

Intracellular Protozoa

Problems for Intracellular Pathogens

1. Entry (or how to get inside)
2. Survival (or how to avoid being killed once inside)
3. Metabolism and Proliferation
4. Preservation of Host Functions
5. Transit (cell-to-cell as well as host-to-host)

Entry into Host Cells

- specialized structures
 - apical complex (Apicomplexa)
 - polar tube (Microsporidia)
- phagocytosis (macrophages)

MACROPHAGES

- found in virtually every tissue in body/play many roles
- immune system
 - detect, ingest, and destroy infectious agents
 - antigen presentation/initiate T-cells
 - effector cells (killing activity and cytokine secretion)

Macrophage Defenses

- phagocytosis/fusion with lysosome
 - low pH
 - hydrolytic enzymes
 - defensins
- generation of ROI
- secretion of lysosomal enzymes
- antigen processing/presentation
- secretion of pro-inflammatory cytokines

Entry and Survival in Macrophages

Leishmania

- enters by phagocytosis
- fusion with lysosome
- resistant to low pH and hydrolases
- down regulation of host defenses

Trypanosoma cruzi

- direct entry or phagocytosis
- escapes from phagosome
- replicates in host cytoplasm

Toxoplasma gondii

- entry involves apical organelles
- parasitophorous vacuolar membrane devoid of host proteins
- does not fuse with lysosome

Intracellular Survival/*Leishmania*

- proton pump to maintain intraparasite pH
- parasite surface resistant to hydrolases
- degradation of host hydrolases
- down regulation of cytokine response and oxidative burst

Andrews et al (1990) Cell 61, 1277

- hemolytic protein isolated from *T. cruzi*
- optimal activity at pH 5.5
- antibodies against C9 (membrane attack complex of complement) cross-reacts with 65-75 kDa *T. cruzi* protein (Tc-TOX)

