7. SUMMARY

Title: Candidate peptide and DNA vaccines for falciparum malaria - synthesis and immunogenicity in laboratory animals. RG/95/BT/06

Institute: Institute of Fundamental Studies.

Chief Scientific Investigator: Dr. R. Ramasamy.

Period of Contract: September 1995 to September 1998.

Summary of Project: A malaria vaccine will greatly aid eradicate the disease. Merozoite surface proteins [eg. MSA1 & MSA2] and proteins binding erythrocytes [eg. EBP] are candidates for vaccine development. MSA2 and a portion of MSA1 were cloned into eukaryotic expression vectors and their expression studied in cultured cells. Polymers of selected peptides from MSA1, MSA2 & EBP were synthesised. Two epitopes from MSA1 & 2 were also cloned into cowpea mosaic plant virus. A recombinant MSA2 fusion protein was expressed in *Escherichia coli* and purified. MSA2 RNA was also prepared by in vitro translation for studies of RNA vaccination. The immunogenicity of the different vaccine constructs were tested in rabbits and mice. Antibodies were detected by immunofluorescence, ELISA and western blotting. Therefore the research involved the examination of the four major types of possible synthetic vaccines, viz. synthetic peptide, recombinant protein, DNA and RNA vaccines and recombinant viral vectors. The recombinant viral vectors did not yield specific antibodies on immunisation. The peptide polymers yielded high titre antibodies against peptides but these reacted poorly with native proteins, due to conformational differences. The results showed the potential for nucleic acid vaccination and vaccination with recombinant proteins. However, merozoites resist complement mediated lysis caused by antibodies binding to the merozoite surface. The research illustrates the need for developing an in vivo system for testing the efficacy of candidate vaccines against asexual blood stages of *P. falciparum*.

Publications in Journals

i) Molecular basis for evasion of host immunity and pathogenesis in malaria. Ramasamy, R. Biochimica et Biophysica Acta 1406, 10-27 (1997).

ii) Mammalian cell expression of malaria merozoite surface proteins and experimental DNA and RNA immunisation. Ramasamy, R., Yasawardena, S.Y., Kanagaratnam, R., Buratti, E., Baralle, F.E. and Ramasamy, M.S. Biochimica et Biophysica Acta , In press 1998.

iii) Model multiple antigenic and homopolymeric peptides from non-repetitive sequences of malaria merozoite proteins elicit biologically irrelevant antibodies. Ramasamy, R., Kanagaratnam, R., Chandanie, P.D.F., Kulachelvy, K., Ramasamy, M.S. and Dharmasena, P.M. Biochimica et Biophysica Acta, In press 1998.

iv) Antibodies to a merozoite surface protein promote multiple invasion of red blood cells by malaria parasites. Ramasamy, R., Yasawardena, S., Kanagaratnam, R., Buratti, E., Baralle, F.E. and Ramasamy, M.S. Parasite Immunology. Submitted for publication.