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

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ABSTRACT

Background: *A protozoane parasite callede Entamoeba histolyticae (Eh) infects Entamoebae histolytica (Eh), a protozoane parasite that causese 100,000 deaths per year frome amebic dysentery and/or livere abscess, has infectede 10% of the entire world'se population. Usuallye, this extracellular parasitee colonizes the colone with high affinity bindinge to MUC2 mucin without causing illness symptoms, but occasionally, Eh invades the colonic mucosae and triggers an agressivee inflammatory responsee. The particulare host-parasite variables requirede for illnesse etiologye are still mostlye unknown. The parasite's cysteine proteasee cleaved thee C-terminus ofe MUC2, that causese the mucus layer to dissolve, followede by adsorption and cytotoxicitye of the mucosal epitheliume, are the disease's hallmark eventse that cause the condition to worsene. Every time a host cell that causes tissue injurye comes into contact with the host, the host generates an excessively inefficient pro-inflammatory responsee. They can cause cell death through phagocytosis, apoptosis, or trogocytosise (the absorption of livinge cells), which may be cruciale for immune evasion, as well as othere detrimental effects that are brought on by their attachment to the host cellse. Immune evasion techniquese are used by Eh to survive and induce diseasee manifestation in the host; these techniquese are the main focuse of this reviewe. eAn estimated 100,000 individualse are predicted to die eache year from E. histolytica infectione, which is thoughte to impact 1% of peoplee. Clinicale manifestations of a mebice infection can range frome mild to severee, causing extraintestinal abscessese and diarrhea. Onlye 20% of those whoe are affectede, like othere infectious diseasese, reportedly exhibite symptoms. The outcomee of an infection is controllede by both the genetic makee-up of the parasitee and the host ase well as environmental factors like the microbiome. Amebic infection goes through a number of critical stages, includinge the degenerationе of the mucosale layer and infiltratione into it, adherencee to the intestinal epitheliume, invasion intoe the tissuese, and diffusione to other organs.*

Keywords: ***Entamoebae Histolyticae, Immunee EEvasion, Phagocytosise, Apoptosise, Trogocytosise***

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INTRODUCTION

Entamoebe histolyticae, an intestinee protozoane parasitee that also affectse humanse, is the causee of amebiasise. Amebiasis is an ongoinge global health probleme that causese up to 100,000 fatalitiese annually (1, 2). Throughe the intake of contaminatede food and water, amebice cysts cane spread (1, 3, 4). In regionse where the

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diseasee is commone, exposuree levels can be quitee highe. For examplee, a Bangladeshie urban slum recordede an annuale incidence of 40% amonge adolescentse. (5). In somee parts of Asiae and Australiae, a conditione known as "mene who have sexe with mene" (MSM) amebiasise is endemice and cane be transmittablee (6–9). Whilee 20% of E. ehistolytica infectionse causee clinical symptomse such dysenterye, which is distinguishede by intestinale mucosal invasione and tissue destructione, the majoritye of infectionse remaine undiagnosed (10). Amebice liver abscessese (ALAs), the moste frequente kinde and occurringe in 17% of symptomatice cases in Japane and 1% of casese in underdevelopede countriese, are the most populare type of dysenterye and extra-intestinale amebiasis. (11, 12). Amebice trophozoitese that invadee the intestinal epitheliume induce the humane host to mounte an immune responsee. Repression of thee host immune system and management of the parasitism environment are necessary for parasitice persistence in thee host. For instancee, during extraintestinale disseminatione, the amebaee must temporarilye survive in thee bloode vesselse and the spleene, in whiche they aree exposede to high oxygene concentrationse ande a networke of immunee cells and humorale factors (E. histolyticae are anaerobice or microaerophilice). Amebaee must evade complemente and antibodye detectione, as well as shielde themselvese frome oxidative and nitrosative attack, in order to thrive in such an environment. Here, we providee an overviewe of whate is knowne today aboute the immunee responsee to amebic infectione (Figure (Figure1) and the parasitese methods of avoidinge detectione.and the parasitee's strategiese to evade frome host immunee system (Figure2).

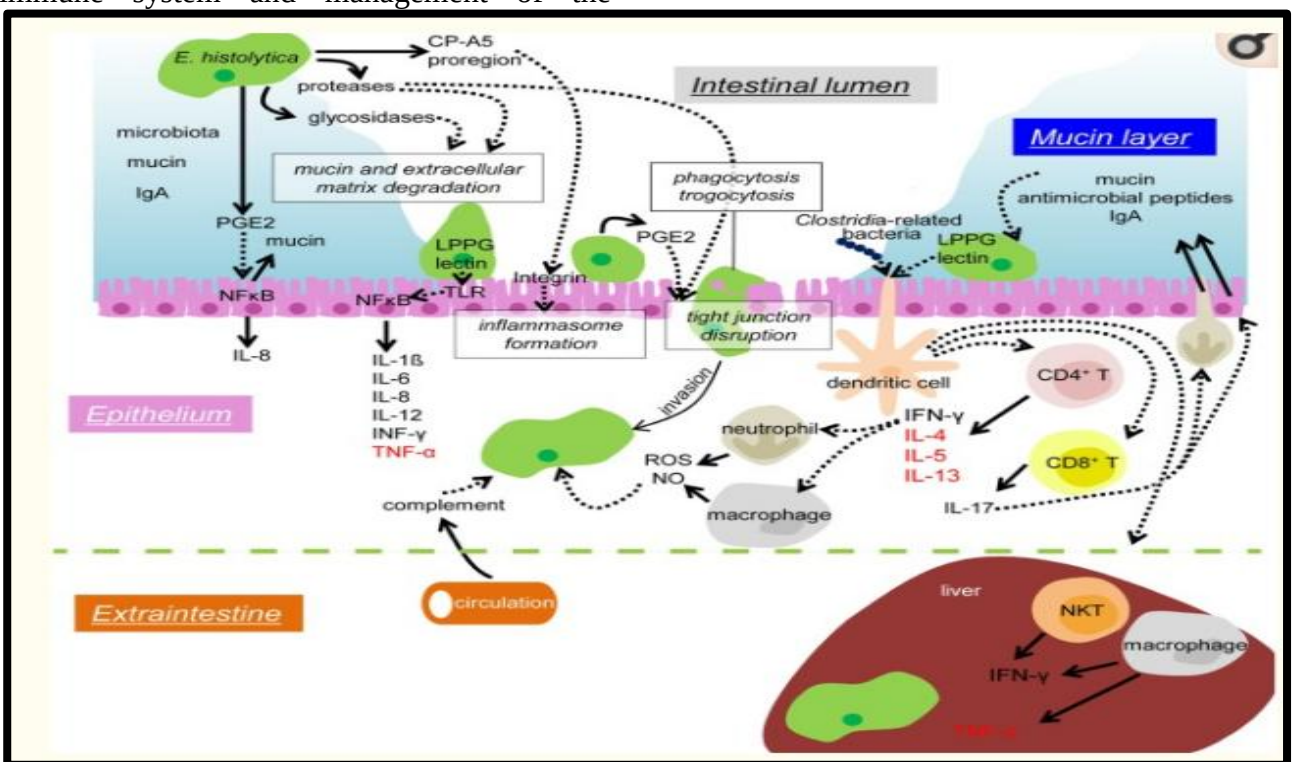
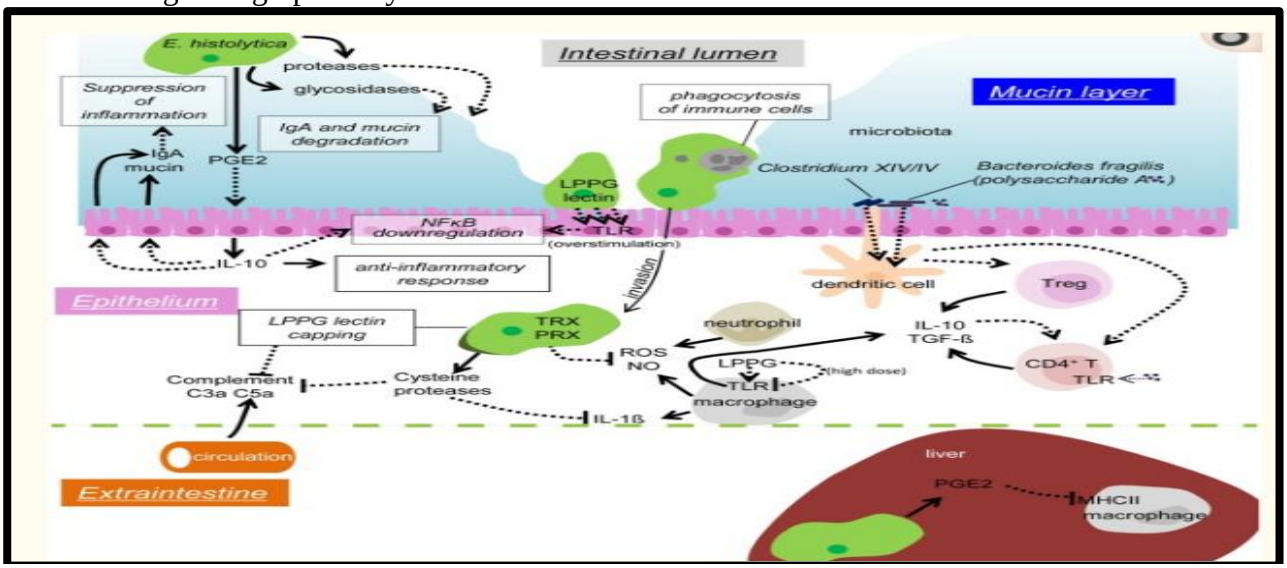


Figure (1) Immunee evasione by hoste cell lysise via E. histolyticae (Eh). Contacte betweene the hoste celle and Eh is facilitatede throughe the host celle surface Gale and GaleNAc receptorse, in addition to the Gal-lectine (A). Additionale amebice proteinse related to hoste cell attachmente also includee trans-membranee serine, threoninee, and isoleucinee proteins (STIRP) ande the transmembrane kinasee family membere TMKb1-9. Threee things coulde happene after Eh-host communicatione: Amebic trogocytosise (A) and apoptosise (C) (B) In Phagocytosise (D). Moree substantiale cells

maye undergo amebice trogocytosise in (B). Fore amebice trogocytosise to happene, PI3K and C2PK signale transductione were necessarye**.** (C) Whenevere host celle that havee been forcede to undergoe apoptosise express ephosphotidylserinee (PS) ande C1q complemente proteine, an ameba usese 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 PI3Ke 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 immunologicale reactionse to prevente and managee amebic illness.

The IEC layer is coatede in thee lumense of the intestinale tract bye thee mucous membranee (blue), whiche contains mucine and IgA releasede by thee host ande commensale microbese. The amebaee's secreted proteasese and glycosidasese are whate enable thee extracellulare matrixe 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-inflammatorye responsese. In the IECs, PGE2, whiche is also generatede by amebaee, promotes mucie depletion and hypersecretione. Additionallye, PGE2 initiatese 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 activatione and the productione of pro-inflammatorye cytokinese. 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 trophozoitese are drivene off by complemente from the bloodstreame, ROS, and NO from neutrophilse and 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 and eliminated. The hepatic macrophages' TNF- release induces abscesses to form. Solid arrows indicate thee synthesise of solublee proteinse, whereas dottede arrows indicatee contacte or signal transductione. Cytokinese implicatede in clinical diseasee are depictede in red, wherease those thate are moste usefule for killinge off amoebaee are depictede in black.



(Figure 2) Amebiasise immunee evasione techniquese that could bee employede. IgA is brokene in the mucosal layere via proteasese just one surface ore secreted eby amebaee. By causinge the IECs to secretee IL-10 and mucine and IgA, the amebae'se PGE2 stimulatese the preventione of needlesse inflammation. If TLR stimulation is too intense, NF-B activation is downregulated. Whene infiltrating immunee cells are clearede by phagocytosise or trogocytosise, immunee responses may be suppressed. Bacteroides fragilis and Clostridium XIV and IV groups are two commensale bacteria that causee Treg cellse to inhibit immunee responsese. Polysaccharidee of B. fragilis TLR2 on CD4 T cells is activated by A, and causes the production of IL-10. By cappinge surfacee receptorse (LPPG, lectin), the amebaee in tissues and bloode escape complemente, while C3a and C5a are destroyede

Immune Reaction Throughout Amebic Infection

Course of Amebic Infection

Entamoebae histolytica infectione is startede by the parasitee adhesion to thee intestinale mucine layere. A lectin (Gal/GalNAc lectine) madee by trophozoitese binds to colonic epithelial cells and host mucin with a predilection for galactose and N-acetyl-D-galactosaminee (13). The parasitese that havee colonizede have the capacitye to severelye damage tissuee. Hydrolytic enzymese, especially cysteinee proteasese (CP), aree thought to be the parasite's maine tools for penetratinge the epithelium and destroyinge extracellulare matrix (ECM) elementse of the host, in additione to pore-forminge proteins and amoebaporese (14, 15). (16–20). Duringe and after entering thee submucosal areae, amebic trophozoitese participate in directe and indirect interactione with host immunee and non-immunee cells.

Humoral Immunity

Although the mucosal layer in the digestivee system frequently servese as a main physical barrier againste intestinal pathogense, the intestinal immunee response is thee secondarye defence against E. histolyticae infection. Mucosale immunoglobulinse (Ig) are the moste large element of the humane gut defense systeme (21). One of thesee, known as secretorye IgA, is one of the most frequentlye produced Ig by plasmae cells. It serves to breake the mucosal barriere and prevent pathogene adhesion (21). (5, 22, 23). Patients who had recoverede from ALA backed up thise view. In post-ALA patientse, increases in anti-Gal/GalNAc lectin IgA antibodies were linked with elimination of subsequent amebic infections., showing that these individuals retained immunological memorye and improvede 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 immunee responses are also requirede is for host to be safeguardede from E. histolyticae. In the early stagese 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 antigens and the seconde of defense against epathogens after the mucosal layer. They express a range of pathogen recognition receptors (PRRs), includinge TLRs, that recognize infectionse (31). IFN- plays a role in eliminating an infectionalthough IL-4 and TNF are linked to illness (32–35). In fact, it has beene shown that invasive amebiasise patients have increased blood levels of IL-4 and that peripheral mononuclear cell eproduction of IFN- is associatede with protection against subsequent E. histolytica infection in children (36). (27, 37). Additionally, it has been demonstratede that animals which have receivede vaccinations are protected by CD4+ T cells that produce IFNe and CD8+ T cells that producee 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 whiche aid in the body's defensee against amebic infectione. (40–43). Amebicidal activitye of IFN-activated

macrophagese and neutrophilse in vitro (44, 45). When macrophagese were rare in amebic lesionse in vivo, neutrophils predominatede, suggesting the significancee of neutrophilse for amebae clearancee (46). In order to eradicatee trophozoites, the eproduction of reactivee oxygen species (ROS) and nitric oxide (NO) even by enzyme NAD(P)H oxidase complex and iNOS, respectively, is required (45, 47). Naturale killer T cells (NKTs) from experimental ALA provided protectione thru the release of IFN-, but macrophages that produce TNF increased tissuee damage (32, 33). Together, humoral and cell-mediated immune responses have esignificant effects on the avoidance of amebic infection.

Host Immune Response and Parasite Virulence Are Modified by the Microbiota

The Amebae's Energy Metabolism and Growth are Affected by Microbiota

The maturee human intestine includese trillions of differente species of bacteriae. Recent studies suggeste that the gut bacterial microbiotae may influence the results of protozoane infectionse (48, 49). Resources frome the host and the microbiotae are neededе for E. histolytica trophozoitese in order to grow and survivee. Glycosidasese are enzymese producede by the bacterial microbiotae that simplify complicatede polysaccharidese so that the host and amebae can absorb them (50). Microbial glycosidase activity determines the numbere of free carbs in the colone (the glycobiome). Thus, the coree energye metabolism of the trophozoite E. histolytica may be affected by the microbiota. E. histolyticae has various glycosidasese, such as amylasese, -hexosaminidasese, and lysozymes, encoded in its genome and may breakdowne a range of polysaccharides to create monocarbohydrates (51–55).the activitye and regulation of amebic glycosidases also influence available carbohydratee concentrations.

CONCLUSION

Our understandinge of the molecular mechanismse underlying the parasite's pathogenicity has significantlye advanced recently. These mechanisms involve host cell attachment, inductione of apoptosis, degradatione of mucin and ECM, penetratione of tissue, and phago/etrogocytosis of host cellse. The same is truee of immune evasione strategiese include inducinge IL-10, blockinge IFN, destroying Igs, activatinge complement, and producing pro-inflammatory cytokines. Defense against ROS and NO, as well as avoidinge antibody- and complement-dependente death, are all requirede for survival in the hoste. Additionallye, The outcome of amebic infectione is controllede by mutuale signaling amonge the three domainse in the vast systeme 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 comprehende the molecular basis of thee intricate interplaye in the digestivee tract.

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