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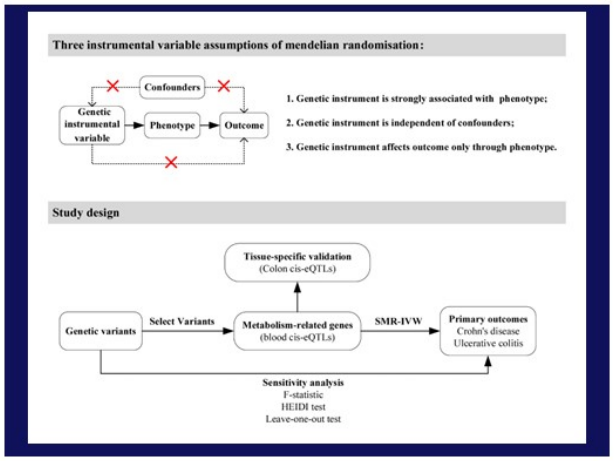
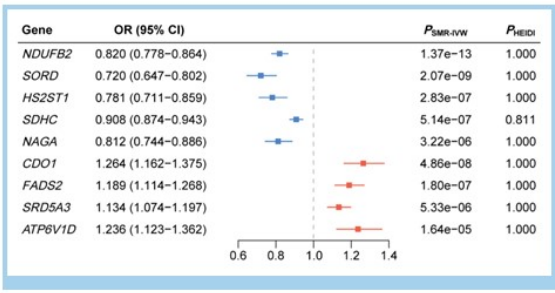
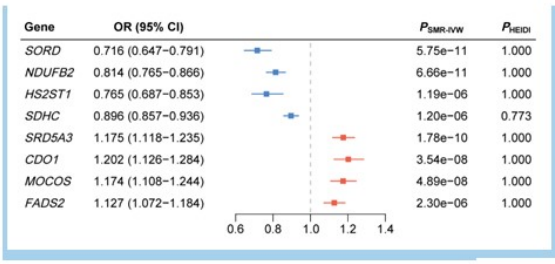
Metabolism-related genome-wide Mendelian randomization identifies potential causal genes for inflammatory bowel disease



Overview of this MR study design



The MR results for the association between the expression of metabolism-related genes and the risk of CD



The MR results for the association between the expression of metabolism-related genes and the risk of UC

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Genome-wide Mendelian randomization implicates metabolism-related gene expression in inflammatory bowel disease in European populations

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Keywords: Metabolism. Inflammatory bowel disease. Crohn's disease. Ulcerative colitis. Mendelian randomization.

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Abbreviations

IBD	inflammatory bowel disease
CD	Crohn's disease
UC	ulcerative colitis
TCA	tricarboxylic acid
RCTs	randomized controlled trials
MR	Mendelian randomization
GO	Gene Ontology
KEGG	Kyoto Encyclopedia of Genes and Genomes
IVs	instrumental variables
Cis-eQTLs	cis-expression quantitative trait locus
eQTLs	expression quantitative trait loci
GTEx	Genotype-Tissue Expression
GWAS	genome-wide association studies
IIBDGC	International Inflammatory Bowel Disease Genetics Consortium
SMR-IVW	summary data–based Mendelian randomization inverse-variance weighted
SNPs	single-nucleotide polymorphisms
LD	linkage disequilibrium
HEIDI	heterogeneity in dependent instruments
OR	odds ratio
CI	confidence interval
SD	standard deviation
FDR	false discovery rate
ETC	electron transport chain
OXPHOS	oxidative phosphorylation
SUCNR1	succinate receptor
AR	androgen-androgen receptor
PUFAs	polyunsaturated fatty acids
EPA	eicosapentaenoic acid

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docosahexaenoic acid

DHA

Abstract

Background: The impact of metabolism-related genes on inflammatory bowel disease remains unclear. This study aimed to identify the causal relationships between metabolism-related genes and inflammatory bowel disease.

Methods: We performed summary-data-based Mendelian randomization analysis to investigate the associations of metabolism-related genes with inflammatory bowel disease.

Results: In the first priority, genetically predicted SORD (CD: odds ratio [OR], 0.716, 95% confidence interval [CI], 0.647−0.791; UC: OR, 0.720, 95% CI, 0.647−0.802), NDUFB2 (CD: OR, 0.814, 95% CI, 0.765−0.866; UC: OR, 0.820, 95% CI, 0.778−0.864), HS2ST1 (CD: OR, 0.765, 95% CI, 0.687−0.853; UC: OR, 0.781, 95% CI, 0.711−0.859), and SDHC (CD: OR, 0.896, 95% CI, 0.857−0.936; UC: OR, 0.908, 95% CI, 0.874−0.943) expression were associated with decreased CD and UC risk. Conversely, genetically predicted higher expression of SRD5A3 (CD: OR, 1.175, 95% CI, 1.118−1.235; UC: OR, 1.134, 95% CI, 1.074−1.197), CDO1 (CD: OR, 1.202, 95% CI, 1.126−1.284; UC: OR, 1.264, 95% CI, 1.162−1.375), and FADS2 (CD: OR, 1.127, 95% CI, 1.072−1.184; UC: OR, 1.189, 95% CI, 1.114−1.268) were associated with increased CD and UC risk. In the second priority, we found MOCOS (OR: 1.174, 95% CI: 1.108−1.244) was presumptively associated with CD, the NAGA (OR: 0.812, 95% CI: 0.744−0.886) and ATP6V1D (OR: 1.236, 95% CI: 1.123−1.362) were associated with UC.

Conclusion: This study provides genetic support for a potential causal relationship between metabolism-related genes and the risk of inflammatory bowel disease. Our findings should be interpreted with caution given the inherent limitations of Mendelian randomization analysis, and further research is warranted to validate these results.

Keywords: Metabolism. Inflammatory bowel disease. Crohn's disease. Ulcerative colitis. Mendelian randomization.

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Introduction

Inflammatory bowel disease (IBD), mainly encompassing Crohn's disease (CD) and ulcerative colitis (UC), imposes a substantial global burden. Despite treatment advances, the complex etiology of IBD challenges therapeutic efficacy, with highly variable patient responses to traditional anti-inflammatory drugs and immune-targeted biologics (1). Consequently, there is an urgent need to explore alternative approaches beyond immune modulation, with metabolic reprogramming emerging as a promising intervention (2).

Metabolic reprogramming refers to the dynamic adaptation of cellular metabolism to meet physiological or pathological demands (3). Accumulating evidence has identified significant metabolic reprogramming (e.g., in antioxidant defense, fatty acid metabolism, glycolysis, and the TCA cycle) within the IBD intestinal microenvironment, implicating these pathways in disease pathogenesis (4). Preclinical research suggests interventions modulating metabolic pathways also show therapeutic potential in IBD (5). However, translational challenges persist due to interspecies differences, limiting applicability of animal or cellular studies to humans.

Large-scale population-based cohort studies have identified metabolism-associated genes differentially expressed in IBD patients (6) but these findings often lack clarity on causality. Observational studies cannot reliably distinguish whether metabolic changes are causes, consequences, or merely correlates of IBD due to confounding and reverse causality biases (7). Moreover, ethical and financial constraints preclude randomized controlled trials (RCTs) to systematically investigate causal relationships between thousands of metabolism-related genes and IBD.

Mendelian randomization (MR) provides a robust alternative to overcome these challenges. By leveraging genetic variants as instrumental variables, MR can assess causal effects between exposures and outcomes, offering quasi-randomized evidence less prone to confounding and reverse causality (8). Additionally, MR also allows identification of candidate pathways by evaluating the impact of gene expression changes on disease risk. For instance, recent MR research has elucidated causal roles of mitochondrial dysfunction in various cancers, identifying actionable

targets (9).

Compared to databases such as Gene Ontology (GO) and Reactome, Kyoto Encyclopedia of Genes and Genomes (KEGG) offers more comprehensive and focused coverage of metabolic pathways. Therefore, in this study, we extracted metabolism-related genes from the KEGG and conducted an MR analysis to evaluate the causal relationships between the expression of metabolism-related genes and the risk of CD and UC.

Materials and Methods

Study design

Firstly, to identify metabolic reprogramming characterized by genetic predisposition in the metabolism-related genomes, we extracted a list of 1,683 known human metabolism-related genes from the KEGG database (10) (http://www.genome.jp/kegg/). These genes are categorized into 11 classes of metabolic pathways (carbohydrate metabolism, energy metabolism, lipid metabolism, nucleotide metabolism, amino acid metabolism, metabolism of other amino acids, glycan biosynthesis and metabolism, metabolism of cofactors and vitamins, metabolism of terpenoids and polyketides, biosynthesis of other secondary metabolites, xenobiotics biodegradation, and metabolism). Then, instrumental variables (IVs) for metabolism-related genes in blood were used for MR analysis of CD and UC, respectively. Subsequently, further validation was performed on the colon tissue. Finally, a series of sensitivity analyses were conducted to assess the robustness of the results.

Data sources

To generate cis-expression quantitative trait locus (Cis-eQTLs) IVs for metabolism-related genes, genetic variants that are robustly associated with gene expression were extracted using expression quantitative trait loci (eQTLs) statistics obtained from the eQTLGen Consortium (11) (https://www.eqtlgen.org/cis-eqtls.html). The eQTLGen consortium contains thousands of genetic loci regulating blood gene

expression from 31,684 individuals. The tissue-specific expression of eQTLs data retrieved from the Genotype-Tissue Expression (GTEx) project (12) was used to assess the impact of tissue-specific candidate gene expression on CD and UC. Genome-wide association studies (GWAS) summary statistics for CD (cases: 5,956; controls: 14,927) and UC (cases: 6,968; controls: 20,464) outcomes were obtained from the International inflammatory bowel disease Genetics Consortium (IIBDGC) (13). All diagnoses of CD and UC were based on accepted radiologic, endoscopic, and histopathologic evaluation (13). Table 1 provides details of the data sources for this study. All original studies from which the data were derived had received prior ethical approval from their respective Institutional Review Boards.

Mendelian randomization

We utilized the summary data–based MR inverse-variance weighted (SMR-IVW) method (14) for MR analysis. SMR-IVW is an extension of the SMR that allows the performance of IVW MR analyses on omics and GWAS summary data (14). SMR-IVW differs from SMR in that SMR-IVW allows for the inclusion of multiple single-nucleotide polymorphisms (SNPs), whereas the latter only considers the effect of the top SNP on the outcome. Previous studies have demonstrated that multi-SNP-based SMR tests are more powerful than single-SNP-based tests (14,15). Therefore, we adopt SMR-IVW as our main analytical method. Referring to previous protocols, we applied the default parameters of a multi-SNP-based test for MR analysis (https://yanglab.westlake.edu.cn/software/smr/#Multi-SNP-basedSMRtest).

Specifically, to ensure strong associations between IVs and gene expression, we selected only SNPs that passed a p-value threshold (default value: $5x10^{-8}$). Then, the SNPs are pruned for linkage disequilibrium (LD) using a weighted vertex coverage algorithm with an LD r2 threshold (default value: 0.9) and a window width (default value: 500). In colon tissue, since there were not enough IVs for MR analysis, p-value threshold was set to 1×10^{-5} with reference to previous studies (15).

Sensitivity analysis

We performed a series of sensitivity analyses to assess the robustness of the results. First, we calculated the F-statistic ($beta^2/se^2$) (16) for each IV to minimize weak instrument bias. The IVs were considered sufficiently strong when F-statistic > 10. Second, we used the heterogeneity in dependent instruments (HEIDI) test to distinguish pleiotropy from linkage (17) where PHEIDI <= 0.05 was considered likely due to pleiotropy and therefore discarded from the analysis. Then, we conducted a leave-one-out analysis to evaluate whether MR estimation is driven or biased by a single SNP that might have a pleiotropic effect. Leave-one-out analysis re-estimates the effect by sequentially removing one SNP at a time. When the removal of a SNP causes a dramatic change in the estimate, it is suggested that the outlier SNP is interfering with the MR estimate (18). Finally, we calculated the statistical power of this MR (19). Genes with consistent results in both CD and UC will be prioritized first, whereas those unique to either subtype will be prioritized second.

SMR-IVW analysis was implemented using the SMR-IVW software and the HEIDI test was conducted using the SMR software (v1.3.1). Other analyses were performed in the R software (v4.3.0). The causal estimates were expressed as odds ratio (OR) with 95% confidence interval (CI) for one standard deviation (SD) change in metabolic gene expression level. To avoid increasing the risk of type I errors in a large number of genetic analyses, we applied Bonferroni (20) and false discovery rate (FDR) correction (21).

Results

Baseline characteristics

In the analysis of CD, a total of 1,110 and 418 metabolism-related genes from blood and colon tissue, respectively, were included in the MR analysis. For UC, 1,112 and 422 metabolism-related genes from blood and colon tissue, respectively, were assessed. All IVs exhibited F-statistics greater than 10, confirming strong instrument

strength. To ensure the robustness of findings, only genes demonstrating consistent effects in both blood and colon tissue analyses were considered valid results. Results obtained solely from a single dataset are deemed inconclusive due to the lack of replication. The statistical power analyses indicated that the majority of MR estimates had sufficient power (**Table 2**).

Crohn's disease

Following Bonferroni (threshold: 0.05/1,110) and FDR correction, genetically predicted one SD increase in the expression of SORD (odds ratio [OR]: 0.716; 95% CI: 0.647–0.791, FDR=1.32e-09), NDUFB2 (OR: 0.814; 95% CI: 0.765–0.866, FDR=1.50e-09), HS2ST1 (OR: 0.765; 95% CI: 0.687–0.853, FDR=1.09e-05), and SDHC (OR: 0.896; 95% CI: 0.857–0.936, FDR=1.10e-05) was associated with a significantly reduced risk of CD (**Fig 1A**). Conversely, higher genetically predicted expression levels of SRD5A3 (OR: 1.175; 95% CI: 1.118–1.235, FDR=3.48e-09), CDO1 (OR: 1.202; 95% CI: 1.126–1.284, FDR=4.63e-07), MOCOS (OR: 1.174; 95% CI: 1.108–1.244, FDR=6.09e-07), and FADS2 (OR: 1.127; 95% CI: 1.072–1.184, FDR=1.93e-05) were associated with an increased CD risk (**Fig 1A**). These findings were consistently observed in colon tissue analysis (**Table 3**). Furthermore, the HEIDI test (all PHEIDI > 0.05) supported the robustness of these results (**Fig 1A**), while leave-one-out sensitivity analyses ruled out significant bias from individual IVs (**Fig 2A**).

Ulcerative colitis

For UC, Bonferroni (threshold: 0.05/1,112) and FDR correction revealed that genetically predicted one SD increase in the expression of NDUFB2 (OR: 0.820; 95% CI: 0.778–0.864, FDR=4.27e-12), SORD (OR: 0.720; 95% CI: 0.647–0.802, FDR=3.37e-08), HS2ST1 (OR: 0.781; 95% CI: 0.711–0.859, FDR=3.00e-06), SDHC (OR: 0.908; 95% CI: 0.874–0.943, FDR=4.98e-06), and NAGA (OR: 0.812; 95% CI: 0.744–0.886, FDR=2.53e-05) was associated with decreased UC risk (Fig 1B). In contrast, elevated expression levels of CDO1 (OR: 1.264; 95% CI: 1.162–1.375,

FDR=6.19e-07), FADS2 (OR: 1.189; 95% CI: 1.114–1.268, FDR=2.00e-06), SRD5A3 (OR: 1.134; 95% CI: 1.074–1.197, FDR=3.98e-05), and ATP6V1D (OR: 1.236; 95% CI: 1.123–1.362, FDR=1.04e-04) were associated with increased UC risk (**Fig 1B**). These associations were consistently replicated in colon tissue analysis (**Table 3**). Sensitivity analyses, including the HEIDI test and leave-one-out plots, confirmed the robustness and reliability of these findings (**Figs 1B and 2B**).

Discussion

This study suggests that metabolic reprogramming characterized by genetic predisposition plays a causal role in IBD (**Fig 3**). Among the identified genes, SORD, NDUFB2, HS2ST1, SDHC, SRD5A3, CDO1, and FADS2 demonstrated consistent causal effects on both CD and UC. Additionally, MOCOS was specifically associated with CD, while NAGA and ATP6V1D were implicated in UC.

The SORD gene encodes sorbitol dehydrogenase, which plays a significant role in sorbitol degradation (22). Clinical data revealed increased fecal sorbitol in active IBD patients (23). Mouse studies indicate that high sorbitol worsens intestinal inflammation by promoting C. difficile infection and growth (23). These findings align with our findings of a strong causal effect of SORD expression on decreased IBD risk.

NDUFB2 is a core component of the electron transport chain (ETC) complex I and is essential for oxidative phosphorylation (OXPHOS). Experimental models have demonstrated that complex I deficiency leads to spontaneous intestinal inflammation and increased colitis sensitivity (24). Our study therefore supports a pathogenic role for NDUFB2 in IBD risk, which underscores the need for mechanistic investigation. HS2ST1, an enzyme for heparan sulfate 2-O-sulfation, regulates cellular senescence (25). Although MR suggests its association with IBD risk, further experimental validation is required to elucidate its mechanism of action. SDHC, a subunit of succinate dehydrogenase, regulates succinate levels in the tricarboxylic acid (TCA) cycle. Succinate, a pro-inflammatory metabolite shaped by gut microbiota, plays a key role in IBD, with elevated levels in serum and fecal samples of patients, where it promotes macrophage activation through Na+-dependent transport, contributing to persistent inflammation (26). Moreover, succinate also

modulates immune responses through its receptor SUCNR1, which drives intestinal inflammation and fibrosis, as shown by its increased expression in CD tissues and experimental colitis models (27). Consistently, our findings indicate that SDHC is a relevant candidate pathway for IBD.

SRD5A3 encodes steroid 5-alpha reductase, mainly involved in glycosylation and steroid hormone synthesis (28). However, how sex hormones influence IBD pathogenesis remains unclear (29). Although our MR results implicate androgen metabolism in IBD, the lack of sex-stratified data means further studies are needed. CDO1 encodes cysteine dioxygenase 1, a key enzyme in taurine synthesis. Available research also suggests an association between taurine metabolism and IBD (30). However, the precise mechanism linking CDO1 to IBD remains unclear, and the correlation identified by MR requires further experimental validation.

FADS2, encoding delta-6 desaturase, regulates synthesis of long-chain omega-3 polyunsaturated fatty acids (PUFAs) such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (31). The effect of omega-3 fatty acids on IBD remains controversial. Daily supplementation with EPA and DHA has been reported effective in reducing CD relapse (32). However, a study with a median follow-up of 5.3 years found no significant reduction in the incidence of a composite outcome of IBD and other autoimmune diseases with fish oil containing EPA and DHA supplementation (33). Thus, our genetic evidence suggests a causal link between the PUFA synthesis pathway and IBD, although further research is needed to confirm and elucidate this relationship. Our study also implicates MOCOS in CD pathogenesis. This gene encodes an enzyme essential for the activity of several oxidases, and its polymorphisms have been linked to altered IBD drug metabolism(34), though mechanisms need clarification. Similarly, the causal associations of NAGA and ATP6V1D with UC risk are novel findings that merit further study to elucidate their roles.

Several strengths enhance the potential of our findings to inform IBD therapies. Firstly, comprehensive MR analysis minimized bias due to confounders and reverse causation, strengthening causal inference. Secondly, by including nearly all known human metabolism-related genes, our study systematically identified

causative metabolic genes underlying IBD, providing promising translational relevance. Thirdly, the causal relationships identified were consistently validated in both blood and intestinal tissues. Moreover, the inclusion of IBD cases confirmed by endoscopic and histological diagnoses minimized diagnostic misclassification, adding robustness to the results. However, several limitations should be acknowledged. Firstly, as the GWAS cohort utilized in this study comprises European populations, our findings may not be directly applicable to non-European populations. Validation across diverse ancestries is therefore required, owing to population-specific genetic or lifestyle factors that may influence MR estimates. Second, pleiotropy is an inherent challenge in MR. Genetic instruments may affect IBD risk through biological pathways independent of the exposure of interest. Pleiotropy cannot be definitively ruled out, even when sensitivity analyses yield consistent estimates. Furthermore, the subsequent development of specific multivariate MR and colocalization analyses may further address this issue. Third, MR estimates reflect lifetime exposure, yet cannot infer tissue, time, and dose-specific effects. Moreover, pharmacological modulation could produce divergent outcomes. Fourth, in our colon tissue analysis, we relaxed the p-value threshold to boost statistical power, at the risk of introducing weakly correlated IVs. While informative, these tissue-specific results must be validated in larger-scale GWAS. Fifth, a further consideration is that the effect sizes from MR are generally modest, suggesting each gene individually exerts only a limited influence on IBD pathogenesis. This statistical significance does not necessarily translate to practical importance. Current research still lacks quantitative evidence of the actual effects of single or multiple genes on IBD, focusing instead on qualitative analyses of differential expression, and MR analyses are no exception. Consequently, future research should develop novel methodologies to quantitatively estimate the magnitude of practical effects exerted by different gene expressions on IBD. Sixth, as the GWAS data utilized comprised a mixed-sex cohort, our MR estimates are potentially confounded by sex differences. Consequently, further sex-stratified analyses will be necessary in future studies. Seventh, some genes were excluded from the MR analysis due to a limited number of IVs, which may have led to the underestimation of the effects of these genes.

Eighth, our MR estimates may be further compromised by the absence of disease subtypes and severity grading in the IBD GWAS data. More detailed data will be required in future studies to assess the impact of IBD heterogeneity on the results.

Conclusions

This study provides genetic support for a potential causal relationship between metabolism-related genes and the risk of IBD. These findings enhance our understanding of the metabolic pathways involved in IBD. However, owing to the inherent limitations of MR, we emphasize that our findings cannot be directly extrapolated to clinical practice. Further studies are needed to investigate the underlying biological mechanisms in more detail and to validate these candidate pathways for clinical applications.

Key Points

Aspect	Summary
What was previously known	Metabolic alterations are implicated in the pathogenesis of Inflammatory Bowel Disease (IBD), but evidence from observational studies is confounded and cannot establish causality. The specific metabolism-related genes that drive disease risk remained largely unidentified.
What the study adds	This genome-wide Mendelian randomization study systematically identifies causal relationships between metabolism-related gene expression and IBD risk. It robustly identifies seven genes (SORD, NDUFB2, HS2ST1, SDHC, SRD5A3, CDO1, FADS2) influencing both Crohn's disease and ulcerative colitis, and three genes (MOCOS,

	NAGA, ATP6V1D) specific to one subtype.
Clinical implications	The findings provide hypothesis-supporting evidence for candidate metabolic pathways in inflammatory bowel disease, serving as a complement to experimental and clinical research.

Competing interests

All authors declare no competing interests.

Data availability statements

Detailed information is provided in the Data sources section, and all data are publicly accessible.

Ethics approval

The data used in our study were retrieved from publicly available databases, and therefore, no additional ethical approval was required.

Artificial intelligence

The authors declare that no artificial intelligence or AI-assisted technologies were used to generate scientific content or draw conclusions in this study.

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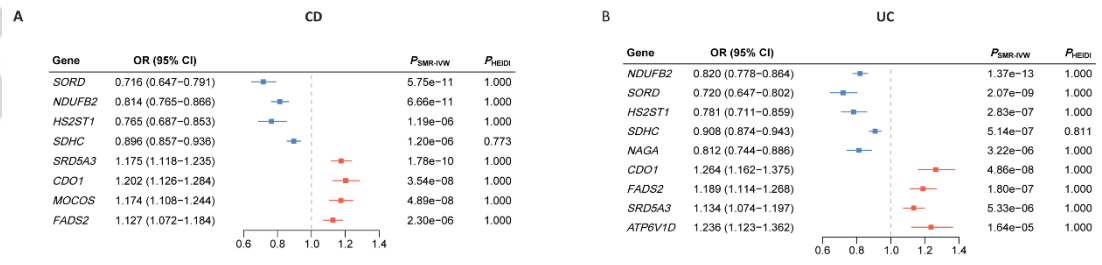

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Fig 1. The MR results for the association between the expression of metabolism-related genes and the risk of CD and UC. (A) The MR results for the association between the expression of metabolism-related genes and the risk of CD; (B) The MR results for the association between the expression of metabolism-related genes and the risk of UC. CD, Crohn's disease; UC, ulcerative colitis; MR, Mendelian randomization; HEIDI, heterogeneity in dependent instruments; SMR-IVW, summary data–based MR inverse-variance weighted.

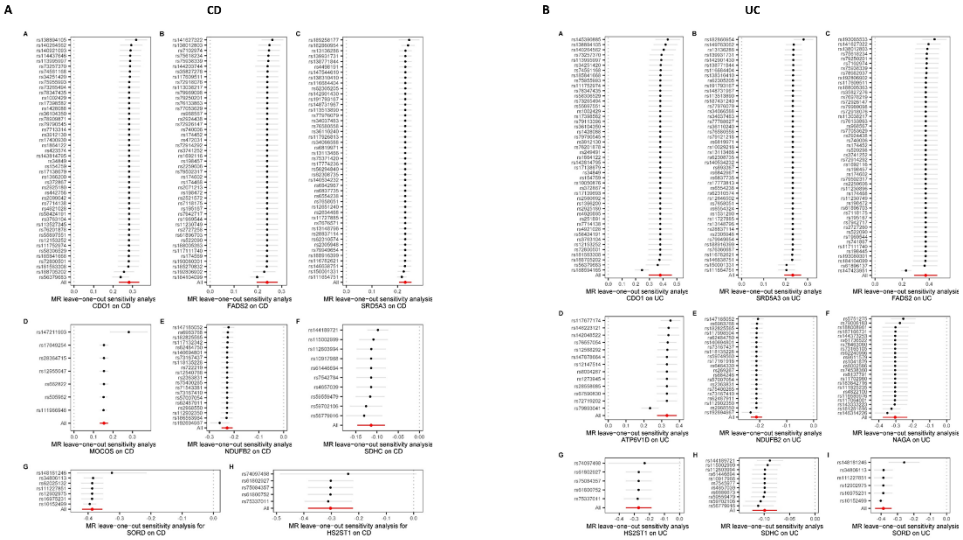

Fig 2. The leave-one-out sensitivity analysis for CD and UC. (A) The leave-one-out sensitivity analysis for CD; (B) The leave-one-out sensitivity analysis for UC. CD, Crohn's disease; UC, ulcerative colitis; MR, Mendelian randomization.

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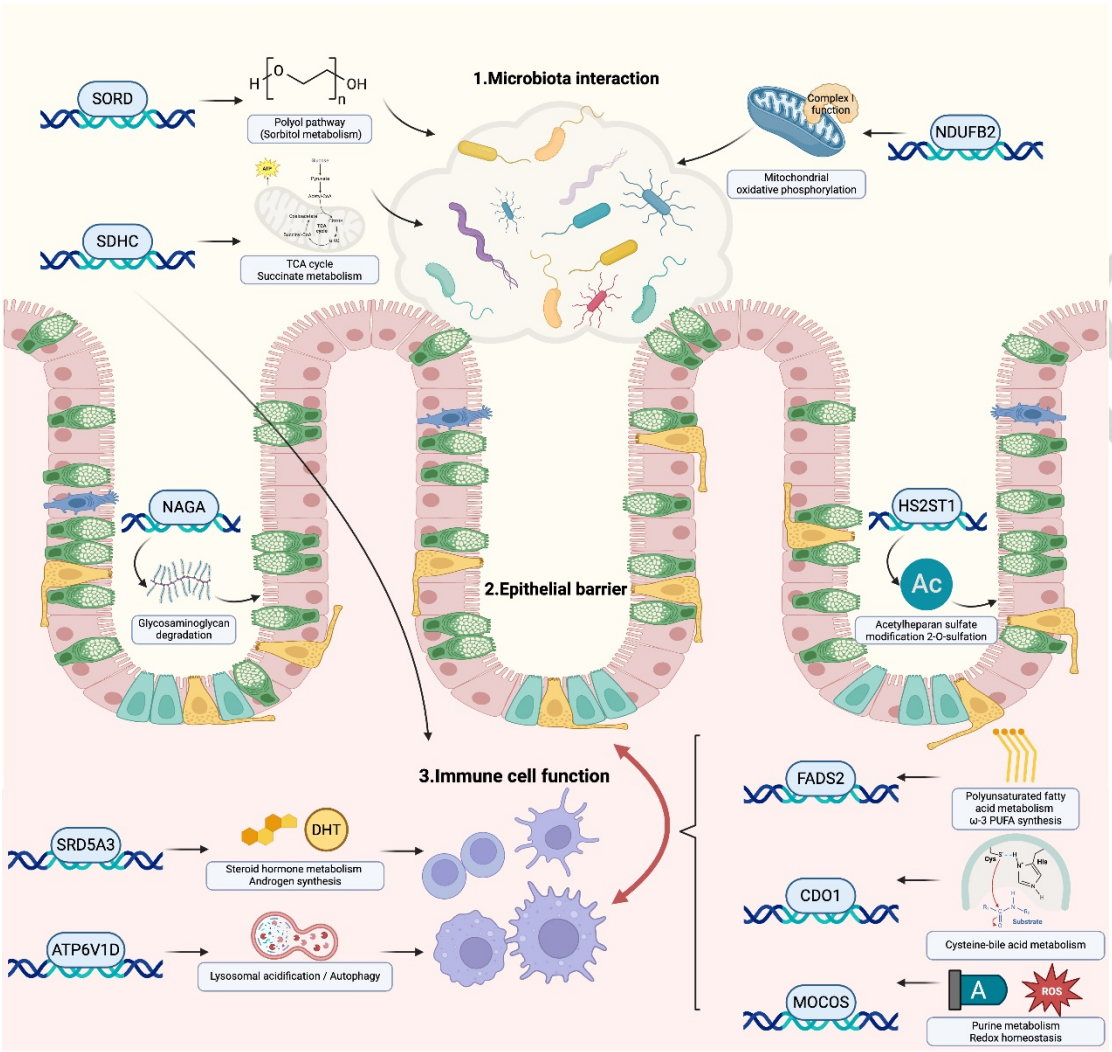

Fig 3.Metabolism-related candidate pathways linking causal genes to IBD pathogenesis.Created with BioRender.com

Table 1. Data sources in this MR analysis.

MR:

Trait	Consortium	Case definition	Ancestry	Cases	Controls	Sample sizes	PMID
CD	IIBDGC	Diagnosis was based on accepted radiologic, endoscopic, and histopathologic evaluation	European	5,956	14,927	20,883	26192919
UC	IIBDGC	Diagnosis was based on accepted radiologic, endoscopic, and histopathologic evaluation	European	6,968	20,464	27,432	26192919
Blood cis-eQTLs	eQTLGen Consortium	Not applicable	European	Not applicable		31,684	34475573
Colon cis-	GTEx						

Mendelian randomization; PMID: PubMed ID; IIBDGC: The International inflammatory bowel disease Genetics Consortium; CD: Crohn's disease; UC: ulcerative colitis; Cis-eQTLs: cis-expression quantitative trait locus; GTEx: Genotype-Tissue Expression.

Table 2. The statistical power of this MR.

outcome	gene	OR	statistical power
CD	*SORD*	0.716	0.98
CD	*NDUFB2*	0.814	1.00
CD	*HS2ST1*	0.765	0.72
CD	*SDHC*	0.896	0.91
CD	*SRD5A3*	1.175	1.00
CD	*CDO1*	1.202	1.00
CD	*MOCOS*	1.174	0.78

CD	*FADS2*	1.127	1.00
UC	*NDUFB2*	0.82	1.00
UC	*SORD*	0.72	0.99
UC	*HS2ST1*	0.781	0.74
UC	*SDHC*	0.908	0.90
UC	*CDO1*	1.264	1.00
UC	*FADS2*	1.189	1.00
UC	*SRD5A3*	1.134	1.00
UC	*ATP6V1D*	1.236	0.99
OR, Odds Ratio; CD, Crohn's disease; UC, ulcerative colitis.			

Table 3. MR replication results of metabolic genes in colon on CD and UC.

Probe ID	Gene	Beta	SE	$P_{SMR-IVW}$	P_{HEIDI}	OR (95% CI)
CD						
ENSG00000140263	*SORD*	-0.186	0.062	0.003	0.852	0.830 (0.735-0.937)
ENSG00000090266	*NDUFB2*	-0.140	0.029	0.000	1.000	0.870 (0.821-0.921)
ENSG00000153936	*HS2ST1*	-0.310	0.106	0.003	1.000	0.733 (0.596-0.902)
ENSG00000143252	*SDHC*	-0.219	0.048	0.000	0.821	0.803 (0.731-0.883)
ENSG00000128039	*SRD5A3*	0.111	0.029	0.000	1.000	1.118 (1.057-1.183)
ENSG00000129596	*CDO1*	0.118	0.042	0.005	1.000	1.126 (1.037-1.222)
ENSG00000075643	*MOCOS*	0.128	0.059	0.031	0.998	1.137 (1.012-1.277)
ENSG00000134824	*FADS2*	0.118	0.048	0.013	1.000	1.125 (1.025-1.236)

UC						
ENSG00000090266	*NDUFB2*	-0.133	0.028	0.000	1.000	0.876 (0.828-0.925)
ENSG00000140263	*SORD*	-0.160	0.047	0.001	0.768	0.852 (0.778-0.934)
ENSG00000153936	*HS2ST1*	-0.197	0.058	0.001	1.000	0.821 (0.732-0.920)
ENSG00000143252	*SDHC*	-0.183	0.036	0.000	0.867	0.833 (0.775-0.894)
ENSG00000198951	*NAGA*	-0.261	0.096	0.006	1.000	0.770 (0.638-0.929)
ENSG00000129596	*CDO1*	0.110	0.042	0.008	1.000	1.116 (1.029-1.210)
ENSG00000134824	*FADS2*	0.112	0.045	0.013	1.000	1.119 (1.024-1.222)
ENSG00000128039	*SRD5A3*	0.093	0.020	0.000	1.000	1.098 (1.056-1.141)
ENSG00000100554	*ATP6V1D*	0.105	0.051	0.039	0.987	1.111 (1.005-1.228)

MR, Mendelian randomization; CD, Crohn's disease; UC, ulcerative colitis.