Research uncovers links between gut microbiota and response to IBD treatment

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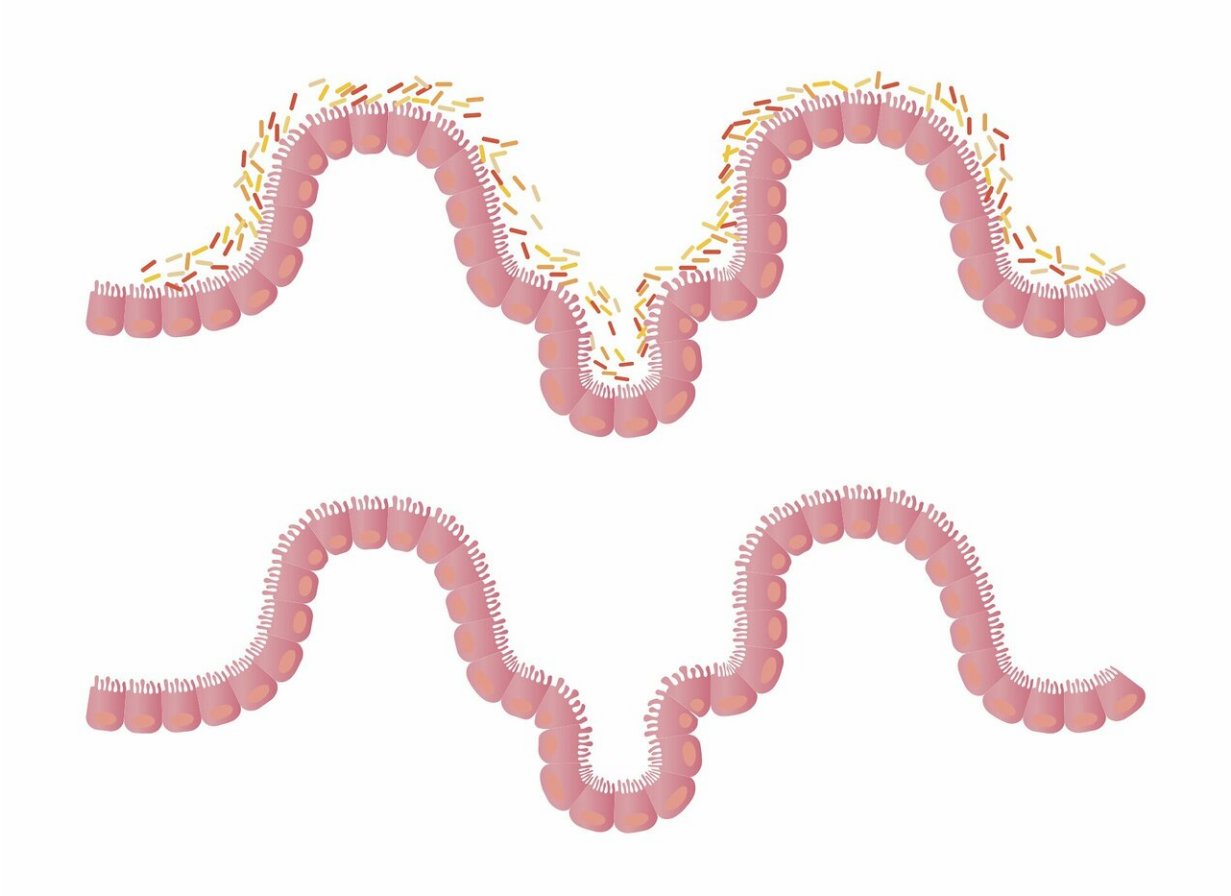

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A team of scientists from Saudi Arabia have published a study in

Bosnian Journal of Basic Medical Sciences, where they explored the gut microbiota of patients with inflammatory bowel disease (IBD).

Senior author, Dr. Sherif Edris, from Department of Biological Sciences, Faculty of Science, King Abdulaziz University, Jeddah, and Princess Al Jawhara Albrahim Center of Excellence in Research of Hereditary Disorders (PACER-HD), King Abdulaziz University, Jeddah, Saudi Arabia and his team investigated whether these microbiota could explain why some patients don't respond to a common IBD treatment called anti-TNF-α therapy. The study aimed to identify microbial structures in the gut that could serve as potential indicators of whether a patient will respond to this therapy.

What is IBD and anti-TNF-α therapy?

Inflammatory bowel disease (IBD), including primary subtypes, Crohn's disease and ulcerative colitis, is a chronic and relapsing inflammatory condition of the gastrointestinal tract that occurs following immune system dysregulation. IBD affects approximately 6.8 million people worldwide, and can occur at any age, but it's often diagnosed in individuals aged 15–35. Common clinical symptoms of IBD are abdominal pain, diarrhea, weight loss, and bloody stools. It can also lead to complications such as malnutrition, anemia, and increased risk of colon cancer.

Anti-TNF-α therapy is a form of biological therapy that is used in the treatment of various autoimmune diseases, including rheumatoid arthritis, psoriasis, and inflammatory bowel diseases (IBD) like Crohn's disease and ulcerative colitis.

TNF-α, or tumor necrosis factor alpha, is a cytokine, a type of protein in the body that plays a crucial role in inflammation. It is produced by immune cells and is found in higher levels in individuals with

autoimmune disorders, contributing to the inflammation and damage seen in these conditions.

Anti-TNF-α therapy works by blocking the action of TNF-α, thereby reducing inflammation. The therapy typically involves the use of biologic drugs, which are medicines made using living organisms, and these drugs can bind to TNF-α in the bloodstream and neutralize it. Some of these drugs include infliximab, adalimumab, and etanercept.

It's important to note that while anti-TNF-α therapy can be very effective for some individuals, it does not work for everyone, and some people can experience side effects.

Traditional medication for IBD involves anti-TNF-α therapies, which, though successful in many patients, has a subset of individuals who do not respond. The researchers' mission was to look into this mystery of non-response and to uncover whether the gut's bacteria composition, the microbiome, could be a contributing factor. Anti-TNF-α therapy is a type of treatment used for these conditions that targets a protein in the body contributing to inflammation. However, not all patients respond to this treatment, and scientists don't yet fully understand why this is the case.

The role of the microbiome

In recent years, scientists have become increasingly interested in the gut microbiota, a complex ecosystem of trillions of microorganisms that inhabit our digestive tracts, and their role in health and disease. Changes in the composition of these microbial communities, a condition known as dysbiosis, have been linked to various diseases, including IBD.

The study involved a careful analysis of stool samples from a group of Saudi Arabian patients with IBD who were classified as responders and

non-responders to anti-TNF-α therapies.

The team used a technique called 16S rRNA gene sequencing, a next-generation sequencing technologies method that identifies and quantifies the bacteria present in a sample, offering a snapshot of the gut's bacterial communities.

Interestingly, the team did not find significant differences in the overall composition of the gut microbiota between the two groups. However, they did observe moderate changes, with certain bacterial groups being more prevalent in the non-responders compared to the responders.

Specifically, non-responders had more of certain types of bacteria, including Proteobacteria and Actinobacteria, which have been associated with various health issues, such as inflammation and metabolic disruption. By contrast, the proportion of a group of bacteria known as Bacteroidetes decreased in non-responders compared with responders.

At a more detailed level, the non-responders showed a decrease in the populations of Bacteroidaceae and Lactobacillaceae, two families of bacteria that play important roles in the gut ecosystem. The Lactobacillaceae family, for instance, contributes to the fermentation of kefir, a type of fermented milk drink that has been suggested to have beneficial effects for IBD.

Conversely, non-responders showed an increased abundance of other bacterial families, including Bifidobacteriaceae, Lachnospiraceae, Enterobacteriaceae, and Muribaculaceae. The team believes that the increased presence of these bacteria could promote inflammation and worsen conditions in primary non-responders.

Potential biomarkers

Another crucial part of the study was identifying potential bacterial biomarkers—indicators that could help predict whether a patient will respond to anti-TNF-α treatment. These included bacteria like Klebsiella, Eubacteriaceae, RF32, B. animalis, and Muribaculaceae.

The concentration of these bacteria increased in patients who did not respond to the treatment. On the other hand, the population of Bacteroides fragilis, a human-friendly bacterium, decreased in non-responders, which is in line with previous studies.

While these results are promising, the researchers acknowledge the need for larger studies to validate these findings. If proven, these microbiota biomarkers could help health care providers predict whether a patient will respond to anti-TNF-α therapy, thereby improving treatment strategies for individuals with IBD.

The team's discoveries could potentially help improve IBD treatment by providing a more tailored approach—personalized medicine, which aims to tailor medical treatment to the individual characteristics of each patient. Understanding the role of gut microbiota in disease and treatment response could open up new therapeutic avenues, not only for IBD but for a variety of other health conditions as well.

At present, IBD treatments often involve a process of trial and error to find the most effective method for each patient. However, if doctors could predict a patient's response to specific therapies using biomarkers, they could prescribe the most effective treatment straight away, saving time and minimizing the patient's discomfort.

The study's findings could stimulate new areas of research, potentially leading to the development of novel treatments for IBD and other related conditions. For example, therapies that aim to modify the gut microbiota , such as the use of probiotics or fecal microbiota transplants, are

currently being explored as potential treatments for various diseases.

More information: Hanan Alatawi et al, Attributes of intestinal microbiota composition and their correlation with clinical primary nonresponse to anti-TNF-α agents in inflammatory bowel disease patients, *Bosnian Journal of Basic Medical Sciences* (2022). DOI: 10.17305/bjbms.2021.6436

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