

Model multiple antigenic and homopolymeric peptides from non-repetitive sequences of malaria merozoite proteins elicit biologically irrelevant antibodies

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Abstract

Three model peptides containing B-epitopes from conserved, non-repetitive regions of the merozoite surface antigens, MSA2 and MSA1, and the erythrocyte binding protein EBP of *Plasmodium falciparum* were synthesised. The peptides incorporated GPG spacers and C residues at the N and C termini, and were polymerised by oxidation to form cystine bridges. Multiple copies of essentially the same peptide sequences were also synthesised on a branching lysyl matrix to form a tetrameric multiple antigen peptide. Rabbits were immunised with the polymerised and multiple antigen peptides, in alum followed by Freund's adjuvant, and the antibody responses examined by IFA and ELISA. Reproducible antibody responses were obtained against the MSA1 and EBP but not MSA2 peptides. IgG antibody levels detected by ELISA after three injections of antigen in alum, increased significantly after further immunisation in Freund's adjuvant. IgG levels were largely maintained for at least 23 weeks after the final immunisation. IgM antibodies, generally detectable only after immunisation in Freund's adjuvant, were absent 23 weeks later. Antibody titres against the native protein on fixed parasites, assayed by IFA, were three to five orders of magnitude lower than the corresponding ELISA titres against the peptides. Antibody-dependent inhibition of *P. falciparum* growth in vitro could not be demonstrated with the immune rabbit sera. The MSA1 and EBP peptides elicited cross-reactive antibodies. The results suggest that the selected non-repetitive sequences are conformationally constrained in the native proteins and only a small proportion of the anti-peptide antibodies bind to the native proteins. The significance of the findings for the development of peptide vaccines and the use of peptides in immunoassays is discussed. © 1999 Elsevier Science B.V. All rights reserved.

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