WP23

PLASMID DNA ENCODING A PLASMODIUM FALCIPARUM SERA5 POLYPEPTIDE, MICROBIAL EPITOPES AND CHEMOKINE GENES INDUCES CROSS-SPECIES PROTECTION IN MICE AND OLIVE BABOONS

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Plasmodium falciparum malaria vaccines that could cross-protect against other human *plasmodium* species including *P. knowlesi* would have enormous safety, economic and manufacturing advantages. In this study, we investigated the safety, immunogenicity and cross-protective efficacy of plasmid DNA encoding a polypeptide of 38 amino acid residues of *P. falciparum* serine repeat antigen 5 (*Pf*SERA5), two microbial epitopes (BCG and TT) and a chemokine gene. Olive baboons (*Papio anubis*) and BALB/c mice were vaccinated with pIRES plasmids encoding SERA+BCG+TT with either CCL5 or CCL20 in pIRES vector. Control animals were given pIRES that did not contain any malaria, microbial or chemokine sequences. Mice and baboons were later challenged with *P. berghei* ANKA and *P. knowlesi* H strain parasites respectively. Plasmid DNA vaccine safety, efficacy and immunogenicity was assessed by reactogenicity at injection sites, parasitaemia profiles, T cell immune responses, survivorship, and antibody responses to SE36, a recombinant construct derived from SERA5. The plasmid DNA vaccines were well tolerated in mice and olive baboons. Vaccinated mice had a 31.45-68.69% cumulative parasite load reduction with enhanced survival while vaccinated baboons demonstrated 60% parasitaemia suppression. There was a significant CD4+ and CD8+ cell subset activation (P=0.00238 and P=0.0478 respectively), SE36-specific baboon IgG antibody in vaccinated group comparison with controls which received only pIRES and elevated Th1/Th2 mice cytokines. Plasmid DNA encoding *Pf*SERA5 polypeptide, microbial epitopes and chemokine adjuvants are safe, immunogenic and cross-protective against heterologous *P.berghei* and *P. knowlesi* challenge infections. This suggests that SERA5-based DNA vaccines could be optimized further to become part of a species transcending malaria vaccine.

Keywords: Malaria, Cross-protection, DNA vaccines, *Pf*SERA5, Adjuvants, Chemokines