. falciparum* MSP-1.

FOOTNOTES

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