Human lymphocyte proliferative response to a sporozoite T cell epitope correlates with resistance to falciparum malaria.

Abstract:

To identify vaccine relevant T cell epitopes on the circumsporozoite (CS) protein of Plasmodium falciparum, the lymphocyte proliferative responses to 10 CS protein derived peptides were studied in 28 adult Kenyans, and correlated with resistance to malaria. Eight peptides, six of which were not overlapping, induced proliferation of lymphocytes from one to five volunteers, suggesting either genetic restriction of response to each of the T epitopes, or dominance of some T sites on the immunizing sporozoites. The 28 volunteers were radically cured of malaria and during the next 126 days 25 of the 28 were reinfected. Resistance to malaria was not correlated with antibodies to malaria Ag, but was significantly correlated with lymphocyte responses to CS protein residues 361-380 and 371-390. Among the 25 volunteers who became re-infected with malaria, lymphocytes from only two responded to a peptide including residues 361-380 of the P. falciparum CS protein, and only one to peptide 371-390. In contrast, lymphocytes from all three volunteers who did not become infected responded to peptide 361-380 ($p = 0.003$), and lymphocytes from two of the three responded to peptide 371-390 ($p = 0.023$). The significant correlation between proliferation to peptides 361-380 and 371-390 and resistance to malaria suggests that at least one epitope within these overlapping peptides is involved in a protective cellular immune response. The data support inclusion of these residues in future CS protein vaccines