

# **PRECISION** NUTRITION THE SCIENCE OF USING FOOD TO HEAL

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# PRECISION NUTRITION THE SCIENCE OF USING FOOD TO HEAL

#### **One Size Does Not Fit All**

The best diet for someone with IBD might be the one that's tailored to fit their distinct biological and clinical characteristics.

When someone is newly diagnosed with inflammatory bowel disease (IBD), one of the very first questions they ask is "What can I eat?" While clinicians usually provide broad guidance, the scientific evidence related to nutrition and IBD is limited. To further complicate matters, certain foods may seem to help some patients heal and yet can cause problems for others—and there's no way to predict who will fall into which group. Patients are often left to experiment with various diet plans on their own, or to attempt to track which foods seem to coincide with flares.

Our new Precision Nutrition Initiative is designed to change that. Last year, we received a generous donation from Jonathan D. Rose, MD, PhD, chair of our Intestinal Pathology Research Program, which enabled us to launch this innovative program. Since then, we've received additional funding from UnitedHealth Group Research & Development, allowing us to further expand the program. The Precision Nutrition Initiative has great potential to benefit patient health, while lowering reliance on costly drugs, because it aims to identify specific biomarkers (biological indicators of response to diet) that may eventually be used to provide personalized dietary guidance.

"We are pioneers in this area of IBD research; we're building an entirely new concept," says Andres Hurtado-Lorenzo, PhD, vice president, translational research programs for the Crohn's & Colitis Foundation. "No other institution has such a devoted effort focused on precision nutrition."

Scientists already suspect that many patients have unique biological characteristics that cause their body to ramp up inflammation or calm it down when they eat certain foods. However, they're still sorting out which biomarkers are most important. If they can pinpoint the connection between specific biomarkers and foods, patients might one day be able to take a simple blood or stool test and learn which foods will make them sicker or help them heal.

"We want to be able to say, 'You have a microbiome profile that makes you respond favorably to certain foods,' or 'You have a genetic mutation that will convert that food into an inflammatory substance, so you should avoid it,''' says Hurtado-Lorenzo. That kind of science-based guidance would be game-changing for patients; it might even one day allow some to reach remission simply by altering their diet.

The following four studies provide an overview of our work to expand our understanding of precision nutrition.

#### Using Artificial Intelligence to Predict Response to Diet

Why can one person with IBD enjoy a certain food, such as a tomato, while another finds that tomatoes can exacerbate symptoms? Thanks to a three-year grant from our Precision Nutrition Initiative, researchers at the University of California, San Diego hope to find out.

Investigator Pieter Dorrestein, PhD, and co-lead investigator Rob Knight, PhD, are creating a food-specific metabolomic signature for thousands of popular foods. Essentially, they're describing foods based on the metabolic end products that can be found in the body after someone eats them. Using their grant, Dorrestein and Knight will next attempt to use artificial intelligence to determine what someone ate simply by analyzing a sample of their blood, urine, or stool.

## In other words, they'll be able to tell what someone ate without even asking them.

The research team is hoping to prove that this is possible, and that they can use this methodology to show not only which foods someone consumed, but also which nonfood substances were ingested in the process. "One tomato may have fungicide on it, and another may not. One piece of beef may have antibiotics in it, and the other might not," Dorrestein explains. "Those differences might influence the microbiome significantly."

Knight and Dorrestein will be analyzing the gut microbiomes of participants to see whether differences in their composition may alter how digested food end products (metabolites) affect disease progression. "We hope to find some foods that are universally good [for IBD patients], but we also expect individuals to respond in different ways," says Knight. §

#### Matching Patients to an Anti-Inflammatory Diet

Many patients with Crohn's disease try to load up on foods that are generally believed to fight inflammation, but could following a specific anti-inflammatory plan be the key to controlling the condition? The answer might be in your genes. Maitreyi Raman, MD, from the University of Calgary, is using a three-year grant from the Precision Nutrition Initiative to identify clinical and biological patterns that might be used to predict which patients can quickly reach remission, simply by following a specific antiinflammatory diet.

"We hope to find some foods that are universally good...but we also expect **individuals to respond in different ways.**"

— Rob Knight, PhD Precision Nutrition Grant Recipient University of California, San Diego





The hope is that we can eventually **use food as treatment.**"

-KONSTANTINOS GERASIMIDIS, PHD, Precision Nutrition Grant Recipient University of Glasgow, Scotland

Raman has long been focused on the impact of diet on IBD. She has already conducted studies including some funded by the Foundation—which suggested that an anti-inflammatory diet often improves the gut microbiome and, in turn, patients' symptoms. Now she plans to use this grant to test her hypothesis in a clinical trial.

Participants will be randomly assigned to follow a prescribed anti-inflammatory diet—which includes plenty of fruits and vegetables, fatty fish at least twice a week, and minimally processed foods-or be part of the control group (which won't make dietary changes). Participants will be tested when the study begins and when it ends 12 weeks later to see how their eating habits have impacted the makeup of their microbiome, immune activity, and inflammatory markers. Raman and her team hope to figure out which patients respond, based on their unique biochemistry, and convert the data they gather on each patient into a multifactorial score that takes a person's genetics, microbiome, and metabolism into account.

"First, we have to show that this diet works. If it does, we want to figure out which patients respond and create a score that would enable us to recommend this diet to select patients in the future," she says.

#### Determining Which Foods Keep Teens in Remission

Seventeen days. That's all it takes for more than 50% of pediatric and adolescent Crohn's disease patients who achieve remission on a liquid diet to relapse after they return to their normal diet. Konstantinos Gerasimidis, PhD, a researcher and professor of clinical nutrition at the University of Glasgow, wants to find out why.

In many countries (often outside the U.S.), exclusive enteral nutrition—which involves providing nutrition via a feeding tube that goes into the stomach—is a well-established treatment for pediatric and adolescent Crohn's disease. "What's fascinating about this liquid diet is it works equally, if not better than high doses of steroids. Eighty-five percent of patients reach clinical remission, and their systemic inflammatory markers and gut inflammation get better, too," Gerasimidis says. But you can't stay on a liquid diet forever, and what happens next seems to be a coin toss.

Gerasimidis and his colleagues think they can tip the odds in a patient's favor by having them



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follow a dietary plan called CD-TREAT. They've already published preliminary results which found that Crohn's disease patients who stick to CD-TREAT—a solid food diet that mimics key nutrient characteristics of the liquid diet, and limits gluten and fiber—showed improvement in gut inflammation and reduced disease activity.

Using a three-year grant from the Precision Nutrition Initiative, they now aim to determine if teenagers who go on CD-TREAT immediately after achieving remission on a liquid diet will fare better than those who resume their normal eating habits. Participants will be randomly assigned to each group and asked to keep food diaries for 21 days. Researchers will also collect urine and stool samples to attempt to measure biomarkers related to the consumption of specific foods and gut inflammation.

Just as not all drugs work for all IBD patients, Gerasimidis says that food triggers are likely individualized. "We might find out that excluding a dietary component works in one patient but not another, and it might depend on the type of microbiome the patient has," he explains. "We're interested not just in dietary triggers, but also in how those triggers interact with the immune system and gut microbiome." §

#### Learning Who Benefits Most from Avoiding Processed Foods

Whole foods are healthy for everyone, but are highly processed ones especially damaging for certain IBD patients? Zhaoping Li, MD, PhD, of the University of California, Los Angeles, will be using a three-year grant from the Foundation's Precision Nutrition Initiative to investigate. Dr. Li plans to use biological data to identify signatures that may be used to predict who is most apt to reach remission by following a whole foods diet.

Dr. Li has seen firsthand how the same foods can impact two people very differently. To understand why, she and her research team will be running a randomized trial, including more than 100 people with mild-to-moderate Crohn's disease. One group will follow their usual diet; the other will follow a carefully orchestrated whole foods diet.

Eating fewer processed foods and more whole/ natural ones has already been associated with a wide variety of health perks, such as lower risk of heart disease and cancer. But Li believes this way of eating may also be beneficial for at least a subset of IBD patients, if not all.

"We're going to be looking at who responds, and try to identify the characteristics of a responder's gut microbiome, as well as genetic data from patients' DNA and RNA," she says. (9)

### Donor Spotlight: Dr. Jonathan D. Rose

Philanthropist Jonathan D. Rose, MD, PhD, is a steadfast champion and friend to the scientific research community, supporting a diverse array of research projects at leading institutions across the country.

As chair of the Crohn's & Colitis Foundation's Intestinal Pathology Research Program, Dr. Rose provides valuable support to the Foundation's research program. Dr. Rose recently made a major commitment to advancing IBD research with a meaningful grant to help the Foundation launch a robust, multi-institution research program to explore the role of diet's impact on IBD.

Central to all patients with IBD is how they manage their diet and food intake while living with a disease that affects their gastrointestinal tract. Yet, just as Crohn's disease and ulcerative colitis are highly individualized diseases, how one patient reacts to a particular food or diet may be very different from another patient's experience. The need to understand how diet affects disease, particularly at the individual patient level, is a critical gap in the IBD field's understanding of the disease, and an area of opportunity to make a significant impact on patients' quality of life. Our ability to launch this research program would truly not be possible without Dr. Rose's visionary support and leadership. 😵

### UnitedHealth Group Research & Development

UnitedHealth Group Research & Development is a diversified healthcare company dedicated to helping people live healthier lives, and helping to make the health system work better for everyone. UnitedHealth Group offers a broad spectrum of products and services through two distinct platforms: UnitedHealthcare, which provides healthcare coverage and benefits services; and Optum, which provides information and technology-enabled health services. §

### **Help Us Change Lives**

Through your support of the Crohn's & Colitis Foundation, you are helping to accelerate the discovery of new treatments and cures for Crohn's and colitis, and supporting those who are struggling with the physical and emotional toll of living with IBD. Help us create a better tomorrow for those suffering from IBD by making a gift to the Crohn's & Colitis Foundation today.

To make a contribution to the Crohn's & Colitis Foundation, please visit crohnscolitisfoundation.org/microscope.



#### Learn more at crohnscolitisfoundation.org

The Crohn's & Colitis Foundation is the leading nonprofit organization focused on both research and patient support for inflammatory bowel disease (IBD). The Foundation's mission is to cure Crohn's disease and ulcerative colitis, and to improve the quality of life for the millions of Americans living with IBD. Our work is dramatically accelerating the research process through our database and investment initiatives. We also provide extensive educational resources for patients and their families, medical professionals, and the public.