

Studies on molecular and cell biological strategies for the control of Malaria

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Abstract

Malaria is a major public health problem in many tropical countries including Sri Lanka. The Jaffna peninsula has experienced a steady increase in the incidence of malaria since 1991. The increasing incidence of chloroquine resistant parasites and the failure of traditional eradication measures have prompted the development of alternative prophylactic and therapeutic tools for the control and management of this disease. The present study investigated two alternative methods for the control of falciparum malaria, that in principle may also be applicable to vivax malaria. Synthetic oligonucleotides administered exogenously have been demonstrated to specifically block expression of eukaryotic genes in nucleated cells. The effects of antisense oligodeoxynucleoside phosphorothioates based on *Plasmodium falciparum* dihydrofolate reductase-thymidylate synthase and a 45 kDa merozoite surface antigen mRNA on malaria parasite growth were examined in vitro. The oligonucleotides produced sequence- independent but dose-dependent inhibition of invasion of merozoites into red blood cells. It is clear in this study that oligonucleotides, because of their polyanionic nature, interfere with the binding of merozoites to receptors of the red blood cells. Hence clinically acceptable polyanions may be used for malaria therapy, particularly useful for drug resistant and complicated malaria. DNA vaccination may provide many advantages over the conventional vaccine methods and this approach was also investigated in this present study. The coding sequences for two N-terminal fragments of a *P. falciparum* 185 kDa merozoite surface protein were cloned into eukaryotic expression plasmid vectors VR1020 and VR1012. Both constructs were able to express MSAI polypeptide when transfected into cultured Cos cell line derived from the monkey kidney. Intramuscular and intradermal inoculations of rabbits with the both plasmids have elicited antibodies to MSAI. These studies on experimental DNA immunisation in rabbits provide important information to further develop DNA vaccines for malaria and other infectious disease.