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IMMUNE RESPONSE TO ENTAMOEBA HISTOLYTICA, AN ENTERIC PARASITE

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Abstract
Entamoeba histolytica belongs to the protozoan parasite that causes amoebiasis, a disease that is common in underdeveloped nations. The establishment of an amoebic infection requires the interaction of pathogenic elements for invasion and tissue destruction, as well as immune responses to defend the host. We examine E. histolytica pathogenicity and describe current understanding on immune response as well as evasion of the immune system strategies while suffering from amoebiasis.

Introduction

The parasitic infection entamoeba histolytica can affect human intestine and causes amoebiasis. Diarrhea, dysentery, and colitis are all clinical manifestations of amoebiasis. Sometimes, virulents amoeba could perhaps left intestinal tract or infiltrate another organ, including brain, lungs or liver. Causes amoebic abscess in these organs. Approximated an E. histolytica infects more than 50 million people worldwide [1]. It's the major problem of health on emerging nations as well as tropical regions around worldwide, including Africa, Mexico, America, South and Central Asia [2]. It may have serious long-term consequences, especially in children. Infectious diseases using the parasite have been discovered in developing nations. Persons who are high-risk groups affected include immigrants and tourists return from endemic areas. as well as the HIV patients [3].

Trying to establish infection of amoebic necessitates delicate equilibrium of Immunological and pathogenic. Intestine amoebas inhabit the external mucus layer and consume bacteria. A mechanism of which harmful pathogens amoebae infiltrates host do not fully clear, many critical procedures on the passageway had been identified, like mucosal layer degradant, ability to adhere to the intestinal mucosa, epithelial cell damage, as well as distribution into other organ. When amoeba infiltrate a tissue, an immune-system mounts an attack versus all parasite. It summarized existing understanding on pathogenic organisms E. histolytica onto immune responses all through amoebiases [4]. in this review,

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also we go through some of the mechanisms that amoeba uses to avoid detection by the immunological system of the host.

Clinical Signs and Symptoms

Amoebiasis with Luminal Amoebae

Most infectious E. histolytica is asymptomatically. A few percentages of infectious individuals (15-25%) developed infection symptom. Age, poor nutrition, pregnancy, cancerous, alcohol consumption, corticosteroids usage, along with the host gut microbiome are all risk factors linked with disease severity. Symptoms of amoebic colitis range between mild to severe diarrhea [5]. The fact of little E. histolytic isolated is more pathogenicity, as well as the fact that only a small number of infectious persons developed amoebiases, strong suggests the variable genomics occurs through isolated amoeba so as human. Many investigations were carried out to determined pathogenicity marker. Analysis of nucleotides DNA polymorphism on noncoded areas as well as on coded gene of chitinases or serinerich of E. histolytic confirming proteins which significant genomics differences occur through E. histolytica by different geographical mobilities. This genomics variation happens of pathogenic E. histolytica and non-pathogenic cultured [6]. Furthermore, an E. histolytica independents analytical isolated associates with clinically outcomes of various identifying geographically origin chosen (SNPs) throughout the strain of E. histolytica pathogen and non-pathogen [7]. Furthermore, family genes and potential pathogenic role are throughout most polymorphism. Distribution of E. histolytica genome shorts retrotransposon (SINEs) was studied. The findings of EhSINE1 as well as EhSINE2 are highly polymorphism throughout the strains of E. histolytica [8]. As a result, the genomic variation of SINEs has been suggested as an approach for typing E. histolytica strains. Only a small genetic correlation of amoebiases were identified in humans. In research from Bangladesh who were intensive monitoring of E. histolytica infectious in three years, an association between MHC antigens, (HLA) antigens class II, as well as suggesting amoebiases. class II HLA alleles DQBI*O6OI also the haplotype heterozygous DQBI*O6OI/DRBI*15O1 are found to have a possible association [9]. Likewise, in an investigation from Mexico of various regions, some of northern with highly estimated occurrence, another from the center which reduced the occurrence estimated, the HLA-DQB1*02 alleles were found among those with liver abscess amoebic at a higher frequency than in healthy individuals. Furthermore, in the population of Mexico, haplotypes HlA-DRBI*O8/-DQBI*O4 has been little common in patients with amoeba compared to controls, indicating a defensives trend versus the disease development [10]. Polymorphism within leptin receptor gene was found to be directly linked among E. histolytica susceptible infectious and genetic markers. Leptin is an adipocyte-produced hormone which reduces the foods intake, affects an immunity, as well as suppresses of malnourished kids. Malnutrition makes children more susceptible to E. histolytica; a link of both leptin function and amoebiasis was investigated. Mutations of sensitivity receptors were linked to an increasing receptivity of intestine blockage [11].

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Amoebic Disease Disseminated

Most affected organs of extra intestine amoebic is a liver, it manifests of amoebic livers abscess. Within 2-4 weeks of infection, the patient presenting sign or symptom such as fever but also ongoing right upper quadrant pain. Furthermore, roughly some of those with chronic diarrhea, dysenteries, losing of weight, pain in the abdomen. Images studying verify abscesses existence, which is located upon that lobe in the right hepatic's [12] Amoebic liver abscesses are interesting in that they would seem in patients between the ages of 25 and 45 and its more in men ten times than women. Causes of this imbalance also unknown. The explanation of this disparity corelated to complement activated, as women sera more considerably successful than serum from men in killing E. histolytic trophozoites, and this attempting to kill effects were mediate via complements [13]. Second explanation of sex disparity the level of testosterone increased mice sensitivity of liver abscesses by inhibiting secretion of interferon gamma. Lung is the secondary common part affected by intestinal amoebiases [14]. Amoebiasis in pulmonary is mostly caused by liver abscesses extension, however, could be caused by directly disseminated of intestinal tumors from blood circulations and lymph's. Amoeba can enter the heart after a liver abscess ruptures. Relatively uncommon complications of such a higher mortality ratio. Brain abscess is uncommon mode by invasive amoeba. This condition was commonly fatal, and it consistently begins with colon infection [15].

Diagnosis by Laboratory

Because diarrheal diseases continue to be the second leading reason for children mortality and morbidity in developed nations, E. histolytica was the major pathogen in this disease, diagnostic of E. histolytica should be improving. Microscopy, serology, antigen recognition [16], identification of nucleic acid use (PCR), as well as colonoscopy are all diagnostic tools for detecting E. histolytica. no required microscopy for diagnosing. The interaction of methods, such as detection of antibodies or antigens, as well as pcr, is recommended to diagnose E. histolytica. Usage of different methods improved amoebic specific and sensitive diagnostic. Due to limited resources, this research still not feasible in lots of endemic places [17].

Models for Investigating Amoebiasis

Because of E. histolytica the amoebiasis research has become very difficult, using persons as its nature sole host. As a result, research into those diseases requires appropriation through vivo model of animals but also ex-vivo studies methods. While no models of animals exist the replicates that entire human diseases cycling, there are lots of resistance and susceptible animal laboratories as well as methods of cultures axenic for trophozoite [18]. In the laboratory, using animals such as mouse, hamster, cat and pig were to examine amoebiasis. The mouse is the most widely used model among these. Some inbreeding mouse types, C57Bl/6 (B6) or BAlB/C, infectious resistant, whereas others, C3H or CBA, infectious vulnerable [19]. Mice are frequently injected with cecum by E. histolytica trophozoites for a study of intestinal amoebiasis, while a similar model for guinea pigs was also utilized [20]. In a severe infection model for amoeba colitis, the trophozoite was introduced within intestinal loop. Pigs are also

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employed as infection of intestine models. Pigs injected by trophozoite intraperitoneally piglets or adults receive injections by trophozoite with washing closed-jejunal loops [21]. Hamsters are widely used to imitate amoebic liver abscess when trophozoites are injected in the portal veins. Amoebas are also injected into pigs' portal veins as a model for hepatic amoebiasis. By using immunodeficient (SCID), humanized model of amoebiasis was created. mice implanted with human intestinal tissue. Humans' intestinal epithelium cells can release cytokines that are inflammatory in response to infection, according to the SCID mouse-human intestines xenografts (SCIDHU-INT) models [22]. Ex vivo infection models have been established in order to limit the use of animals. The intestine loop of human, for example, may be infectious with trophozoites ex-vivo. In addition, three-dimensional representations of infectious created tissues using check-liver cuts sections rather than hamster intestinal slices. By growing sinusoidal endothelial cells of the liver and hepatocytic of collagen-I 3D matrix sandwichs, developing in vitro humans' three-dimensional model of liver for invasions E. histolytica [23].

Pathogenicity of E. histolytica

If the cyst of amoeba enter an intestinal tract, they release trophozoite cling colon mucosal layers. It may survive in the colon, grazing upon common bacterium without illness signs. likewise unclear conditions, when the microbiome's equilibrium is disrupted (dysbiosis), mucosal barriers breaching by amoebas then cling straight next to epithelium outer layer of intestines. After that amoeba trigger the lysis of host cell, inflammation, as well as immune system recruitments cells like neutrophil. During this process, amoebic movement, phagocytes, while trogocytoses the major pathogens components. Finally, amoebas cause extracellular matrix breakdown and tight junction rupture, allowing tissue invasions but, on certain one, diffusion into neighboring organ [24].

The Microbiomes

In the upper mucosal layer's amoebas still there, far from epithelial while E. histolytica enters a healthy person that has an intact intestinal barrier. Amoebas eat bacteria and mucus sugars to produce an asymptomatic infection. Because both the microbiome and microbes compete on bound site in mucosal layers, mucus serves as a shield to maintain a healthy balance [25]. A surface lectin mediates in colon mucus layers E. histolytica was adhesion. Amoebas that interact directly in beneficial bacterium of its existence, not just like nutrition sources, it is building pathogens as well [26]. animal infections by E. histolytica without germs failed to result in sickness, although pathogenicity of E. histolytica was restored after bacterial inoculation. Commensal lactobacilli microbes which is partial from health microbiome are phagocytosed preferentially by amoebas [26]. Other bacteria, however, appear to be involved in E. histolytica pathogenesis. a type of bacteria linked to inflammatory intestine. Similarly, E. histolytica coculture, with intestinal live bacterium elicited a defense mechanism towards oxidative stress in the parasite. While a mixed of E. histolytica and the strain of probiotic, this reaction was not detected [27].

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Amoeba Attachment to the Intestinal Epithelium and Mucus Barrier Destruction

Amoebas release glycosidases and proteinases during a dysbiosis state, which degrades layers of mucin also exposes the epithelium of intestine. Various glycosidases, which include N-acetylgalctosamidase, N-acetyl-glycosaminidases, galactosidases, N-acetyl-hexosaminidases, are secreted by E. histolytica and mucins digestion carbohydrates chain way. Mucin's protein backbone later destroyed via cysteine proteinase numerous activities. Genomic E. histolytica's contains Fifty proteinase genes [28]. In laboratory mice, Ehcp-A5 has a critical pathogenic role, notably in invasion and liver abscesses formations. EhCP-A5 has recently been found to stimulate hosts matrix metalloproteinases, who efficiently destroy extracellular matrix proteins [29]. Furthermore, EhCP-A5 can cause inflammation in the absence of proteinase activity. Outside of its catalytic site, Ehcp-A5 possesses argininеglycineaspartates pattern that serves as an integrin binding site. Ehcp-A5 and integrin bind together causes an inflammation response by activating inflammasome NLRp3. Furthermore, Ehcp-A5 RGD peptides link into v3 integrins, which in goblets cell, causing secretion of mucus or water, resulting in cavitations and depletions of mucus [30]. E. histolytica employs lectin GaI/GaINAc to bind with GaI and GaINAC residues in exposed epithelial cell membranes.

Host Cell Lysis Induction

Come into direct contact with epithelial cells, either through a cellular-contacts methods or through releasing for lytic chemicals. The initial step in E. histolytica's cytotoxic action is cell adhesion. The lectin GaI/ GaINAC amoeba's biggest adhesive molecules also necessary to touch E. histolytica dependent mediating killed cells, evidenced through suppression in cytotoxic as well as cytopathic activity amoebas followed lectin inhibition. Cytotoxicity of caspase-3 is activated upon interaction, however the signaling route that induces apoptosis is not well understood. One probable mechanism is an increase in intracellular calcium levels in host cells, which results in many proteins dephosphorylated on tyrosine, resulting in caspase-3 activation. Cells are killed when K channels are activated, resulting in K ion outflow [31]. Furthermore, adhesion-dependent trophozoite activation which resulting of molecule amoebic ejection which were responsible to effects of cytotoxicity relation to tissue impassioned, Amoebapores contain soluble proteins that can form oligomer pores at cellular membranes. The big purpose present by kill bacterium within vacuoles amoeba's phagocyte. oligomeric holes in cell membranes. Secreted amoebapores, may cause cells necrosis of the epithelium as well as leukocytes. Amoebapores function within the invasive amoeba's process has not been demonstrated. Cysteine proteinases play a role in basal membranes breakdown, allows amoeba to enter tissue or destroying the tissue of the liver, while phospholipases A2 is responsible to other hemolytic parasites activities [32].

Trogocytoses, Phagocytoses, Motility

In addition to cytotoxicity, E. histolytica exploits its motility, phagocytosis, and trogocytoses mechanisms like pathogens. movement of amoeba aided via interaction between parasites and extracellular matrix protein that resulting remodeling by cytoskeletons [33]. Erythrocyte phagocytes,

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bacterial, as well as dead cells were essential to survive trophozoite. E. histolytica isolates with higher pathogenicity erythrocyte phagocytosed with substantially high ratio [34], whereas clone of E. histolytica phagocytoses deficiencies similarly low harmful. Trophozoite promote apoptotic cells digestion, implying the amoeba cause apoptosis prior to phagocytoses. Furthermore, trophozoites in hamster liver abscesses can directly phagocytoze hepatocytes [35]. Amoebic phagocytic receptors have yet to be found. The GaI/GaINAc lectin recently appeared to operate like erythrocytes phagocytosis receptors. Even though E. histolytica's cytoskeletal components are simple, as express just one kind of action, it is motile exceedingly, and phagocytosis executes efficiently quietly. Acetylation was among the most common changes, then phosphorylation [36]. EhRhoI E. histolytica has control phagocytoses via attaching onto actin developing protein EhForminI with EhProfilinI within phagocytoses nucleus area, like Rho GTPases, which are recognized as controllers of the cytoskeleton made of actin in cells of mammals. EhPIPKI enzyme of amoeba, that produce PtdInS P2, appeared to enrich on phagocyte cup at beginning until closure it disappears on phagosome after plasma membrane pinched off them [37]. Then, in eukaryotes, complexes of endosomal sorting needed at orchestrate membranes transportation remodels mechanism such as endocytoses. ESCRT-111 amoebic protein involved on phagocytoses via engaging with protein vps to assemble phagosomes and intraluminal vesicle. Trogocytosis, a method by which amoebas chew on bits of living cells, is another harmful mechanism. This mechanism requires the involvement of acidic lysosomes and AGC group kinase 1 [38].

Immune Reaction to Entamoeba histolytica

The host initiates a series of immunological reactions in response to amoeba contacts along with an invasion of the gut epithelium in order to protect itself against the parasite. As a result, several evasions mechanism that amoeba evolving in, withstand pathogeneses and immune responses prolong that life. Another extensive research showed fewer immune responses learned within invasive amoeba [39].

Defense of Innate Immunity

Defenses of innate immunity are met with the invaded amoeba. Although the antimicrobial factor “acid” is successful in the stomach, amoeba cysts have been resistant to it. Epithelial cells cover by thick coating mucus mucin later on intestine. epithelial cells of intestine detecting carbohydrates recognition when amoebas reaching epithelial. GaI/GaINAc lectin domain binding with TlR-2 and TlR-4 [40]. When these TLRs are activated, NF- B is activated, resulting inflammatory cytokines generation like, interleukin IL-1, IL12, IL8, IL6, IFN-, also tumor necrosis factor-alpha, that promoting inflammatory as well as control host immune cell functions. Furthermore, E. histolytica trophozoites demonstrate the GPl anchored-molecular-complex called (LPPG) lipo-peptido-phosphoglycan on their cell surface. TLR-2 recognizes LPPG and induces the release of IL-10. Trophozoites are also known to produce proteins of immunomodulatory which induce epithelium cell for generate cytokines before initiating contact cell [41]. IL-1 is present in cysteinproteinases. It expected that neutrophils are the first innate immune cells to infiltrate the intestines throughout an amoebic infection according to strong neutrophil chemoattractant IL-8.IL-1 is present in cysteinproteinases. Infection with amoeba have another pro-

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inflammatory cytokine its "TNF ", and its production has been linked to E. histolytica diarrhea induced among children and destructing tissue on an amoeba livers abscess through a rat models [42]. Amoebas are subjected to the complement system after they leave the intestinal tract and enter the circulation. As evidenced, women serum is more effective for complements-mediated amoebolysis, which is an important thing at innate immune versus amoeba. Some studies revealed that cell membrane proteins of humans produce E. histolytica via trogocytosis also exhibit these surface proteins. A mechanism results in human sera lysis in resistance. E. histolytica infection characterization via severe inflammatory of several neutrophils invading .it may travel to infection sites coming from the circulation, the perform antimicrobe tasks such as ingestion, degranulation, and the creation the extracellular neutrophil traps (NET) [43]. Neutrophils appear to have a defense role against this parasite, since lower neutrophil counts result in greater levels of amoebiasis. E. histolytica trophozoites have recently been shown to be able to trigging NET information. The reaction was elicited via different receptors, which signaling activating cascade on neutrophils including RAf/MEk/ERk not PkC or RoS [44]. The NET even discovered to non just prevent amoebic migrating also additionally killing those direct. Other defenses of innate mechanism versus amoebae linked with receptors leptin mutations (q223r). The location of leptin activity has been identified as the epithelial of intestine, it needs signal of leptin receptors via STAt3. Furthermore, the mutation reduces infiltrations of neutrophils at infectious sites, as a result of impaired neutrophil chemotaxis through leptin. Macrophages are also implicated in amoebic defense. TLR-2 and TLR-4 on macrophages recognize amoebas, generating huge range for inflammation of cytokine which include Interleukin 6, IL12, and IL1. Activated macrophages can kill E. histolytica by producing (NO) nitric oxide, antibacterial chemical which inhibit critical enzyme on metabolism of amoeba. IFN-'s amoebic impact is due to activated macrophages, which generate NO as great deal through l-arginine, NO substrates (NOS-II) synthases. Amoebae defend themself against macrophages by E. histolytica arginases manufacturing, the enzymes which hydrolysis catalyzes the for l-arginine into urea as well as l-ornithine [45].

Response of Cellular Immunity

Immune responses mediated by cells are also crucial in the host's defense versus E. histolytica. In the infection of early stages of intestine epithelial identify the amoebic into lectin GaI/GaINAc attaching TlR-2 as well as TlR-4. Activates Nf-B on epithelium, resulting in the generation of inflammatory cytokines. Furthermore, variety of cells, like dendritic cells, detect amoeba at TlRs then turns on lymphocyte T-cells [46]. CD marker 4 T-cell found the crucial into amoebic gastrointestinal with C3H/Hej mouse as their results of depletion of fewer lesion of intestine also fewer amoebae. As a result, for the disease, inflammatory T cells were added. Cytokine T-cell, on the other hand, can alter the disease progression. It depends on whether immune response is ThI / Th2. IFN-, a Th1 cytokine, protects against a parasitic infection, while Th2, IL-4, has been linked to both the invasion of the disease and acute phases of infection [47]. Although CD marker 4 T-cell is IFN primary source, NKT may additionally generate this cytokine and protect against amebic liver abscess. In vitro, IFN- may activate neutrophils and macrophages, resulting in direct amoebic action. In a similar way CD8 cytotoxic T

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lymphocytes can harm amoebas directly or indirectly through their creation for IL-17 [48]. At the level of the intestinal epithelium, IL-17 has several effects against amoebas, including induction of mucin as well as antimicrobial peptides, as well as stimulation or IgA transportation through the epithelium [49]. IL-10 is an additional cytokine produced by CD4 T cells that has a significant protective impact against intestinal amoebiasis. This cytokine was found to play in epithelium of intestine for improve B6 mice's natural resistance to intestinal amoebiasis utilizing chimeras in resistant (B6) mouse strain and susceptibility (C3E). Furthermore, activation of macrophage via TlR2, TlR4 into amoeba lPPG production IL10. In an amoeba infection model, a subset of regulating T cells was discovered. These regulatory T cells, which express CCR9 chemokines receptors, play a role in resolutions and control an inflammation of reaction disease by E. histolytica [50]. These studies suggest that cell-mediated immune reactions are vital in the fight toward E. histolytica infections.

The Conclusions

Amoebiasis remains a major public health concern in poor countries. Nonetheless, the prevalence and incidence of amoebiasis keeps on increasing globally as a result of travel and emigration from endemic areas to developed countries. In infection during the reaction, activation of all adaptive and innate immunity, in order to regulate E. histolytica invasion or remove it, that utilizes several pathogenic components as defense measures. The immune response appears to be mostly efficient, as most infected asymptomatic people remain, with just little amoebiasis invasion progressing [51]. Regarding the immune response there is few knowledge about such parasite. levels of chemokines, cytokines, immunoglobulin, as well as the function of immune cells, will continue to be studied in asymptomatic carriers as well as individuals with invasive illness. in amoebiasis, neutrophil roles control must investigate, existing leukocytes models merely producing damage tissues of collateral permits penetrating the parasites appears incompletely. Trophozoite can identifying by neutrophils and generate NET, that can trap and kill amoebas [52]. Future research should focus on the mechanisms that cause tissue harm in order to establish better treatments and preventive measures for amoebiasis [53]. In the end, a combination of sanitation education campaigns and basic research upon the pathology of E. histolytica an infection will undoubtedly direct our efforts toward, hopefully, eradicating amoebiasis one day.

References

1. Shirley DT, Farr L, Watanabe K, Moonah S. A review of the global burden, new diagnostics, and current therapeutics for amebiasis. Open Forum Infect Dis 5: ofy161, 2018.
2. Marie C, Petri WA Jr. Regulation of virulence of Entamoeba histolytica. Annu Rev Microbiol 68: 493–520, 2014.
3. Petri WA Jr, Mondal D, Peterson KM, Duggal P, Haque R. Association of malnutrition with amebiasis. Nutr Rev 67, Suppl 2: S207–S215, 2009.
4. Watanabe K, Gatanaga H, Escueta-de Cadiz A, Tanuma J, Nozaki T, Oka S. Amebiasis in HIV-1-infected Japanese men: clinical features and response to therapy. PLoS Negl Trop Dis 5: e1318, 2011.

ISSN: 2776-1010 Volume 4, Issue 7, July 2023

5. Singh A, Banerjee T, Kumar R, Shukla SK. Prevalence of cases of amebic liver abscess in a tertiary care centre in India: A study on risk factors, associated microflora and strain variation of Entamoeba histolytica. PLoS One 14: e0214880, 2019.
6. Haghighi A, Kobayashi S, Takeuchi T, Masuda G, Nozaki T. Remarkable genetic polymorphism among Entamoeba histolytica isolates from a limited geographic area. J Clin Microbiol 40: 4081–4090, 2002.
7. Gilchrist CA, Ali IK, Kabir M, Alam F, Scherbakova S, Ferlanti E, Weedall GD, Hall N, Haque R, Petri WA Jr, Caler E. A multilocus sequence typing system (MLST) reveals a high level of diversity and a genetic component to Entamoeba histolytica virulence. BMC Microbiol 12: 151, 2012.
8. Kumari V, Iyer LR, Roy R, Bhargava V, Panda S, Paul J, Verweij JJ, Clark CG, Bhattacharya A, Bhattacharya S. Genomic distribution of SINEs in Entamoeba histolytica strains: implication for genotyping. BMC Genomics 14: 432, 2013.
9. Duggal P, Haque R, Roy S, Mondal D, Sack RB, Farr BM, Beaty TH, Petri WA Jr. Influence of human leukocyte antigen class II alleles on susceptibility to Entamoeba histolytica infection in Bangladeshi children. J Infect Dis 189: 520–526, 2004.
10. Hernández EG, Granados J, Partida-Rodríguez O, Valenzuela O, Rascón E, Magaña U, EscamillaTilch M, López-Reyes A, Nieves-Ramírez M, González E, Morán P, Rojas L, Valadez A, Luna A, Estrada FJ, Maldonado C, Ximénez C. Prevalent HLA class II alleles in Mexico City appear to confer resistance to the development of amebic liver abscess. PLoS One 10: e0126195, 2015.
11. Duggal P, Haque R, Roy S, Mondal D, Sack RB, Farr BM, Beaty TH, Petri WA Jr. Influence of human leukocyte antigen class II alleles on susceptibility to Entamoeba histolytica infection in Bangladeshi children. J Infect Dis 189: 520–526, 2004.
12. Wuerz T, Kane JB, Boggild AK, Krajden S, Keystone JS, Fuksa M, Kain KC, Warren R, Kempston J, Anderson J. A review of amoebic liver abscess for clinicians in a nonendemic setting. Can J Gastroenterol 26: 729–733, 2012.
13. Snow M, Chen M, Guo J, Atkinson J, Stanley SL Jr. Differences in complement-mediated killing of Entamoeba histolytica between men and women—an explanation for the increased susceptibility of men to invasive amebiasis? Am J Trop Med Hyg 78: 922–923, 2008.
14. Shamsuzzaman SM, Hashiguchi Y. Thoracic amebiasis. Clin Chest Med 23: 479–492, 2002.
15. Maldonado-Barrera CA, Campos-Esparza MR, Muñoz-Fernández L, Victoria-Hernández JA, Campos-Rodríguez R, Talamás-Rohana P, Ventura-Juárez J. Clinical case of cerebral amebiasis caused by E. histolytica. Parasitol Res 110: 1291– 1296, 2012.
16. Haque R, Kress K, Wood S, Jackson TF, Lyerly D, Wilkins T, Petri WA Jr. Diagnosis of pathogenic Entamoeba histolytica infection using a stool ELISA based on monoclonal antibodies to the galactose-specific adhesin. J Infect Dis 167: 247– 249, 1993.
17. Ryan U, Paparini A, Oskam C. New technologies for detection of enteric parasites. Trends Parasitol 33: 532–546, 2017.
18. Diamond LS, Harlow DR, Cunnick CC. A new medium for the axenic cultivation of Entamoeba histolytica and other Entamoeba. Trans R Soc Trop Med Hyg 72: 431–432, 1978.

ISSN: 2776-1010 Volume 4, Issue 7, July 2023

19. Hamano S, Asgharpour A, Stroup SE, Wynn TA, Leiter EH, Houpt E. Resistance of C57BL/6 mice to amoebiasis is mediated by nonhemopoietic cells but requires hemopoietic IL-10 production. J Immunol 177: 1208–1213, 2006
20. Kaur U, Khurana S, Saikia UN, Dubey ML. Immunogenicity and protective efficacy of heparan sulphate binding proteins of Entamoeba histolytica in a guinea pig model of intestinal amoebiasis. Exp Parasitol 135: 486–496, 2013.
21. Girard-Misguich F, Cognie J, Delgado-Ortega M, Berthon P, Rossignol C, Larcher T, Melo S, Bruel T, Guibon R, Chérel Y, Sarradin P, Salmon H, Guillén N, Meurens F. Towards the establishment of a porcine model to study human amebiasis. PLoS One 6: e28795, 2011.
22.. Zhang Z, Wang L, Seydel KB, Li E, Ankri S, Mirelman D, Stanley SL Jr. Entamoeba histolytica cysteine proteinases with interleukin-1 beta converting enzyme (ICE) activity cause intestinal inflammation and tissue damage in amoebiasis. Mol Microbiol 37: 542–548, 2000.
23. Petropolis DB, Faust DM, Deep Jhingan G, Guillen N. A new human 3D-liver model unravels the role of galectins in liver infection by the parasite Entamoeba histolytica. PLoS Pathog 10: e1004381, 2014.
24. Sperandio B, Fischer N, Sansonetti PJ. Mucosal physical and chemical innate barriers: Lessons from microbial evasion strategies. Semin Immunol 27: 111–118, 2015.
25. Burgess SL, Petri WA Jr. The intestinal bacterial microbiome and E. histolytica infection. Curr Trop Med Rep 3: 71–74, 2016.
26. Iyer LR, Verma AK, Paul J, Bhattacharya A. Phagocytosis of gut bacteria by Entamoeba histolytica. Front Cell Infect Microbiol 9: 34, 2019.
27. Varet H, Shaulov Y, Sismeiro O, Trebicz-Geffen M, Legendre R, Coppée JY, Ankri S, Guillen N. Enteric bacteria boost defences against oxidative stress in Entamoeba histolytica. Sci Rep 8: 9042, 2018.
28. Tillack M, Biller L, Irmer H, Freitas M, Gomes MA, Tannich E, Bruchhaus I. The Entamoeba histolytica genome: primary structure and expression of proteolytic enzymes. BMC Genomics 8: 170, 2007.
29. Thibeaux R, Avé P, Bernier M, Morcelet M, Frileux P, Guillén N, Labruyère E. The parasite Entamoeba histolytica exploits the activities of human matrix metalloproteinases to invade colonic tissue. Nat Commun 5: 5142, 2014.
30. Cornick S, Moreau F, Chadee K. Entamoeba histolytica cysteine proteinase 5 evokes mucin exocytosis from colonic goblet cells via v3 integrin. PLoS Pathog 12: e1005579, 2016.
31. Marie C, Verkerke HP, Theodorescu D, Petri WA Jr. A whole-genome RNAi screen uncovers a novel role for human potassium channels in cell killing by the parasite Entamoeba histolytica. Sci Rep 5: 13613, 2015.
32. Vargas-Villarreal J, Olvera-Rodríguez A, MataCárdenas BD, Martínez-Rogríguez HG, SaidFernández S, Alagón-Cano A. Isolation of an Entamoeba histolytica intracellular alkaline phospholipase A2. Parasitol Res 84: 310–314, 1998.

ISSN: 2776-1010 Volume 4, Issue 7, July 2023

33. Labruyère E, Guillén N. Host tissue invasion by Entamoeba histolytica is powered by motility and phagocytosis. Arch Med Res 37: 253–258, 2006.
34. Trissl D, Martínez-Palomo A, de la Torre M, de la Hoz R, Pérez de Suárez E. Surface properties of Entamoeba: increased rates of human erythrocyte phagocytosis in pathogenic strains. J Exp Med 148: 1137–1143, 1978.
35. Blazquez S, Rigothier MC, Huerre M, Guillén N. Initiation of inflammation and cell death during liver abscess formation by Entamoeba histolytica depends on activity of the galactose/N-acetyl-Dgalactosamine lectin. Int J Parasitol 37: 425–433, 2007.
36. Hernández-Cuevas NA, Jhingan GD, Petropolis D, Vargas M, Guillen N. Acetylation is the most abundant actin modification in Entamoeba histolytica and modifications of actin's amino-terminal domain change cytoskeleton activities. Cell Microbiol 21: e12983, 2019.
37. Sharma S, Agarwal S, Bharadwaj R, Somlata, Bhattacharya S, Bhattacharya A. Novel regulatory roles of PtdIns(4,5)P2 generating enzyme EhPIPKI in actin dynamics and phagocytosis of Entamoeba histolytica. Cell Microbiol 21: e13087, 2019.
38. Somlata, Nakada-Tsukui K, Nozaki T. AGC family kinase 1 participates in trogocytosis but not in phagocytosis in Entamoeba histolytica. Nat Commun 8: 101, 2017.
39. Kantor M, Abrantes A, Estevez A, Schiller A, Torrent J, Gascon J, Hernandez R, Ochner C. Entamoeba histolytica: Updates in clinical manifestation, pathogenesis, and vaccine development. Can J Gastroenterol Hepatol 2018: 4601420, 2018.
40. Kammanadiminti SJ, Mann BJ, Dutil L, Chadee K. Regulation of Toll-like receptor-2 expression by the Gal-lectin of Entamoeba histolytica. FASEB J 18: 155–157, 2004.
41. . Yu Y, Chadee K. Entamoeba histolytica stimulates interleukin 8 from human colonic epithelial cells without parasite-enterocyte contact. Gastroenterology 112: 1536–1547, 1997.
42. Helk E, Bernin H, Ernst T, Ittrich H, Jacobs T, Heeren J, Tacke F, Tannich E, Lotter H. TNF-mediated liver destruction by Kupffer cells and Ly6Chi monocytes during Entamoeba histolytica infection. PLoS Pathog 9: e1003096, 2013.
43. Yipp BG, Petri B, Salina D, Jenne CN, Scott BN, Zbytnuik LD, Pittman K, Asaduzzaman M, Wu K, Meijndert HC, Malawista SE, de Boisfleury Chevance A, Zhang K, Conly J, Kubes P. Infectioninduced NETosis is a dynamic process involving neutrophil multitasking in vivo. Nat Med 18: 1386–1393, 2012.
44. Díaz-Godínez C, Fonseca Z, Néquiz M, Laclette JP, Rosales C, Carrero JC. Entamoeba histolytica trophozoites induce a rapid non-classical NETosis mechanism independent of NOX2-derived reactive oxygen species and PAD4 activity. Front Cell Infect Microbiol 8: 184, 2018.
45. Elnekave K, Siman-Tov R, Ankri S. Consumption of L-arginine mediated by Entamoeba histolytica L-arginase (EhArg) inhibits amoebicidal activity and nitric oxide production by activated macrophages. Parasite Immunol 25: 597–608, 2003.
46.. Sharma M, Bhasin D, Vohra H. Differential induction of immunoregulatory circuits of phagocytic cells by Gal/Gal NAc lectin from pathogenic and nonpathogenic Entamoeba. J Clin Immunol 28: 542–557, 2008.

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47. Guo X, Stroup SE, Houpt ER. Persistence of Entamoeba histolytica infection in CBA mice owes to intestinal IL-4 production and inhibition of protective IFN-gamma. Mucosal Immunol 1: 139– 146, 2008.
48. Guo X, Barroso L, Lyerly DM, Petri WA Jr, Houpt ER. CD4 and CD8 T cell- and IL-17-mediated protection against Entamoeba histolytica induced by a recombinant vaccine. Vaccine 29: 772–777, 2011.
49. Cao AT, Yao S, Gong B, Elson CO, Cong Y. Th17 cells upregulate polymeric Ig receptor and intestinal IgA and contribute to intestinal homeostasis. J Immunol 189: 4666–4673, 2012.
50. Rojas-López AE, Soldevila G, Meza-Pérez S, Dupont G, Ostoa-Saloma P, Wurbel MA, VenturaJuárez J, Flores-Romo L, García-Zepeda EA. CCR9 T cells contribute to the resolution of the inflammatory response in a mouse model of intestinal amoebiasis. Immunobiology 217: 795– 807, 2012.
51. Kantor M, Abrantes A, Estevez A, Schiller A, Torrent J, Gascon J, Hernandez R, Ochner C. Entamoeba histolytica: Updates in clinical manifestation, pathogenesis, and vaccine development. Can J Gastroenterol Hepatol 2018: 4601420, 2018.
52. Fonseca Z, Uribe-Querol E, Díaz-Godínez C, Carrero JC, Rosales C. Pathogenic Entamoeba histolytica, but not Entamoeba dispar, induce neutrophil extracellular trap (NET) formation. J Leukoc Biol 105: 1167–1181, 2019.
53. Ghosh S, Padalia J, Moonah S. Tissue destruction caused by Entamoeba histolytica parasite: Cell death, inflammation, invasion, and the gut microbiome. Curr Clin Microbiol Rep 6: 51–57, 2019.