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Sporozoite-induced Plasmodium cynomolgi ceylonensis malarial infections in toque monkeys; a natural challenge system for evaluation of vaccine efficacy

Asexual blood stage (ABS) vaccine candidates against malaria are generally evaluated by protection against a challenge infection with ABS parasites. We have tested the ABS vaccine candidate based on MSP1p19, in the *Plasmodium cynomolgi*-toque monkey (*Macaca sinica*) host-parasite system, which is highly analogous to *P. vivax* in humans. Protective efficacy was evaluated by challenging immunized animals with ABS parasites of *P.cynomolgi* (trophozoite-induced infections). In the present study, we explored the possibility fo using a natural parasite challenge; sporozoite inoculation through infectious mosquito bites. *Plasmodium cynomolgi ceylonensis* infections were induced in malaria naïve toque monkeys, via infectious *Anopheles tessellates* mosquite bites (sporozoiute-induced infections). Eight and two animals were infected by 3-10 and 66 infectious mosquito bites respectively. They were monitored fo rpatent infections for 19 days, by microscopic examination of giemsa-stained, thick and thin blood films. The animals became patent in 9-12 days, and showed a peak parasitaemia of 0.24*/2.17 (geometric mean*/STD). The number of infectious bites showed no correlation with the pre-patent period, course of parasitaemia, peak parasitaemia or day of peak parasitaemia.

Sporozoite-induced infections in the eight monkeys were compared with trophozoiteinduced infections in another eight animals. In the sporozoite-induced infections, parasitaemias from day eight were considered for comparison , allowing seven days for preerythrocytic development. The peak parasitaemia in trophozoite-induced infections was significantly higher (1.63*/1.84) than that of sporozoite-induced

infections (p=0.0050, as was the course of parasitaemia (=0.002). No significant difference was observed in the day of peak parasitaemia. This indicates that the ABS challenge system may have represented an unnatural, highly stringent mode of evaluation in previous immunization trials, and suggests the protective efficacy would have been different if tested against a natural challenge system.