

ORAL PRESENTATION

Open Access

Identification and characterization of novel *Plasmodium falciparum* cyclophilins and their roles in the antimalarial actions of cyclosporin A and derivatives

Alejandro Marin-Menendez, Angus Bell*

From Parasite to Prevention: Advances in the understanding of malaria
Edinburgh, UK. 20-22 October 2010

Background

Cyclophilins are distributed widely among different organisms and are proposed drug targets for a number of diseases including HIV and hepatitis C infection and ischemia. Cyclophilins play roles in folding and chaperoning of cellular proteins and are the major receptors for the immunosuppressive drug cyclosporin A (CsA). CsA and certain non-immunosuppressive derivatives (e.g., valsopodar) possess potent antimalarial activity. We are interested in the role (if any) played by cyclophilins in parasite killing by cyclosporins. We, and others, have previously characterized two CsA-binding cyclophilins (PfCYP19A and PfCYP19B) but a family of genes encoding uncharacterized cyclophilins/cyclophilin-like proteins is also seen in the *P. falciparum* genome (Figure 1).

Results and conclusions

All but three of the cyclophilin/cyclophilin-like genes (or in the case of the larger proteins, their CYP domains) were cloned identically into a pET vector encoding a C-terminal His₆-tag and eight of them were successfully expressed in *Escherichia coli* and purified using nickel-chelate affinity chromatography. All of the recombinant proteins showed chaperone activity on model substrates, while only PfCYP19A and PfCYP19B demonstrated peptidyl-prolyl isomerase (foldase) activity and were bound by CsA. Our data suggest the existence of a cyclophilin-type chaperone family whose partner proteins are not yet known but might include proteins exported to the host erythrocyte.

Published: 20 October 2010

doi:10.1186/1475-2875-9-S2-O3

Cite this article as: Marin-Menendez and Bell: Identification and characterization of novel *Plasmodium falciparum* cyclophilins and their roles in the antimalarial actions of cyclosporin A and derivatives. *Malaria Journal* 2010 **9**(Suppl 2):O3.

Department of Microbiology, School of Genetics and Microbiology, Moyné Institute of Preventive Medicine, Trinity College Dublin, Dublin 2, Ireland



Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit



© 2010 Marin-Menendez and Bell; licensee BioMed Central Ltd. This is an open access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

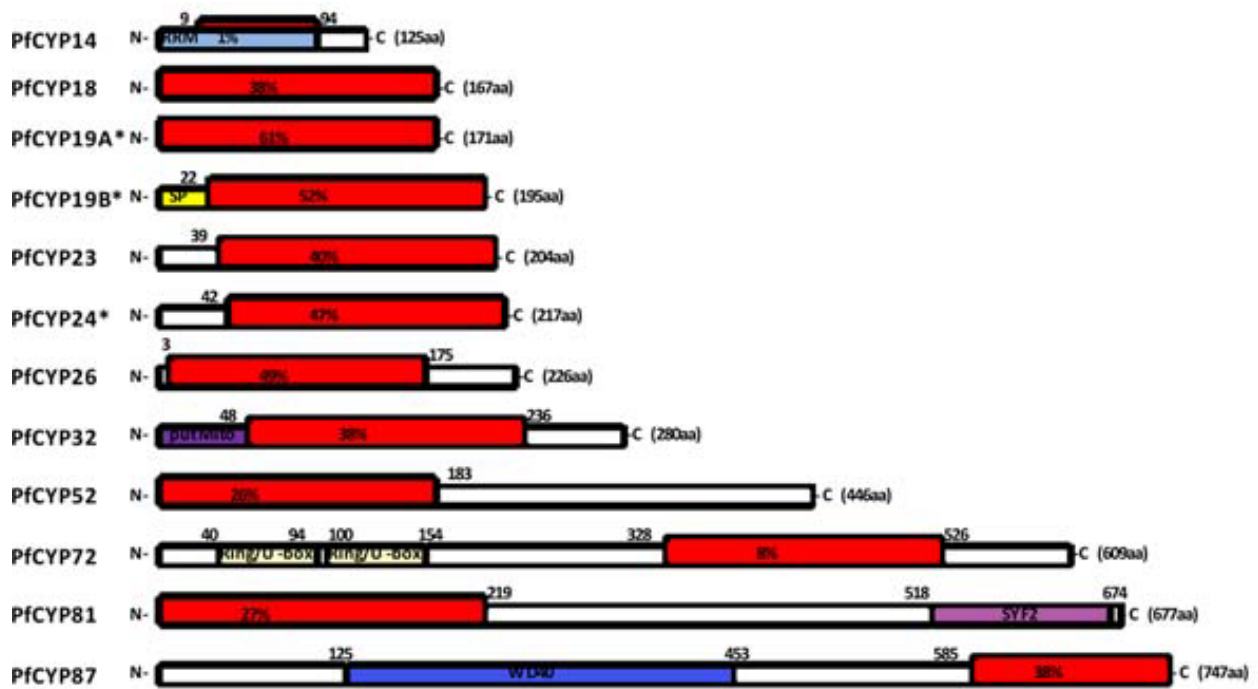


Figure 1 Domain architectures of *P. falciparum* cyclophilin and cyclophilin-like proteins annotated in PlasmoDB. Differently-coloured boxes indicate recognizable domains; red boxes indicate cyclophilin/cyclophilin-like domains with numbers indicating % identities to human cyclophilin A(hCYP18). RRM, RNA recognition motif; SP, signal peptide; putMito, putative mitochondrial signal; SYF2, splicing factor 2; WD40, WD40 domain.