

PRE-CLINICAL EVALUATION OF MALARIA VACCINE CANDIDATE MSP-1(42) WITH DIFFERENT ADJUVANTS

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The *P. falciparum* merozoite surface protein (MSP-1) is recognized as promising vaccine candidate against erythrocytic stage. MSP-1 vaccines that give protection in animal models require complete Freund's adjuvant, which is not approved for human use. In this study, we evaluate safety and immunogenicity in *rhesus* model of MSP-142 formulated with novel adjuvant systems that being developed for clinical use. A five dose series (week 0, 4, 13, 21 and 30) of MSP-142 was administered by intramuscular injection with five adjuvants (alum and GSK adjuvants; ASO1, ASO2, ASO5 and ASO8). Safety data from *rhesus* monkeys demonstrate that all five MSP-142 vaccines are safe. There were no significant toxicities associated with immunization observed through out the course of study. Antibody response data indicate that both 42/ASO2 and 42/ASO1 vaccines significantly elicited higher levels of anti-MSP-142 antibody than the 42/alum vaccine. The produced antibody not only reacted to MSP-142 by ELISA, but also recognized native antigen on merozoite confirming that the recombinant MSP-142 protein is correctly folded. The MSP-142 vaccines produced a robust T cell response. All vaccines tested generated high stimulation index (SI) even with alum adjuvanted vaccine. *Rhesus* cytokine ELISPOT assay was used to evaluate Th1/Th2 polarization. The two formulations of MSP-142 vaccine (42/ASO2 and 42/ASO1), which induced high titers of antibody, demonstrated different cytokine response profiles. Both vaccines induced comparable levels of IFN- γ response after the 3rd dose, however the IL-5 response was greatly suppressed in animals receiving 42/ASO1. As judged by the ratio of IFN- γ /IL-5, the 42/ASO1 induced more vigorous Th1 response (IFN- γ /IL-5 = 4.2) where as 42/ASO2 induced rather mixed Th1/Th2 response (IFN- γ /IL-5 = 0.75). The 42/alum induced the lowest ratio of IFN- γ /IL-5, which was 0.53. The IFN- γ response generated by both 42/ASO2 and 42/ASO1 persists at least 24 weeks after vaccination. The difference of Th1/Th2 polarization of the 42/ASO2 and 42/ASO1 vaccines warrants further comparative development of these vaccine candidates.

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