Review On The Role Of Host Immune Response In Protection And Immunopathogenesis During *Entamoeba Histolytica*

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ABSTRACT

Background: A protozoan parasite called *Entamoeba histolytica* (Eh) infects *Entamoeba histolytica* (Eh), a protozoan parasite that causes 100,000 deaths per year from amebic dysentery and/or liver abscess, has infected 10% of the entire world's population. Usually, this extracellular parasite colonizes the colon with high affinity binding to MUC2 mucin without causing illness symptoms, but occasionally, Eh invades the colonic mucosae and triggers an aggressive inflammatory response. The particular host-parasite variables required for illness etiology are still mostly unknown. The parasite's cysteine protease cleaved the C-terminus of MUC2, that cause the mucus layer to dissolve, followed by adsorption and cytotoxicity of the mucosal epithelium, are the disease's hallmark events that cause the condition to worsen. Every time a host cell that causes tissue injury comes into contact with the host, the host generates an excessively inefficient pro-inflammatory response. They can cause cell death through phagocytosis, apoptosis, or trogocytosis (the absorption of living cells), which may be crucial for immune evasion, as well as other detrimental effects that are brought on by their attachment to the host cells. Immune evasion techniques are used by Eh to survive and induce disease manifestation in the host; these techniques are the main focus of this review. An estimated 100,000 individual deaths are predicted to die each year from *E. histolytica* infection, which is thought to impact 1% of people. Clinicale manifestations of a mebic infection can range from mild to severe, causing extraintestinal abscesses and diarrhea. Only 20% of those who are affected, like other infectious diseases, reportedly exhibit symptoms. The outcome of an infection is controlled by both the genetic make-up of the parasite and the host as well as environmental factors like the microbiome. Amebic infection goes through a number of critical stages, including the degeneration of the mucosal layer and infiltration into it, adherence to the intestinal epithelium, invasion into the tissues, and diffusion to other organs.

**Keywords:** *Entamoebae Histolyticae*, Immune Evasion, Phagocytosis, Apoptosis, Trogocytosis

INTRODUCTION

*Entamoebae histolyticae*, an intestine protozoan parasite that also affect human, is the cause of amebiasis. Amebiasis is an ongoing global health probleme that cause up to 100,000 fatalities annually (1, 2). Through the intake of contaminated food and water, amebice cysts cane spread (1, 3, 4). In regione where the
disease is common, exposure levels can be quite high. For example, a Bangladeshi urban slum recorded an annual incidence of 40% among adolescents. (5). In some parts of Asia and Australia, a condition known as "men who have sex with men" (MSM) amebiasis is endemic and can be transmissible (6–9). While 20% of E. histolytica infection cause clinical symptoms such as dysentery, which is distinguished by intestinal mucosal invasion and tissue destruction, the majority of infection remain undiagnosed (10). Amebic liver abscesses (ALAs), the most frequent kind and occurring in 17% of symptomatic cases in Japan and 1% of cases in underdeveloped countries, are the most popular type of dysentery and extra-intestinal amebiasis. (11, 12). Amebic trophozoites that invade the intestinal epithelium induce the human host to mount an immune response. Repression of the host immune system and management of the parasitic environment are necessary for parasite persistence in the host. For instance, during extraintestinal dissemination, the amebae must temporarily survive in the blood vessels and the spleen, in which they are exposed to high oxygen concentration and a network of immune cells and humoral factors (E. histolyticae are anaerobic or microaerophilic). Amebae must evade complement and antibody detection, as well as shield themselves from oxidative and nitrosative attack, in order to thrive in such an environment. Here, we provide an overview of what is known today about the immune response to amebic infection (Figure (1)) and the parasites' methods of avoiding detection and the parasite's strategies to evade from host immune system (Figure 2).

**Figure (1)** Immune evasion by host cell lysis via E. histolytica (Eh). Contact between the host cell and Eh is facilitated through the host cell surface GalNAc receptor, in addition to the Galectin (A). Additional amebic protein related to host cell attachment also include trans-membrane serine, threonine, and isoleucine proteins (STIRP) and the transmembrane kinase family member TMKb1-9. Three things could happen after Eh-host communication: Amebic trogocytosis (A) and apoptosis (C) (B) In Phagocytosis (D). More substantial cells
maye undergo amebice trogocytosise in (B). Fore amebice trogocytosise to happene, PI3K and C2PK signale transductione were necessarype. (C) Whenevere host celle that havee been forcede to undergo apoptosis express ephosphotidylserine (PS) and C1q complemente proteine, an ameba usees the amebice calreticuline receptore to opsonizee the cellse. In (D), phagocytosise occurs on bothe the smallere cell and thee cell that is apoptosizinge. Signale transductione for phagocytosise, thate is also mediatede by PI3K and EhC2PKe, influencese actin polymerizatione. Transmembranee Kinasee (TMK), C2 Protein Kinasee (PI3K), and Phosphatidylinositole 3 Kinasee (PI3K) 39 (TMK39).

Mechanisms of E. histolytica trophozoite colonization and invasion and host immunological reactionse to prevente and managee amebic illness.

The IEC layer is coatede in thee lumense of the intestinale tract bye thee mucous membrane (blue), whiche contains mucine and IgA releasede by thee host ande commensale microbose. The amebae's secreted proteasee and glycosidasee are whate enable thee extracellulare matrix and mucin to breake downe. Inflammasomese are producede as a resulte of EhCP-pro-domaine A5's interactione with integrine, activatione of which leadse in pro-inflammatoriy responsese. In the IECs, PGE2, whiche is also generatede by amebaee, promotes mucie depletion and hypersecretestione. Additionally, PGE2 initiateese a chain of signallinge pathways thate activatee NF-B in the IECse and culminatee in the releasee releasee IL-8. As a resulte of the Gale/GalNAc lectine (lectin) and LPPGe on the amebae's surface bindinge to TLR2, IEC experiencese NF-B activacione ande the productione of pro-inflammatoriy cytokine. Furthermore, PGE2e interferes withe the tight junctione function of thee epithelium ande promotes amebice infiltratione. The clearancee of host cellse and invasion intoe the host tissuee are both madee much easiere by phagocytosise and trogocytosise. Invadinge trophozoitee are drivene off by complemente from the bloodstreame, ROS, and NO from neutrophilise ande macrophagese. The activatione of CD4, CD8, and NKT cells, the Gal/GalNAc lectin, and LPPG enhance protective cellular immunity. CD4 T cells producee IFN-, IL-4, IL-5, and IL-13, whilee CD8 T cells producee IL-17. The productione of mucine, bacteriocinse, and IgA intoe the intestinale lumen is enhancede by IL-17, which also promotese neutrophil infiltratione. When disseminatede to the liver by the densee, which is mediatede by IFN-secretede by NKT cellse, the amebaee are adherede to ande eliminated. The hepatic macrophagese' TNF- release induces abscesses to form. Solid arrows indicate thee synthesis of solublee proteine, whereas dottede arrows indicatee contacte or signal transductione. Cytokine implicatede in clinical diseasee are depictede in red, whereas those thate are moste usefule for killinge off amoebaee are depictede in black.
Amebiasis immune evasion techniques that could be employed. IgA is broken in the mucosal layer via protease just one surface or secreted by amebae. By causing the IECs to secrete IL-10 and mucin and IgA, the amebae's PGE2 stimulates the prevention of needleless inflammation. If TLR stimulation is too intense, NF-B activation is downregulated. When infiltrating immune cells are cleared by phagocytosis or trogocytosis, immune responses may be suppressed. Bacteroides fragilis and Clostridium XIV and IV groups are two commensale bacteria that cause Treg cells to inhibit immune responses. Polysaccharide of B. fragilis TLR2 on CD4 T cells is activated by A, and causes the production of IL-10. By capping surface receptors (LPPG, lectin), the amebae in tissues and blood escape complemente, while C3a and C5a are destroyed

Immune Reaction Throughout Amebic Infection

Course of Amebic Infection

Entamoeba histolytica infection is started by the parasite adhesion to the intestinal mucin layer. A lectin (Gal/GalNAc lectin) made by trophozoite binds to colonic epithelial cells and host mucin with a predilection for galactose and N-acetyl-D-galactosamine (13). The parasites that have colonized have the capacity to severely damage tissue. Hydrolytic enzyme, especially cysteine protease (CP), are thought to be the parasite's main tools for penetrating the epithelium and destroying extracellular matrix (ECM) elements of the host, in addition to pore-forming proteins and amoebaporese (14, 15). (16–20). During and after entering the submucosal areae, amebic trophozoite participate in directe and indirect interactione with host immune and non-immunene cells.

Humoral Immunity

Although the mucosal layer in the digestive system frequently serve as a main physical barrier against intestinal pathogene, the intestinal immune response is the secondaer defense against E. histolyticae infection. Mucosal immunoglobulin (Ig) are the moste large element of the humane gut defense systeme (21). One of these, known as secretory IgA, is one of the most frequently produced Ig by plasmae cells. It serves to break the mucosal barrier and prevent pathogene adhesion (21). (5, 22, 23). Patients who had recovered from ALA backed up this view. In post-ALA patiente, increases in anti-Gal/GalNAc lectin IgA antibodies were linked with elimination of subsequent amebic infections., showing that these individuals retained immunological memorye and improved immune responsee (24, 25). IgG levels, on thee other hand, can either protect against or not protect against amebic illnessese depending on the majore IgG subclassese induced by infection (i.e., IgG1 and IgG2 induced by Th2 and Th1, respectively) (26, 27).

Cell-Mediated Immunity

Cell-mediated immune responses are also requirede for host to be safeguardede from E. histolyticae. In the early stagee of infection, intestinale epithelial cellse (IECs) bind to and identify the carbohydratee recognition domaine of the Gal/GalNAc lectin via TLR-2/4, which activates NF-B and causes the production of top player cytokines such IL-1, IL-6, IL-8, IL-12, IFN-, and TNF- (28–30). IECs are the first host cells to come into contact with microbial/parasitee antigene and the seconde of defense against pathogene after the mucosal layer. They express a range of pathogen recognition receptorse (PRRs), including TLRs, that recognize infectione (31). IFN- plays a role in eliminating an infectionalthough IL-4 and TNF are linked to illness (32–35). In fact, it has been shown that invasive amebiasis patiente have increased blood levels of IL-4 and that peripheral mononuclear cell eproduction of IFN- is associatede with protection against subsequent E. histolyticae infection in children (36). (27, 37). Additionally, it has been demonstratede that animals which have receivde vaccinations are protected by CD4+ T cells that produce IFNede and CD8+ T cells that produce IL-17 (38, 39). IL-17 increasese neutrophil infiltratione, mucin and antimicrobiale peptide secretione is induced, and IgA transporte across the intestinale epithelium rises, all of which aid in the body's defense against amebic infectione. (40–43). Amebicidal activitiee of IFN-activated
macrophages and neutrophils in vitro (44, 45). When macrophages were rare in amebic lesion in vivo, neutrophils predominated, suggesting the significance of neutrophils for amebae clearance (46). In order to eradicate trophozoites, the eproduction of reactive oxygen species (ROS) and nitric oxide (NO) even by enzyme NAD(P)H oxidase complex and iNOS, respectively, is required (45, 47). Natural killer T cells (NKTs) from experimental ALA provided protection thru the release of IFN-γ, but macrophages that produce TNF increased tissue damage (32, 33). Together, humoral and cell-mediated immune responses have esignificant effects on the avoidance of amebic infection.

**CONCLUSION**

Our understandinge of the molecular mechanisms underlying the parasite's pathogenicity has significantly advanced recently. These mechanisms involve host cell attachment, induction of apoptosis, degradation of mucin and ECM, penetration of tissue, and phago/endoctyosis of host cells. The same is true of immune evasion strategies include inducing IL-10, blocking IFN, destroying Igs, activating complement, and producing pro-inflammatory cytokines. Defense against ROS and NO, as well as avoiding antibody- and complement-dependent death, are all required for survival in the host. Additionally, The outcome of amebic infection is controlled by mutuale signaling among the three domaines in the vast system of the humane, microbiota, and parasite with polymorphic genetic backgrounds. Further research is required to explaine the molecular basis of the complexe interaction in the intestinale ecosysteme and to comprehend the molecular basis of thee intricate interplaye in the digestivee tract.

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