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RESEARCH ARTICLE

Characteristics and Dynamic Changes of Gut Microbiota in Cats with Colitis

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Colitis is a significant factor that poses a threat to animal health and welfare, and its association with the gut microbiota has been extensively studied. However, there is limited information available on the changes in gut microbial composition in cats with colitis. Here, we investigated the gut microbial composition and variability of cats during colitis. Our findings indicated that *Firmicutes*, *Actinobacteriota*, and *Proteobacteria* were abundant in all the samples. However, there were significant changes in the gut microbial diversity and composition. Analysis of microbial diversity revealed a significant decrease in gut microbial alpha diversity in cats with colitis, along with notable changes in the gut microbial structure. Bacterial taxonomic analysis demonstrated an obvious increase in the relative abundance of 1 phylum (*Firmicutes*) and 10 genera (*Acidithiobacillus*, *Candidatus_Bacilloplasma*, *Shewanella*, *Ferrimicrobium*, *Sellimonas*, *unclassified_Butyricicoccaceae*, *V9D2013_group*, *unclassified_Euzebyaceae*, *UCG_002* and *Providencia*), while the relative abundance of 24 phyla and 475 genera decreased significantly during colitis. Remarkably, 11 phyla and 370 genera completely disappeared among the reduced taxa. Overall, this study demonstrates that colitis can lead to significant alterations in the diversity and composition of the gut microbiota in cats. Moreover, these findings contribute to our understanding of the underlying causes of colitis from the perspective of the gut microbiota and provide a theoretical basis for the development of prevention and treatment strategies.

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INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic inflammatory gastrointestinal disease that occurs in the colorectal mucosa, characterized by intestinal inflammation, rectal bleeding, diarrhea, and weight loss (Ungaro *et al*., 2017). Early investigations revealed that the direct and indirect medical expenses associated with colitis in the United States and Europe exceed $20 billion annually, affecting approximately 3.6 million individuals. Additionally, colitis is also prevalent in animals, particularly cats, dogs, and cattle, seriously threatening their welfare, production performance, and overall health (Waite *et al*., 2023). Although the exact cause of IBD remains unclear, studies have found a close relationship between gut microbial dysbiosis, environmental changes, genetic susceptibility, and IBD (Guo *et al*., 2020). Among them, the gut microbial dysbiosis has been increasingly identified as a significant driving force in the development and persistence of IBD.

The intestine is the primary organ responsible for digestion and absorption, and it is also home to hundreds of trillions of microorganisms (Li *et al*., 2021; Liao *et al*., 2022). These microorganisms, collectively known as gut microbiota, participate in multiple important physiological functions and have a significant impact on host health (Li *et al*., 2023). Research indicated that gut microbiota could positively regulate host health and intestinal homeostasis by producing beneficial metabolites (Zong *et al*., 2020). Additionally, gut microbiota also contribute to food digestion and absorption, as well as nutrient metabolism, through the fermentation of dietary or undigested carbohydrates from the host (Meng *et al*., 2020). Recent studies on gut microbiota have also highlighted their significant roles in maintaining intestinal permeability, facilitating immune system development, and enhancing resistance against pathogenic bacterial infections (Shi *et al*., 2021). However, many endogenous and exogenous factors including diet, age, disease, heavy metals, and pesticides can cause distinct changes in the gut microbial composition (Wu *et al*., 2022; Wu *et al*., 2024). Numerous

studies demonstrated that gut microbial dysbiosis inevitably injured intestinal function and jeopardized the intestinal health (Li *et al*., 2019). Notably, gut microbial dysbiosis can also have negative effects on other organs such as the liver, kidney, and brain, resulting in systemic symptoms (Xu *et al*., 2022). Therefore, the systematic study of the gut microbiota is essential for maintaining host health and understanding the pathogenesis of gastrointestinal diseases.

According to statistics, there are approximately 500 million pet cats in the world, involving 100 different breeds. Moreover, the number of pet cats continues to rise, which drives the development of related industries such as pet medical care, pet food, and pet grooming. These cats have become integral members of families, so any disease that threatens their health should not be overlooked. However, multiple factors including stress response, food and drug allergies, bacterial and parasitic infections all contribute to the high incidence of colitis in cats (Cardenas *et al*., 2022). Currently, colitis has been recognized as one of the important factors affecting the health and development of cats. Previous studies involving dogs, pigs, and mice have demonstrated the importance of gut microbial dysbiosis in the development of colitis (Liu *et al*., 2023). However, the potential relationship between colitis and gut microbiota in cats remains to be further investigated. Therefore, this study aimed to explore gut microbial changes of cats with colitis.

MATERIALS AND METHODS

Sample acquisition: In this study, a total of 14 cats were selected from the United Pet Hospital in Wuhan, China for sample collection and the sample group comprised of 7 healthy cats (CON) and 7 cats with colitis (COL). To minimize the influence of other factors on the gut microbiota, these cats of similar age and immune background were chosen. The health status of all cats was determined by professional veterinarians through observation and diagnosis and cats with colitis were not given any medical treatment prior to sample collection. The healthy cats and cats with colitis were kept in separate areas to prevent infection and sample contamination. A sterile swab was used to collect rectal samples by rotating it. Subsequently, fecal samples were immediately subsampled from the mid-section to minimize contamination. These samples were then snap-frozen using liquid nitrogen and stored at -80°C for DNA extraction and amplicon sequencing.

16S rDNA amplicon sequencing: The specific steps of DNA extraction and amplicon sequencing were referred to previous research (Li *et al*., 2021).

RESULTS

Data acquisition and analysis: In this study, we performed amplicon sequencing on acquired fecal samples to explore the gut microbial changes in cats with colitis. Results indicated that a total of 1,120,404 (CON = 560,446, COL = 559,958) original sequences were generated in the CON and COL groups, with an average of 80,028 (varying from 79,853 and 80,159) reads per sample (Table 1). After quality evaluation of these original sequences, 873,729 (CON = 419,370, COL = 454,359) effective sequences were collected from both groups, with an effective rate approximately 78%. Moreover, results of rarefaction and rank abundance curves analysis show that all the curves gradually saturate, indicating that almost all bacterial taxa in the gut microbiota are identified (Fig. 1A, B, C). According to the 97% nucleotide-sequence similarity, these effective sequences generated by amplicon sequencing were clustered into 13,880 (CON = 12,783, COL = 1,250) OTUs, ranging from 178 to 4,052 OTUs per sample (Fig. 1D, E). Among these recognized OTUs, 153 OTUs were shared in the CON and COL groups, accounting for approximately 1.10% of the OTUs composition.

Table 1: Statistics and quality assessment of sequencing data of samples from the CON and COL groups.

Sample	Raw Reads	Clean Reads	Denoised Reads	Merged Reads	Non-chimeric Reads	Effective (%)
CON1	80148	74697	73836	66433	59997	74.85
CON2	80029	74480	73803	67474	62233	77.76
CON3	80007	75081	73480	58319	48739	60.91
CON4	79945	74343	73310	65109	57496	71.91
CON5	80159	74711	73797	65376	56265	70.19
CON6	79853	71583	71274	69063	66528	83.31
CON7	80305	72439	72219	70397	68112	84.81
COL1	79988	71828	71722	70977	65636	82.05
COL2	80039	72555	72358	69481	57550	71.90
COL3	79957	72188	72123	71531	68385	85.52
COL4	79973	70477	70412	70048	69412	86.79
COL5	80128	72062	71978	71471	66212	82.63
COL6	79858	71801	71688	70033	61369	76.84
COL7	80015	72254	72053	70611	65795	82.22

Analysis of microbial diversity index associated with colitis: Good's coverage estimates showed that over 99% of the bacterial phenotypes were found in all samples, demonstrating a satisfactory sequencing depth (Fig. 2A). The comparative analysis results between the CON and COL groups indicated that there were statistically significant differences in the Chao1 (2144.53 ± 426.72 versus 229.83 ± 15.08, P = 0.0041), ACE (2150.59 ± 427.20 versus 233.54 ± 15.39, P = 0.0041) and Shannon (8.04 ± 0.68 versus 4.14 ± 0.43, P = 0.00067) indices, demonstrating that colitis dramatically decreased the gut microbial diversity and abundance (Fig. 2B, C, D). Furthermore, results of beta diversity analysis indicated that the samples from the CON and COL groups exhibited a tendency to separation (Fig. 2E, F). This finding implies that there is substantial distinction in the principal constituents of gut microbiota.

Changes in microbial composition associated with colitis: Results indicated that there were 48 phyla recognized from both groups, varying from 14 to 42 phyla per sample (Table 2). The phyla *Firmicutes* (35.04%, 59.26%), *Actinobacteriota* (23.93%, 16.30%) and *Proteobacteria* (11.66%, 17.34%) were the three most dominant phyla in CON and COL groups, accounting for over 70% of the bacterial composition (Fig. 3A). Other phyla such as *unclassified_Bacteria* (3.77%, 0.067%), *Gemmatimonadota* (2.03%, 0.014%), *Methylomirabilota* (2.00%, 0.0022%), *Myxococcota* (1.75%, 0.0070%) and

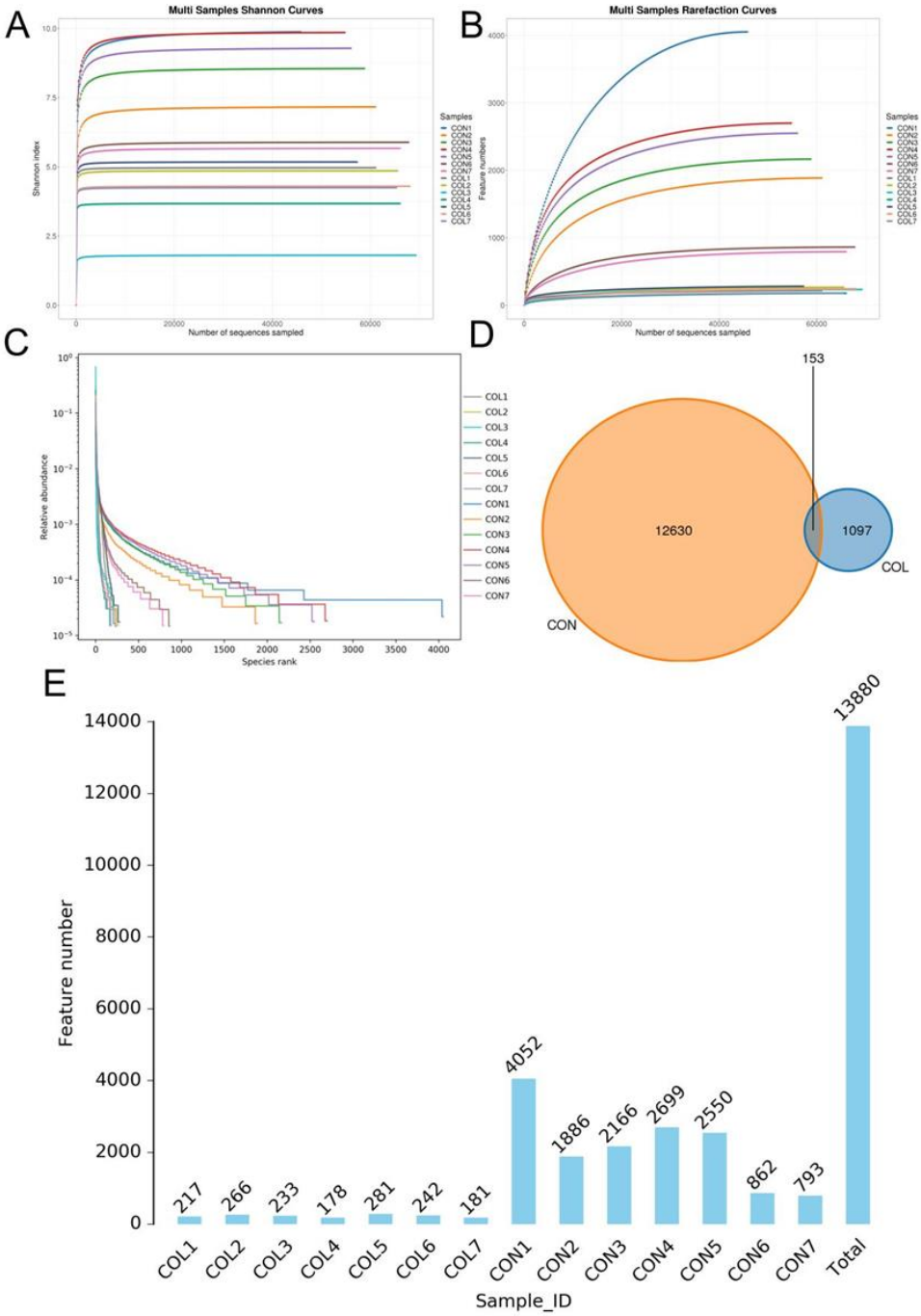

Fig. 1: Analysis of sequencing depth and OTUs quantity. Rarefaction curves (A, B) and rank abundance curves (C) indicated the sequencing depth and uniformity. D: In the Venn diagram, orange and blue represent the number of OTUs in the CON and COL, respectively. E: Histogram of OTUs distribution.

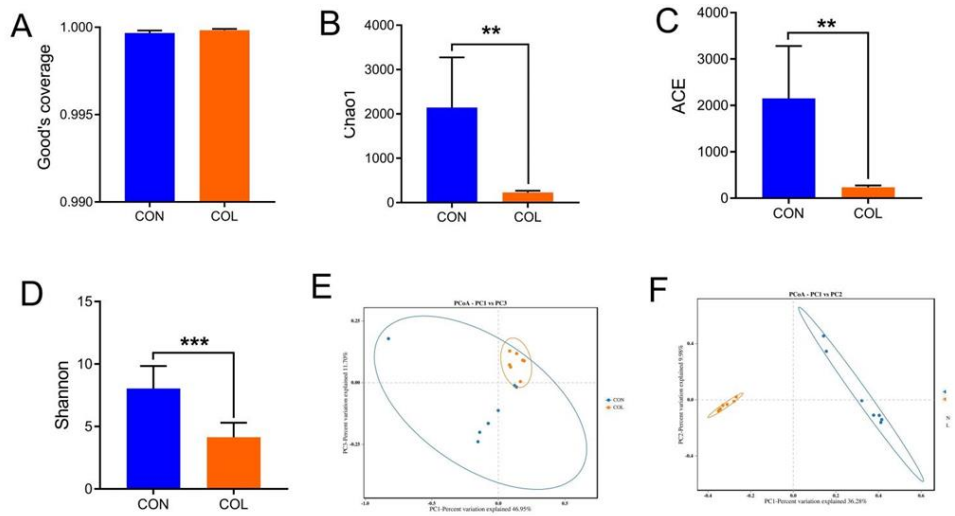

Fig. 2: Effects of colitis on gut microbial alpha and beta diversities in cats.

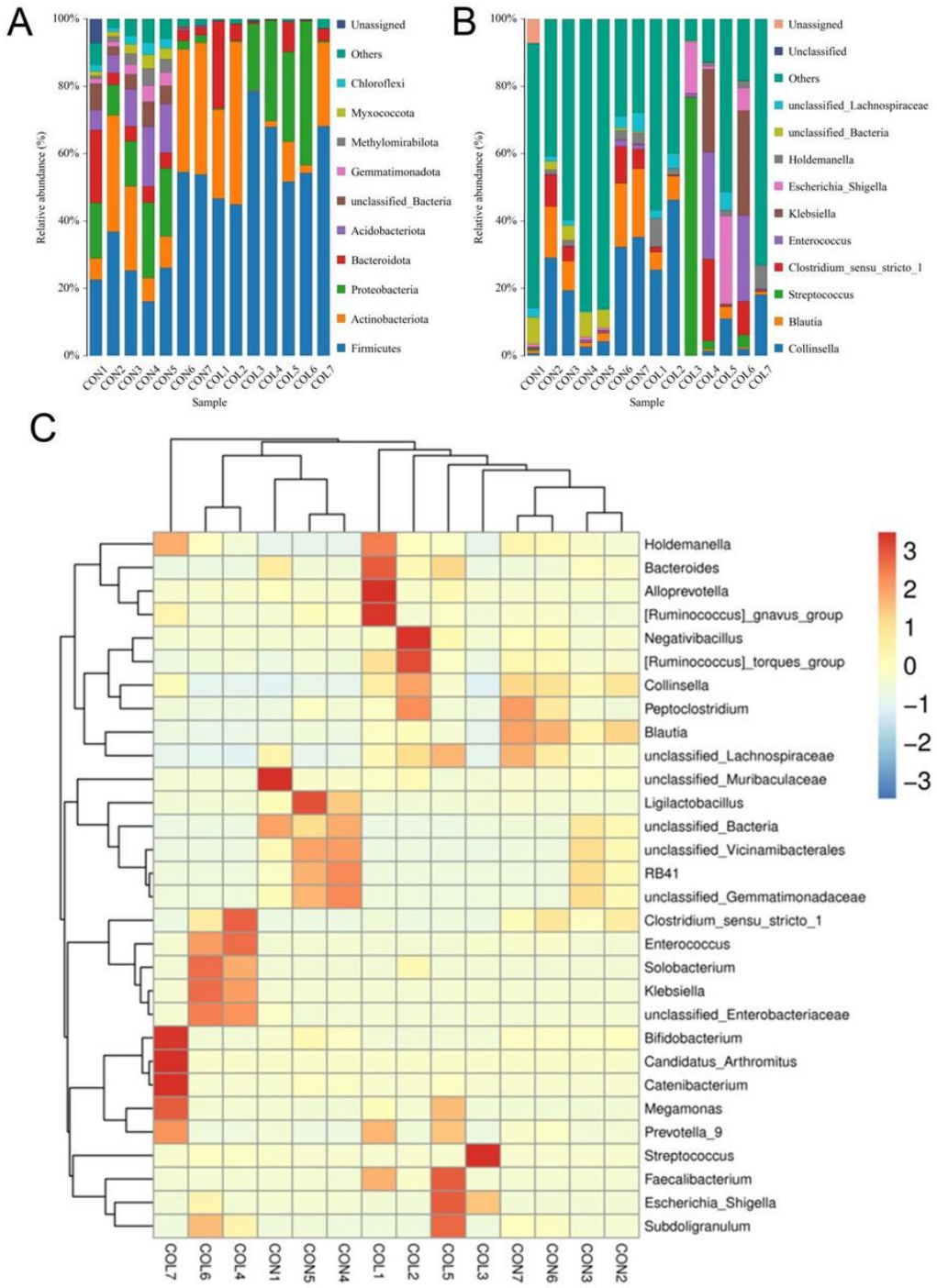

Fig. 3: The species and abundance distribution of dominant bacteria at the phylum (A) and genus (B) levels. C: Clustering heat map of bacterial genera.

Table 2: Statistics of bacterial species at different classification levels in samples from the CON and COL groups.

Sample	Kingdom	Phylum	Class	Order	Family	Genus
CON1	1	33	78	199	353	556
CON2	1	31	75	196	334	520
CON3	2	42	102	249	442	788
CON4	1	33	82	218	373	589
CON5	2	34	84	226	382	582
CON6	2	30	59	137	225	391
CON7	1	27	57	147	250	423
COL1	1	15	23	49	81	117
COL2	1	14	20	39	71	121
COL3	2	21	30	69	117	164
COL4	1	19	33	73	108	150
COL5	1	16	27	61	86	119
COL6	1	15	23	42	71	111
COL7	1	15	27	55	82	129
Total	2	48	120	324	628	1283

Chloroflexi (1.71%, 0.0072%) in the CON and COL groups were detected in low abundances. To further explore the effects of colitis on gut microbial composition, 1,283 genera were identified from both groups. Among these genera, *Collinsella* (19.13%), *Blautia* (10.51%) and *Clostridium_sensu_stricto_1* (4.73%) were abundantly found in the CON group, accounting for more than 34% of total bacterial composition (Fig. 3B). On the other hand, *Collinsella* (14.67%) was the most dominant genus in the COL group, followed by *Streptococcus* (12.69%) and *Enterococcus* (8.68%). Furthermore, clustering heatmaps can be used to visualize the type and abundance distributions of dominant bacteria between both groups, as well as the changes in gut microbial composition during colitis (Fig. 3C).

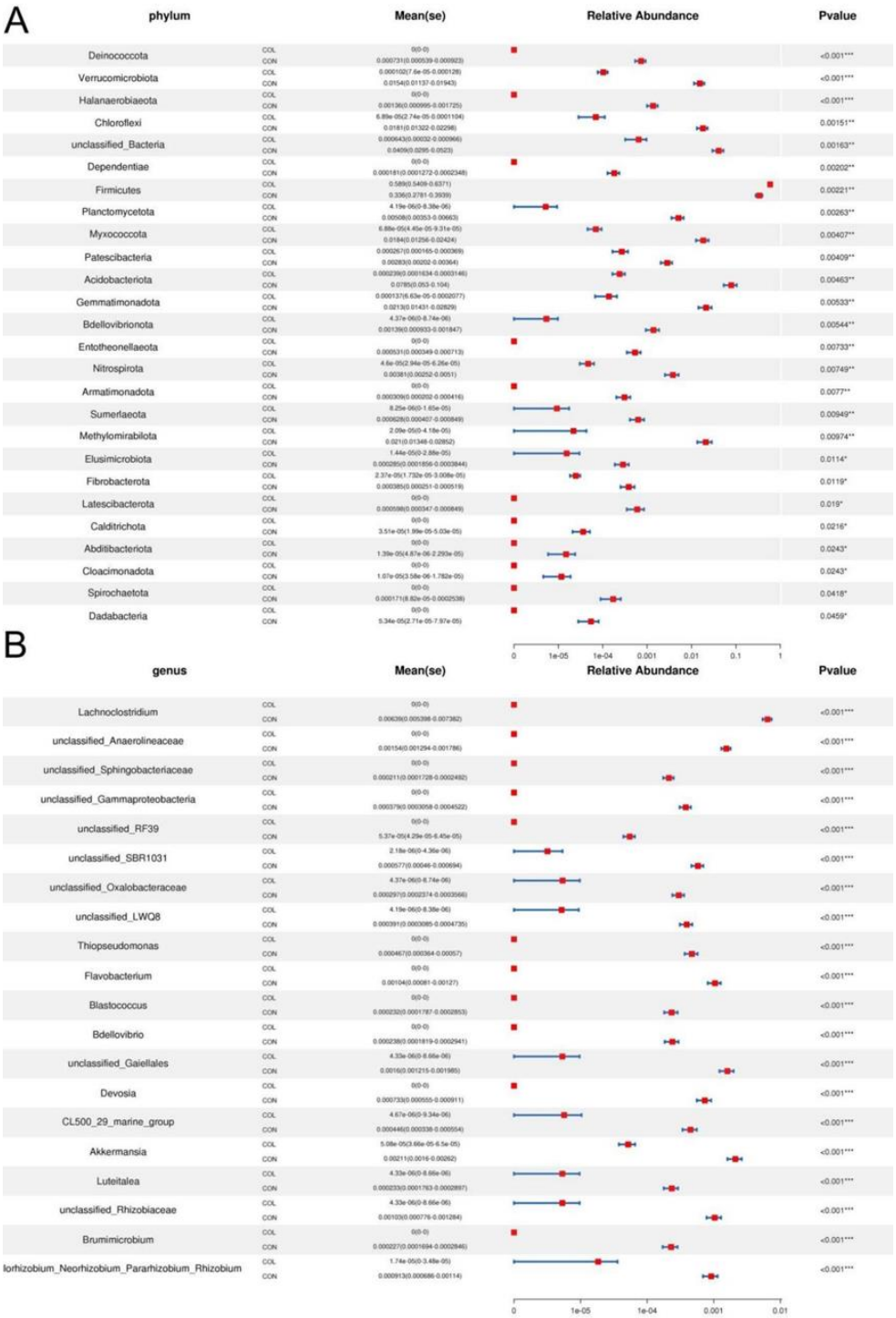

Fig. 4: Statistics of bacterial differences between the CON and COL groups at the phylum (A) and genus (B) levels. This figure shows only part of the results.

At the phylum level, the COL group indicated significantly higher abundances of *Firmicutes*, whereas the CON group enriched for *Deinococcota*, *Verrucomicrobiota*, *Halanaerobiaeota*, *Chloroflexi*, *unclassified_Bacteria*, *Dependentiae*, *Planctomycetota*, *Myxococcota*, *Patescibacteria*, *Acidobacteriota*, *Gemmatimonadota*, *Bdellovibrionota*, *Entotheonellaeota*, *Nitrospirota*, *Armatimonadota*, *Sumerlaeota*, *Methylomirabilota*, *Elusimicrobiota*, *Fibrobacterota*, *Latescibacterota*, *Calditrichota*, *Abditibacteriota*, *Cloacimonadota*, *Spirochaetota*, and *Dadabacteria* (Fig. 4A, 4B). Additionally, we also detected that 485 genera were markedly different between the CON and COL groups. Among them, the proportions of 10 genera (*Acidithiobacillus*, *Candidatus_Bacilloplasma*, *Shewanella*, *Ferrimicrobium*, *Sellimonas*, *unclassified_Butyricicoccaceae*, *V9D2013_group*, *unclassified_Euzebyaceae*, *UCG_002* and *Providencia*) dramatically increased, whereas the relative abundances of 475 (*Weissella*, *Lactobacillus*, *Lachnospiraceae_NC2004_group*, *Succinivibrio*, *Prevotella_7*, *Akkermansia*, *Lachnoclostridium*, *Aquicella*, *Bacillus*, *Cellvibrio*, *Gemmatimonas*, *Acidibacter*, *Streptomyces*, *Phaselicystis*, *Bradyrhizobium*, *Nocardioides*, *Steroidobacter*, *Rhizobacter*, *Bilophila*, *Legionella*, *Haliangium*, *Reyranella*, *Bosea*, and *Ohtaekwangia*, etc.) genera dramatically decreased during colitis. Notably, 370 bacterial genera in the gut microbiota such as *Thiopseudomonas*, *Flavobacterium*, *Blastococcus*, *Bdellovibrio*, *Brumimicrobium*, *Moheibacter*, *Sinibacillus*,

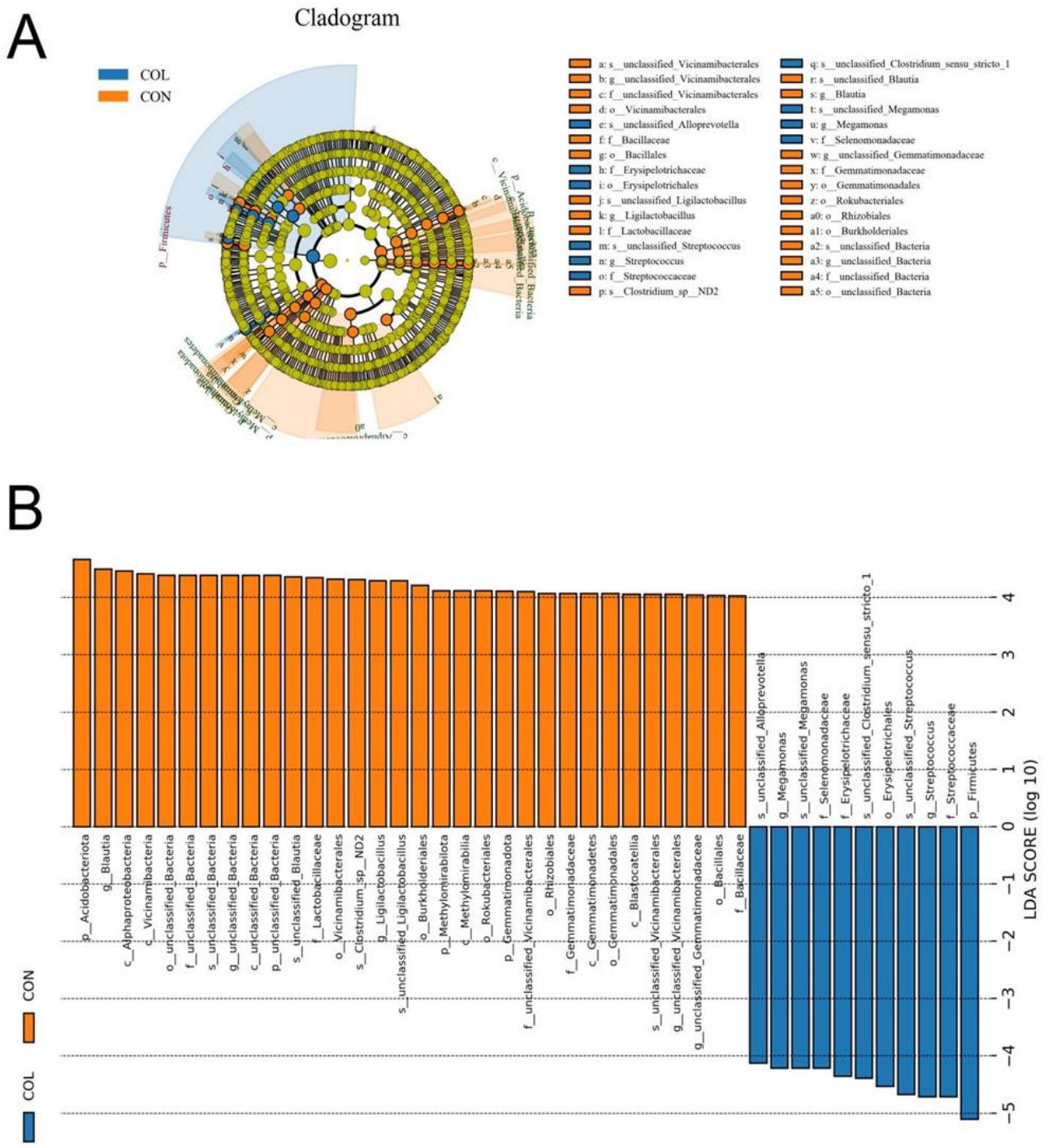

Fig. 5: Differential taxa in the gut microbiota of cats associated with colitis. A: LEfSe analyzes cladograms. B: LDA value distribution histogram

Pseudogracilibacillus, *Aequorivita*, *Truepera*, *Pseudofulvimonas*, *Tepidimicrobium*, *Marinimicrobium*, *Halocella*, *Fermentimonas*, *Pusillimonas*, *Alcanivorax*, *Sporocytophaga*, *Taibaiella*, *Georgenia*, *Aliidiomarina*, *Solirubrobacter*, *Marinospirillum*, *Puia*, *Kribbella*, *Herpetosiphon*, etc. even disappeared during colitis. To further identify differential taxa associated with colitis exposure, we also performed LEfSe analysis. We also observed that *Ligilactobacillus* in the CON group were dramatically preponderant than COL group, while the *Streptococcus* and *Megamonas* were lower (Fig. 5A, B).

Correlation network analysis: Bacillus was positively associated with P3OB_42 (0.921), unclassified_Bacteria (0.90), RB41 (0.90), unclassified_Gemmatimonadaceae (0.88), Ligilactobacillus (0.84), unclassified_ Vicinamibacterales (0.83) and unclassified_ Vicinamibacteraceae (0.83) (Fig. 6). Blautia was positively related to Collinsella (0.90). Libanicoccus was positively associated with Blautia (0.92) and unclassified_ Clostridia_UCG_014 (0.88). Sphingomonas was positively related to Bacillus (0.93), P3OB_42 (0.92), unclassified_ Vicinamibacterales (0.90), unclassified_ Bacteria (0.89), unclassified_Vicinamibacteraceae (0.89), RB41 (0.884601789), unclassified_Gemmatimonadaceae (0.85) and P3OB_42 (0.83).

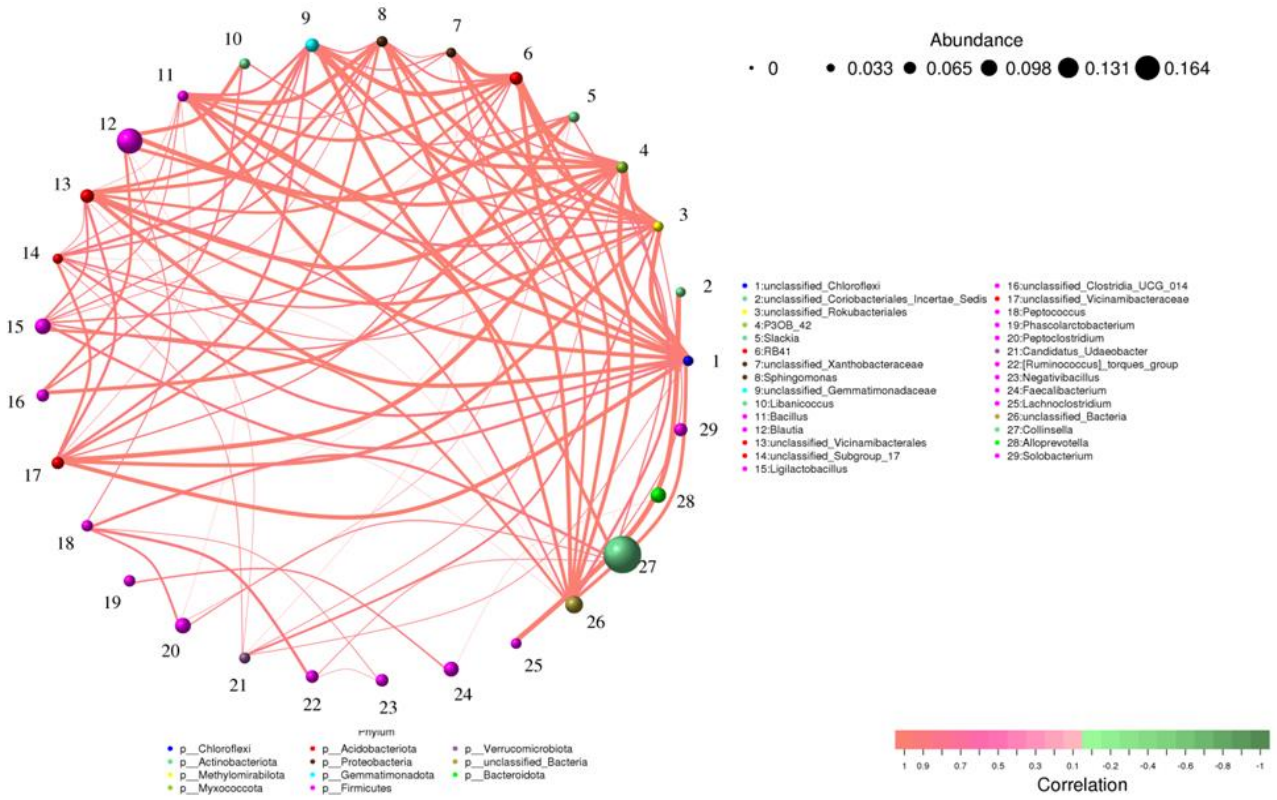

Fig. 6: Network diagram showing the correlations between bacteria. Positive correlations between different bacteria are represented by red lines.

DISCUSSION

Colitis is a significant global health issue that contributes to decreased animal productivity and increased mortality rates, posing a serious threat to animal welfare, livestock development, and the agricultural economy. However, controlling colitis is challenging due to various factors such as immunity, genetics, environment, and bacterial infections. The gut microbiota was demonstrated to play vital roles in immunity, intestinal barrier function, disease prevention and metabolism (Ma *et al*., 2020; Jabeen *et al*., 2023). Recent research has highlighted the significant role of gut microbiota in diarrhea, constipation, and intestinal cancer (Wang *et al*., 2022). Previous research on gut microbiota and colitis has primarily focused on horses, dogs, mice, and pigs, revealing the key role of gut microbiota in the development and treatment of colitis. However, the relationship between gut microbiota and colitis remains unclear. Here, our objective was to analyze and compare the gut microbial compositions and changes of healthy cats and cats with colitis.

Early investigations have shown that the gut microbiota is a dynamic system that undergoes physiological fluctuations due to various factors such as age, gender, and environment (Li *et al*., 2021). However, it has been demonstrated that some external stimuli, such as intestinal inflammation, antibiotics, and environmental pollutants can have an impact on the growth and survival of intestinal microorganisms, which may cause gut microbial dysbiosis and subsequently affect the hos health (Zhang *et al*., 2023). To investigate the potential negative effects, we hypothesized that colitis could induce gut microbial dysbiosis by altering the gut microbial diversity and abundance, thereby further compromising the host health. This study revealed that colitis significantly reduced the Chao1, ACE, and Shannon indices of the gut microbiota, indicating notable changes in the diversity and abundance of gut microbiota. Several previous studies have also reported negative effects of gut-related diseases on the host gut microbiota, which is consistent with the findings of this study. For instance, Li *et al*. (2021) demonstrated that diarrhea can reduce the gut microbial diversity and lead to gut microbial dysbiosis in giraffes. Similarly, Cao *et al*. (2021) found that colitis can cause gut microbial dysbiosis and injury intestinal barrier function of mice. The balanced gut microbiota is crucial for maintaining intestinal permeability and preventing the invasion of pathogens (Zhang *et al*., 2022). Conversely, the disturbance of gut microbiota can compromise the intestinal barrier function, making individuals more susceptible to pathogenic bacteria and resulting in various pathological consequences. Furthermore, the opportunistic pathogens can also become pathogenic during gut microbial dysbiosis, leading to increased morbidity in the host (Ding *et al*., 2023; Ren *et al*., 2023). It is worth noting that reduced diversity in gut microbiota is commonly observed in several chronic diseases (Yang *et al*., 2019). Therefore, hosts affected by colitis may be at a higher risk of experiencing additional complications and intestinal dysfunction.

In this study, we observed that *Firmicutes*, *Actinobacteriota* and *Proteobacteria* were the most prevalent bacterial phyla in the gut microbiota, regardless of health status. Moreover, these bacterial phyla have also been identified as the core flora in other mammals,

including pigs, cattle, and dogs, highlighting their significance in the intestinal microbial community system. Although the dominant bacterial phyla remained consistent, we noticed significant changes in the abundance of some bacterial phylum in the COL group compared to the CON group. Moreover, we also noticed changes in the types of the dominant bacterial genera in both groups. Early investigations have demonstrated that *Streptococcus* can cause severe infections such as sepsis, phlegmon, pneumonia, and trachitis (Catton *et al*., 2023). *Enterococcus* was demonstrated to result in life-threatening cardioperiostitis, cardioperiostitis and sepsis. Furthermore, the treatment of *Enterococcus* infection is often challenging as many antibiotics commonly used in the clinic have proven ineffective due to the presence of inherent and acquired resistance. In this study, the changes in the abundances of several bacterial phyla and dominant genera further support the detrimental impact of colitis on the gut microbiota.

Previous studies have demonstrated that colitis can have a profound impact on the composition and structure of the gut microbiota, leading to dysbiosis. Notably, variations in specific bacteria have been found to potentially correlate with the phenotype of the host. In this study, we observed significant reduction in certain intestinal bacteria such as *Weissella*, *Lactobacillus*, *Blautia*, *Herbinix*, *Lachnospiraceae_NC2004_group*, *Succinivibrio*, *Prevotella_7*, and *Akkermansia* in cats with colitis and these changes may disrupt intestinal homeostasis and function. As the acknowledged intestinal beneficial bacterium, *Akkermansia* was previously demonstrated to gradually decrease during the development of enteritis (Bian *et al*., 2019). Moreover, *Akkermansia* also participated in the positive regulation of metabolic balance and negatively associate with low-grade inflammation, obesity, diabetes and cardiometabolic disease. *Weissella* has long been considered as a potential beneficial bacterium due to the positive regulation of intestinal development, growth performance and disease resistance (Kavitake *et al*., 2020). *Lactobacillus*, primarily residing in the gastrointestinal tract, is an important and potentially beneficial bacterium due to its various physiological functions and health benefits for the host. Additionally, *Lactobacillus* can enhance the host's disease resistance by improving the intestinal environment, inhibiting the growth of harmful bacteria, and stimulating the immune system (Wang *et al*., 2022). Apart from these beneficial properties, it also demonstrates significant potential in areas such as maintaining gut microbial homeostasis, reducing oxidative stress, lower cholesterol and the treatment of chronic diarrhea and antibiotic-associated diarrhea. *Succinivibrio*, *Herbinix* and *Prevotell* have been demonstrated to possess a wide range of metabolic capabilities related to the utilization of carbohydrates (Mechelke *et al*., 2017). On the other hand, *Lachnospiraceae*, which primarily inhabit the intestines, are considered beneficial bacteria due to their role in metabolizing various carbohydrates and reducing inflammation (Zhao *et al*., 2017). The metabolism of carbohydrates by the gut microbiota is a crucial process that provides nutrients and energy to the host. Therefore, a decrease in the abundances of *Succinivibrio*, *Herbinix*, *Prevotell* and *Lachnospiraceae* can potentially impact host growth, development, and energy intake. Notably, the reduced abundance bacteria, such as *Akkermansia*, *Blautia*, *Lachnospiraceae*, *Weissella* and *Lactobacillus*, have been found to potentially produce short-chain fatty acids (SCFAs). SCFAs have multiple physiological functions and beneficial effects on host health. Research indicates that SCFAs play a positive role in regulating host metabolism, immune system, cancer prevention, inflammation relief, and cholesterol reduction (Mirzaei *et al*., 2021). Recent studies have also shown that SCFAs can regulate energy intake and appetite through the brain-gut axis, thereby reducing obesity-induced cardiovascular dysfunction and diabetes (Murugesan *et al*., 2018). Furthermore, SCFAs also contribute to maintaining gut microbial balance and intestinal permeability, playing an important role in intestinal homeostasis and function. Consistent with the current study, previous research has found that gastrointestinal disease like diarrhea and enteritis significantly reduces SCFAs-producing bacteria (Li *et al*., 2021). We hypothesized that colitis could affect the intestinal environment of cats, leading to a decrease in the survival of these bacteria.

Gut microbial dysbiosis is increasingly recognized as a significant contributor to several diseases. Research indicates that the microorganisms residing in the intestines can cooperate with each other in symbiotic, synergistic, or antagonistic ways to maintain intestinal homeostasis and balance the gut microbial ecosystem (Hu *et al*., 2016). Consequently, alterations in the population of certain bacteria in the intestine can directly or indirectly impact the functions of other bacteria, thereby aggravating gut microbial imbalance (Li *et al*., 2023). Our study also revealed noteworthy correlations between specific bacteria that experienced significant changes and other bacterial species. This study imparts a crucial message that colitis could directly or indirectly affect gut microbiota, potentially magnifying the impact of colitis on the gut microbiota.

Conclusion: In summary, this study dissected gut microbial changes of cat with colitis. The findings revealed significant alterations in the gut microbiota of cats with colitis, including a decrease in microbial diversity and abundance. Meanwhile, we also observed significant decreases in the abundances of numerous bacterial phyla and genera during colitis. These results enhance our understanding of feline gut microbiota and highlight the potential role of gut microbial dysbiosis in the development or worsening of colitis. Moreover, this study provides a theoretical foundation for addressing and managing feline colitis by targeting the gut microbiota.

Author contributions: QX and JL conceived and designed the experiments. QX wrote the manuscript. QX, YZ, ZZ, SG, QM contributed to the sample collection and reagents preparation. QM and JL revised the manuscript. All the authors reviewed the manuscript.

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Conflict of interest: The authors declare that they have no competing interests.

REFERENCES

Bian X, Wu W, Yang L, *et al*., 2019. Administration of Akkermansia muciniphila ameliorates dextran sulfate sodium-induced ulcerative colitis in mice. Front Microbiol 10: 2259.

Cao C, Zhu B, Liu Z, *et al*., 2021. An arabinogalactan from Lycium barbarum attenuates DSS-induced chronic colitis in C57BL/6J mice associated with the modulation of intestinal barrier function and gut microbiota. Food Funct 12: 9829-43.

Cardenas V, Lozzi R, Roman H, *et al*., 2022. Cat scratch lesions as a manifestation of chronic colitis due to spirochetosis. Rev Esp Enferm Dig 114: 693-94.

Catton E, Bonsor D, Herrera C, *et al*., 2023. Human CEACAM1 is targeted by a Streptococcus pyogenes adhesin implicated in puerperal sepsis pathogenesis. Nat Commun 14: 2275.

Ding X, Jiang H, Zhang R, *et al*., 2023. Comparative analysis of nasal microbial community between tibetan sheep with different ages. Pak Vet J 43: 723-731.

Guo X, Liu X and Hao J, 2020. Gut microbiota in ulcerative colitis: insights on pathogenesis and treatment. J Dig Dis 21: 147-59.

Hu J, Nie Y, Chen J, *et al*., 2016. Gradual Changes of Gut Microbiota in Weaned Miniature Piglets. Front Microbiol 7: 1727.

Jabeen Z, Bukhari SA, Malik SA, *et al*., 2023. Improved gut microbiota escalates muscle function rehabilitation and ameliorates oxidative stress following mechanically induced peripheral nerve injury in mice. Pak Vet J 43(4): 707-713.

Kavitake D, Devi P and Shetty P, 2020. Overview of exopolysaccharides produced by Weissella genus - A review. Int J Biol Macromol 164: 2964-73.

Li S, Qi Y, Chen L, *et al*., 2019. Effects of Panax ginseng polysaccharides on the gut microbiota in mice with antibiotic-associated diarrhea. Int J Biol Macromol 124: 931-37.

Li A, Liu B, Li F, *et al*., 2021. Integrated Bacterial and Fungal Diversity Analysis Reveals the Gut Microbial Alterations in Diarrheic Giraffes. Front Microbiol 12: 712092.

Li A, Wang Y, Kulyar M, *et al*., 2023. Environmental microplastics exposure decreases antioxidant ability, perturbs gut microbial homeostasis and metabolism in chicken. Sci Total Environ 856: 159089.

Liao J, Liu Y, Yi J, *et al*., 2022. Gut microbiota disturbance exaggerates battery wastewater-induced hepatotoxicity through a gut-liver axis. Sci Total Environ 809: 152188.

Liu Q, Jian W, Wang L, *et al*., 2023. Alleviation of DSS-induced colitis in mice by a new-isolated Lactobacillus acidophilus C4. Front Microbiol 14: 1137701.

Ma Z, Wang H, Ma X, *et al*., 2020. Modulation of gut microbiota and intestinal barrier function during alleviation of antibiotic-associated diarrhea with Rhizoma Zingiber officinale (Ginger) extract. Food Funct 11: 10839-51.

Mechelke M, Koeck D, Broeker J, *et al*., 2017. Characterization of the arabinoxylan-degrading machinery of the thermophilic bacterium Herbinix hemicellulosilytica-Six new xylanases, three arabinofuranosidases and one xylosidase. J Biotechnol 257: 122-30.

Meng Q, Luo Z, Cao C, *et al*., 2020. Weaning alters intestinal gene expression involved in nutrient metabolism by shaping gut microbiota in Pigs. Front Microbiol 11: 694.

Mirzaei R, Afaghi A, Babakhani S, *et al*., 2021. Role of microbiota-derived short-chain fatty acids in cancer development and prevention. Biomed Pharmacother 139: 111619.

Murugesan S, Nirmalkar K, Hoyo-Vadillo C, *et al*., 2018. Gut microbiome production of short-chain fatty acids and obesity in children. Eur J Clin Microbiol Infect Dis 37: 621-25.

Ren Y, Zhaxi Y, Liu M, *et al*., 2023. Revealing the fungi microbiome difference of suffolk cross with tibetan sheep on plateau. Pak Vet J 43: 748-756

Shi Z, Fang Z, Gao X, *et al*., 2021. Nuciferine improves high-fat diet-induced obesity via reducing intestinal permeability by increasing autophagy and remodeling the gut microbiota. Food Funct 12: 5850-61.

Ungaro R, Mehandru S, Allen PB, *et al*., 2017. Ulcerative colitis. Lancet 389: 1756-70.

Waite O, Yaffy D and Kathrani A, 2023. Repeat histopathology and culture of colonic biopsy specimens after treatment for Escherichia coli-associated granulomatous colitis in a cat. JFMS Open Rep 9: 172078390.

Wang K, He KY, Yang JY, *et al*., 2022. Lactobacillus Suppresses Tumorigenesis of Oropharyngeal Cancer via Enhancing Anti-Tumor Immune Response. Front Cell Dev Biol 10: 842153.

Wang M, Cha R, Hao W, *et al*., 2022. Nanocrystalline cellulose cures constipation via gut microbiota metabolism. Acs Nano 16: 16481-96.

Wu S, Wang Y, Iqbal M, *et al*., 2022. Challenges of fluoride pollution in environment: Mechanisms and pathological significance of toxicity-A review. Environ Pollut 304: 119241.

Wu X, Liu Y, Li Y, *et al*., 2024. Molecular mechanism of thiram-induced abnormal chondrocyte proliferation via lncRNA MSTRG.74.1-BNIP3 axis. Pestic Biochem Phys 201: 105847.

Xu Z, Jiang N, Xiao Y, *et al*., 2022. The role of gut microbiota in liver regeneration. Front Immunol 13: 1003376.

Yang Y, Misra B, Liang L, *et al*., 2019. Integrated microbiome and metabolome analysis reveals a novel interplay between commensal bacteria and metabolites in colorectal cancer. Theranostics 9: 4101-14.

Zhang L, Guo H, Gu J, *et al*., 2023. Metagenomic insights into dietary remodeling of gut microbiota and antibiotic resistome in meat rabbits. Sci Total Environ 874: 162006.

Zhang Y, Tan P, Zhao Y, *et al*., 2022. Enterotoxigenic Escherichia coli: intestinal pathogenesis mechanisms and colonization resistance by gut microbiota. Gut Microbes 14: 2055943.

Zhao L, Zhang Q, Ma W, *et al*., 2017. A combination of quercetin and resveratrol reduces obesity in high-fat diet-fed rats by modulation of gut microbiota. Food Funct 8: 4644-56.

Zong X, Fu J, Xu B, *et al*., 2020. Interplay between gut microbiota and antimicrobial peptides. Anim Nutr 6: 389-96.