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Microbiota and IBD: Introduction and Mechanism

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ABSTRACT. *IBD is a worldwide disease leading to abdominal discomfort and pain caused by microbiota imbalance and some other factors such as genetic and the environment. Further research on both microbiota and IBD and the link between them may indicate some possible treatment to the disease according to ways to acquire different groups of microbiotas and balance the proportion. IBD infection has increased rapidly in the past decade and it is important to find effective treatment soon.*

KEYWORDS： *Micorbiota; IBD; Introduction; Mechanism; Infection*

1. Introduction

1.1 IBD

IBD, or known as inflammatory bowel disease, including ulcerative colitis (UC) and Crohn's disease (CD). Crohn's disease is chronic inflammation of any part of the digestive tract, although usually involves the terminal small bowel, cecum and anus. The most common signs and symptoms include diarrhea, crampy or steady pain in the right lower abdomen, pain or bleeding with a bowel movement. The general symptoms that may occur in some patients are fatigue, weight loss and low-grade fevers. While ulcerative colitis is an acute or chronic inflammation of the colon. Signs and symptoms include inflammation of colon tissue and it can produce sores and ulcers; it is usually limited to the colon and rarely affects the small intestine, except for the terminal ileum. Common signs and symptoms include frequent loose stools, lower abdominal discomfort and pain, fever, lethargy,

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appetite loss, weight loss, bowel incontinence and anemia. Occasionally, other body organs may be involved, for example eye problems, joint problems, neck or back pain, skin rashes, liver and bile duct problems and/or kidney problems.

IBD has become a global disease with accelerating incidence worldwide in the 21st century while its accurate etiology remains unclear. People who are infected with UC have increased 4 times during 1981-2000 in China. UC infection increases first and the increase infection of CD goes next. IBD's infection cases mainly concentrate in North America and Oceania. Since 1990, incidence has been rising in newly industrialized countries in Africa, Asia, and South America, including Brazil and Taiwan, which leads to the suspect of the prevalence between IBD infection and the environment.

It is also estimated that IBD could be driven by genetic susceptibility, environmental and microbial factors. The genetic mutations of NOR2 and CRAD15 on Chromosome 16 have been proved that they maintain a close relation with the incidence of rate of IBD. The possibility of infection monozygotic twines is higher than dizygotic twines. White people have higher possibility of infection than African American. As for environmental factors are smoking and diet. Smoking can boost the formation of thrombus and increase the danger of CD, while fast food can also increase the rate of infection. Microbiota also plays an important role in the pathology of IBD.

1.2 Microbiota

Microbiota is the community of microbes living inside human body. They mainly co-exist with human. They can help with digestion, develop and differentiate host's intestinal epithelium, regulate immune system, protect against other bacteria which might cause disease, produce vitamin B and maintain tissue homeostasis. Microbiota can be categorized into five groups, Firmicutes, Bacteroidetes, Archaea, Actinobacteria and Proteobacteria. The majority are Firmicutes and Bacteroidetes.

It is important for human to maintain the proportion of the five groups. The proportion differentiates in different organs. There are several factors that could

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reflect the proportion including age, antibiotics, diet lifestyle the immune system, evolutionary history and host genetics.

Human acquire most of their microbiota in the first three months after born. The environment plays an important role in acquiring microbiota instead of genes. Dysbiosis, which means the imbalanced status of human microbiota, would probably lead to diseases such as IBD. The way of acquiring microbiota might inspire us ways to balance the proportion and treat the disease caused by dysbiosis.

2. Mechanism

2.1. Environmental factor

To begin with, Researchers found that smoking can boost the formation of thrombus and increase the danger of CD (a kind of branch disease about the IBD). Additionally, the prevalence of the fast food also can increase the rate of infection. More reaches unveiled that the prevalence of refrigerator keeps a same pace with the morbidity of IBD: Psychrophile inside the refrigerator can also infect those who are sensitive to psychrophilic bacteria. It means that people will eat such bacterial and then being infected.

2.2. Genetic factor

Firstly, the racial differences: (comparing the possibility of infection) monozygotic twines are higher than dizygotic, immediate relative is high, spouses is less, the white people are higher than Africa-American. Furthermore, researchers uncovered that the genetic mutation of NOR2 and CRAD15 on Chromosome 16 have been proved that they maintain a close relation with the incidence of rate of IBD.

2.3. Immune factor

Firstly, the epithelial barrier of IBD patients has defect. And the proof that bolster this conclusion is that researchers find that whether patients with or without inflammation, they have decreased ability to resist but increased permeability.

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What's more, IBD patients have epithelial innate immune disorder. Patients with IBD have something different on the expression of TLRS in intestinal epithelium with the normal people. TLR3 and TLR5 are expressed in intestinal epithelium of normal people, but TLR2 and TLR4 are hardly detected. As the CD was active, TLR3 decrease, conversely, TLR4 increase as the CD and UC was active. Moreover, TLR5 is usually inhabited due to its basal expression, but flagellin can bind TLR5 to agravate inflammation in IBD damaged mucosa.

Finally, IBD patients have functional APC antigen recognition and processing disorder. Increased TLR4 expression has been found in the medully DCs. Another animal experiment found that activated DCs had longer life span, thus maintaining inflammatory response.

2.4. Infection factor

To begin with such experience onset this discovery: Intestinal flora and the pathogenesis of IBD (mice experiment). In mouse DSS model Bacteriodes and Clostridium increased, suggesting that intestinal flora may be involved in the pathogenesis of DSS colitis in mice. Another experiment was also meaningful, related to the discovery of infection: IBD animal models with the immune deficiency that cased by transgenic or elimination methods: intestinal inflammation will not occur in the intestinal sterile environment, but will occur if the normal intestinal flora is back to normal.

Comparing to that of normal ones, the fecal and intestinal mucosal floral of IBD patients have traits like increasing content significantly, the composition is significantly different, and the discrepancy of structure of intestinal flora also exist in different time period of diseases.

To prove the first feature above, what you have to do is do rRNA prob quantification and the next step is to extract CD patients' fecal samples. The result is that bacterial concentration was significant higher than the normal group, and more than 30% of them belong to atypical bacteria. And the next experiment is that Swidssinski boosts16S rRNA gene sequence analysis technology and then extracted colonoscopy biopsy specimens of 305 patients with intestinal inflammation and 40 controls. They found that the mucosal bacterial content of

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patients with intestinal inflammation was significantly higher than of controls, especially in patients with CD.

As for the second feature, researchers find that there is a microecological imbalance in IBD patients. The advantage of opportunistic pathogens is higher than that of physiological bacteria, and it is more prominent in active period. Helicobacter family is also suspected to be associated with IBD, and Fusiform proteus is associated with UC, researchers also found that Escherichia coli also have a significant relation with CD.

As we talk about the mechanism that intestinal flora plays a role in IBD, the first theory is that the immune system of normal intestinal mucosa is immune tolerant to the normal flora in the intestinal tract. When the intestinal flora is out of balance, a large number of proliferating pathogenic bacteria active the intestinal immune system, and the activated immune system cannot tolerate the change flora in the intestine, resulting in excessive immune response. Researchers group (Duchmann) finds that normal people had tolerance to their own intestinal bacteria, but this tolerance was broken in IBD patients.

And another theory relate to Normal flora (probiotics) competition mechanism with intestinal pathogens. For instance, the probiotics will occupy the space, or compete for essential nutrition and epithelial attachment points. And they could produce anti-microbial ingredients, volatile fatty acids, modified cholic acid, adverse to the growth environment of pathogenic bacteria and inducing immune cells to gather. Probiotics could even activate appropriate immune and inflammatory responses.

It is said that for the normal people, their intestine is covered with mucus from ileum to colon, thus protecting intestinal mucosa from bacterial invasion. However, for those IBD patients, the mucus barrier of intestinal mucosa disappeared, and the intestinal epithelium adhered to a layer of bacterial shell, which was mostly found at the bottom of epithelial crypt, and even scattered in intestinal epithelial cells, thus activating mucosal immunity, destroying immune tolerance and inducing the onset of IBD.

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Although the cause of the loss of mucous barrier in IBD patients is still unknown, there are some evidences other than what was mentioned above that shows IBD may also be associated with smoking, stimulating food, etc.

References

[1] Hails W, SchOlmerich J, Gross V, et al. The role of the resident intestinal flora in acute and chronic dextral sulfale sodium- induced cols in mice. Eur J Gastroenterol Hepatol, 2000, 12:267-273.
[2] Tanrog JD, Richardson JA, Cmft JT. et al. The germ-free siale prevents development of gut and joint inflammatory disease in HLA-B27 transgenic rats. Exp Med, 1994, 180:2359-2364.
[3] Sellon RK, Tonkonogy S, Schulm M, et al. Resident enteric bacteria are necessary for development of spontaneous colitis and immune system activation in interleukin--1o-- mice. Infect linITlun, 199B.66:5224—5231.
[4] Seksik P Rigottier-Gois L, Gramet G, et al. Alterations of the dominant fecal bacterial groups in patients with Crohn's disease of the colon. Gut, 2003, 52:237242.
[5] Swidsinski A. Ladhoff A, Pemthaler A, et al. Mucosal flora inflammatory bowel disease. Gastroenterology, 2002, 122: 44-54
[6] Swidsiski A, Loening-Baucke V, Herber A; Mucosal flora in Crohn's disease and ulcerative colitis: an overview. [J] Physiol Pharmacol. 2009 Dec; 60 Suppl 6: 61-71.
[7] Darfeuille-Michand A, Boudeau J, Bulois P, et al. High prevalence of adherent-invasive Escherichia coli associated with ileal mucosa in Crohn's disease Gastroenterology, 2004, 127: 412-421
[8] Ohkusa T, Okayasu l, Ogihara T et al. Induction of experimental ulcerative colitis by fusobacterium varium isolated from colonic mucosa of patients with ulcerative colitis [J] Gut, 2003, 52:79.
[9] Zhang L, Day A, MeKenzie G, et al; Nongastric Helicobacter species detected in the intestinal tract of children. [J]. Clin Microbiol, 2006. 44(6): 2276.
[10] Ryan P, Kelly RG, Lee G, et al. Bacterial. DNA within granulomas of patients with Crohn's disease detection by laser capture mierodissection and PCR[J]. Am J Gastroenterol, 2004, 99 (8): 1539.
[11] Duchmann R, May E, Heike M, et al. T cell specificity and cross re-activity towards enterobacteria, bacteroides, bifidobacterium, and antigens from resident intestinal flora in humans [J]. Gut, 1999, 44 (6): 812.