INTRODUCTION
The inflammatory bowel diseases (IBD), incorporating ulcerative colitis and Crohn's disease, are complex, chronic inflammatory diseases of the gastrointestinal tract. Even within the broad diagnostic categories mentioned, each disease is strikingly heterogeneous. Clinically, enormous variation is seen in anatomic location/extent, disease behavior, associated extraintestinal manifestations, and response to therapy. Although the exact details of disease pathogenesis remain elusive, the generally accepted hypothesis is that IBD occurs as a result of an inappropriate and exaggerated mucosal immune response to ubiquitous environmental factors (most likely commensal microflora) in genetically susceptible hosts. It is hypothesized that multiple genes influence both the development and progression of IBD, with both gene-gene and gene-environment interactions accounting for the observed heterogeneity. It is possible that genetic variation, to some extent, modulates the host susceptibility and response to commensal bacteria, potentially via increased risk of altered mucosal barrier function or altered immune response.

The 2005 Nobel prize in Physiology and Medicine awarded to Robin Warren and Barry Marshall is a reminder that the solution to some human diseases does not reside solely within the host but rather might be found at the interface with the microbial environment. Moreover, it seems that certain basic developmental features and functions of the mammalian immune system depend on interactions with the human microbiome. Unlike opportunistic pathogens, which elicit immune responses that result in tissue damage during infection, some symbiotic bacterial species have been shown to prevent inflammatory disease during colonization. Therefore, the microbiota has the potential to exert both pro- and anti-inflammatory responses, and the composition of the bacterial communities in the gut may be intimately linked to the proper functioning of the immune system. As IBD is a disorder of mucosal inflammation, the mucosa-associated microflora seems to be of great relevance to the disease process. Differences have been observed between the dominant fecal microbiota and the mucosa-associated microbiota at different sites of the colon and rectum in IBD versus healthy subjects. Alterations in the microflora
community structure due to other triggers like antibiotic therapy or infectious colitis, can promote the development of IBD.

We believe that genetic epidemiology and functional genomics represent a turning point in the understanding of the pathogenesis of IBD and may provide novel biomarkers able to integrate the existing clinical classifications. It is generally believed that there may be a number of "susceptibility genes" that confer a general predisposition to IBD. Other "modifier genes," although they don't initiate disease, then act to influence specific phenotypic characteristics such as disease behavior, complications, and treatment response, among others. The intracellular nucleotide-binding oligomerization domain (NOD), Nod-like proteins or receptors (NLR) are a family of sensors of intracellularly encountered microbial motifs and 'danger signals' that have emerged as being critical components of the innate immune responses and of inflammation in mammals. Several Nod-like receptors, including Nod1, Nod2, NALP3 (NACHT-LRR-PYD-containing protein), Ipaf (ICE protease-activating factor) and Naip (neuronal apoptosis inhibitor protein), are strongly associated with host responses to intracellular invasion by bacteria or the intracellular presence of specific bacterial products. An additional key function of Nod-like receptors is in inflammatory conditions, which has been emphasized by the identification of several different mutations in the genes encoding Nod1, Nod2 and NALP3 that are associated with susceptibility to inflammatory disorders. Both "susceptibility" and "modification" may be further influenced by interaction with environmental factors. Although proposed several years ago, genetic findings to date have generally been consistent with this conceptual model. Indeed, if this model is true, it is presumed that eventually, knowledge of a patient's genotype and altered microflora may allow the clinician to apply a molecular classification to his/her disease and, presumably, better predict both the future disease course and appropriate therapeutic options.