New research paper supports using microbiome data to develop potential probiotic therapies

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In a new paper published by the journal *Gastroenterology*, researchers from University Hospitals (UH) Cleveland Medical Center and Case Western Reserve University School of Medicine, review studies about the microbiome's role in disease and health, and discuss tactics for developing probiotics to modulate the microbiome through leveraging microbiome data. They illustrate these tactics by using Crohn's disease (CD) as an example.

According to the authors, gut microbes may influence a number of health-related issues including diseases such as CD and other degenerative diseases, including obesity, diabetes, cancer, autism and cardiovascular disease.

"The microbiome consists of bacteria, fungal and viral constituents in the gut. We have come to learn how the interaction between these communities, as well as potential interaction with the body can affect health and disease," said Senior Author Mahmoud Ghannoum, Ph.D., Director, Integrated Microbiome and the Center for Medical Mycology at UH and Case Western Reserve University.

"An imbalance of the gut microbiota composition, called dysbiosis, may initiate or exacerbate several diseases. Furthermore, the imbalance may form a biofilm, which can create a barrier to the absorption of medications and create an environment encouraging growth of harmful bacteria and fungal components," said Dr. Ghannoum, who has been studying the microbiome for decades.

In their paper, intestinal biofilms that developed in CD were targeted for modulation, and then beneficial microbial strains that could potentially interrupt and disrupt the biofilms were identified.

Through further analysis, four biotherapeutic strains of beneficial bacteria and fungi were selected due to their efficacy in neutralizing the

organisms creating the biofilms.

"These strains were shown to have anti-biofilm activity and to interfere with epithelial cell damage caused by the bacteria and fungus found in CD," said Dr. Ghannoum.

In addition to the selected microorganisms, the enzyme amylase was added to the formulation to enhance biofilm abrogation.

The researchers studied the effects in mice and humans. In humans, 49 healthy volunteers enrolled to participate in four weeks of once-a-day formulation consumption.

The comprehensive intestinal microbiome, representing bacterial and fungal communities, profiles were assessed at the start of the study and following four weeks of probiotic consumption.

"The microbiome (both bacteria and fungi) of our subjects was compared with those reported by the Human Microbiome Project (HMP) for healthy subjects as a control for bacterial abundance," said Dr. Ghannoum.

"When the volunteers' microbiome profiles were analyzed, the changes indicated the effects could be of great benefit to healthy individuals with digestive issues," he said.

Following this preliminary study, another clinical study was conducted (recently completed and submitted for publication) to test effects of the formulation on healthy individuals with self-reported gastrointestinal symptoms such as flatulence, bloating, and abdominal discomfort.

"The second study showed that the formulation reduced the severity and frequency of overall GI symptoms and positively modulated specific

symptoms, such as flatulence, bloating, stool regularity, constipation, and abdominal discomfort) to a statistically significant degree compared to placebo," said Dr. Ghannoum.

"In addition, the formulation appeared to improve irritability while possibly reducing anxiety, emotional stress, and improving overall score on an anxiety symptom questionnaire. Importantly, the research subjects tolerated the formulation very well in comparison to individuals who had received a placebo."

"Studies such as these and additional studies demonstrating that changes in the gut microbiome balance following probiotic modulation can be sustained by either diet modification or maintenance dietary supplementation that has been designed to address the specific microbiome profile of the target condition," he said.

Dr. Ghannoum said that the rational design and appropriate experimental and clinical studies could be applied to other cohorts of individuals based on health and demographic factors to provide insights into gut microbiota composition, microbial interplay with probiotics and potential effects on host organisms.

Through the analysis of big microbiome data sets, researchers have started to appreciate the microbiome composition differences between different cohorts of individuals. That has lead to the opportunity to leverage such data insights for targeted microbiome solution development.

"Introducing an additional or adjuvant/supporting therapy that can modulate the gut microbiota and/or prevent gut microbiome dysbiosis may be a new approach to targeted microbiome product development. Not only does this approach have the potential of restoring the microbiome balance, but it may also help achieve better response to the

currently used approaches," said Dr. Ghannoum.

The probiotic formulation developed through this data-powered design process was launched in market by BIOHM Health Inc. as a general wellness probiotic. Dr. Ghannoum is co-founder of BIOHM.

"We launched BIOHM to build off this process of utilizing microbiome data to create nutritional solutions that are built off the actual microbiome profiles of thousands and metadata of real individuals, allowing for truly targeted innovation," said Afif Ghannoum, CEO of BIOHM Health Inc. and Dr. Mahmoud Ghannoum's son.

Importantly Afif Ghannoum strongly noted that the probiotic currently in market has not been proven to, nor is not intended to prevent, treat or cure CD or any other condition or disease.

More information: Rachael Gowan et al, Modulating the Microbiome for Disease Treatment, *Gastroenterology* (2023). DOI: 10.1053/j.gastro.2023.01.017

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