Malaria parasites co-opt human factor H to prevent complement-mediated lysis in the mosquito midgut.


Abstract

Human complement is a first line defense against infection in which circulating proteins initiate an enzyme cascade on the microbial surface that leads to phagocytosis and lysis. Various pathogens evade complement recognition by binding to regulator proteins that protect host cells from complement activation. We show that emerging gametes of the malaria parasite Plasmodium falciparum bind the host complement regulator factor H (FH) following transmission to the mosquito to protect from complement-mediated lysis by the blood meal. Human complement is active in the mosquito midgut for approximately 1 hr postfeeding. During this period, the gamete surface protein PfGAP50 binds to FH and uses surface-bound FH to inactivate the complement protein C3b. Loss of FH-mediated protection, either through neutralization of FH or blockade of PfGAP50, significantly impairs gametogenesis and inhibits parasite transmission to the mosquito. Thus, Plasmodium co-opts the protective host protein FH to evade complement-mediated lysis within the mosquito midgut.

Beteiligte Abteilungen und Gruppen

Infektionsbiologie

HKI-Autoren

Prof. Dr. Peter F. Zipfel   Prof. Dr. Christine Skerka