PARASITOLOGY

Conserved invasion

New research shows that the different life cycle stages of the malaria parasite *Plasmodium* spp. use a conserved mechanism to invade host cells.

After ingestion of infected blood, malarial parasites are fertilized in the mosquito midgut, where they develop into ookinetes. Ookinetes invade midgut epithelial cells, move through the cytoplasm, and subsequently develop into oocysts and then sporozoites at the basal lamina. A membrane-attack complex and perforin (MACPF) protein has previously been shown to be necessary for host-cell invasion by *Plasmodium berghei* sporozoites. Now, reporting in *Proceedings of the National Academy of Sciences USA*, Kadota *et al.* have found that another, ookinete-specific, MACPF protein (which they named membrane-attack ookinete protein, MAOP) is necessary for host-cell invasion by *P. berghei* ookinetes.

The authors identified a MACPF-domain-containing protein from analysis of the *P. berghei* ookinete expressed sequence tag (EST) database, and BLAST searches revealed homologues in several *Plasmodium* species. Immunofluorescence microscopy analysis showed the protein to be specifically expressed at the ookinete stage of the *Plasmodium* life cycle.

The authors then examined the effect of a mutation in the *maop* gene on the ability of *P. berghei* to infect the insect host. Although *P. berghei maop* mutants developed into mature ookinetes in the *Anopheles stephensi* midgut, they were unable to infect the insect vector and develop into oocysts. Electron microscopy analysis revealed that the *maop*-disrupted parasites were unable to penetrate the midgut epithelial cells and analysis of infected epithelial cells showed that only the membranes of those infected with wild-type parasites were degraded.

This study shows that the molecular basis of host-cell invasion is conserved between the ookinete and sporozoite stages, and the use of a conserved MACPF domain provides a potential new target for antimalarial compounds.

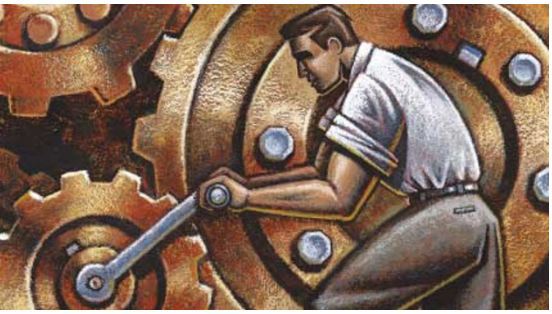
Jane Saunders

References and links

ORIGINAL RESEARCH PAPER Kadota, K. *et al*. Essential role of membrane-attack protein in malarial transmission to mosquito host. *Proc. Natl Acad. Sci. USA* **101**, 16310–16315 (2004).

BACTERIAL PHYSIOLOGY

The dynamic ParM engine



ParM is a bacterial structural homologue of actin that segregates plasmids prior to cell division. Reporting in *Science*, Garner *et al.* show that ParM assembles into a dynamic polymerization engine.

ParM is encoded in the *par* operon, a partitioning locus harboured on the R1 drug-resistance plasmid. Together with ParC (centromere) and ParR (DNA-binding protein), ParM (ATPase) functions to position plasmid pairs at opposite ends of rod-shaped bacteria, ensuring plasmid distribution to both daughter cells following division.

ParM was known to polymerize to form filaments that extended along the length of the cell, with plasmids located at the ends of the filaments. But until now, how the ParM machine functions has not been clear. ParM was labelled and filament assembly monitored by dual-colour fluorescence microscopy. Unlike actin filaments, which assemble unidirectionally, ParM filaments assembled bidirectionally with monomers added to both ends of the filaments.

Assembly kinetics were analysed using fluorescence resonance energy transfer (FRET), revealing that ParM assembles into filaments 300 times faster than actin. A filament long enough to touch both ends of a rod-shaped bacterium was assembled in 10 μs. After growing the length of a rod-shaped bacterium, ParM filaments abruptly began to disassemble. A *parM* mutant unable to hydrolyse ATP formed a stable filament, indicating that switching between elongation and disassembly is a nucleotide-dependent dynamic instability, which has previously only been observed for eukaryotic microtubules.

Furthermore, Garner *et al.* confirmed that ParM polymerization stimulates ParM ATPase activity, and that ParM–ADP rapidly dissociates from the polymer. Assembly and disassembly of ParM filaments does not require any accessory factors, probably because it serves only to segregate plasmids.

Replicated plasmids are joined at their centromeres and bound up with ParR. The authors propose that ParM assembles into filaments that scout around the bacterial cell for these plasmid complexes and that bound plasmid complexes stabilize the filaments, preventing disassembly and maintaining plasmid segregation.

Whether disassembly begins at a specific filament terminus and whether MreB, another structural actin homologue, functions to segregate chromosomes using a similar mechanism are questions that should now be addressed. Finding a polymer with dynamic instability in bacteria that has no similarity to tubulin indicates convergent evolution in these lineages and reveals that bacteria are far more sophisticated than was once appreciated.

Susan Jones

References and links

ORIGINAL RESEARCH PAPER Garner, E. C. *et al*. Dynamic instability in a DNA-segregating prokaryotic actin homolog. *Science* **306**, 1021–1025 (2004)