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Nutrition, Gut Microbiota and Immunity: Therapeutic Targets for IBD

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Preface

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic debilitating diseases that occur in populations around the world. The diseases can manifest at any age, and therefore represent a clinical challenge for pediatricians, internists, family practitioners, and surgeons. The underlying etiology is multifactorial, where host genetic polymorphisms account for a minority of the risk for disease development, emphasizing the importance of environmental factors such as the gut microbiota. Supportive of this notion, epidemiologic associations show a significant increase in IBD incidence over the past few decades associated primarily with residence in industrialized nations.

Current therapeutic modalities for IBD are largely targeted at suppression of the innate and adaptive immune response. Commonly used therapies include mesalamine, corticosteroids, thiopurine analogues (azathioprine or 6-mercaptopurine), methotrexate, and anti-tumor necrosis factor- α agents. There is also limited use of natalizumab, a biologic targeting the α 4-integrin adhesion molecules. While effective for many patients, these therapeutic strategies are not universally effective. Furthermore, they are each associated with the risk of serious and sometimes fatal adverse events.

An alternative approach to the treatment of IBD is to change the environmental factors that contribute to the etiology or perpetuation of inflammation. Leading targets for this alternative approach to therapy are the principal contents of the gastrointestinal tract – our diet and the human gut microbiota. Indeed, there is reason to believe that the composition of our diet and the gut microbiota might have a synergistic effect on inflammation related to IBD.

This monograph includes summaries of talks presented at the 79th Nestlé Nutrition Institute Workshop held in New York on the 28th and 29th of September 2013. The speakers in the symposium addressed our current understanding of the epidemiology and biologic underpinnings that manifest as CD and UC; the gut microbiota, its function, and how it may interact with

nutritional status in perpetuating IBD; the potential for manipulation of the gut microbiota through the use of prebiotics, probiotics, antibiotics, and fecal transplantation, and the current role of and future prospects for nutritional interventions in the management of these diseases.

Despite advances in the treatment of IBD, a substantial proportion of patients experience relapse of the disease every year. Many of these patients still require surgery. Although surgery represents a cure for UC, it is associated with lifelong alteration in bowel function and risks of other complications. For CD, surgery is generally only a temporizing measure as disease recurrence is common. Given the incomplete effectiveness of our current immunosuppressive therapies and their associated toxicities, there is a real need for alternative treatment strategies. Altering key environmental exposures that drive the inflammatory response could open new avenues to treat these debilitating lifelong diseases.

James D. Lewis

Frank M. Ruemmele

Gary D. Wu

Foreword

Inflammatory bowel disease (IBD) currently affects 1 in 200 people in the United States. The incidence of IBD has been gradually increasing globally in the past several decades. While the explanation for this increase is not totally clear, environmental factors, including changes in the diet, may be a key factor.

The 79th Nestlé Nutrition Institute Workshop held in New York City in September 2013 carries on the theme from the 77th Nestlé Nutrition Institute Workshop, where world experts gathered in Panama City to present their latest findings on how nutrient status can modulate immunity and improve health conditions in pediatric patients. This workshop chaired by Prof. Lewis, Prof. Ruemmele and Prof. Wu focused on the complex relationship between nutrition, inflammation and the microbiome as it relates to IBD; this is arguably the hottest area of IBD research currently.

Previously, the theories on pathogenesis of IBD suggested a combination of genetic susceptibility and immune and external environmental factors. In recent years, the gut microbiota has greatly gained in importance and has been accepted as the 4th element in the pathogenesis of IBD. These relationships are complex and not independent since IBD patients may have a genetic susceptibility that leads to abnormal immune responses directed against the intestinal microbiota.

Currently, over 160 genetic susceptibility genes have been identified for IBD, the most prevalent of these are Nod2, an important intracellular pathogen recognition sensor, and ATG 16L1, important in autophagy, killing and processing of phagocytized bacteria. However, the function of many of the other genes identified has not been fully characterized.

The gut microbiota consists of both protective and aggressive microbes, and the balance between these populations is important, not only in the pathogenesis of IBD, but also in the ongoing inflammatory response. A better understanding of the complex interactions, particularly the role of the gut microbiota in the inflammatory process, holds the key for potential for targeted therapy in

the future. The ability to selectively alter the composition and thus the function of the gut microbiome through diet, prebiotic and probiotic therapy may be a very attractive treatment alternative for patients with IBD. There is already good evidence in the medical literature that total enteral nutrition is highly efficacious in inducing remission in pediatric Crohn's disease. In these patients, there is a significant shift in the gut microbiota following the successful enteral therapy; however, the causal relationship has not been established to date.

On behalf of Nestlé Nutrition Institute and Nestlé Health Science, we would like to thank the Chairmen, Prof. James Lewis, Prof. Frank M. Ruemmele and Prof. Gary Wu for their diligent work in assembling such a distinguished group of researchers, clinicians and speakers. We would also like to thank all the speakers for their hard work in putting together such outstanding presentations. The energy throughout the meeting, the interest among the participants and the quality of the questions posed to the speakers were all testaments to the quality of the meeting and the importance of this topic. We hope that important collaborations will result from the many positive interactions during this workshop.

Finally, we would like to thank Natalia Wagemans, Mélanie Costinas, Bernice Hammer and Mélanie Pittier who worked tirelessly in the background to ensure the meeting ran smoothly and made it the resounding success that it was.

We look forward to a follow-up NNI Workshop in the near future to review the advances in this exciting field of research.

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