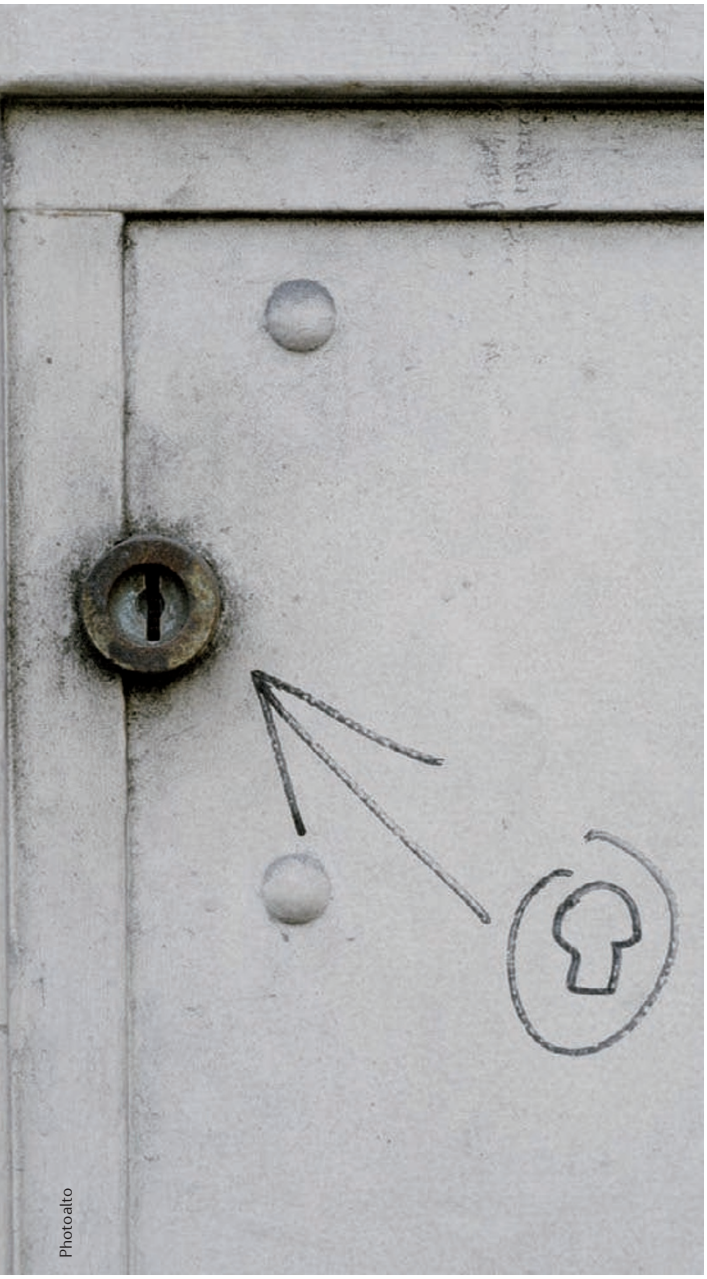

PARASITOLOGY

Plasmodium protein portal

Plasmodium parasites modify the host erythrocyte in which they replicate by exporting proteins that influence cellular properties such as rigidity, adherence and permeability. Although this is a crucial process, the mechanism of export is not understood. de Koning-Ward and colleagues, writing in a recent issue of *Nature*, have now identified a protein complex that may be responsible for *Plasmodium* protein export.

After they enter the erythrocyte, *Plasmodium* parasites are encased in a membrane-bound compartment, the parasitophorous vacuole (PV). Exported proteins are secreted from the parasite into the PV by the secretory machinery, and their subsequent transport across the PV membrane is mediated by an amino-terminal signal sequence that is known as the *Plasmodium* export element (PEXEL) or host targeting (HT) sequence.

de Koning-Ward and colleagues were interested in identifying the elusive transporter involved in the export of these *Plasmodium* proteins. They searched among the proteins that could be detected in detergent-insoluble membranes for those that adhered to the criteria that they had set for a transporter: it must be made at the correct time, be unique to *Plasmodium* and contain a power source. Using these criteria they identified a heat shock protein (HSP) family member, HSP101.

The authors also identified another protein, which they called PTEX150, with a similar expression pattern to HSP101. Biochemical experiments showed that these proteins interact with each other and are localized at the PV membrane. Three additional proteins that interact with HSP101 and PTEX150 were identified: an uncharacterized protein, a thioredoxin-like protein and the previously identified exported protein 2 (EXP2). Immunoprecipitations showed that known exported proteins interact, either directly or indirectly, with HSP101, PTEX150 and EXP2.

Of the three translocon proteins tested, EXP2 was most tightly associated with the membranes. This, combined with the structural similarity of EXP2 to bacterial porins, raises the possibility that EXP2 may form the membrane-spanning pore through which the exported proteins are extruded. Attempted deletions of the gene encoding PTEX150 were unsuccessful, emphasizing the importance of the exported proteins for the growth of the parasite and the possibility of targeting this transporter system for therapeutic intervention.

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ORIGINAL RESEARCH PAPER de Koning-Ward, T. F. *et al.* A newly discovered protein export machine in malaria parasites. *Nature* **459**, 945–949 (2009)