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Review article

The interplay between *Blastocystis* and human gut microbiota

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ABSTRACT. Gut microbiota, consisting of multiple beneficial microorganisms, significantly impacts host health. Recent investigations have revealed that the gut microbiota influences the pathogenicity of eukaryotes such as *Blastocystis*, and conversely, the protist can impact the composition of the bacterial community. This review focuses on both, beneficial and adverse interactions between *Blastocystis* and human gut microbiota communities. *Blastocystis* can modulate both the structure and composition of the gut microbiota. Research has demonstrated that *Blastocystis* colonization is associated with increased gut microbiota diversity, a higher abundance of beneficial bacteria like Firmicutes and Clostridiales, and reduced *Bacteroides*, indicating a potential beneficial relation. However, its exact role is still unknown, and it may be associated with dysbiosis in some gastrointestinal disorders such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). Moreover, some researchers presented the contradictory study results of interactions between specific *Blastocystis* subtypes and gut bacteria. The bidirectional influence between microorganisms is complex, with distinct subtypes that can display varying effects on the microbiota. These discrepant findings might reflect variations in the host factors, microbial environment, or strain-level diversity.

Keywords: *Blastocystis,* gut microbiota, interaction

Introduction

Blastocystis spp. (*Blastocystis*) is the most prevalent enteric protist present in the human and animals gastrointestinal tract [1,2]. *Blastocystis* infection typically occurs through the fecal-oral route [3]. Currently, it exhibits a high genetic diversity, and based on sequence analyses of the small subunit ribosomal RNA (SSU rRNA) gene, at least 44 subtypes (STs) have been identified to date [1,4,5]. Of these, ST1–ST10, ST12, ST14, ST16, ST23, ST35 and ST41 have been found in humans [1,6,7]. Although *Blastocystis* infections are usually, asymptomatic, there are many cases of people who could suffer serious non-specific gastrointestinal symptoms such as abdominal pain, diarrhea, nausea, vomiting, bloating, and anorexia, as well as less frequent skin lesions [8–11]. The genetic diversity of *Blastocystis* adds complexity, with some subtypes being more frequently detected in symptomatic individuals, while others are commonly found in asymptomatic populations. Therefore, it is believed that the pathogenicity of *Blastocystis* subtypes is determined mainly by the interaction with the intestinal microbiota and the host's immune response [12–14]. Some subtypes, such as ST1, ST4, and ST7, have been associated with health disorders in humans and, on the other hand, ST3 has been reported as a non-pathogenic subtype [1,9,15]. Moreover, a number of studies suggested that *Blastocystis* is a member of the commensal gut microbiota and showed both a higher richness and a higher evenness of the gut bacterial microbiota in people colonized with *Blastocystis* [2,16–18]. There are many study results strongly suggesting that *Blastocystis* colonization may be closely related to an anti-inflammatory response favoring changes in the bacterial composition of the gut microbiota [16]. Conversely, some studies report that *Blastocystis* may be associated with reduced beneficial bacteria and an altered gut microbiota composition [19]. In contrast,

some authors demonstrated the influence of bacteria on *Blastocystis* pathogenicity [20]. The protist can be referred to as a pathobiont, implying that it is native to a host's microbiota but can promote disease under certain conditions in the host, including gut dysbiosis.

Blastocystis may colonize the human intestine for a long time and is frequently identified in stool samples from individuals with no gastrointestinal complaints. Therefore, the question of whether a protist should be considered a pathogen or a commensal often arises [2,21]. Nonetheless, the eradication of *Blastocystis* is necessary in cases where it is the only symptom agent, the patient's complaints persist and in patients with a large number of cysts in feces (>5 cysts in the field of vision) [22,23]. A number of antimicrobial drugs, including metronidazole, trimethoprim-sulfamethoxazole (TMP-SMX), nitazoxanide, paramomycin, iodoquinol, ketoconazole, and tinidazole, have been used to treat *Blastocystis* infection [24]. Metronidazole is a first-line drug and an effective therapy. Trimethoprim–sulfamethoxazole (TMP – SMX) is a second-choice therapy selected when the initial one has not been effective or for patients with metronidazole intolerance [24].

The researchers still cannot clarify what factors determine asymptomatic *Blastocystis* colonization or symptomatic disease. Tsaousis et al. suggest that *Blastocystis* is a part of the human gut transient microbiota from early life, but often goes undetected due to limitations in detection methodology [25]. It is essential to systematically map the conflicting evidence on *Blastocystis* pathogenicity. The main subjects addressed in this review are *Blastocystis* and gut microbiota interactions to (1) determine the triggers of *Blastocystis* pathogenicity, (2) link bacterial species with *Blastocystis* colonization, and (3) understand how *Blastocystis* affects the gut microbiota and vice versa.

The effect of *Blastocystis* on gut microbiota

A growing body of literature suggests *Blastocystis* is important in the human gut microbiota, where it is increasingly viewed as a commensal with roles in immune modulation and maintaining bacterial diversity [13,18,26,27]. Healthy individuals often show a link between *Blastocystis* colonization and increased bacterial diversity, a higher abundance of beneficial bacteria like Firmicutes and Clostridiales, and a lower abundance of *Bacteroides* [28,29]. However, its exact role is still debated, and it may be linked to dysbiosis in some gastrointestinal disorders such as IBS–constipation and inflammatory bowel disease (IBD) [19,30,31]. Moreover, few studies have investigated the interactions between *Blastocystis* subtypes and microbiota [13,27]. In general, *Blastocystis* is a common eukaryote in the healthy intestinal microbiota. Its presence is often linked with the high diversity and richness of bacterial communities [13]. However, a comprehensive understanding of how *Blastocystis* and the gut microbiota interact is still lacking, and the relationship is complex and debated.

Human gut microbiota

The term of gut microbiota refers to the composition of bacteria, viruses, archaea, and eukaryotes that colonize the gastrointestinal tract, mainly the large intestine. This complex ecosystem plays a key role in maintaining human health by fulfilling various physiological functions such as host metabolism and immune system, fermenting nondigestible fiber, and providing barriers to pathogens [32]. According to the data from the Metagenomics of the Human Intestinal Tract (MetaHIT) project and the Human Microbiome Project (HMP) together human gut microbiota consists of more than 250 strictly anaerobic species classified into five different phyla of bacteria, of which 60 to 80% belong to the largest Firmicutes, and less to the Bacteroidetes, the Proteobacteria, the Actinobacteria, the Verrucomicrobiota, and, to a lesser extent, one Archea phylum, the Euryarchaeota [33–37].

The human gut microbiota is established during and immediately after birth, though some early colonization may occur in the womb. An infant's gut is rapidly colonized by microorganisms from its mother and the environment, with the composition significantly influenced by factors such as the mode of delivery (vaginal vs. cesarean), infant feeding methods (breastfeeding vs. formula), and host genetics or ethnicity [38,39]. In addition, diet, nutritional status, prenatal events, geographical location, antibiotic treatment, and age are all major external factors that shape the gut microbiota throughout a human life [40–44]. The microbiota reaches a balanced state of high diversity and richness in the years following life, establishing a commensal relationship with the host, and this process is crucial

for immune system development [45]. The gut microbiota has numerous crucial functions, including digestion and the production of vitamins, regulating the immune system by protecting against pathogens, maintaining the gut barrier, and controlling metabolic activities. Consequently, a healthy and diverse gut microbiota is fundamental for overall health, as imbalances, known as dysbiosis, are linked to various diseases [46,47]. Integrative analyses show that alterations of the gut microbiota are linked to chronic diseases like autoimmune disorders, obesity, diabetes, IBS, metabolic syndrome, depression, and allergies through mechanisms involving inflammation, immune system regulation, and metabolic pathways [48–52].

The composition of the microbiota is shaped by both host and environmental selective pressures. The GI tract uses a dynamic, multi-layered intestinal barrier to protect the host immune system from the gut microbiota, which limits injury and maintains homeostasis. The barrier system integrates physical (the epithelial and mucus layers, which form a physical and anatomical barrier), biochemical (enzymes and antimicrobial proteins), and immunological (IgA and epithelia-associated immune cells – T cells, B cells, macrophages, and dendritic cells, which provide a specific immune response) factors for protection [53]. The longevity of an individual microbe is determined by its contribution to the host's essential functions, such as metabolism, immune system regulation, and development. Gut microbes must be adapted to a specific lifestyle due to fewer biochemical niches in the gut compared to other environments. The energy can be derived from dietary and host carbohydrates through processes like fermentation and sulfate reduction. An organism's phenotypic traits, such as its ability to withstand the gut's acidic environment, metabolize specific nutrients, or evade the host's immune system, determine its ability to colonize and survive in the gut. These traits act as a selective filter, making survival limited to organisms that possess the right characteristics to thrive in that particular niche [54]. Factors shaping the GI microbiota are:

– Diet, especially the availability of microbiota-accessible carbohydrates (MACs) from dietary fiber. Extreme animal- or plant-based diets cause wide-ranging and rapid alterations to the gut microbiota in humans, as shown by studies where microbial community structure shifts within days of a dietary change [55].

– Intestinal mucus built around the large highly glycosylated gel-forming mucin MUC2 secreted by goblet cells [56]. The outer mucus layer is a unique „niche" in the gut that acts as a separate microbial habitat from the main lumen, leading to different bacterial behavior [57]. The mucin O-glycosylation patterns are determined by the specific glycosyltransferases (GTs) [58], which influences the gut microbiota composition. Alterations in this glycosylation process, often due to factors like disease or infection, can change the available sugars on the mucin surface, thereby affecting which bacteria can adhere to, thrive in, or degrade the mucus.

– Mutation or lateral gene transfer [59,60]. The appearance of new bacterial functional traits can lead to the exploitation of different resources or the creation of new metabolic byproducts. These byproducts can then create new niches for other bacteria to colonize or for the original bacteria to adapt to, driving a cycle of increasing functional and genetic diversity within the community.

– The presence of sulphated compounds in the colon – whether originating from inorganic sources (such as sulphates and sulphites) or organic ones (such as dietary amino acids and host-derived mucins) – can affect certain bacterial groups, including sulphate-reducing bacteria. These microbes are natural components of the gut microbiota and have been associated with the development of intestinal conditions like IBD, IBS, and colorectal cancer [61].

– The way bile acids are distributed throughout the small and large intestine can likewise influence the dynamics of the gut bacterial community, as extensively discussed in the literature [62,63].

– The influence of the host immune system mainly involves organizing and segregating bacterial populations to prevent opportunistic penetration of host tissues, while effects targeting specific species are less likely because of the extensive functional redundancy present within the microbiota [54,64–67]. The antimicrobials (both host-derived and administered) play a key role in shaping the gut microbiota.

– Numerous environmental factors have been linked to shaping the microbiota, including geographic location, surgical history, smoking, depression, and whether a person lives in an urban or rural setting [68–71].

Single-celled eukaryotes are an important and heterogeneous component of the human intestinal

microbiota. Their categorization as pathogenic, commensal, or beneficial is a major discussion point because many species exhibit a spectrum of effects, from causing disease to contributing to a healthy gut by modulating the immune system. The well-known protist community in the human gut includes *Blastocystis*, *Dientamoeba fragilis*, *Giardia intestinalis, Entamoeba histolytica*, and *Cryptosporidium* spp. The last three species usually contribute to acute gastroenteritis and diarrheal diseases worldwide [72]. However, several intestinal protozoa species, such as *Endolimax nana*, *Iodamoeba butschlii*, and *Chilomastix mesnili*, are not pathogens and might be beneficial inhabitants of the intestine [73]. Retrospective studies on *D. fragilis* and *Blastocystis* show conflicting results regarding their role in gastrointestinal diseases [74,75]. Moreover, recent investigations using technologies like metagenomics and other omics approaches have revealed that the gut microbiota significantly influences the pathogenicity of intestinal protozoa, and conversely, these protozoa can impact the composition of the bacterial community.

The adverse associations of *Blastocystis* on gut microbiota

Blastocystis colonization is thought to be related to changes in the gut bacterial microbiota [76]. Recent studies indicate that *Blastocystis* infection may be associated with alterations in the abundances of both beneficial and harmful intestinal bacteria. Research on the relationship between asymptomatic *Blastocystis* infection and intestinal bacterial composition is ongoing, although this association still needs to be fully understood [13,77, 78].

Behboud et al. reported that individuals carrying *Blastocystis* showed significantly increased mean relative abundances of the beneficial groups *Bifidobacterium* and *Lactobacillus*/*Enterococcus*, as well as of the harmful taxa *Peptostreptococcus* productus and *Escherichia coli*. In contrast, the relative levels of *Bacteroides fragilis* (*B. fragilis*) and *Enterococcus* spp. were markedly reduced compared with the control group [77]. Di Cristanziano et al. found that patients infected with *Blastocystis* consistently harboured bacterial genera associated with a healthy gut, such as the *Eubacterium rectale* and *Eubacterium coprostanoligenes* groups, along with *Roseburia* and *Succinivibrio*. However, the relative abundances of these taxa were uniformly lower than those observed in the control group [78].

It is suggested that ST7 has been involved in promoting gut dysbiosis [80,81]. Moreover, studies have shown that *Blastocystis* ST7 can disturb the microbial equilibrium of the gut, notably by decreasing *Bifidobacterium longum* (*B. longum*) and *Lactobacillus brevis* (*L. brevis*). The researchers demonstrated that ST7 selectively suppressed the growth of beneficial commensals such as *Bifidobacterium* and *Lactobacillus* [19], while increasing the levels of sulphate-reducing bacteria like *Desulfovibrio* in a DSS-induced colitis mouse model [82]. *Desulfovibrio* interacts with epithelial cells of the intestine, triggers apoptosis, and intensifies gut inflammation, worsening DSS-induced colitis [83,84]. Furthermore, microbiota profiling of patients with diarrhea revealed that ST7 was the dominant subtype, and its presence correlated with higher levels of *Escherichia–Shigella*, a bacterial group frequently observed in individuals with IBD [81,85]. Additionally, ST1 has been associated with pathogenicity in two contexts: (1) diarrhea-predominant irritable bowel syndrome (IBS-D) in Indonesian adolescents and (2) colorectal carcinoma [86,87].

Blastocystis may influence the gut–brain axis by altering the gut microbial composition, which in turn affects gut-brain communication. Research has shown that in a rat model, chronic colonization with *Blastocystis* ST4 is associated with colonic hypersensitivity and behavioral alterations, such as increased anxiety- and depression-like behaviors. These behavioral changes were associated with a decreased abundance of beneficial bacteria (*Clostridium*, *Pseudomonas*, and *Rhodoplanes*) and an increased abundance of potentially harmful or opportunistic bacteria (*Anaerovorax, Oscillospira*, and *Parabacteroides*). This imbalance can lead to inflammation and metabolic issues, which in turn can alter behavior through the gut-brain axis [88]. Furthermore, *Blastocystis* infection may disrupt gut microbial metabolite profiles. A significant reduction in the levels of SCFAs, especially acetate and propionate, was observed in infected rats [88]. SCFAs are crucial mediators of the gut–brain axis, influencing the development and progression of neurodegenerative diseases [89].

Blastocystis may influence both the composition and diversity of gut microbiota, causing dysbiosis, which has been proposed as a contributing factor to IBS [90]. The presence of protist may be associated

with a decreased *Firmicutes/Bacteroidetes* ratio in individuals with metabolic disorders compared to healthy controls [91]. Some studies suggest a synergistic relationship between *Blastocystis* and *Clostridium difficile* in patients with diarrhea, where their co-detection may be linked to more severe gastrointestinal symptoms [92,93].

The beneficial associations of *Blastocystis* on gut microbiota

Many studies, including Audebert et al., report that colonization with *Blastocystis* is associated with a higher diversity of the human intestinal bacterial microbiota, characterized by a greater abundance of Clostridia and a lower abundance of Enterobacteriaceae. These findings suggest that *Blastocystis* colonization is often associated with a healthy gut microbiota rather than dysbiosis [94]. A study found that healthy children colonized with *Blastocystis* had higher gut microbiota diversity and a greater proportion of beneficial bacteria compared to those who were not colonized with the organism. This suggests that *Blastocystis* colonization is associated with a healthy gut in this population and may even be beneficial, as higher diversity is considered a hallmark of a healthy gut [95,96].

Even et al. found that *Blastocystis* colonization significantly impacted higher-level taxonomic diversity in the gut microbiota, and also noted higher relative abundances of *Ruminococcaceae* and *Clostridiales* in colonized individuals. Interestingly, it has been observed that patients with multiple *Blastocystis* STs have a greater diversity of gut bacteria compared to those with a single subtype [97]. The 2025 study by Castañeda et al. found that individuals positive for the protist showed distinct gut bacterial and eukaryotic profiles compared to those without the organism [98]. The research suggests that *Blastocystis* colonization is associated with increased microbial diversity and specific bacterial taxa, including *Bacteroides*, *Prevotella*, *Oscillibacter*, *Faecalibacterium*, and *Alistipes*. This correlation indicates that *Blastocystis* may act as an ecosystem engineer, contributing to a more diverse and potentially more stable gut microbial community. The study also showed that individuals colonized with *Blastocystis* were found to have a higher prevalence of the bacteria *Bacteroides uniformis*, *Oscillibacter* sp., and *Prevotella copri*. *Blastocystis* colonization may increase the abundance of short-chain fatty acid (SCFA)-producing bacteria, leading to beneficial microbial functions that contribute to gut health. Machine learning models, including random forest classifiers, supported findings on the beneficial effect of the protist, identifying *Faecalibacterium* and *Bacteroides* as predictors of *Blastocystis* colonization. The anti-inflammatory properties of *Faecalibacterium prausnitzii* and its role in maintaining gut health may contribute to the observed microbiota stability in the presence of *Blastocystis*. Similarly, the function of *Bacteroides ovatus* in breaking down complex carbohydrates supports a diverse and balanced microbial community. This indicates *Blastocystis* colonization could promote beneficial microbes for gut homeostasis [99–101].

Recent research has identified that higher *Blastocystis* colonization intensity is associated with an increased abundance of taxa such as *Alistipes* and *Lachnospira*, which are known to have anti-inflammatory properties and play a role in maintaining gut homeostasis [102–104]. Additionally, lower intensities of *Blastocystis* colonization are associated with a higher abundance of beneficial bacteria such as *Akkermansia*. *Akkermansia muciniphila* is known to help maintain the gut's protective mucus layer, improve metabolic health, and is considered a marker for a healthy gut microbiota. These studies suggest that the interaction between *Blastocystis* and the microbiota is complex and might be modulated by the protist's intensity during the gut colonization [105].

Current research suggests that *Blastocystis* ST1 colonization has beneficial effects on gut health by promoting a beneficial microbial ecology, which in turn increases short-chain fatty acid (SCFA) production [106]. In addition, the researchers support the statement indicating a positive correlation between *Blastocystis* colonization and *Akkermansia muciniphila*, a key bacterial species in the human gut microbiota [107,108]. In mouse models of colitis, the administration of *Akkermansia muciniphila* has been shown to reduce the severity of dextran sulfate sodium (DSS)-induced colitis. Its protective effects are linked to strengthening the intestinal barrier, decreasing inflammation, and restoring a balanced gut microbiota [105,109]. Notably, *Blastocystis* ST1 colonization markedly increased the abundance of the genus *Akkermansia*, and ST1-colonized mice showed reduced severity of DSS-induced colitis [106].

A study on gut eukaryotic composition found that *Blastocystis*-positive individuals had a higher

abundance of *Entamoeba coli*, while *Blastocystis*-negative individuals had a higher abundance of opportunistic fungi, such as *Candida albicans*. This suggests that the presence of *Blastocystis* is associated with a different eukaryotic microbial profile compared to its absence, and that *Blastocystis* colonization is linked to distinct eukaryotic communities in the gut. The fungal communities are altered in irritable bowel syndrome (IBS), and studies show an increased presence of the class Saccharomycetes and specific species like *Candida albicans* and *Saccharomyces cerevisiae* [110]. Furthermore, the ability of *Candida albicans* to act as both a harmless commensal and a life-threatening pathogen is an example of opportunistic infection. In a healthy host, the gut's resident bacteria and a strong immune system keep *C. albicans* in check, maintaining a state of balance. In an immunocompromised host, however, this balance is disturbed, allowing the fungus to overgrow, become more virulent, breach the mucosal barrier, and enter the bloodstream [111,112]. Additionally, *C. albicans* can contribute to the development of colitis and Crohn's disease [113].

A large-scale metagenomics study indicated that *Blastocystis* colonization can be associated with a healthier gut microbiota by enriching beneficial bacteria like *Firmicutes* and *Clostridiales* and simultaneously decreasing the abundance of *Bacteroides*, a genus often linked to dysbiosis [28]. In a mouse model of colitis *Blastocystis* ST4 increased the abundance of beneficial, short-chain fatty acid (SCFA)-producing bacteria (*Clostridia*), leading to improved recovery and reduced damage to the colon [114]. It has also been demonstrated that while *Blastocystis* ST4 colonization it inhibits the growth of the pathogenic *Bacteroides vulgatus* when co-incubated with other intestinal bacteria [115]. Billy and colleagues have reported that long-term colonization with *Blastocystis* ST3 in a rat model of colitis altered the gut's microbial composition without reducing bacterial richness and promoted a faster recovery from dinitrobenzene sulphonic acid-induced colitis [76]. The studies suggest that *Blastocystis* ST3 may promote microbial ecosystem stability and aid in the recovery of the gut lining during inflammation.

Changes in the gut microbiota's composition and the production of microbial metabolites are strongly linked to metabolic dysregulation and diseases like obesity, type 2 diabetes, and cardiovascular issues [116]. Research suggests *Blastocystis* may play a beneficial role in metabolic health by being associated with lower body mass index (BMI), improved glucose metabolism, and favorable lipid profiles, which are often linked to healthier diets [28,6,117,118]. This suggests *Blastocystis* may play a role in regulating body weight and fatness, potentially by influencing gut microbial metabolites like short-chain fatty acids (SCFAs), which can reduce systemic inflammation and improve insulin sensitivity. Linear discriminant analysis by Kim et al., revealed that the *Blastocystis*-positive group had higher levels of bacteria such as *Faecalibacterium*, *Prevotella* 9, Rikenellaceae, Acidaminococcaceae, *Phascolarctobacterium* and Muribaculaceae, while the *Blastocystis*-negative group showed higher abundance of the *Enterococcus* genus and its related families and orders, such as *Enterococcus hirae*, *Enterococcus faecalis*, *Enterococcus durans*, *Enterococcaceae*, *Lactobacillales*, and *Bacilli*. This suggests a potential link between the presence of *Blastocystis* and an enrichment of certain gut microbes, with *Enterococcus* species being characteristic of a *Blastocystis*-negative state [119]. Additionally, in another study, at the phylum level, Firmicutes and Bacteroidetes were enriched in *Blastocystis* carriers, while *Proteobacteria* were enriched in non-carriers [120]. The genera *Prevotella*, *Faecalibacterium*, *Flavonifracter*, *Clostridium*, *Succinivibrio*, and *Oscillibacter* were enriched in protist carriers, and *Escherichia, Bacteroides, Klebsiella*, and *Pseudomonas* were enriched in non-carriers. *Blastocystis*-positive individuals appear to have gut microbiota composition associated with eubiosis, while those with *Blastocystis*-negative stools frequently exhibit a microbiota similar to dysbiosis [120].

The effect of gut microbiota on *Blastocystis*

Recent research shows the human gut microbiota is crucial in how intestinal protozoa affect a person's health by influencing the host's immune response and altering the balance between parasitic and commensal states. It is providing new insights into how factors such as bacterial composition and diversity can determine whether an infection like *Blastocystis* or other eukaryotes remains asymptomatic or leads to disease, and is opening doors for novel therapeutic strategies.

The pathogenicity of the common gut protozoan *Blastocystis* is highly dependent on its interactions

with the host gut microbiota. The research shows that *Blastocystis* isolates from asymptomatic individuals can transition to a more pathogenic state when co-cultured with bacterial suspensions from symptomatic individuals. The transition is accompanied by increased protease activity, a key virulence agent, which highlights the interaction between *Blastocystis* and the gut microbiota [20]. Jeffery et al.'s study revealed that *Blastocystis* was significantly less prevalent in the antibiotic-treated group compared to non-antibiotic treated controls. The explanation for the observed differences in *Blastocystis* prevalence, is that the antibiotic-induced disruption of the gut microbiota negatively affects protist. Antibiotics, while targeting bacteria, can cause „collateral damage" to beneficial bacteria, and *Blastocystis* may be dependent on this disrupted bacterial community for survival [121]. This dependence can lead to secondary extinctions, making *Blastocystis* less prevalent in antibiotic-treated individuals.

Rajamanikam et al. demonstrated the influence of bacteria on *Blastocystis* pathogenicity [20]. In their experiment, *Blastocystis* isolated from a symptomatic individual was co-cultured with a bacterial suspension of *Blastocystis* from an asymptomatic individual. The protist demonstrated increased growth and reduced potential pathogenic expressions. For the first time, the study results demonstrate evidence on the influential role of gut microbiota in altering the characteristics of the parasite. Their study found that asymptomatic *Blastocystis* in the gut can become pathogenic due to the influence of the surrounding intestinal microbiota, showing that the same protist subtype can exhibit different behaviors depending on its microbial environment [20].

Comparative genomic analysis reveals *Blastocystis* has evolved through gene loss, gene gain via horizontal transfer, and changes in genome structure to adapt to diverse animal guts [122]. Genomic streamlining is the process by which organisms, especially symbiotic and parasitic ones, reduce their genome size by eliminating non-essential DNA, leading to faster replication, increased gene density, and more efficient resource use [123,124]. Lind et al. found evidence consistent with host adaptation within *Blastocystis*. A *Blastocystis* strain from herbivorous tortoises has carbohydrate-digesting enzymes which does not occur in other *Blastocystis* isolates because it acquired some through horizontal gene transfer from bacteria, including bacteria that also colonize the tortoise gut [120]. The discovery of plant-specific carbohydrate digesting enzymes in some of *Blastocystis* subtypes suggests that, like some ciliates and many gut bacteria, protists may ferment plant carbohydrates [125]. This metabolic capability is significant for energy production and aligns with the roles of other gut microbes like ciliates and bacteria.

Conclusions

Blastocystis colonization is related to changes in the gut bacterial microbiota. The studies indicate evidence that *Blastocystis* infection may be associated with alterations in the abundances of both beneficial and harmful intestinal bacteria. Moreover, the gut microbiota significantly influences the pathogenicity of the protist. *Blastocystis* is native to a host's microbiota but can promote disease under certain conditions in the host, including gut dysbiosis and reactions of the host's immune system as well as the protist subtype. Research on the relationship between asymptomatic *Blastocystis* infection and intestinal bacterial diversity and richness is ongoing, although this association still needs to be fully understood.

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