Immunopathogenesis of *Entamoeba histolytica*

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*Entamoeba histolytica* is an enteric protozoan parasite that infects up to 10% of the world’s population resulting in 100,000 deaths per year from amebic colitis and liver abscess.\(^{(1)}\) The parasite’s distribution is worldwide. Humans are infected by two morphologically identical species of amoebae: *Entamoeba histolytica* Schaudinn, 1903, which is pathogenic and is capable of causing invasive amebiasis (but remains as a harmless commensal in the majority of infections), and *Entamoeba dispar* Brumpt, 1925, which is not pathogenic. Biochemical, immunological, genetic, and clinical characteristics support the existence of the two different and well-defined species.\(^{(2)}\) This important finding has clarified the long-standing issue of interconverting amoebae and has explained the low percentage of individuals with clinical symptoms.

1. **THE LIFE CYCLE OF *E. HISTOLYTICA***

   During the life cycle of *E. histolytica*, three stages are recognized: the trophozoite or invasive form, the cyst which is the infective and transmission form, and the metacyst. When the cyst reaches the small intestine, it excysts releasing a quadrinucleated amoeba which divides twice and gives rise to eight uninucleated daughter trophozoites. The motile trophozoites (10–40 \(\mu\)m) colonize the large intestine, where they multiply by binary fission and may cause lesions or form typical tetranucleated cysts (8–20 \(\mu\)m diameter) to complete the life cycle.\(^{(3)}\) The trophozoite surface is highly pleomorphic
exhibiting lobopodia, endocytotic stomata, filopodia, and posterior uroid. Trophozoites lack mitochondria, peroxisomes, and a typical Golgi apparatus and endoplasmic reticulum; they also lack a structured cytoskeleton and cytoplasmic microtubules (only observed during nuclear division). The cytoplasm contains numerous digestive vacuoles and a conspicuous nucleus.\textsuperscript{5} \textit{E. histolytica} is considered to be a very primitive eukaryote and its metabolic pathways deviate from those of complex eukaryotes.\textsuperscript{4}

2. PATHOGENESIS OF \textit{E. HISTOLYTICA}

Pathogenesis is defined as the origination and development of a disease. In \textit{E. histolytica} infections, disease causation involves a series of distinct events: (1) colonization of the colon, (2) disruption or dissolution of non-specific host defenses (e.g., mucus glycoproteins) by enzymes or toxins (secretagogues), (3) attachment of amoebae to colonic epithelial cells, and (4) lysis of enterocytes and inflammatory cells leading to amebic invasion resulting in colonic ulceration and/or dissemination of the parasites to soft organs causing amebic abscesses.\textsuperscript{5}

Adherence Mechanisms

\textit{E. histolytica} adherence in the gut is important not only for colonization but also for invasion of the large bowel. Colonic biopsies of patients with intestinal amebiasis have shown amebic trophozoites in the lumen and adherent to the mucus layer in areas devoid of ulceration. Areas of focal ulceration were characterized by amoebae in the lesion and mucus depletion.\textsuperscript{6} Animal models of the disease have confirmed that the sequence of events involves (1) trophozoite colonization of the mucus layer (Fig. 1A), (2) depletion of goblet cell mucin, (3) amebic adherence to enterocytes (Fig. 1B) followed by cytolysis of the cells, and finally (4) trophozoite invasion into the lamina propria and crypts.\textsuperscript{7,8} \textit{In vitro} studies with trophozoites and target cells have elucidated the molecular basis of amebic adherence mechanisms. Even though a variety of surface proteins that mediate adherence to target cells (Table I) have been described in \textit{E. histolytica}, the galactose lectin\textsuperscript{9,10} is the most important and is central in pathogenesis. Evidence for this is suggested by the inhibition of adherence and cytolysis of target cells in the presence of galactose, \textit{N}-acetyl-d-galactosamine (Gal/GalNAc), and purified colonic mucins.\textsuperscript{11,18} Indeed, the Gal/GalNAc lectin is involved in amebic colonization of the colonic mucus blanket\textsuperscript{19} and in adherence and cytolysis of a variety of target cells. The nonreduced lectin (260 kDa) is composed of two subunits of 170 and 35 Kda.\textsuperscript{20} The 170-kDa