

oocyst number in the mosquito midgut. Several combinations of homologous and heterologous antigen-delivery prime boost strategy were also evaluated and the results suggested that antibody titers and transmission-blocking activities by the three prime-boost strategies (DNA prime/DNA boost, DNA prime/protein boost, and protein prime/protein boost) were comparable with slightly better immunogenicity of heterologous antigen-delivery prime/boost as compared to DNA/DNA alone. These results demonstrate potent immunogenicity of DNA vaccines encoding Pvs25 and Pvs28 and warrant further evaluation in non-human primates.

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### **PRE-CLINICAL EVALUATION OF THE MALARIA VACCINE CANDIDATE *P. FALCIPARUM* MSP1<sub>42</sub> FORMULATED WITH NOVEL ADJUVANTS OR WITH ALUM**

**Pichyangkul S, Gettayacamin M, Miller RS, Lyon JA, Angov E, Tongtawe P, Ruble DL, Heppner DG Jr, Kester KE, Ballou WR, Diggs CL, Voss G, Cohen JD and Walsh DS**

We compared the safety and immunogenicity of the recombinant *Plasmodium falciparum* MSP1<sub>42</sub> antigen formulated with four novel adjuvant systems (AS01B, AS02A, AS05 and AS08) to alum in rhesus monkeys. All five formulations of MSP1<sub>42</sub> were safe and immunogenic. Whereas, all MSP1<sub>42</sub> formulations tested generated high stimulation indices for lymphocyte proliferation (ranging from 27 to 50), the AS02A and AS01B formulations induced the highest levels of specific anti-MSP1<sub>42</sub> antibody. ELISPOT assays showed that the AS02A and AS01B vaccine formulations-induced different cytokine response profiles. Using the ratio of IFN- $\gamma$ /IL-5 secreting cells as the metric, the AS01B formulation induced a strong Th1 response, whereas the AS02A formulation induced a balanced Th1/Th2 response. The IFN- $\gamma$  response generated by AS02A and AS01B formulations persisted at least 24 weeks after final vaccination. The notable difference in Th1/Th2 polarization induced by the AS02A and AS01B formulations warrants comparative clinical testing.

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### **REEMERGENCE AND PERSISTENCE OF VIVAX MALARIA IN THE REPUBLIC OF KOREA**

**Pacha L, Lee HS, Bradley K, Tobler S, Littlebird FD, Maza JP, Hemingway A, Pettit K, Baker A, Kim H, Lee W, Lee J, Yang B, Jung G and Klein TA**

After the Republic of Korea (ROK, South Korea) was declared malaria-free in 1979, *Plasmodium vivax* malaria reemerged in 1993, putting Korea's military and civilians and US soldiers at risk for the disease. Our goals were to provide an overview of the reemergence and persistence of malaria in Korea, identify improvements for control, and assess the ongoing and future threat of malaria in Korea. We identified all reported malaria cases in ROK civilians, ROK military

and US soldiers in 1993-2003. For US soldiers, we studied morbidity reports for persons currently and previously assigned to duty in Korea. Military cases were interviewed to determine incubation periods, probable sites of exposure and compliance with the use of personal protective measures (PPM). Malaria cases peaked in 1998 (1,156 cases) in the ROK active duty military population and declined thereafter. Peaks in ROK civilian cases (1580) and discharged Korean soldiers (1273) were not seen until 2000, with subsequent declines in cases. Malaria cases in US soldiers deployed to Korea peaked in 1997 at 27 and averaged 18.3 per year during 1998-2003. Cases due to exposure in Korea and reported in US soldiers outside the ROK peaked in 1999 at 42 and declined thereafter. Interviews were conducted with 68 military cases between 2001 and 2003. Both short (1-4 months) and long (9-13 months) incubation periods were seen. The most probable sites of exposure were training areas within 25 km of the Demilitarized Zone separating North and South Korea. In 2003, one case was ascribed to exposure at a training site near Yongin, approximately 35 Km south of Seoul. Proper wear of the uniform limits exposed body surface (uniform discipline) and was the most commonly employed PPM; 57 (83.8%) patients reported practicing uniform discipline during field exercises. Only 18 (26.5%) reported having permethrin-treated uniforms. Forty-four (64.7%) patients reported using N,N-diethylmetatoluamide (DEET). Of these, only 29 (65.9%) reported using the US military extended duration formulation. Vivax malaria persists in the ROK. Transmission has occurred primarily along the highly fortified DMZ between North and South Korea. Barriers to communication and coordination with North Korea make eradication in the near future unlikely. Therefore, control measures (surveillance, environmental interventions, use of PPM and clinical awareness) must be continued and improved.

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## **SAFETY AND IMMUNOGENICITY OF RTS,S+TRAP MALARIA VACCINE, FORMULATED IN THE AS02A ADJUVANT SYSTEM, IN INFANT RHESUS MONKEYS**

**Walsh DS, Pichyangkul S, Gettayacamin M, Tongtawe P, Siegrist CA, Hansukjariya P, Kester KE, Holland CA, Voss G, Cohen J, Stewart AV, Miller RS, Ballou WR and Heppner DG Jr**

Malaria vaccine RTS,S combined with thrombospondin-related anonymous protein (TRAP) and formulated with AS02A (RTS,S+TRAP/AS02A) is safe and immunogenic in adult humans and rhesus monkeys (*Macaca mulatta*). Here, RTS,S+TRAP/AS02A was administered on a 0-, 1-, and 3-month schedule to three cohorts of infant monkeys, along with adult comparators. Cohort 1 evaluated 1/5, 1/2, and full adult doses, with the first dose administration at one month of age; cohort 2 monkeys received full adult doses, with the first dose administration at one versus three months of age; and, cohort 3 compared infants gestated in mothers with or without previous RTS,S/AS02A immunization. Immunization site reactogenicity was mild. Some infants, including the phosphate-buffered saline only recipient, developed transient iron-deficiency anemia, which is considered a result of repeated phlebotomies. All RTS,S+TRAP/AS02A