PLASMID DNA ENCODING A PLASMODIUM FALCIWARM SERA5 POLYPEPTIDE, MICROBIAL EPITOPIES AND CHEMOKINE GENES INDUCES CROSS-SPECIES PROTECTION IN MICE AND OLIVE BAOONS

Nyamongo W. Onkoba 1,2, Ruth M. Mumo 1,2, Charles Omwandho 2, Horace Ochanda 3, Hastings S. Ozwa 1, Thomas G. Egwang 4

1Tropical and Infectious Diseases Department, Institute of Primate Research, P. O. Box 24481-
00502 Nairobi, Kenya.
2Department of Biochemistry, University of Nairobi, P. O. Box 30197-00100 Nairobi, Kenya
3School of Biological Sciences, University of Nairobi, P. O. Box 30197-00100 Nairobi,
Kenya
4Med Biotech Laboratories, P. O. Box 9364 Kampala, Uganda

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 (PfSERAS5), 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 SERAS5. 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 PfSERAS5 polypeptide, microbial epitopes and chemokine adjuvants are safe, immunogenic and cross-protective against heterologous P.berghei and P. knowlesi challenge infections. This suggests that SERAS5-based DNA vaccines could be optimized further to become part of a species transcending malaria vaccine.

Keywords: Malaria, Cross-protection, DNA vaccines, PfSERAS5, Adjuvants, Chemokines