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EDITORIAL

Mucosal Microbiota: Closer to the Pathology, Closer to the Truth?

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Irritable bowel syndrome (IBS) is a frequently-encountered chronic gastrointestinal disorder characterized by recurrent abdominal pain accompanied by changes in fecal morphology and bowel habits [1]. The pathogenesis of IBS is associated with genetic loci, aberrant stress responses, diet, age, geographic origin, prior infection, alterations of the gut microbiome composition, and antibiotic use. Currently, the diagnosis of IBS is solely based on symptom criteria, and in most cases, only limited tests are performed to exclude other organic gastrointestinal diseases [2]. A growing body of research suggests that gut microbes are important for IBS pathogenesis due to their contributions to host biochemical and metabolic processes. A well-functioning microbiota inhabiting the human gastrointestinal tract is highly host-adapted, benefiting the host by participating in immunity, resistance to pathogen colonization, intestinal growth and differentiation, and the regulation of numerous intestinal functions [3]. Alteration of the composition of the intestinal microbiota termed "dysbiosis" has been described in IBS patients, suggesting that the intestinal microbiome and IBS pathogenesis are linked. Recent studies, for example, have reported altered intestinal flora and metabolites in patients with IBS, including a decrease in microbial diversity and richness and a decrease in the level of beneficial intestinal bacteria, such as *Bifidobacterium* [3, 4]. These studies, however, are limited by small sample size, and heterogeneity in selection criteria, detection methods, and the sampled intestinal segment, with inconsistent and inconclusive results. IBS is usually classified into four types: predominant-diarrhea (IBS-D), constipation-predominant (IBS-C), mixed bowel habits (IBS-M), and unclassified (IBS-U) [5]. Though many groups reported differences in intestinal microbiota composition among IBS-C, IBS-M, and IBS-D [6], Pittayanon et al. summarized 6 studies of 130 IBS-M patients finding no significant differences among subtypes [7], casting doubt on the significance of this finding.

Since fresh intestinal mucosal tissue is difficult to obtain, prior studies primarily concentrated on the composition of fecal microbiota and metabolites [8], although some researchers claimed that mucosal microbiota is a more important contributor to the occurrence of intestinal diseases due to their proximity to the intestinal epithelium, as compared with fecal microbiota [9, 10], consistent with known host–microbial interactions involving bioactive bacterial components such as lipopolysaccharide and fermentative metabolites such as short-chain fatty acids that activate host cognate receptors [11]. Additionally, Jingze Yang et al. have shown that the changes in mucosal microbiota are related to the synthesis and secretion of serotonin by host intestinal enterochromaffin cells which further promotes the progression of IBS [10]. Contrariwise, the changes in the composition of the fecal microbiota and metabolites are more likely to be determined by dietary patterns [12]. Therefore, investigating the changes in microbiota and metabolites obtained from the mucosa of IBS patients may provide a deeper understanding of the pathogenesis of IBS [1].

The gut bacterial composition is highly dependent on the sample type and regional location. The sigmoid colon and ileum are two different ecosystems with different structures and functions [13]. Though many researchers have reported the microbiota composition, few focused on its function [14]. Since congruent bacterial communities in different locations may have completely different host effects, deciphering the function and host interactions of the microbiota in different intestinal regions may provide additional insight into IBS pathogenesis. However, many questions remain regarding the significance of the associations of the composition of the gut microbiota and metabolites as obtained from fecal and mucosal samples regarding the pathophysiology of IBS.

In this issue of *Digestive Diseases and Sciences*, Hou et al. [15] reported a multifaceted microbiota study that included 14 IBS-C patients, 20 IBS-D patients, and 20

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healthy controls (HCs). The authors compared changes in intestinal flora composition among IBS subtypes, between samples obtained from feces and intestinal mucosa, and among different intestinal sites. Furthermore, the correlation between the composition of the intestinal flora and clinical manifestations of IBS patients was also analyzed. The authors showed that the community richness and diversity of IBS-C and IBS-D patients were significantly lower than those obtained from HC. Although there was no significant difference in composition and diversity between samples obtained from IBS-C and IBS-D subjects, several common bacteria in the intestinal tract exhibited notable trends: IBS-C had increased *Eggerthella* and *Ferrovibrio* compared with HC, whereas IBS-D had a higher prevalence of the *Christensenellaceaæ_R-7_group*. IBS-D had higher *Prevotella-9* and *Collinsella* and lower *Bifidobacterium, Blautia, Eggerthella, Ferrovibrio,* and *Marvinbryantia* compared with IBS-C. Furthermore, there were significant differences in the changes of intestinal microflora in mucus obtained from different intestinal segments. The bacterial count at the terminal ileum was lower than that at the rectosigmoid junction. In the patients with IBS, the prevalence of *Bacteroides caccæ* at the junction of the rectosigmoid increased 1.9 times and *Clostridium histilyticum* increased 1.7 times compared with that of the ileum. There were also significant differences between the fecal samples of IBS patients and the related bacteria in the mucosal samples. Compared with HC, the number of *Bacteroides caccæ* decreased in the fecal samples of IBS patients but increased in the mucosal samples. In contrast, the content of *Roseburia* decreased in feces but increased in mucosal specimens. Correlation analysis of the composition of the intestinal mucosal flora and clinical symptoms of patients suggested that the composition of intestinal mucosal microflora might be able to better predict the symptoms of IBS than the fecal microflora composition. Although the number of patient samples collected in this research was limited, this is the first report of multi-dimensional analysis of the changes in intestinal microflora composition of IBS patients among different patient subtypes, sample types, and intestinal mucosal segments.

The study was limited to a relatively small sample size and lack of matching of samples according to age and gender between groups, increasing the possibility that confounding factors could possibly distort the findings. Furthermore, dietary habits that simultaneously affect the composition of intestinal flora and metabolites were not considered. Also, the authors only collected samples at a single time point. A longitudinal investigation and prospective validations in the future would further improve the accuracy of the conclusion on cause–effect relationships.

In conclusion, Yangfan Hou et al. presented the landscape of microbiota in both feces and the intestinal mucosa of IBS patients. We believe this work not only provides a set of comprehensive data that investigators can further analyze to understand the pathogenesis of IBS but also inspires researchers in this field to focus on mucosal microbiota instead of fecal microbiota.

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