

Fine structure of *Plasmodium falciparum* subtelomeric sequence

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The organization of *Plasmodium falciparum* subtelomeric sequences has received much attention in the last years, in particular for what concerns instability and recombination aspects. Terminal and non-terminal deletions as well as duplications are frequent events in these regions. Length polymorphism also affects the tandemly repetitive rep20 region present at most chromosomal ends.

In contrast with this plasticity, most of *P. falciparum* chromosomal ends were shown to maintain with high fidelity a terminal region of about 40 kb. Comparison of the four extremities of the two completely sequenced *P. falciparum* chromosomes led to suggest that they share a modular organization of the region, proximal to rep20, which harbours members of gene families (var, rif, stevor) involved or presumed to be involved in antigenic variation .

Recently it has been shown that subtelomeric regions belonging to heterologous chromosomes associate to form clusters or bouquet-like structures (in asexuals and gametocytes, respectively). This fact led to assume that telomere alignment brings non-homologous chromosome ends close together, forming a structural framework facilitating ectopic recombination through gene conversion events.

In an attempt to better understand the basis of end-association of heterologous chromosomes, we investigated the extent of similarity between chromosome ends for which annotated sequences are presently available. Pairwise dot-plot comparisons performed at increasing stringencies indicated a high degree of sequence similarity both between the two ends of the same chromosome and between ends of different chromosomes. In order to better define the organization of subtelomeric regions proximal to rep20, we first analyzed by multiple alignment all the members of the rif and stevor families available in databases.

Members of the stevor family cluster together, whereas rif members appear to fall into two separate groups. By combining the data from dot-plot and protein cluster analyses we propose a scheme for the sequenced subtelomeric regions proximal to rep20 region in which we identify portions that are highly conserved at different ends, portions that were duplicated at particular ends, as well as variability hotspots (variable protein domains and rep20 region).

Possible mechanisms and their biological implications are discussed.