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PARASITOLOGY

Basigin opens the door to malaria

> Two genetic approaches confirmed that basigin is the receptor for *P. falciparum*.

Plasmodium falciparum is one of the *Plasmodium* species that cause malaria, a disease that is initiated by parasitic infection of erythrocytes. Several host receptors and *P. falciparum* ligands that mediate invasion have been described, but different parasite strains have differential dependencies on known receptors. Crosnier *et al.* now reveal that basigin (also known as CD147, EMMPRIN and leukocyte activation antigen M6) is a receptor for the parasite invasin reticulocyte-binding protein 5 (Rh5) and appears to be required for invasion by all *P. falciparum* strains.

Rh5 is a member of a multi-protein family of *P. falciparum* erythrocyte invasion ligands but, unlike for all other members of the family, attempts to delete the gene that encodes Rh5 did not recover viable parasites in any *P. falciparum* strain, suggesting that it may be essential for invasion. To find the Rh5 receptor, the authors screened recombinant ectodomain fragments of 40 erythrocyte receptors using AVEXIS (avidity-based extracellular interaction screen), leading to the identification of basigin as the Rh5 receptor. The authors then tested the invasion capabilities of nine standard laboratory strains in the presence of a soluble version of the basigin extracellular domain or a basigin-specific monoclonal antibody and found that invasion was potently inhibited in a dose-dependent manner in all cases. Similarly, invasion of six Senegalese field isolates was inhibited by the addition of the basigin-specific monoclonal antibody.

Two genetic approaches confirmed that basigin is an important erythrocyte invasion receptor for *P. falciparum*. First, RNA interference was used to decrease the cell surface levels of basigin on erythrocytes that were differentiated from haematopoietic stem cells, and this reduced parasite entry. Second, invasion of erythrocytes of the Ok^{a-} blood group, which carry a mutation in the putative Rh5-binding loop of basigin, was also reduced.

The finding that a single receptor–ligand pair may mediate the entry of all *P. falciparum* strains into erythrocytes is an important step forward in understanding the invasion process and provides a focus for new therapeutics. However, as deletion of other putative invasion proteins also decreases invasion, albeit in a strain-specific manner, parasite invasion is clearly a complex process that requires multiple interactions.

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ORIGINAL RESEARCH PAPER Crosnier, C. *et al.* Basigin is a receptor essential for erythrocyte invasion by *Plasmodium falciparum*. *Nature* 9 Nov 2011 (doi:10.1038/nature10606)