High-density mapping of the MHC identifies a shared role for HLA-DRB1*01:03 in inflammatory bowel diseases and heterozygous advantage in ulcerative colitis.

Abstract:
Genome-wide association studies of the related chronic inflammatory bowel diseases (IBD) known as Crohn's disease and ulcerative colitis have shown strong evidence of association to the major histocompatibility complex (MHC). This region encodes a large number of immunological candidates, including the antigen-presenting classical human leukocyte antigen (HLA) molecules. Studies in IBD have indicated that multiple independent associations exist at HLA and non-HLA genes, but they have lacked the statistical power to define the architecture of association and causal alleles. To address this, we performed high-density SNP typing of the MHC in >32,000 individuals with IBD, implicating multiple HLA alleles, with a primary role for HLA-DRB1*01:03 in both Crohn's disease and ulcerative colitis. Noteworthy differences were observed between these diseases, including a predominant role for class II HLA variants and heterozygous advantage observed in ulcerative colitis, suggesting an important role of the adaptive immune response in the colonic environment in the pathogenesis of IBD.
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