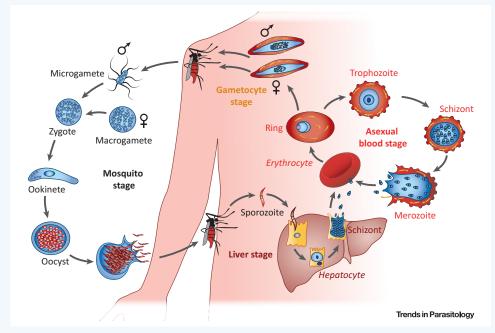
Trends in Parasitology | **Parasite of the Month** *Plasmodium falciparum*

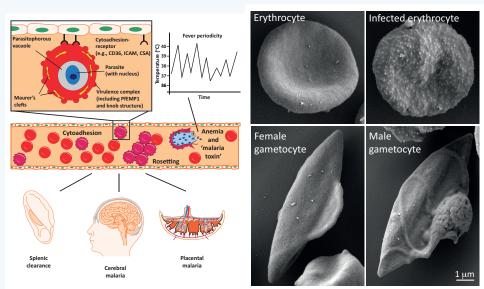
Alexander G. Maier,^{1,*} Kai Matuschewski,² Meng Zhang,¹ and Melanie Rug³

¹Research School of Biology, The Australian National University, Canberra ACT, Australia ²Molecular Parasitology, Humboldt-University, Berlin, Germany

³Center for Advanced Microscopy, The Australian National University, Canberra ACT, Australia



Plasmodium falciparum is the etiological agent of malaria *tropica*, the leading cause of death due to a vector-borne infectious disease, claiming 0.5 million lives every year. The single-cell eukaryote undergoes a complex life cycle and is an obligate intracellular parasite of hepatocytes (clinically silent) and erythrocytes (disease causing). An infection can progress to a wide range of pathologies, including severe anemia and cerebral malaria, which can lead to death. *P. falciparum* repeatedly replicates over the course of 48 h inside erythrocytes, resulting in exponential growth and rapid disease progression. As the single most important infectious disease afflicting children, no other pathogen has exerted a higher selection pressure on the human genome. Over 20 polymorphisms, including the sickle-cell trait, have been selected in human populations, despite severe fitness costs, since they offer protection against fatal *P. falciparum* infections. No effective vaccine exists, but several curative treatments are available.



Trends in Parasitology





Trends in Parasitology, June 2019, Vol. 35, No. 6 © 2018 Published by Elsevier Ltd. https://doi.org/10.1016/j.pt.2018.11.010 481

Trends in Parasitology

KEY FACTS:

No known reservoir; *P. falciparum* has a tight species barrier.

Sporozoites are injected into the skin by female Anopheles mosquitoes, travel to the liver and initiate silent expansion in hepatocytes.

Tissue sequestration due to the expression of parasite-encoded proteins leads to knob formation on the infected erythrocyte membrane.

Three genomes: a nuclear genome (23.2 Mb encoding 5,370 genes); a mitochondrial genome (6 kb) and an apicoplast genome (35 kb).

Continuous red blood cell infections and complete life cycle can be maintained in lab setting alongside both forward and reverse genetics strategies.

DISEASE FACTS:

Major cause of infant mortality, mostly in sub-Saharan Africa. Major factor for poverty in resource-poor settings.

Disease is caused by the asexual blood stages. Symptoms include signature fever-chill periodicity, fatigue and headache. Morbidity and mortality are due to a broad spectrum of pathologies, including metabolic acidosis, organ failure, anemia and coma.

Slow acquisition of partial, short-lived immunity even after years of continuous re-infections.

Treatment with artemisinin-based combination therapy is lifesaving, but no causal prophylactic drug in use. Resistance in the field has developed to all available antimalarial drugs.

Insecticide-treated bed nets have major impact on reducing transmission.

TAXONOMY AND CLASSIFICATION:

PHYLUM: Apicomplexa CLASS: Aconoidasida ORDER: Haemosporida FAMILY: Plasmodiidae GENUS: Plasmodium SPECIES: P. falciparum

*Correspondence: alex.maier@anu.edu.au (A.G. Maier).

Trends in Parasitology | Parasite of the Month

Acknowledgments

This work was supported by the Alliance Berlin Canberra 'Crossing Boundaries: Molecular Interactions in Malaria', which is cofunded by a grant from the Deutsche Forschungsgemeinschaft (DFG) for the International Research Training Group (IRTG) 2290 and the Australian National University. The authors acknowledge the assistance of Microscopy Australia at the Centre for Advanced Microscopy, The Australian National University.

Resources

www.who.int/malaria/en/ www.cdc.gov/malaria/ www.plasmodb.org

Literature

- 1. Laveran, A. (1880) A new parasite found in the blood of malarial patients. Parasitic origin of malarial attacks. Bull. Mem. Soc. Med. Hosp. Paris 17, 158–164
- 2. Trager, W. et al. (1976) Human malaria parasites in continuous culture. Science 193, 673-675
- 3. Sachs, J. et al. (2002) The economic and social burden of malaria. Nature 415, 680-685
- 4. Gardner, M.J. et al. (2002) Genome sequence of the human malaria parasite Plasmodium falciparum. Nature 419, 498-511
- 5. Haldar, K. et al. (2007) Malaria: mechanisms of erythrocyte invasion and pathological correlates of severe disease. Annu. Rev. Pathol. 2, 217-249
- 6. Langhorne, J. et al. (2008) Immunity to malaria: more questions than answers. Nat. Immunol. 9, 725-732
- 7. Maier, A.G. et al. (2009) Malaria parasite proteins that remodel the host erythrocyte. Nat. Rev. Microbiol. 7, 341-354
- 8. Miller, L.H. et al. (2013) Malaria biology and disease pathogenesis: insights for new treatments. Nat. Med. 19, 159–167
- 9. de Koning-Ward, T.F. et al. (2015) Advances in molecular genetic systems in malaria. Nat. Rev. Microbiol. 13, 399-312

10. Cowman, A.F. et al. (2016) Malaria: biology and disease. Cell 167, 610-624

