019 A

GENETIC VARIATION IN THE C-TERMINAL MEROZOITE SURFACE PROTEIN 1 OF PLASMODIUM: A LEADING MALARIA VACCINE CANDIDATE

C-terminal processing fragments of P. falciparum Merozoite Surface Protein 1 (MSP1), p42 and p19, are major targets of vaccine development. Allelic variation in

MSP1 is principally dimorphic and sequences from MAD20 from Papua New Guinea, and K1 from Thailand, strains serve as representative types for the two dimorphs. In order to design optimal MSP1p19 and/or MSP1p42 based vaccine candidates with limited polymorphism, the extent of allelic diversity in different malaria endemic areas needs to be properly evaluated. In the present study, we have investigated the sequence variation in P. falciparum MSP1 C-terminal 42 kDa region (spanning blocks 15-17) in 21 natural isolates from Kataragama in Sri Lanka and in 18 isolates from Ndiop in Senegal. Of the 21 parasite isolates from Kataragama, there were 12 and 18 MAD20 and K1 prototypes respectively, with 9 isolates showing mixed infection with both MAD20 and K1 prototypes. PCR analysis of the 18 parasite isolates from Ndiop, revealed that all 18 isolates were of MAD20 origin and 4 of these isolates were positive for both prototypic alleles. The 30 MAD20 prototype sequences from both Kataragama and Ndiop, consisted of 14 different genotypes showing polymorphism at a total of 18 amino acid residue positions. In contrast, the 22 K1 prototype isolates from both Kataragama and Ndiop, consisted of only 2 different genotypes, showing polymorphism at a total of 2 amino acid residue positions. The 52 nucleotide and deduced amino acid sequences from Kataragama and Ndiop, encoding the MSP1p19 domain were highly conserved, with amino acid variations at only four positions. The most highly represented sequence variant was the prototype Q-KNG-L, found in all 22 K1 types, as well as in 3 of 12, and 17 of 18 MAD20 sequences from Sri Lanka and Senegal respectively. In addition, there were 8 E-TSR-L prototypes, and 1 of the more rare (but found also in isolates of Indian origin) E-TSG-L type in Sri Lanka, and 1 E-KNG-L type in Ndiop. No sequences with the relatively rare F, replacing L, in the fifth position were observed in these samples. Together these data suggest that the PfMSP1p42 protein in particular is under immune pressure, and that the long term effectiveness of a vaccine based on this antigen would be likely to be limited. In contrast the PfMSP1p19 shows considerably greater conservation, probably due to restraints imposed by its structural requirements.