

Erythrocyte membrane remodelling and destruction by malaria parasites

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In the clinical phase of malaria infection, the parasite cells (merozoites) invade their host erythrocytes and create an intracellular vacuole, inside which they replicate. In addition, they modify the erythrocyte membrane to create sites of adhesion to endothelia, the cause of severe clinical disease in *P. falciparum* cases. When the daughter parasites are mature, after about 48 h, they need to break through both vacuole and erythrocyte membranes in order to invade new erythrocytes. The process by which they escape ("egress") is a highly ordered sequence of secretion, activation and proteolytic events, culminating in explosive release of the new parasites for the next round of infection.

We have used video microscopy, electron and X-ray tomography along with mutants and pharmacological blockers of different steps in egress, to study membrane disruption and breakage during the process of egress. This work has revealed new steps in egress and an unexpected role for the major merozoite surface complex MSP1.

Hale, VL, Watermeyer, JM, Hackett, F, Vizcay-Barrena, G, van Ooij, C, Thomas, JA, Spink, MC, Harkiolaki, M, Duke, E, Fleck, RA, Blackman, MJ & Saibil, HR (2017) Parasitophorous vacuole poration precedes its rupture and rapid host erythrocyte cytoskeleton collapse in *Plasmodium falciparum* egress. PNAS 114, 3439-3444.

Watermeyer, JM, Hale, VL, Hackett, F, Clare, DK, Cutts, EE, Vakonakis, I, Fleck, RA, Blackman, MJ & Saibil, HR (2016) A spiral scaffold underlies cytoadherent knobs in *Plasmodium falciparum*-infected erythrocytes. Blood 127, 343-351.

Das S, Hertrich N, Perrin AJ, Withers-Martinez C, Collins CR, Jones ML, Watermeyer JM, Fobes ET, Martin SR, Saibil HR, Wright GJ, Treeck M, Epp C, Blackman, MJ (2015) Processing of *Plasmodium falciparum* merozoite surface protein msp1 activates a spectrin-binding function enabling parasite egress from RBCs. Cell Host Microbe 18, 433-444.