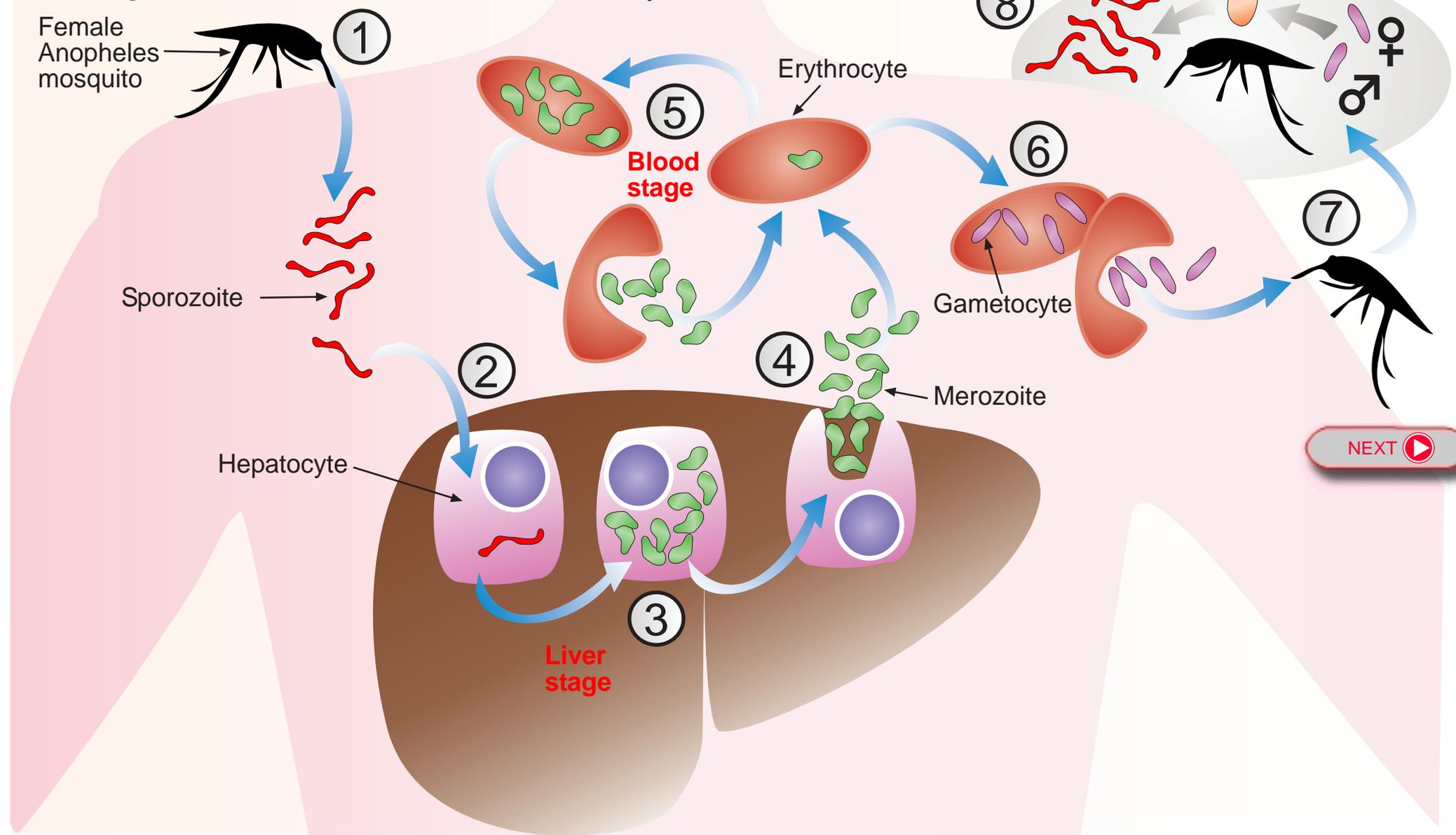


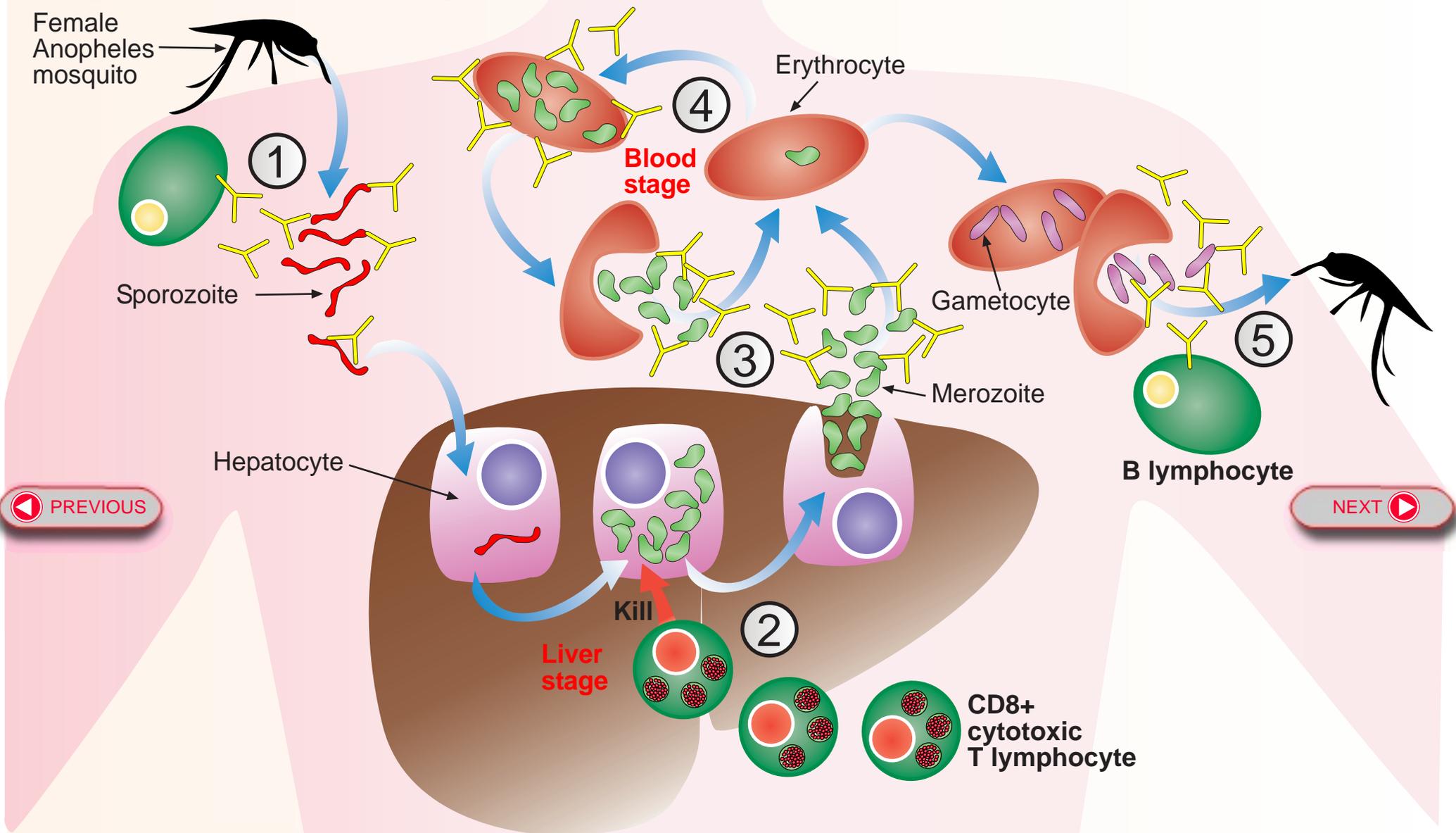
Life-cycle of *Plasmodium falciparum*



NEXT ▶

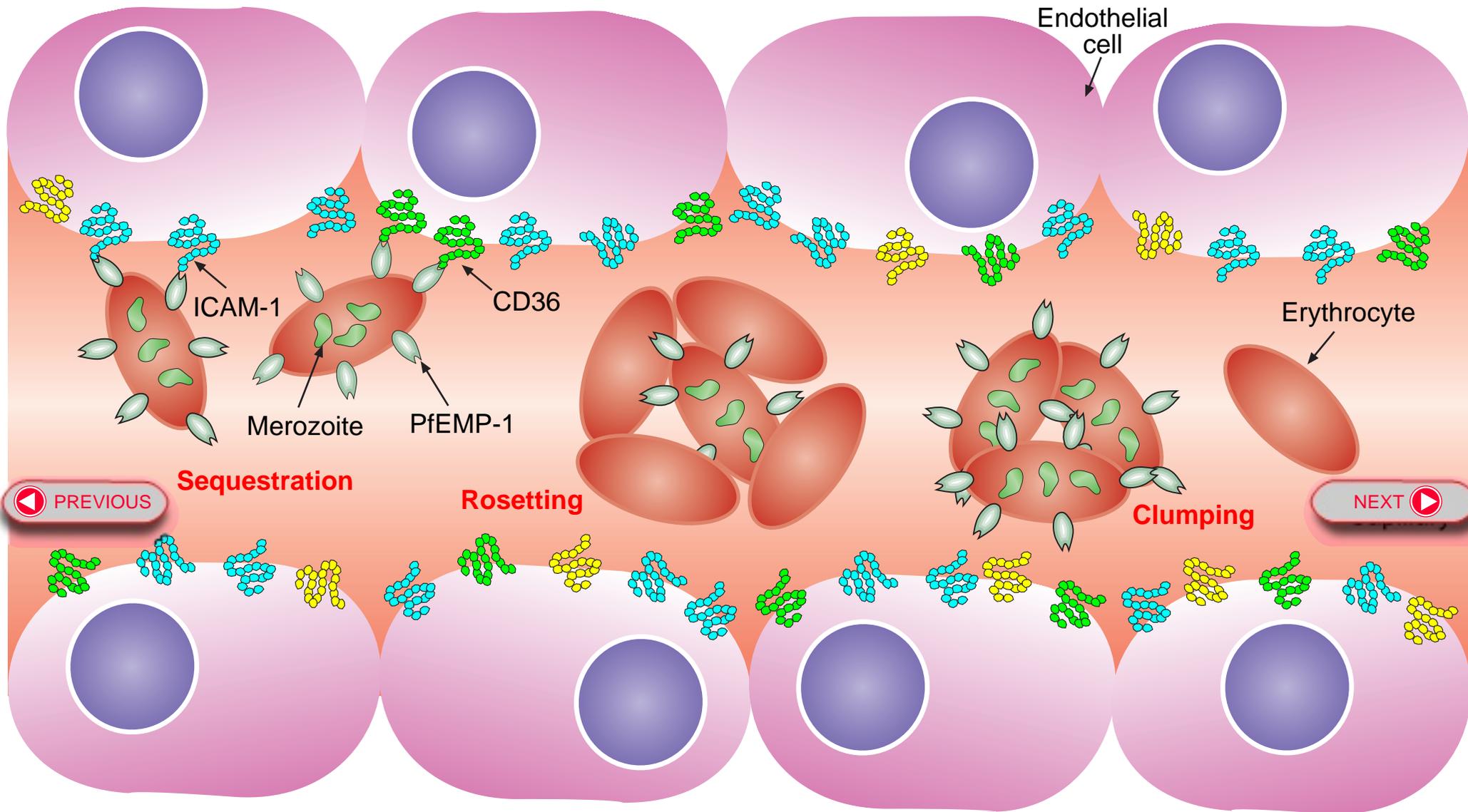
(1) The female Anopheles mosquito is the carrier of sporozoites which are injected along with saliva into the human host during a blood feed. (2) The sporozoites gain access to blood vessels and traffic to the liver where they penetrate hepatocytes. (3) Sporozoites differentiate into merozoites that rapidly divide asexually. (4) Merozoites are released from ruptured hepatocytes and enter erythrocytes. (5) Merozoites reproduce asexually in erythrocytes and re-infect other erythrocytes. (6) Some merozoites differentiate into male and female gametocytes. (7) Gametocytes are taken up by a female Anopheles mosquito during a blood feed. (8) In the mosquito, sexual reproduction produces new sporozoites.

Adaptive immune response to *Plasmodium falciparum*



Humoral and cell-mediated immune responses help to control *Plasmodium falciparum* infection. (1) Antibodies to sporozoites enhance removal by phagocytosis and block penetration of hepatocytes. (2) CD8+ cytotoxic T lymphocyte responses kill infected hepatocytes via HLA class I antigen recognition. (3) Antibodies to free merozoites released from hepatocytes or erythrocytes enhance removal by phagocytosis and block infection of new erythrocytes. (4) Antibodies to parasite proteins on the surface of infected erythrocytes enhance removal by phagocytosis especially in the spleen. (5) Antibodies to gametocytes enhance removal by phagocytosis and may prevent uptake by feeding mosquitoes.

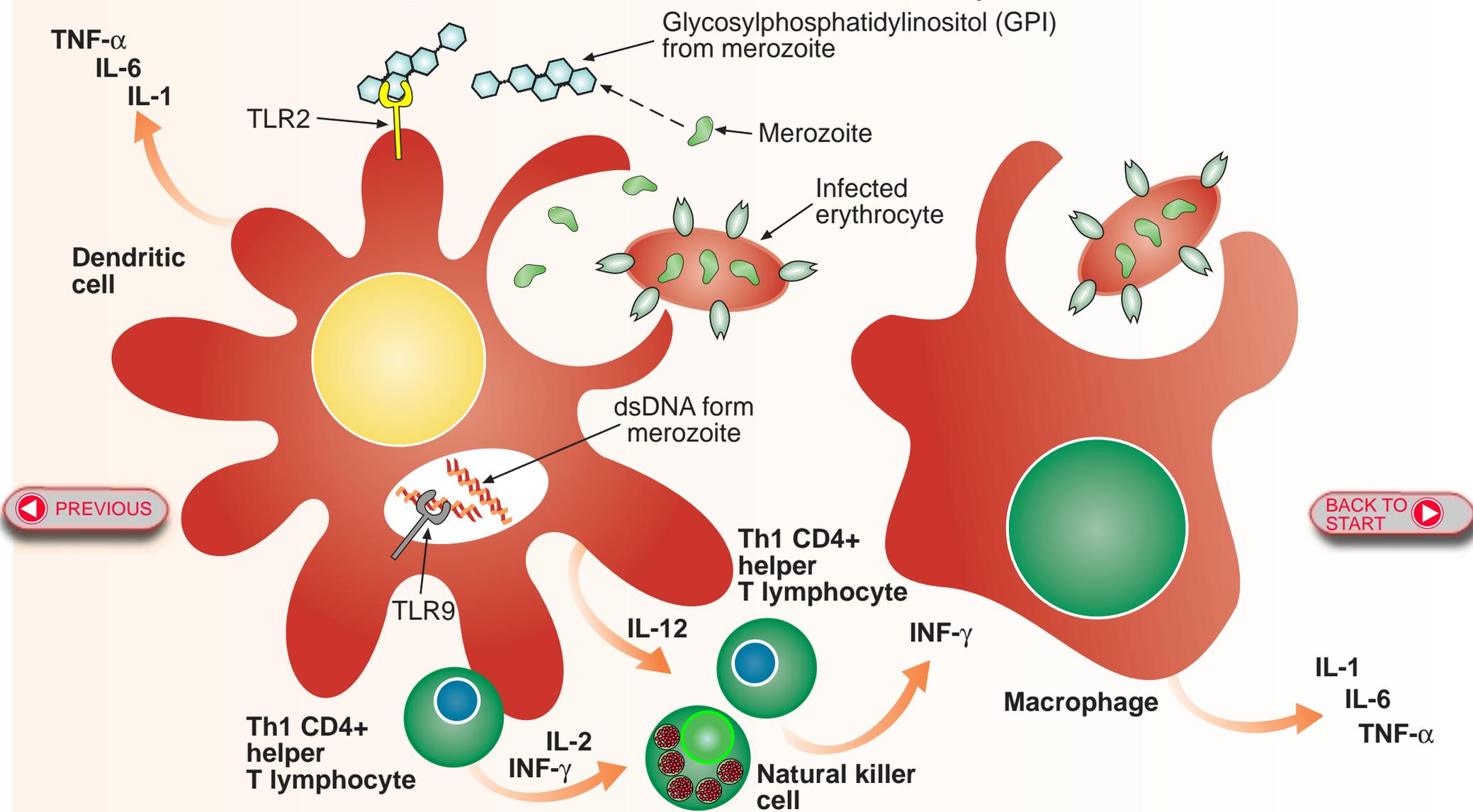
Adhesion of infected erythrocytes to vascular endothelial cells



Infected erythrocytes express parasite derived PfEMP-1 proteins on the cell surface. These proteins have high affinity for membrane receptors such as CD36 and ICAM-1 expressed on vascular endothelial cells. Binding of infected erythrocytes to these receptors (sequestration) allows escape from circulation to the spleen where infected cells are detected and destroyed. In addition, infected erythrocytes can also stick to uninfected erythrocytes (rosetting) or infected erythrocytes can stick together (clumping). Together these cause blockages in blood capillaries that can lead to cerebral malaria, kidney complications (blackwater fever) or respiratory disease.



Innate immune response to *Plasmodium falciparum*



Control of malaria parasite growth is dependent on a strong cell-mediated immune response mainly due to the pro-inflammatory cytokines **IL-12** and **INF-γ**. Innate immune responses to blood stage merozoites occurs by stimulation of pattern recognition receptors such as TLR2 that binds GPI as well as TLR9 that binds parasite dsDNA. Stimulation of these receptors induces secretion of pro-inflammatory cytokines such as **IL-1**, **IL-6**, **TNF-α** that cause fever. **IL-12** activates T cells and NK cells. Recruited CD4+ helper T cells stimulate cell-mediated responses by secretion of **IL-2** and **INF-γ**. This enhances phagocytosis of infected erythrocytes and merozoites and is needed for CD8+ Cytotoxic responses against the infected hepatocytes.

