Multi-cohort, multi-regional metagenomic association study of inflammatory bowel disease patients and non-IBD controls.

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Inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), is a group of chronic inflammatory conditions of the gastrointestinal tract. The incidence and prevalence of IBD have been high mainly in Western countries such as North America, northern and western Europe. In the last two decades, incidences of IBD in Asia and eastern Europe have also risen steadily due to westernized diet and changes in other environmental factors (Kaplan, G. G., 2015). IBD is one of the representative diseases associated with gut microbial dysbiosis. Common changes in the gut microbiome in IBD patients include an increase in facultative anaerobes and a decrease in obligately anaerobic producers of short-chain fatty acids (SCFAs) (Morgan, X. C. *et al.*, 2012). Besides functional dysbiosis of the gut microbiome, multiple factors including host genetics and environmental conditions such as diet also affect immunological responses and inflammation in the intestine; the complex interplay between these factors must be considered. Taking this into account, we performed a multi-cohort metagenomic association study of IBD, utilizing metagenomic shotgun sequencing data of 1,002 cross-sectional stool samples collected from published studies. Sequencing data were pre-processed, and batch corrected with compositionality-aware methods. Clean reads were then aligned to a comprehensive gut microbial genome database HRGM (Kim, CY. *et al.*, In Press) to establish taxonomic profiles of all samples. Batch effects and differences among multi-regional cohorts were assessed, and differently abundant microbial species were then identified.

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