Abstract citation ID: jjad212.1289
P1159
Gene and environment interactions in inflammatory bowel disease: a systematic review of human epidemiologic studies

J. Bai¹, D. Bouwknegt¹, R. Weersma¹, G. Dijkstra¹, K. van der Sloot¹, E. Festen¹,²
¹University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, The Netherlands ²University Medical Center Groningen, Department of Genetics, Groningen, The Netherlands

Background: Complex gene-environment interaction for Inflammatory Bowel Disease (IBD) remains elusive. This systematic review aims to summarize the current evidence of gene and environment interactions in IBD.

Methods: PubMed, EMBASE, Web of Science and Scopus were systematically searched from inception through July 20, 2022 to identify publications examining the interaction effect of genetic variants and environmental factors in IBD. Two investigators independently screened the title/abstract and full text according to the predefined criteria. All eligible studies were graded using STREGA guideline. The protocol was registered on PROSPERO (CRD42023443071).

Results: 4,305 publications were identified and screened, resulting in 36 eligible studies. 17 studies reported statistically significant interactions. The interaction effect of NOD2 and smoking was most frequently investigated and showed variant-specific interaction at rs2066847 regading risk of Crohn’s disease (CD). Gene-smoking interactions were further identified in 1) other IBD risk genes (ATG16L1, IL23R, CALM3), as well as the IBD-genetic risk score (GRS), 2) detoxification genes (GSTP1 and HMOX1), 3) smoking-associated genes (CHRNA3, CHRNAS, PPP1R3C, BDNF), as well as the general smoking-GRS, and 4) the inflammation cytokine gene (IL-1β) using the candidate gene approach. Using the Illumina immune-focused Chip, another 64 smoking interacting variants were identified.

Gene-diet interactions were reported across different nutritional measures, including the intake of fatty acids with CYP4F3 and FADS2, serum level of selenium with SEPHS1and SEPSECS, dietary intake of potassium with IL21, alcohol consumption with IL12B, dietary heme iron intake with FcgRIIA and serum level of 25-hydroxyvitamin D with VDR. No genome wide environment interaction studies (GWEIS) of IBD have been conducted to date, while this strategy holds great potential to unravel the missing heritability influenced by environment factors for IBD.

Conclusion: While past studies have increased insights into potential gene-environmental interactions in the pathophysiology of IBD, current evidence is limited and inconclusive due to lack of replication of presented results, and limited study power. Further research, including GWEIS and clinical trials, is needed for future recommendations on lifestyle and dietary modification, based on individual genetic backgrounds.