

Problems for Intracellular Pathogens

- **Entry into Host Cell**
- **Surviving Host Defenses**
- **Metabolism and Proliferation**
- **Preserving Host Cell Function**
- **Cell-to-Cell Transit**

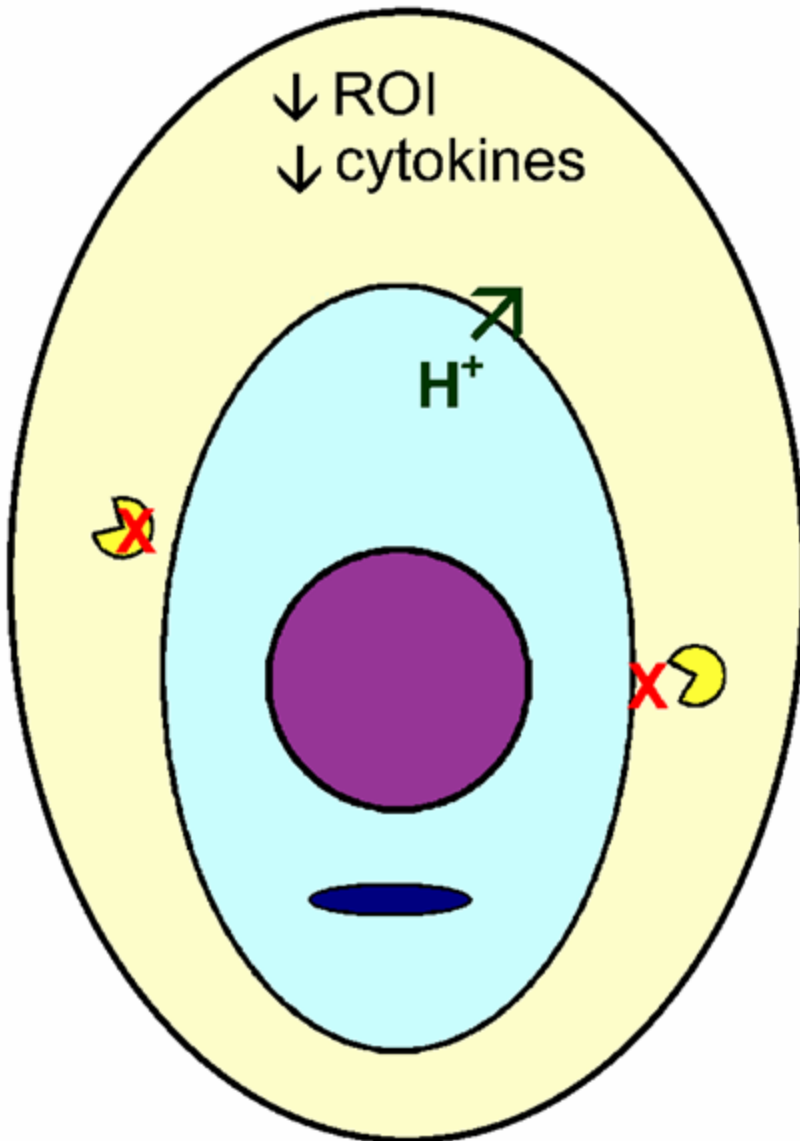
Entry into the Host Cell

- **specialized structures**
 - **apical complex (Apicomplexa)**
 - **polar tube (Microsporidia)**
- **phagocytosis (endocytosis)**
 - **ie, macrophages**

Macrophages as host cells?

- **detect, ingest, and destroy infectious agents**
- **antigen presentation**
- **secrete pro-inflammatory cytokines**

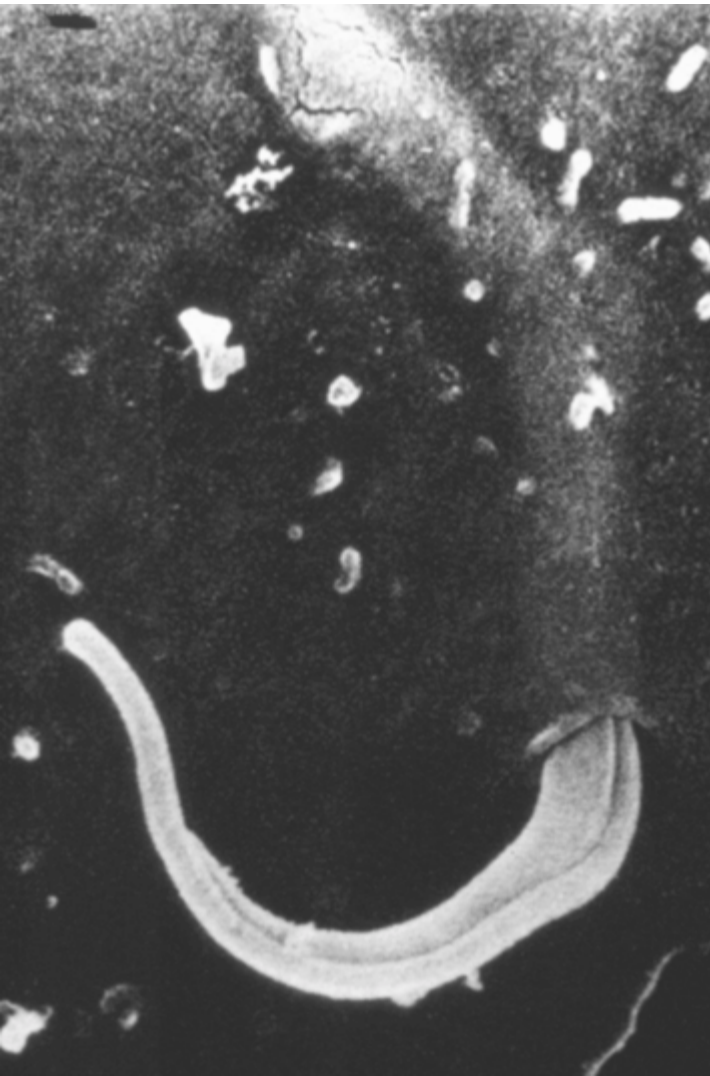
Survival in the Phagolysosome



Leishmania:

- has proton pump to maintain intraparasite pH
- amastigote surface resistant to proteases
- degrades host hydrolases
- down regulates oxidative burst and cytokine response

Invasion by *T. cruzi*



- phagocytosis followed by escape from phagolysosome
- parasite replicates in host cytoplasm

Tc-TOX:

- *T. cruzi* protein with hemolytic activity
- pH 5.5 optimum
- ↑ pH of phagolysosome blocks escape
- C9 antibodies cross-react

Andrews et al (1990) Cell 61:1277

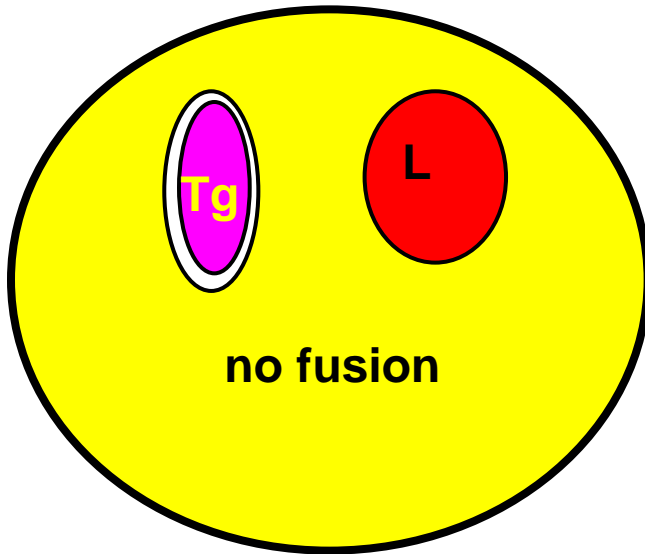
TOXOPLASMA AND MACROPHAGES

tachyzoites

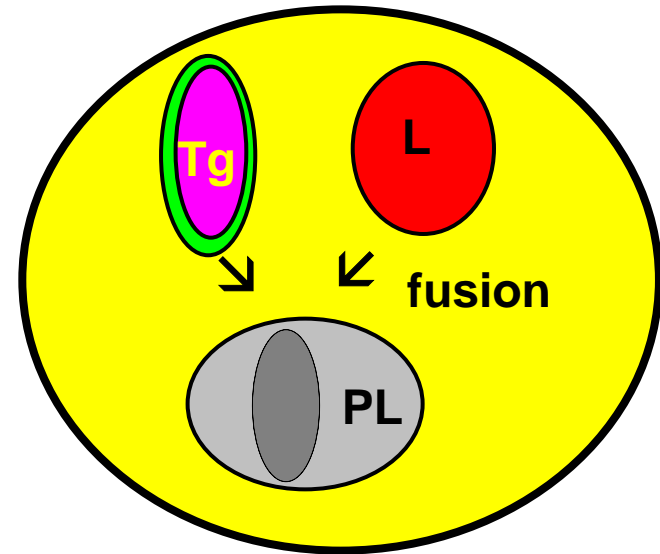
tachyzoites + Ab

↓ invasion

↓ phagocytosis

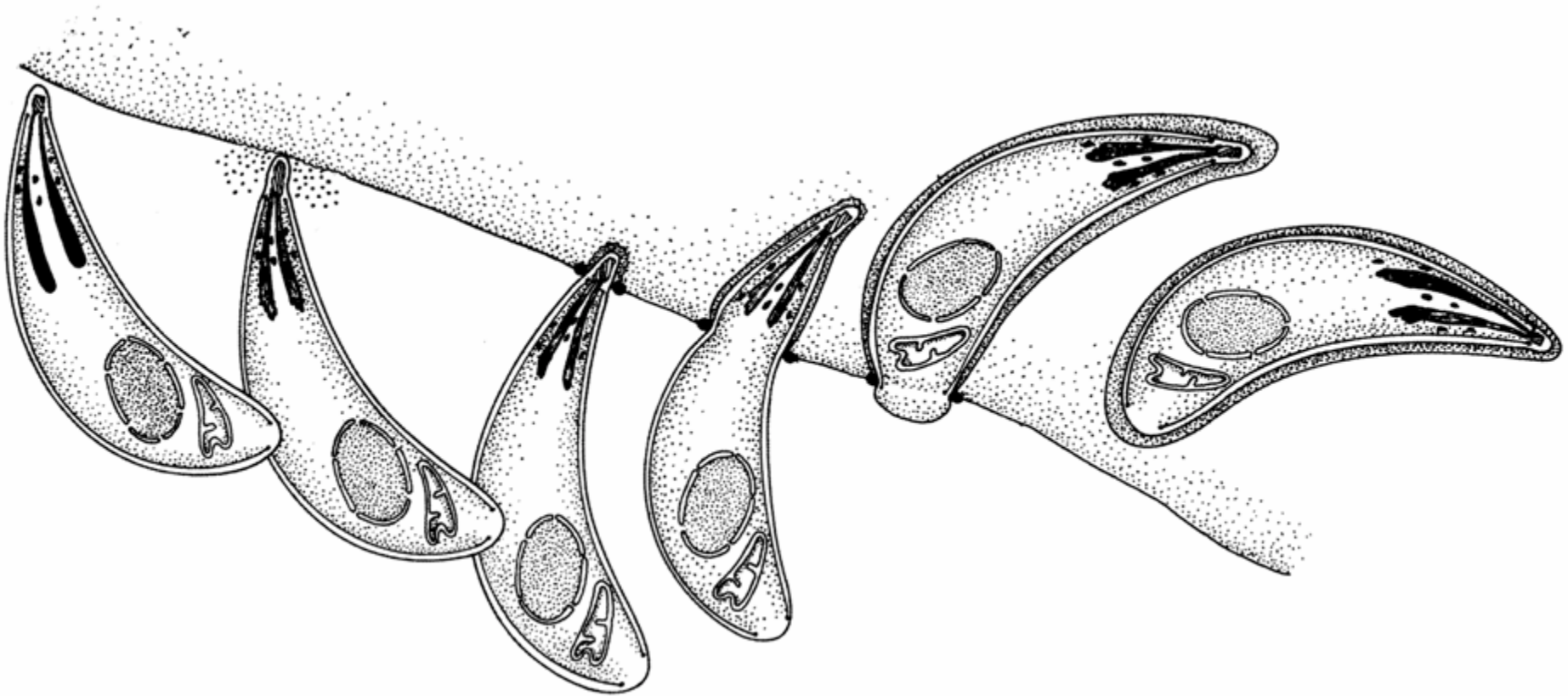


MΦ



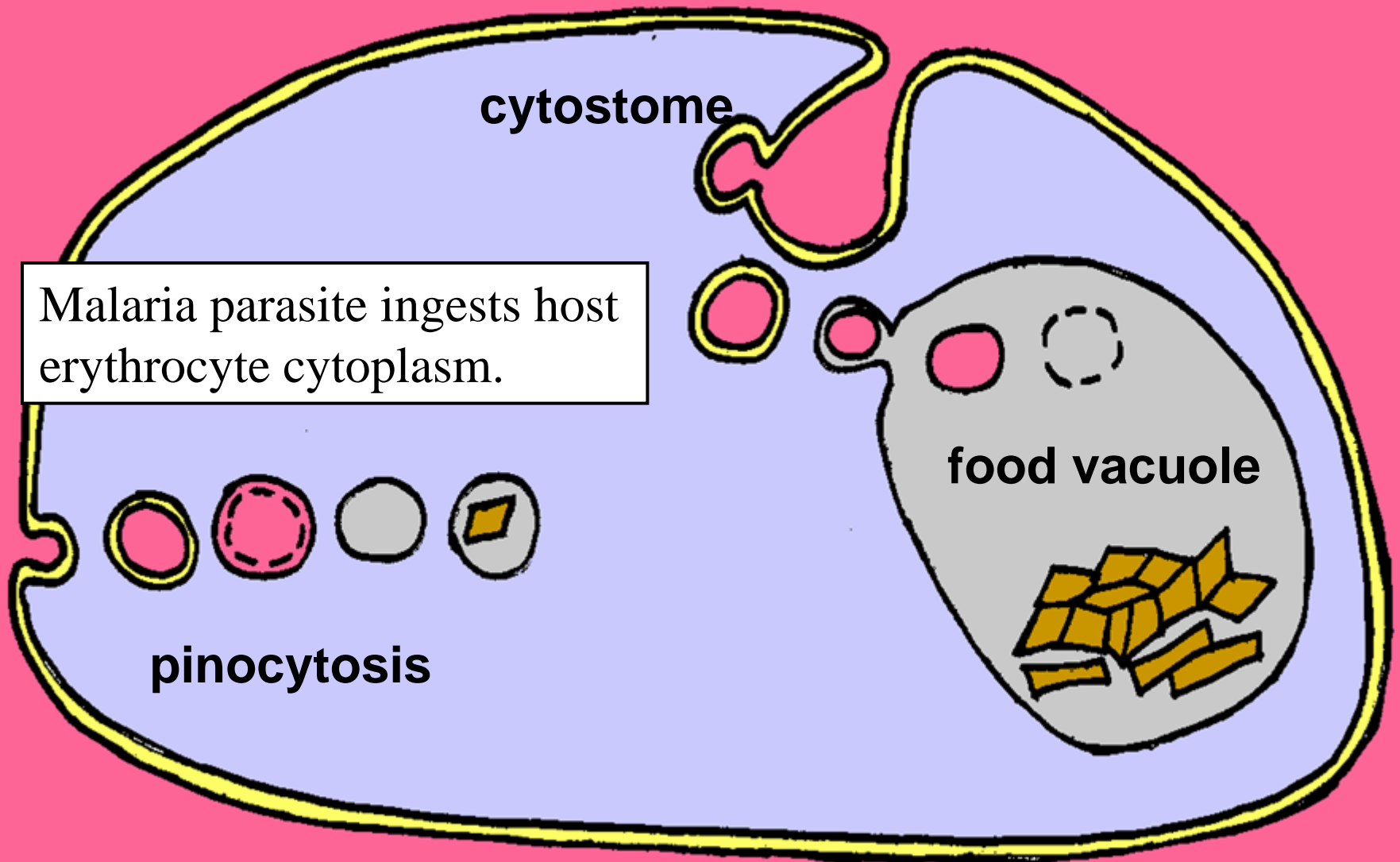
parasite replication

parasite death



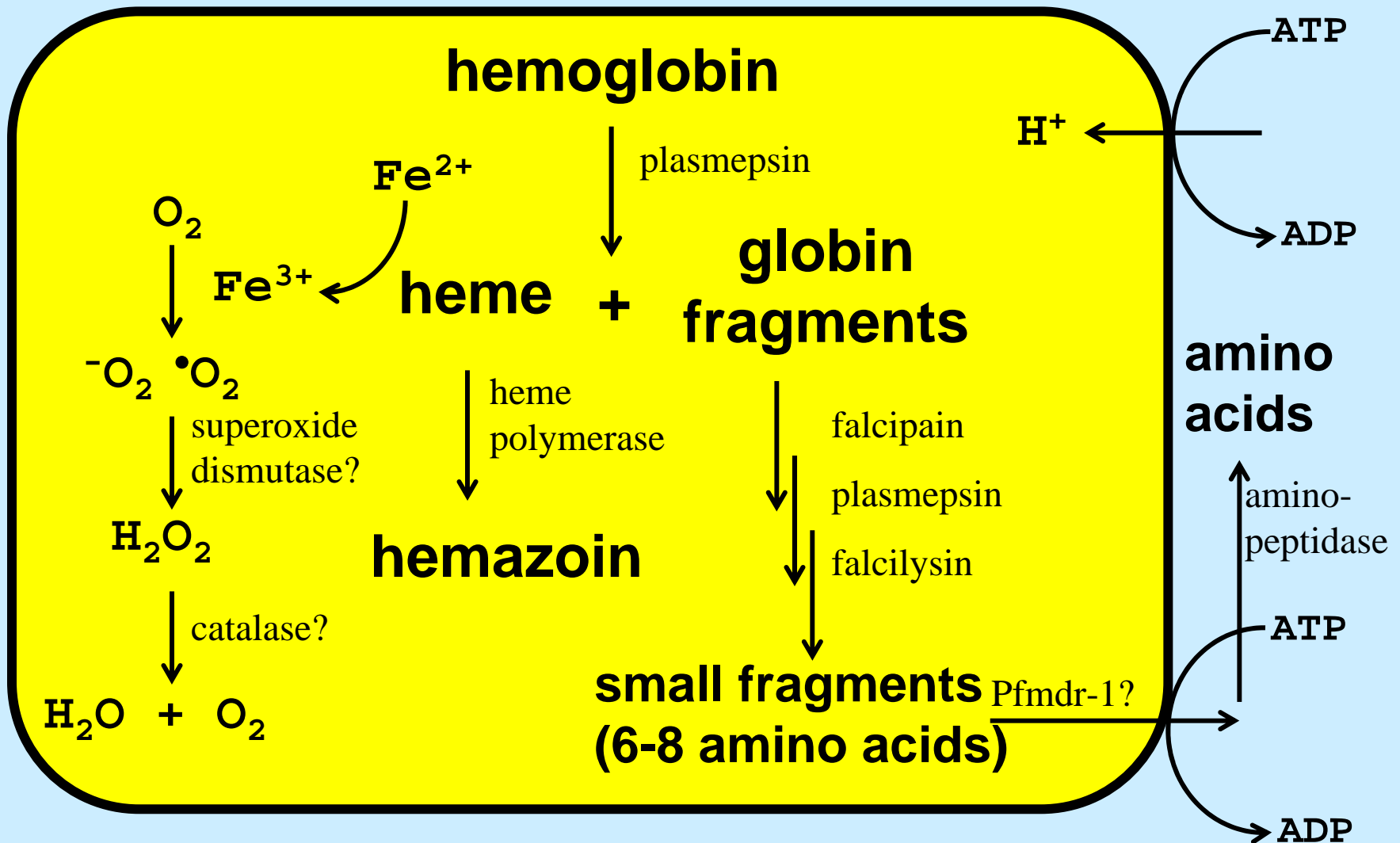
Tachyzoite invasion involves apical organelles and formation of parasitophorous vacuole devoid of host membrane proteins.

Ingestion of Host Cytoplasm



The Food Vacuole

A Specialized Lysosome



Natural Resistance to Malaria

- **inherited erythrocyte disorders associated with protection against malaria:**
 - **sickle-cell anemia**
 - **thalassemia**
 - **G6PD deficiency**
- **all 3 may make the erythrocyte more sensitive to oxidative stress**

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