Inflammatory bowel disease (IBD), like all immune-mediated inflammatory diseases, is believed to occur as a result of an environmental trigger in a genetically predisposed individual. Despite decades of research, the relative contribution of each of these variables (genes and the environment) remains unclear. This session first highlighted Australian research into environmental factors associated with the pathogenesis of IBD, then culminated in an entertaining debate between two international experts on the relative contribution of each of these variables in IBD causality.

The Geelong Epidemiological Crohn’s Colitis Outcome study, established as a population-based inception cohort in 2007, has produced valuable Australian IBD epidemiological data through researchers from St. Vincent’s Hospital, Melbourne. Presenting recent data from this registry, Dr. Ola Niewiadomski showed an inverse association between daily fruit and caffeine intake and the development of ulcerative colitis (UC), but a positive association between fast food intake and development of both Crohn’s disease (CD) and UC. Potential mechanisms for the role of food in the pathogenesis of IBD were discussed, including the effect of food on the microbiota, the mucus layer, and mucosal immunology.

Previous migration studies have demonstrated an increased incidence of IBD among migrants to westernized countries. Dr. Yanna Ko, from Concord Hospital, Sydney, presented research on the effect of migration from Middle Eastern countries to Australia on the incidence of IBD. This prospective case–control study of almost 800 subjects demonstrated that differential IBD environmental risk factors exist between Middle Eastern migrants and Caucasians. In particular, antibiotic use reduced the risk of CD and UC in Middle Eastern migrants but increased the risk of both conditions in Caucasians. Similarly, markers of reduced “hygiene” (rural dwelling, pet ownership, pet feeding, and farm animal contact) reduced CD and UC incidence in Middle Eastern migrants but not Caucasians.

In a highly entertaining debate, Dr. Miles Parkes from Addenbrooke’s Hospital, Cambridge, argued that the answer to the cause of IBD will be found in the genes, whereas Dr. Ashwin Ananthakrishnan from Massachusetts General Hospital, Boston, argued that it will be discovered in the environment. Dr. Parkes argued that studies of IBD causality are confounded by the presence of inflammation that makes it difficult to determine whether the mucosal immunological dysfunction of IBD is the primary event triggering inflammation or vice versa. By contrast, an appeal of genetic studies is that genes are not influenced by inflammation. He argued that twin studies have demonstrated that genes play a pivotal role in determining the composition of the microbiota, the “dysbiosis” of which is unequivocally central to IBD pathogenesis. The important role of genome-wide association studies was discussed, including the seminal paper that demonstrated 163 genetic loci associated with an increased risk of IBD, with considerable overlap of disease-susceptibility loci between CD and UC. Individual mutations associated with defects in innate immunity and autophagy were then presented, including NOD2, ATG16L1, IL23R, and IRGM.

In contrast, Dr. Ananthakrishnan argued that despite an increasing number of IBD-associated loci being identified in recent decades, the overall proportion of disease that can be explained by hereditable factors is less than 15% from most studies. Instead, the changing global epidemiological trends in IBD closely follow global environmental changes of “westernization,” suggesting the central role of the environment in IBD causality. Supporting this hypothesis is the fact that emerging areas of increased IBD incidence (e.g. Asia) are distinct genetically from established regions (e.g. low NOD2 mutations in Asians) but have increasingly similar environments (e.g. levels of hygiene and fast food intake). He argued that data supporting environmental causality of IBD are now emerging from well-designed prospective cohort studies that have demonstrated associations, both positive and negative, between the development of IBD and the following environmental factors—smoking, dietary fiber intake, polyunsaturated fatty acid intake, antibiotic exposure, and breast feeding. His opinion was that environmental factors were a greater determinant of the composition of the microbiota than genetics and that the efficacy of “environmental” treatment strategies (e.g. exclusive enteral nutrition and smoking cessation) in changing natural history outcomes is further evidence of the primary role of environmental factors in IBD pathogenesis.

References