**Helicobacter pylori** may participate in the development of inflammatory bowel disease by modulating the intestinal microbiota

Xiaoyin Bai¹, Lingjuan Jiang², Gechong Ruan¹, Tingting Liu¹, Hong Yang³

¹Department of Gastroenterology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China; ²Department of Medical Research Center, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China.

**Abstract**

Inflammatory bowel disease (IBD) is a non-specific inflammatory disease of the gastrointestinal (GI) tract that is generally accepted to be closely related to intestinal dysbiosis in the host. GI infections contribute a key role in the pathogenesis of IBD; however, although the results of recent clinical studies have revealed an inverse correlation between *Helicobacter pylori* (H. pylori) infection and IBD, the exact mechanism underlying the development of IBD remains unclear. H. pylori, as a star microorganism, has been a focus for decades, and recent preclinical and real-world studies have demonstrated that *H. pylori* not only affects the changes in the gastric microbiota and microenvironment but also influences the intestinal microbiota, indicating a potential correlation with IBD. Detailed analysis revealed that *H. pylori* infection increased the diversity of the intestinal microbiota, reduced the abundance of Bacteroidetes, augmented the abundance of Firmicutes, and produced short-chain fatty acid-producing bacteria such as *Akkermansia*. All these factors may decrease vulnerability to IBD. Further studies investigating the *H. pylori*-intestinal microbiota metabolite axis should be performed to understand the mechanism underlying the development of IBD.

**Keywords:** *Helicobacter pylori*; Inflammatory bowel disease; Intestinal microbiota

**Introduction**

Inflammatory bowel disease (IBD) consists of Crohn’s disease (CD) and ulcerative colitis (UC), and it is a group of complex diseases that have a protracted course characterized by periodical remissions and relapses; in addition, IBD significantly impacts the quality of life and working competence. During the past two decades, our understanding of the pathogenesis of this complex disease has improved significantly. Infection and immune response are generally considered to play a crucial role in the pathogenesis of IBD; however, results of recent studies indicate that not all infections or microbial exposures exert the same effect on the development of IBD. *Helicobacter pylori* (H. pylori), which is well known to lead to chronic atrophic gastritis, peptic ulcers, and gastric cancer, showed an inverse correlation with IBD in several studies with a large sample size, especially a significant negative relationship with CD rather than UC.[¹,²] To date, several hypotheses have been proposed for this inverse correlation, including a negative socioeconomic distribution between harboring *H. pylori* infection and IBD and the counter-effect of *H. pylori* infection on the immune system.[³] However, the exact mechanism underlying this phenomenon remains unclear. In this review, we provide an overview of the studies performed thus far on the intestinal microbiota and IBD and the effect of *H. pylori* on the intestinal microbiota and IBD as a friend or a foe in the pathogenesis of IBD, which highlights the possible benefit of the presence of *H. pylori* in humans.

**IBD and Intestinal Microbiota: Friend or Foe**

The human “microbiota” is defined as an entire ecosystem consisting of bacteria, viruses, fungi, and bacteriophages which cooperatively acts as an entity within the human. The microbiome of a healthy adult has 10¹³–10¹⁵ bacterial cells and an estimated 1000 kinds of various bacterial species; however, the unique population of fecal microbiota in each individual is fairly constant over time, and the fluctuations of these microorganisms’ numbers are considered as a response to developmental or environmental factors, with the most prominent factors being diet and exposure to antibiotics. In the colon of a healthy...
adult, the most abundant bacterial phyla resided are Bacteroidetes and Firmicutes. Other important groups of microorganisms occurring at a lower frequency include Proteobacteria, Actinobacteria, Fusobacteria, and Verrucomicrobia. The host immune system influences the intestinal microbial communities. In addition, alterations in the microbial community, in turn, modulate the outcomes of the intestinal inflammatory disease.

The pivotal mechanism for the development of IBD appears to involve a deregulated immune response to the commensal flora in an individual with genetic susceptibility. Several studies indicate that the disordered intestinal microbiome is the underlying pathogenesis for IBD, and the imbalance between “beneficial” and “harmful” bacteria is defined as dysbiosis. To our knowledge, at least two dominant patterns of alterations in the intestinal microbiota are generally accepted as distinguishing features in patients with IBD. Compared with healthy individuals, patients with IBD show a decrease in the overall diversity and abundance of intestinal microbiota. Meanwhile, mucosal biopsies of patients with IBD reveal a decrease in the abundance of Firmicutes and Bacteroidetes and an increase in the abundance of Proteobacteria and Actinobacteria, which are generally considered the “foes” of IBD. Furthermore, patients with IBD may have a significant reduction of the bacteria number, which may be important in conferring protection from intestinal inflammation. For instance, patients with IBD have decreased levels of short-chain fatty acids (SCFAs) in the stool, indicating the potential role of Ruminococcaceae, which is an important butyrate producer and the key “friend” of IBD.

Recent studies have shown that surprisingly, *H. pylori* has the potential beneficial effects as a friend in asthma, rheumatoid arthritis, and IBD. These novel results change our knowledge regarding *H. pylori*, which is typically a harmful bacterium that leads to the development of multiple gastric diseases. Epidemiological evidence and the interaction of *H. pylori* with other microbiota should be studied to precisely understand the role of *H. pylori*.

**Global Epidemiological Trends of IBD and *H. pylori* with the Interesting Inverse Correlation**

Significant geographic and temporal trends in the incidence of IBD have been reported in several population-based cohort studies. The results revealed that the incidence of IBD, regardless of CD or UC, appears to be increasing in some areas and vary based on geographic location. Interestingly, the incidence and prevalence of IBD are at a low level in Asia, which is an area with a high abundance of *H. pylori*; furthermore, some newly industrialized regions in eastern Asia have shown an increase in the incidence of IBD (for instance, the annual percentage changes in the incidence of CD and UC in Taiwan, China, were +4.0% and +4.8%, respectively) and the prevalence of *H. pylori* infection has presented a decreasing trend (eg, in Hangzhou, China, the prevalence of *H. pylori* infection in juvenile individuals decreased from 21.6% to 17.2% between 2007 and 2014).

Unlike the pathogens that cause classic infective gastroenteritis, such as *Salmonella* and *Campylobacter*, *H. pylori* is a spiral-shaped and Gram-negative bacterium identified in the human gastric mucosa by Marshall and Warren in 1984 and is well known to lead to chronic atrophic gastritis, peptic ulcers, gastric cancer, and mucosa-associated lymphoid tissue lymphoma. *H. pylori* is the most popular bacterial pathogen in humans and is present in the upper gastrointestinal (GI) tract of >50% of the whole population among individuals of all ages. *H. pylori* infection showed a predilection for the young population in developing countries than in industrialized regions, and the incidence of *H. pylori* infection has decreased in industrialized countries in recent years, which demonstrates an interesting inverse geographic and temporal trend for IBD. The risk of *H. pylori* infection is proven to be related to poor living conditions and socioeconomic status early in life. Infective gastroenteritis in the first year of life was listed as a risk factor for IBD; however, several studies have demonstrated a negative correlation between *H. pylori* seropositivity and the development of IBD regardless of age, ethnicity, *H. pylori* test techniques, and IBD subtype. Furthermore, patients with IBD have a significantly increased prevalence of *H. pylori*-negative gastritis. Some studies have reported that *H. pylori* is a GI infection distinct from other infections. The negative association between *H. pylori* infection and IBD was observed both in vivo and in vitro. *H. pylori* deoxyribonucleic acid (DNA) suppressed the release of pro-inflammatory cytokines by dendritic cells and attenuated the severity of colitis in a mouse model of IBD. A recent preclinical study on serum exosomes derived from *H. pylori*-positive gastritis patients showed a potential explanatory pathway for the inverse phenomenon. Other animal studies suggested regulatory T (Treg) cells, T-helper (Th17) cells, regulatory B (Breg) cells, and M2 macrophages might make a positive effect on the protective function of *H. pylori* infection for colitis. In addition, the luminal delivery of *H. pylori* genomic DNA ameliorates the severity of chronic experimental colitis. Several explanatory hypotheses have been proposed for this meaningful phenomenon, including an inverse socioeconomic distribution between harboring *H. pylori* and IBD and the counter-effect of *H. pylori* on the immune system; however, the key mechanism underlying the development of IBD remains unclear. The alteration in microbiota induced by *H. pylori* infection has emerged as a potential explanation.

**H. pylori Infection and the Alteration in the Intestinal Microbiota**

Despite the varying results obtained in different studies, the focus of most recent studies has been the difference in gastric microbiota between patients with and without *H. pylori* infection. Hypochlorhydria and hypergastrinemia induced by *H. pylori* may change the intestinal microbiota. Analysis of the relative abundance of different bacteria along the entire GI tract of a Mongolian gerbil model showed an altered composition of the intestinal microbiota after chronic infection (14 months).
with *H. pylori*. The results revealed differences in microbiota in the distal but not in the proximal portion of the inflamed GI tract. Further molecular analyses revealed that *Akkermansia*, an important member of healthy species in the intestinal mucosa, was the subject of the study. Another *H. pylori*-related experiment performed using the C57BL/6 mouse model of *H. pylori* infection focused on the local and distant microbial community structures and relative microbial abundance. The results of the study revealed that *H. pylori* influenced the microbial population structure of the distal intestine over time. Furthermore, the results of multiple temporal analyses revealed a persistently altered abundance of the intestinal microbiota (1, 3, and 6 months).

A few studies have been performed on the intestinal microbiota in humans infected with *H. pylori*. A study with a small sample size, including 18 Japanese children and adults from five families with or without *H. pylori* infection, aimed to investigate the potential influence of *H. pylori* infection on the intestinal microbiota. The results revealed no significant difference in the intestinal microbiome between the *H. pylori*-positive and *H. pylori*-negative groups. However, the limitations of this study included a small sample size, different age groups, and participants with a kinship relation. The results of a recent study including 47 participants from a region in China with a high prevalence of *H. pylori* infection showed that the species and Shannon index were higher in participants with past or current *H. pylori* infection than in those without *H. pylori* infection. A significant decrease was observed in the abundance of *Bacteroidetes* in patients with past or current *H. pylori* infection, and the average relative abundance of *Firmicutes* showed an increasing trend in the group with previous *H. pylori* infection compared with the *H. pylori*-negative group. Although the exact mechanism underlying the relationship between *H. pylori* infection and changes in the intestinal microbiota has not been established thus far, an interplay with an intact type IV secretion system is thought to induce distinct shifts in the composition of the gut microbiota. Furthermore, *H. pylori*-induced hypochlorhydria and hypergastrinemia in the upper GI have been hypothesized as factors underlying the changes in the microbiota of the large intestine.

Multiple antibiotic regimens have been evaluated for the treatment of *H. pylori* infection, and a 14-day bismuth-containing quadruple therapy has been proposed as the first-line standard regimen. However, the *H. pylori* eradication treatment produced a significant change in the human intestinal microbiome and decreased bacterial diversity. For example, the eradication treatment caused a dramatic decline in *Actinobacteria*. Some patients continued to have an altered intestinal microbiota even 4 years after the eradication treatment. These results were consistent with those reported in a randomized clinical trial in Chinese adults with or without *H. pylori* infection. To explore the significance of the intestinal microbiota, a study investigating the addition of *Clostridium butyricum* as a probiotic to the standard quadruple anti-*H. pylori* therapy is underway. Patients receiving the eradication therapy with the probiotic showed improved GI symptoms and an increased *Bacteroidetes/Firmicutes* ratio. Moreover, it is important to identify whether alterations in the intestinal microbiota affect real-world outcomes. Data from a health insurance database from Taiwan, China, showed that treatment for *H. pylori* infection accounted for a significantly elevated risk of autoimmune diseases or IBD (hazard ratio, 2.36; 95% confidence interval, 2.14–2.59).

To conclude, *H. pylori* infection not only induces changes in the gastric microenvironment but also interacts with microbiota in the large intestine, creating a new physiological balance in the GI tract. Although limited data are available regarding the changes in the intestinal microbiota in humans and animals, the results available thus far demonstrate an “IBD-protective” profile of the intestinal microbiome, such as an increase in alpha- and beta-diversity *Firmicutes* phyla, and *Akkermansia* species. Therefore, we speculate that alterations in the intestinal microbiota induced by *H. pylori* and eradication contribute to the pathogenesis of IBD.

Alterations in the Immune Response Induced by *H. pylori* Affect the Development of IBD

Changes in immune response instead of changes in the intestinal microbiota are more recognized effects of *H. pylori* infection. Several hypotheses have been proposed to elucidate the relationship between *H. pylori* and IBD; however, the exact relationship between *H. pylori* infection and IBD remains unclear. One of the theories suggests that *H. pylori* infection-associated diseases are driven by the expression of Th1 and Th17 cytokines secreted by pathogenic T cells; however, a majority of individuals without symptoms receive protection from Treg-predominant response to *H. pylori* infection by suppressing the Th1, Th17, and Th2 responses not only in the gastric mucosa but also in the rest of the GI tract. *H. pylori*-induced Tregs play an important role in alleviating the symptoms of colitis in models of IBD; in addition, other immune factors are involved in resolving these symptoms. Previous studies demonstrated that *H. pylori* infection alleviated acute and chronic colitis induced by dextran sulfate sodium (DSS), and Breg cells played a critical role in this process. The levels of CD19+ interleukin 10 (IL-10)-producing cells were higher in the *H. pylori*/DSS-cotreated groups than in the DSS-treated groups. Moreover, Breg cells attenuate the mucosal inflammatory responses in the gut. They cooperate with dendritic cells to promote differentiation of Treg cells, leading to the inhibition of effective T cell responses. However, the results of several clinical analyses did not show a difference between symptomatic and asymptomatic patients with *H. pylori* infection in correlation with IBD, which indicated that the classical theory may not be sufficient to explain the relationship between *H. pylori* infection and IBD.

Some protective associations may not be directly driven by *H. pylori*. *H. pylori* infection modifies the composition of the gut microbiota. However, the impact of *H. pylori* on gut microbiota-derived metabolites remains unknown.
Gut microbiota-derived metabolites such as SCFAs and bile acid metabolites are the key factors in the development of IBD. Reduced microbial diversity and SCFA-producing bacteria (such as Ruminococcaceae) and a potential increase in pathogenic bacteria may lead to a decrease in the energy source in epithelial cells, alteration in the differentiation of Treg cells, degradation of mucus, induction of mucosal inflammation, and a change in mucosal permeability. Further studies should aim to identify the metabolite profile of patients with H. pylori infection with or without IBD, and the detailed mechanism underlying the H. pylori-gut microbiota-metabolism axis should be explained.

Summary

The cumulative evidence from preclinical and real-world studies showed a possible negative association between H. pylori infection and IBD. The changes in intestinal microbiota induced by H. pylori infection have the potential to protect against IBD; thus, selective eradication and surveillance of patient subgroups with a high risk of H. pylori-related sequelae (eg, gastric ulcer and cancer) would be more appropriate than the indiscriminate eradication recommended in some guidelines.

Funding

This work was supported by the Natural Science Foundation of Beijing (No. 7202161), the Fundamental Research Funds for the Center Universities (No. 3332021007), and the CAMS Innovation Fund for Medical Sciences (No. 2021–1–12M–001).

Conflicts of interest

None.

References

1. Bartels LE, Jepsen P, Christensen LA, Gerdes LU, Vilstrup H, Dahlup JF. Diagnosis of Helicobacter pylori infection is associated with lower prevalence and subsequent incidence of Crohn’s disease. J Crohns Colitis 2016;10:443–448. doi: 10.1093/ecto-jcc/jow029.
2. Shirzad-Aski H, Besharat S, Kienesberger S, Sohrabi A, Roshandel M. Eradication of Helicobacter pylori colonization and inflammatory bowel disease: a systematic review and meta-analysis. J Clin Gastroenterol 2021;55:380–392. doi: 10.1097/MCG.000000000001415.
3. Sonnenberg A, Genta RM. Low prevalence of Helicobacter pylori infection among patients with inflammatory bowel disease. Aliment Pharmacol Ther 2012;35:469–476. doi: 10.1111/j.1365-2036.2011.04969.x.
4. Nishida A, Inoue R, Inoue R, Inatomi O, Bamba S, Naito Y, Andoh A. Gut microbiota in the pathogenesis of inflammatory bowel disease. Clin J Gastroenterol 2013;11:1–10. doi: 10.1007/s12328-017-0813-5.
5. Nash AK, Auchtung TA, Wong MC, Smith DP, Gesell JR, Ross MC, et al. The gut mycobiome of the Human Microbiome Project healthy cohort. Microbiome 2017;5:153. doi: 10.1186/s40168-017-0373-4.
6. Honda K, Litman DR. The microbiota in adaptive immune homeostasis and disease. Nature 2016;533:57–84. doi: 10.1038/nature18486.
7. Franzosa EA, Sirota-Madi A, Avila-Pacheco J, Fornelos N, Hauser HJ, Reinker S, et al. Gut microbiome structure and metabolic activity in inflammatory bowel disease. Nat Microbiol 2019;4:293–305. doi: 10.1038/s41564-018-0306-4.
8. Yilmaz B, Juillerat P, Oyas O, Ramon C, Bravo FD, Franc Y, et al. Microbial network disturbances in relapsing refractory Crohn’s disease. Nat Med 2019;25:323–336. doi: 10.1038/s41591-018-0308-z.
9. Gonçalves P, Araujo JR, Di Santo JP. A cross-talk between microbiota-derived short-chain fatty acids and the host mucosal immune system regulates intestinal homeostasis and inflammatory bowel disease. Inflamm Bowel Dis 2018;24:558–572. doi: 10.1093/ibd/izy029.
10. Pellicano R, Ianigo G, Fagonee S, Settannis CR, Gasbarrini A. Review: extragastric diseases and Helicobacter pylori. Helicobacter 2020;25 Suppl 1:e12741. doi: 10.1111/hel.12741.
11. Ng SC, Kaplan GG, Tang WP, Zhang Y, Wang C, Underwood FE, et al. Population density and risk of inflammatory bowel disease: a prospective population-based study in 13 countries or regions in Asia-Pacific. Am J Gastroenterol 2019;114:107–115. doi: 10.1038/s41395-018-0233-2.
12. Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchmol EL, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. Lancet 2017;390:2769–2778. doi: 10.1016/S0140-6736(17)32448-0.
13. Shu X, Pung M, Yin G, Jiang M. Investigation of Helicobacter pylori infection among symptomatic children in Hangzhou from 2007 to 2014: a retrospective study with 12,796 cases. PeerJ 2017;5:e2937. doi: 10.7717/peerj.2937.
14. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet 1984;1:1311–1315. doi: 10.1016/0140-6736(84)91116-6.
15. Alarcon T, Llorca L, Perez-Perez G. Impact of the microbiota and gastric disease development by Helicobacter pylori. Curr Top Microbiol Immunol 2017;400:253–273. doi: 10.1007/978-3-319-50520-6_11.
16. Burauco A, Axon A. Epidemiology of Helicobacter pylori infection. Helicobacter 2017;22 Suppl 1:e12403. doi: 10.1111/hel.12403.
17. Torres BZ, Lucero Y, Lagomarcino AJ, Orellana-Manzano A, George S, Torres JP, et al. Review: prevalence and dynamics of Helicobacter pylori infection during childhood. Helicobacter 2017;22:e12399. doi: 10.1111/hel.12399.
18. Ueno T, Suzuki H, Hirose M, Shida T, Ikewakawa K, Matsui H, et al. Influence of living environment during childhood on Helicobacter pylori infection in Japanese young adults. Digestion 2020;101:779–784. doi: 10.1159/000502574.
19. Bernstein CN, Burchill C, Targownik LE, Singh H, Roso LL. Events within the first year of life, but not the neonatal period, affect risk for later development of inflammatory bowel diseases. Gastroenterology 2019;156:2190–2197. doi: 10.1053/j.gastro.2019.02.004.
20. Castano-Rodríguez N, Kaakoush NO, Lee WS, Mitchell HM. Dual role of Helicobacter and Campylobacter species in IBD: a systematic review and meta-analysis. Gut 2017;66:235–249. doi: 10.1136/gutjnl-2015-310545.
21. Tepler A, Narula N, Peak RM Jr, Patel A, Edelson C, Colombel JF, et al. Systematic review with meta-analysis: association between Helicobacter pylori CagA seropositivity and odds of inflammatory bowel disease. Aliment Pharmacol Ther 2019;50:121–131. doi: 10.1111/apt.15306.
22. Piovani D, Danese S, Peyrin-Biroulet L, Nikolopoulos GK, Lytras T, Bonovas S. Environmental risk factors for inflammatory bowel disease. In: The gut microbiome. 2017:659–637. doi: 10.1007/978-3-319-72402-6_11.
23. Shah SC. Friend or foe in inflammatory bowel disease pathogenesis: not all infections are equal. Gastroenterology 2019;157:1441–1442. doi: 10.1053/j.gastro.2019.04.016.
24. Luther J, Owyang SY, Takeuchi T, Cole TS, Zhang M, Liu M, et al. Helicobacter pylori DNA decreases pro-inflammatory cytokine production by dendritic cells and attenuates dextran sulphate-induced colitis. Gut 2011;60:1479–1486. doi: 10.1136/gut.2010.220807.
25. Chen Y, Huang J, Li H, Li P, Xu C. Serum exosomes derived from Hp-positive gastritis patients inhibit MCP-1 and MIP-1α expression.
via NLRP12-Notch signaling pathway in intestinal epithelial cells and improve DS-17 induced colitis in mice. Int Immunopharmacol 2020;88:107012. doi: 10.1016/j.intimp.2020.107012.

26. Zhang H, Dai Y, Liu Y, Wu T, Li J, Wang X, et al. Helicobacter pylori colonization protects against chronic experimental colitis by regulating Th17/Treg balance. Inflamm Bowel Dis 2018;24:1481–1492. doi: 10.1093/ibd/izy107.

27. 2019; Li X, Tan J, Zhang F, Xue Q, Wang N, Cong X, et al. H. pylori infection alleviates acute and chronic colitis with the expansion of regulatory B cells in mice. Inflammation 42:1611–1621. doi: 10.1007/s10753-019-0234-0.

28. Li LN, Liu Y, Zhang HC, Wu T, Dai Y, Wang WH. Helicobacter pylori infection reduces TAMs infiltration in a mouse model of AOM/DDX induced colitis-associated cancer. PLoS One 2020;15: e022840. doi: 10.1371/journal.pone.022840.

29. Owang SY, Luther J, Owang CC, Zhang M, Kao JY. Helicobacter pylori DNA’s anti-inflammatory effect on experimental colitis. Gut Microbes 2012;3:168–171. doi: 10.4161/gmic.19181.

30. Yu Y, Zhu S, Li P, Min L, Zhang S. Helicobacter pylori infection and inflammatory bowel disease: a crosstalk between upper and lower digestive tract. Cell Death Dis 2018:9:961. doi: 10.1038/s41419-018-0998-2.

31. Parsoni BN, Iraz UZ, D’Amore R, Burkitt MD, Eccles R, Lenzi I, et al. Comparison of the human gastric microbiota in hypochlorhydric states arising as a result of Helicobacter pylori-induced atrophic gastritis, autoimmune atrophic gastritis and proton pump inhibitor use. PLoS Pathog 2017;13:e1006653. doi: 10.1371/journal.ppat.1006653.

32. Derrien M, Belzer C, de Vos WM. Akkermansia muciniphila and its role in regulating host functions. Microb Pathog 2017;106:171–181. doi: 10.1016/j.micpath.2016.02.005.

33. Lopez-Siles M, Enrich-Capo N, Aldeguer X, Sabat-Mir M, Duncan FL, Belzer C, et al. Akkermansia muciniphila and its role in regulating host functions. Microb Pathog 2017;106:171–181. doi: 10.1016/j.micpath.2016.02.005.

34. Heimesaat MM, Fischer A, Plickert R, Wiedemann T, Loddenkemper T, Haenen G, et al. The inflammatory response to Helicobacter pylori infection: a role for the cytokine network. Gut Microbes 2012;3:168–171. doi: 10.4161/gmic.19181.

35. Iino C, Shimoyama T. Impact of Helicobacter pylori infection on gut immune responses. J Autoimmun 2014;50:107–113. doi: 10.1016/j.jaut.2014.01.032.

36. Liou JM, Chen CC, Chang CM, Fang YJ, Bair MJ, Chen PY, et al. The microbial metabolites, short-chain fatty acids, regulate colonic Treg cell homeostasis. Science 2013;341:569–573. doi: 10.1126/science.1241165.

37. Smith PM, Howitt MR, Panikov N, Michaud M, Gallini CA, Urbano-Rojas V, et al. Metabolite-sensing receptors GPR43 and GPR109A facilitate dietary fibre-induced gut homeostasis through regulation of the inflammation- some. Nat Commun 2015;6:7354. doi: 10.1038/ncomms8734.

38. Ji J, Yang H. Using probiotics as supplementation for Helicobacter pylori antibiotic therapy. Int J Mol Sci 2020;21:11136. doi: 10.3390/ijms21031136.

39. Lopetuso LR, Napoli M, Rizzatti G, Scalfaferrri F, Franceschi F, Gasbarrini A. Considering gut microbiota disturbance in the management of Helicobacter pylori infection. Expert Rev Gastroenterol Hepatol 2018;12:899–906. doi: 10.1080/17474124.2018.1503946.

How to cite this article: Bai X, Jiang L, Ruan G, Liu T, Yang H. Helicobacter pylori may participate in the development of inflammatory bowel disease by modulating the intestinal microbiota. Chin Med J 2022;135:634–638. doi: 10.1097/CM9.0000000000002008