National Institutes of Health
Office of Nutrition Research

NIH Workshop: Impact of Diet on Mucosal Immunity and Immune-Mediated Digestive Diseases

August 21–22, 2024

Executive Summary

On August 21–22, 2024, the National Institutes of Health (NIH) Office of Nutrition Research (ONR) and the National Institute of Allergy and Infectious Diseases (NIAID), in collaboration with several other NIH Institutes and Offices, convened an NIH-wide workshop focused on the impact of diet on mucosal immunity and immune-mediated digestive diseases. The workshop also examined the current state of the science with respect to critical nutritional factors that regulate the development and function of the intestinal immune system. In addition to ONR and NIAID, workshop sponsors and participants included the National Institute of Diabetes and Digestive and Kidney Diseases, the National Cancer Institute, the National Institute on Aging, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the NIH Office of Dietary Supplements, and the NIH Office of Autoimmune Disease Research within the Office of Research on Women's Health. This broad engagement reflects a strategic refocusing on the importance of nutrition in the development and function of intestinal mucosal immunity and its relevance and impact to the work of virtually every component of NIH.

The workshop brought together NIH staff, research scientists, clinicians, people living with digestive diseases, and advocacy groups with the goals of understanding the current state of the science, identifying knowledge gaps, and discussing research opportunities that could close these knowledge gaps. A quote attributed to the ancient Greek physician Hippocrates—"All disease begins in the gut"—was a touchstone throughout the two-day workshop.

The keynote address and five scientific sessions included presentations and panel discussions on the role of nutrition in maintaining intestinal homeostasis during health and the potential of precision nutrition to alter intestinal disequilibrium during disease states across the lifespan. Overarching topics included the impact of early exposures, including perinatal diet and maternal nutritional status, on the development and maintenance of mucosal homeostasis and gut mucosal immunity, as well as the functional interactions of these systems with the gut microbiome and subsequent development of digestive and immune-mediated diseases. Specific sessions of the workshop focused on:

1. Impact of early dietary exposures on gut mucosal immune development and mucosal homeostasis
2. Production of diet-derived metabolites and their functional interactions with the gut microbiome and host mucosal immune system
3. Impact of diet on intestinal homeostasis and its relationship to development of digestive and immune-mediated diseases, such as autoimmunity disorders and cancer
4. Regulatory immune mechanisms related to tolerance, inflammation, innate and adaptive immunity, and neuroimmune interactions

5. Role of nutrition in maintaining or altering intestinal homeostasis and immunity during health and disease states across the lifespan

In addition, the workshop provided an opportunity for clinicians and researchers to hear from people living with diet- and immune-mediated digestive diseases about their lived experiences. People with digestive diseases, advocacy groups, and research foundations shared their perspectives on the scientific and practical barriers to success in curing or managing symptoms of disease.

Several broad themes emerged during the workshop. Common research findings indicate that additional research is needed to advance the field of immune-mediated digestive diseases. Converging lines of evidence suggest that, in response to diet, the gut microbiome can undergo rapid changes to mediate pathogenic host immune responses. Research into diet/microbiome/immune system interactions may be a particularly fruitful area to target future mechanistic and therapeutic studies. Novel tools and omics technologies are also now available that, for the first time, allow integration of information on the genome, metabolome, microbiome, and environment.

Areas of need for future research in the field of immune-mediated digestive diseases include studies that characterize interactions between the gut and other body systems, such as the respiratory and central nervous systems, that lead to a more comprehensive understanding of the pleiotropic effects of nutrition on human health. In consideration of clinical research studies, additional tools are needed that integrate metadata to enable clinicians, patients, and researchers to quantify key variables related to diet, disease symptoms, and quality of life. Furthermore, harmonization of terms and common measurements related to nutrition, including standardized definitions of “fasting,” “caloric restriction,” “keto diet,” and “high-fat Western diet,” as well as the control diet used in the context of clinical trials or translational research studies are needed.

Interdisciplinary collaboration was a recurring theme throughout the workshop. There was a call to continue and expand partnerships between scientists and clinicians and among patient advocacy groups, researchers, and clinical care teams. In addition, the inclusion of dietitians and nutritionists as critical components of an integrated team that works to improve care, quality of life, and outcomes for people with immune-mediated digestive diseases was highlighted. Additional discussion topics included the impact of food labeling for people living with digestive diseases as well as the need to overcome barriers to accessing healthy foods, including cost and availability.

Over the two days, the wide range of diseases and conditions that were discussed included inflammatory bowel disease, celiac disease, necrotizing enterocolitis, eosinophilic esophagitis, colorectal cancer, food allergies, and metabolic endotoxemia. The identified research gaps and opportunities also ranged the entire translational research spectrum. At the conclusion of the workshop, the NIH organizers expressed their appreciation for the thoughtful contributions of the participants and opportunity for the insights shared to inform a research agenda that aims to fill critical scientific gaps, advance the nutrition field, and improve public health.