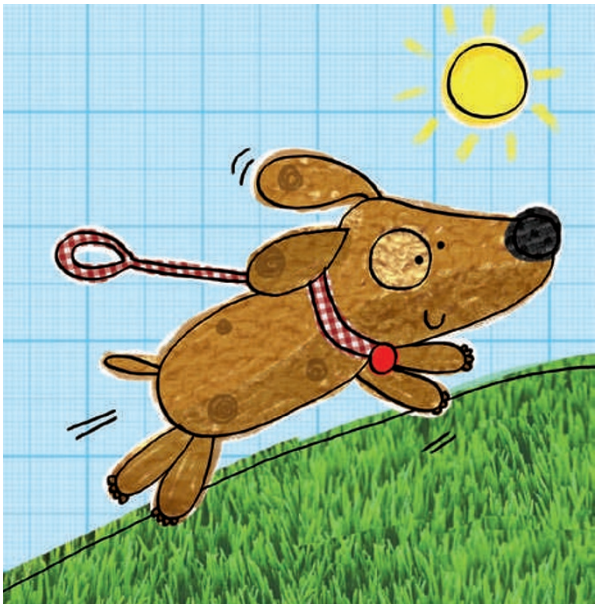
PARASITOLOGY

Signalling the great escape

The blood-stage asexual cycle of the malarial parasite *Plasmodium falciparum* involves invasion of and egress from a host erythrocyte, a process thought to be regulated by a calcium-dependent signalling cascade. Dvorin *et al*. now describe an essential role for the calcium-dependent protein kinase CDPK5 in this process.



CDPK5 is expressed in mature blood-stage schizonts and invasive merozoites, so it is well placed to act as a signal transducer for egress. To investigate its role in the *P. falciparum* life cycle the authors generated parasites in which CDPK5 was joined to a destabilizing domain (DD), forming a fusion protein that was stable only in the presence of the DD stabilizing ligand, Shield 1. In the absence of Shield 1, CDPK5–DD was rapidly degraded and the parasites could not proliferate, indicating that the kinase is required for asexual reproduction. However, development was disrupted in only the final stages of the cycle: ring-stage parasites, trophozoites and schizonts were formed in the presence and absence of Shield 1, but in the absence of Shield 1 most of the parasites stalled as late schizonts and did not exit the infected erythrocytes as merozoites to invade new cells. The arrested schizonts were morphologically normal, but the parasitophorous vacuole membrane and erythrocyte plasma membrane enclosing them were intact, indicating that the developmental block occurs prior to membrane rupture. This suggests that CDPK5 is important for egress from the erythrocyte.

Recently, a *P. falciparum* protease cascade was discovered that is necessary for egress and for maturation of merozoite surface proteins. Interestingly, processing of these proteins was normal in the arrested CDPK5-deficient parasites. On the basis of these results, the authors propose a model in which an egress signal, in parallel with the protease cascade, triggers an increase in calcium that, in turn, activates CDPK5. This kinase then triggers membrane rupture through a series of downstream events, leading to merozoite egress.

CDPK5 is a plant-like kinase with no human homologue and, as such, might be an exciting potential drug target that may enable the arrest of parasite development without affecting the host.

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ORIGINAL RESEARCH PAPER Dvorin, J. D. *et al.* A plant-like kinase in *Plasmodium falciparum* regulates parasite egress from erythrocyes. *Science* **328**, 910–912 (2010)
FURTHER READING Maier, A. G. *et al.* Malaria parasite proteins that remodel the host erythrocyte. *Nature Rev. Microbiol.* **7**, 341–354 (2009)