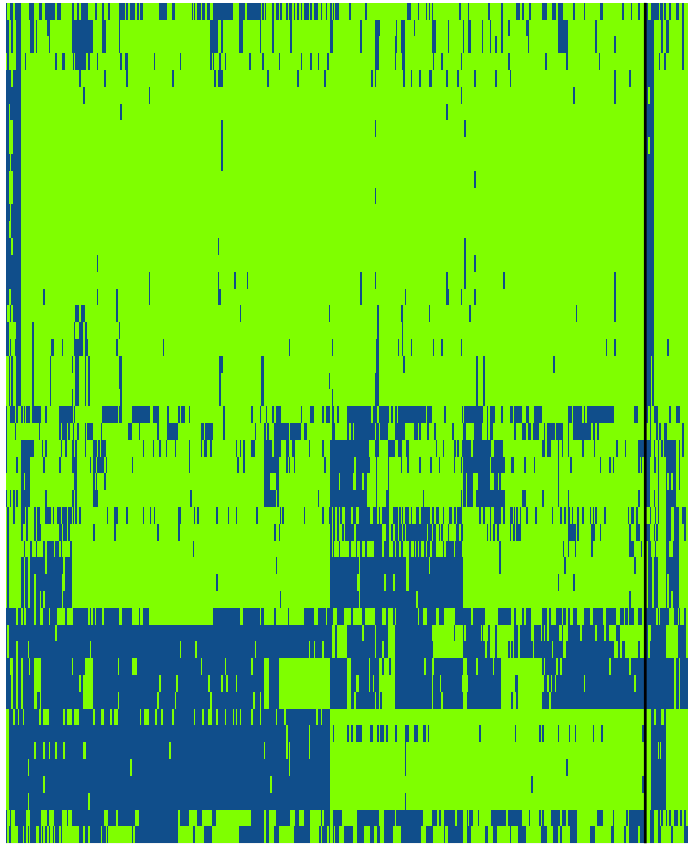
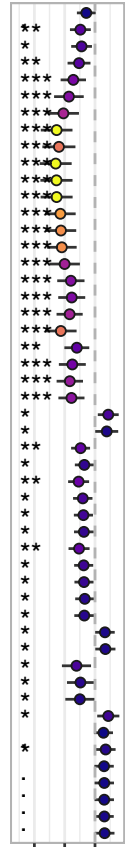


Supplementary Figure 1. The differences of gut microbial (A) within-person diversity (alpha-diversity) and (B) between-person diversity (beta-diversity) across participants without IBS and with IBS subtypes. Alpha-diversity was measured using richness and Simpson's index and their overall differences by IBS subtype was assessed using Kruskal-Wallis test, with pairwise differences assessed using Wilcoxon rank sum test. Between-person diversity was measured by Jaccard dissimilarity and its difference by IBS subtype was assessed using permutational multivariate analysis of variance (PERMANOVA). Figure shows the first two axes of principal coordinate analysis and numbers in parentheses represent the variance explained by each axis. **, p -value <0.01 ; ***, p -value <0.001 .

Alistipes_putredinis (n = 690)

Top 50 hits



- UniRef90_B0MZE7: NO_NAME
- UniRef90_R5V6Q9: Outer membrane receptor for ferrienterochelin and colicins
- UniRef90_R5U729: ABC-type Fe³⁺-hydroxamate transport system periplasmic component
- UniRef90_3YJC8: Bacterial nucleoid DNA-binding protein
- UniRef90_F4MBS6: NO_NAME
- UniRef90_D4IPP2: NO_NAME
- UniRef90_F4MBT7: PepsY domain protein
- UniRef90_F4MBT9: NO_NAME
- UniRef90_R5V672: NO_NAME
- UniRef90_D4IPP5: ABC-type multidrug transport system, ATPase component
- UniRef90_D4IPP4: NO_NAME
- UniRef90_D4IPP1: TonB-dependent Receptor Plug Domain
- UniRef90_D4IPP3: NO_NAME
- UniRef90_R5JYL5: NO_NAME
- UniRef90_3YR20: Flavodoxin
- UniRef90_D4IPP9: NO_NAME
- UniRef90_D4IPN9: NO_NAME
- UniRef90_F4MBS7: NO_NAME
- UniRef90_3YMB9: Transposase
- UniRef90_3YK10: Transposase
- UniRef90_A0A1Q6F927: NO_NAME
- UniRef90_D4INV7: NO_NAME
- UniRef90_3YIQ5: TonB-linked outer membrane protein, SusC/RagA family
- UniRef90_F4MEA3: NO_NAME
- UniRef90_B0MZZ2: Sigma-70 region 2
- UniRef90_B0MXPT: Late embryogenesis abundant protein
- UniRef90_A0A0E2TFE3: Type I restriction enzyme R Protein
- UniRef90_A0A3E5DXN2: GLY-YIG nuclease family protein
- UniRef90_I9RD05: Type I restriction-modification system, M subunit
- UniRef90_F3PUY3: Toxin-antitoxin system, toxin component, Fic family
- UniRef90_B0MTE1: Site-specific recombinase, phage integrase family
- UniRef90_B0MU63: NO_NAME
- UniRef90_B0MYR8: NO_NAME
- UniRef90_B0MYR3: NO_NAME
- UniRef90_B0MYU3: NO_NAME
- UniRef90_B0MYB1: NO_NAME
- UniRef90_B0MVP4: DNA-binding helix-turn-helix protein
- UniRef90_I7JK96: NO_NAME
- UniRef90_A0A1Q6F347: NO_NAME
- UniRef90_B0MXE4: NO_NAME
- UniRef90_B0MXD3: NO_NAME
- UniRef90_B0MXD4: NO_NAME
- UniRef90_I7JE3: NO_NAME
- UniRef90_I7JE2: Mannosyl-glycoprotein endo-beta-N-acetylglucosaminidase
- UniRef90_I7JE4: NO_NAME
- UniRef90_I7JO8: NO_NAME
- UniRef90_I7JIC7: NO_NAME
- UniRef90_I7JH2: NO_NAME
- UniRef90_K6AL85: NO_NAME
- UniRef90_A0A395YXYT: NO_NAME

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samples

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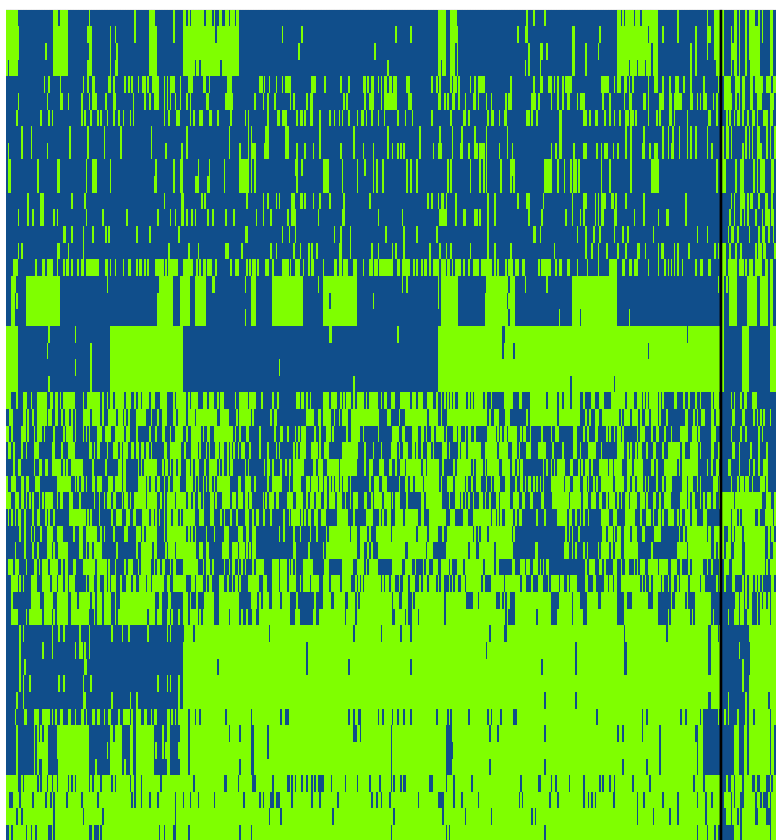
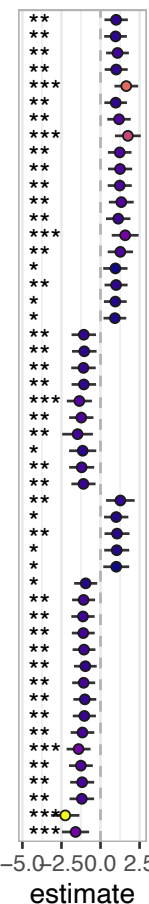
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Supplementary Figure 3. Associations between gene families contributed by *Alistipes putredinis* and IBS-D. Logistic regression model was adjusted for age and sex. *p-value<0.05, **p-value<0.01, ***p-value<0.001; Q: p-value adjusted for Benjamini-Hochberg method.

Bacteroides_vulgatus (n = 475)

Top 50 hits



- UniRef90_D6D3B1: NO NAME
- UniRef90_D6D3B2: NO NAME
- UniRef90_D7J4U0: Multiple inositol polyphosphate histidine phosphatase 1
- UniRef90_A0A1Y3Z862: NO NAME
- UniRef90_F7L6S3: NO NAME
- UniRef90_I8VHR6: NO NAME
- UniRef90_A0A1Y3V3P2: RNA polymerase subunit sigma-70
- UniRef90_A0A069S601: NO NAME
- UniRef90_S0F955: NO NAME
- UniRef90_A0A395B7X4: NO NAME
- UniRef90_A0A396BD89: NO NAME
- UniRef90_A0A1Q6IP00: NO NAME
- UniRef90_A0A0E2TFV4: NO NAME
- UniRef90_D4VBL3: NO NAME
- UniRef90_A0A173Z1G3: NO NAME
- UniRef90_B5D2Q8: Type I restriction modification DNA specificity domain protein
- UniRef90_A0A078RC79: Polysaccharide pyruvyl transferase family protein
- UniRef90_A0A397WM96: Coenzyme F420 hydrogenase, subunit gamma
- UniRef90_A0A397WL34: Glycosyltransferase
- UniRef90_A0A0M1W1J0: Glycosyl transferase
- UniRef90_A0A3E4JJC0: NO NAME
- UniRef90_A0A3E4WDJ6: Glycosyltransferase
- UniRef90_I8VBY0: NO NAME
- UniRef90_A0A3A9HCC7: DUF3989 domain-containing protein
- UniRef90_A0A174VTF7: Tyrosine recombinase XerD
- UniRef90_I9QPR5: NO NAME
- UniRef90_A0A078SUV6: NO NAME
- UniRef90_A0A3E5E9C8: DNA resolvase
- UniRef90_A0A069S312: Arsenical-resistance protein
- UniRef90_A0A396BMU7: DUF4141 domain-containing protein
- UniRef90_A0A139KSW0: Virulence-associated protein E
- UniRef90_A0A1F7RHU8: Plasmid transfer protein
- UniRef90_D1KAH7: NO NAME
- UniRef90_A0A139K4I3: NO NAME
- UniRef90_A7ACH8: PRTFC system protein C
- UniRef90_A0A108T8M8: NO NAME
- UniRef90_F1VJ98: NO NAME
- UniRef90_A0A3E5DNC9: DUF3989 domain-containing protein
- UniRef90_A0A3E5DNE9: DUF3872 domain-containing protein
- UniRef90_A0A3E5DNF2: Glycoside hydrolase
- UniRef90_A0A3E5DLC0: NO NAME
- UniRef90_A0A3E5DS10: ATP-binding protein
- UniRef90_B6W4R3: NO NAME
- UniRef90_A0A396BT80: NO NAME
- UniRef90_F9ZCL7: NO NAME
- UniRef90_A0A396BT81: Four helix bundle protein
- UniRef90_A0A396BB35: DNA-binding protein
- UniRef90_A0A0E2TFE3: Type I restriction enzyme R Protein
- UniRef90_A0A1Y3V160: Transcriptional regulator
- UniRef90_A0A3E4WNB8: Fimbrillin family protein

-5.0 -2.5 0.0 2.5

estimate

samples



ibs_d2



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present



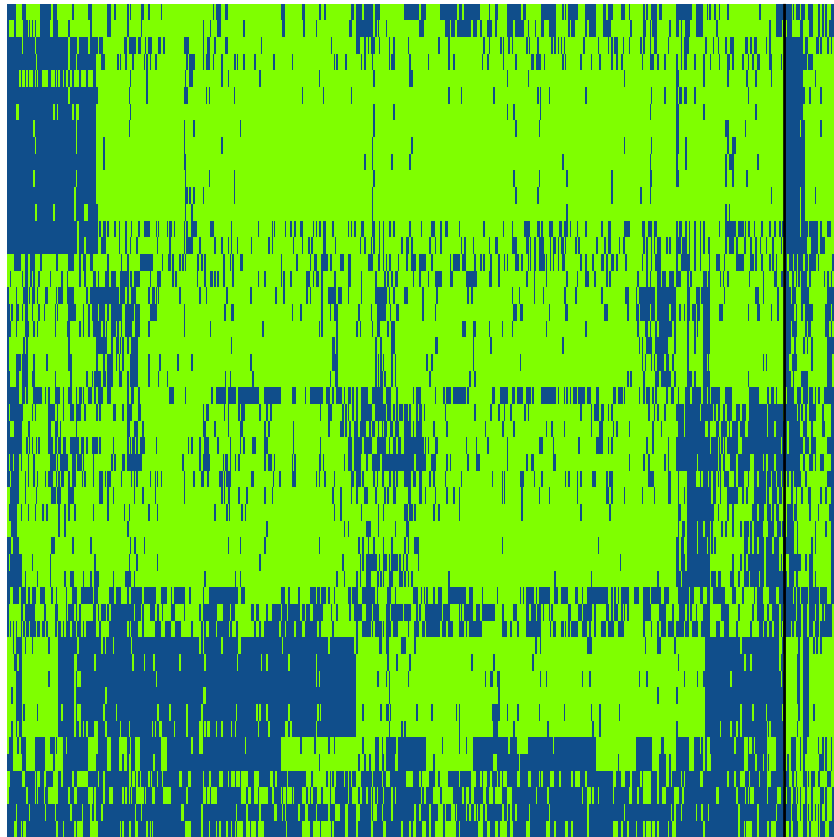
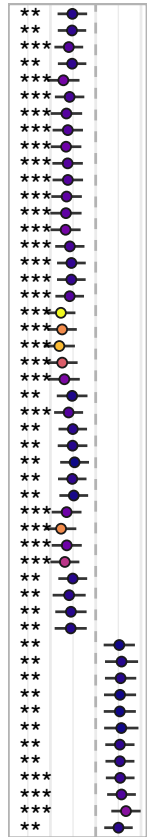
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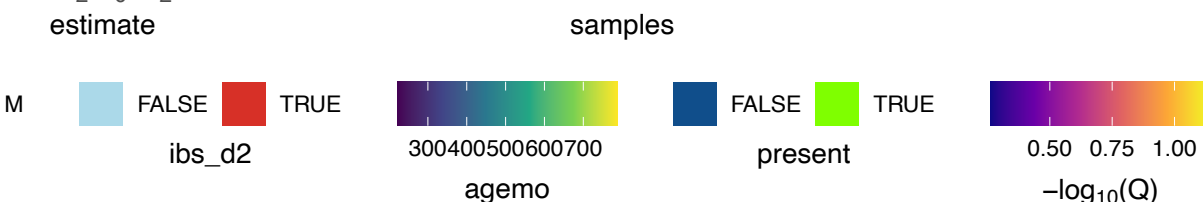
Supplementary Figure 4. Associations between gene families contributed by *Bacteroides vulgatus* and IBS-D. Logistic regression model was adjusted for age and sex. *p-value<0.05, **p-value<0.01, ***p-value<0.001; Q: p-value adjusted for Benjamini-Hochberg method.

Faecalibacterium_prausnitzii (n = 673)

Top 50 hits



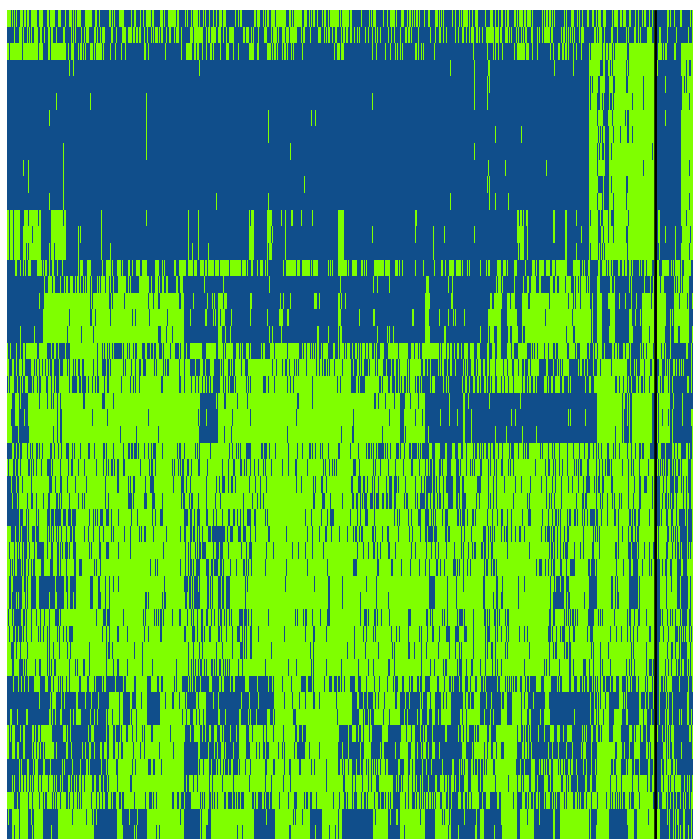
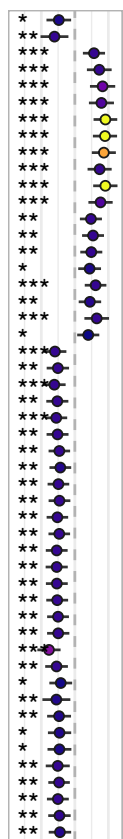
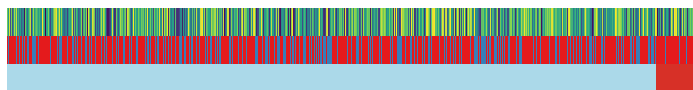
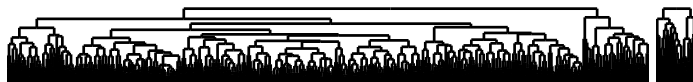
- UniRef90_A0A173STB8: DNA-binding transcriptional regulator HcaR
- UniRef90_A0A173UAZ6: Acylphosphatase
- UniRef90_A0A329UC17: Peptide deformylase
- UniRef90_b6Q137: NO_NAME
- UniRef90_b6QA72: NO_NAME
- UniRef90_b6R91T: Putative membrane protein insertion efficiency factor
- UniRef90_b6Q123: Cysteine desulfurase
- UniRef90_b6R321: Cobalamin biosynthesis protein CobD
- UniRef90_b6QE58: NO_NAME
- UniRef90_b6R019: NO_NAME
- UniRef90_b6Q4M6: NO_NAME
- UniRef90_b6Q331: Ribonuclease Z
- UniRef90_b6R3K4: Predicted ATPase (AAA+ superfamily)
- UniRef90_A0A329TRC0: NO_NAME
- UniRef90_b6R8R8: NO_NAME
- UniRef90_UPI000DE2BD69: NO_NAME
- UniRef90_D6DE93: Suppressor of fused protein (SUFU)
- UniRef90_A0A329TXE4: NO_NAME
- UniRef90_C0EBY0: NO_NAME
- UniRef90_C0EBZ1: NO_NAME
- UniRef90_A0A329TVL8: Class V aminotransferase
- UniRef90_C0EBS6: NO_NAME
- UniRef90_A0A173XS31: Sporulation initiation inhibitor protein soj
- UniRef90_A0A3E2W877: AraC family transcriptional regulator
- UniRef90_A0A2A6ZHK6: NO_NAME
- UniRef90_A0A2A6ZGW2: Lipoprotein signal peptidase
- UniRef90_A0A2A6ZKK1: Acriflavin resistance protein
- UniRef90_A0A2A6ZK27: NO_NAME
- UniRef90_A0A2A7B459: 4-alpha-glucanotransferase
- UniRef90_A0A2A7B7K9: ABC transporter ATP-binding protein
- UniRef90_A0A2A7B4B8: L-glyceraldehyde 3-phosphate reductase
- UniRef90_A0A2A7BK09: Electron transporter RnfD
- UniRef90_A0A2A6ZJB8: Sec-independent protein translocase TatB
- UniRef90_A0A2A6ZG10: RNA pseudouridine synthase
- UniRef90_A0A2A6ZG54: Metalloendopeptidase
- UniRef90_A0A2A7ADM6: NO_NAME
- UniRef90_A0A329UJW8: Helix-turn-helix domain-containing protein
- UniRef90_E2ZLS9: Bacterial mobilization protein MobC
- UniRef90_A0A329U3B9: DNA-binding response regulator
- UniRef90_A0A329UCX6: NO_NAME
- UniRef90_A0A329U8Q4: NO_NAME
- UniRef90_A0A329UAV6: DNA invertase
- UniRef90_A0A329UCF9: NO_NAME
- UniRef90_A0A329U9H9: NO_NAME
- UniRef90_A0A2A7BGG3: NO_NAME
- UniRef90_A0A2A7AHK2: NO_NAME
- UniRef90_A0A329UIK5: FeoB-associated Cys-rich membrane protein
- UniRef90_A0A3E2X512: DUF262 domain-containing protein
- UniRef90_A0A2A7BFW1: NO_NAME
- UniRef90_A0A2A7BC72: Nitrous oxide-stimulated promoter family protein



Supplementary Figure 5. Associations between gene families contributed by *Faecalibacterium prausnitzii* and IBS-D. Logistic regression model was adjusted for age and sex. *p-value<0.05, **p-value<0.01, ***p-value<0.001; Q: p-value adjusted for Benjamini-Hochberg method.

Coprococcus_comes (n = 719)

Top 50 hits



- UniRef90 A0A173XKN5: Hyaluronan synthase
- UniRef90 A0A3E5A5W0: Recombinase
- UniRef90 A0A3E4GLU2: DeoR/GlpR transcriptional regulator
- UniRef90 A0A3E4GL50: HPr family phosphocarrier protein
- UniRef90 A0A3E4GL70: Transcriptional regulator
- UniRef90 A0A3E4GLD9: UPF0261 family protein
- UniRef90 A0A3E4GLE6: ABC transporter permease
- UniRef90 A0A3E4GLE7: ABC transporter permease
- UniRef90 A0A3E4GL27: Sugar ABC transporter ATP-binding protein
- UniRef90 A0A3E4GLE0: Sugar ABC transporter substrate-binding protein
- UniRef90 A0A3E4GL01: Class II aldolase/adducin family protein
- UniRef90 A0A3E4GL89: N-acyl homoserine lactonase family protein
- UniRef90 A0A3E4GLN8: 2-keto-3-deoxygluconate permease
- UniRef90 A0A3E4GLP2: Four-carbon acid sugar kinase family protein
- UniRef90 A0A3E4GLV5: 4-hydroxythreonine-4-phosphate dehydrogenase PdxA
- UniRef90 A0A174SDI2: HTH-type transcriptional regulator immR
- UniRef90 A0A2N5PFG7: NO_NAME
- UniRef90 A0A174PIP6: Conjugal transfer relaxase Tral
- UniRef90 A0A374NU17: Type IV secretory system conjugative DNA transfer family protein
- UniRef90 A0A374NVT0: DUF3991 domain-containing protein
- UniRef90 R5S5L6: Metal dependent phosphohydrolase
- UniRef90 A0A174K1V0: VarZ like family
- UniRef90 C0B9T3: NO_NAME
- UniRef90 C0B573: Renal dipeptidase family protein
- UniRef90 C0B577: ABC transporter, substrate-binding protein, family 5
- UniRef90 R6LPY2: ABC transporter ATP-binding protein
- UniRef90 A0A2N5NTS2: Gamma-glutamylcyclotransferase
- UniRef90 C0B5M7: NO_NAME
- UniRef90 C0B9H7: NO_NAME
- UniRef90 C0B9L3: NO_NAME
- UniRef90 C0BC79: transporter
- UniRef90 C0BB17: NO_NAME
- UniRef90 C0BB04: NO_NAME
- UniRef90 C0BD53: NO_NAME
- UniRef90 R6LEN2: ABC transporter ATP-binding protein
- UniRef90 A0A174K1W4: RTX-I toxin determinant B
- UniRef90 C0BD74: NO_NAME
- UniRef90 C0B8K4: Probable butyrate kinase
- UniRef90 A0A3E4GNW9: Glycine reductase complex selenoprotein B
- UniRef90 R6IMS9: NO_NAME
- UniRef90 C0B6Y0: NO_NAME
- UniRef90 A0A174LCF2: NO_NAME
- UniRef90 A0A3E4GNU7: NO_NAME
- UniRef90 C0B8V3: NO_NAME
- UniRef90 C0B8V1: Efflux ABC transporter, permease protein
- UniRef90 G1VW86: NO_NAME
- UniRef90 C0BEH3: Resolvase, N-terminal domain protein
- UniRef90 A0A3E4GL08: RioB domain-containing protein
- UniRef90 A0A3E4GRH1: ATP-dependent helicase
- UniRef90 A0A3E4GR58: DUF2813 domain-containing protein

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samples

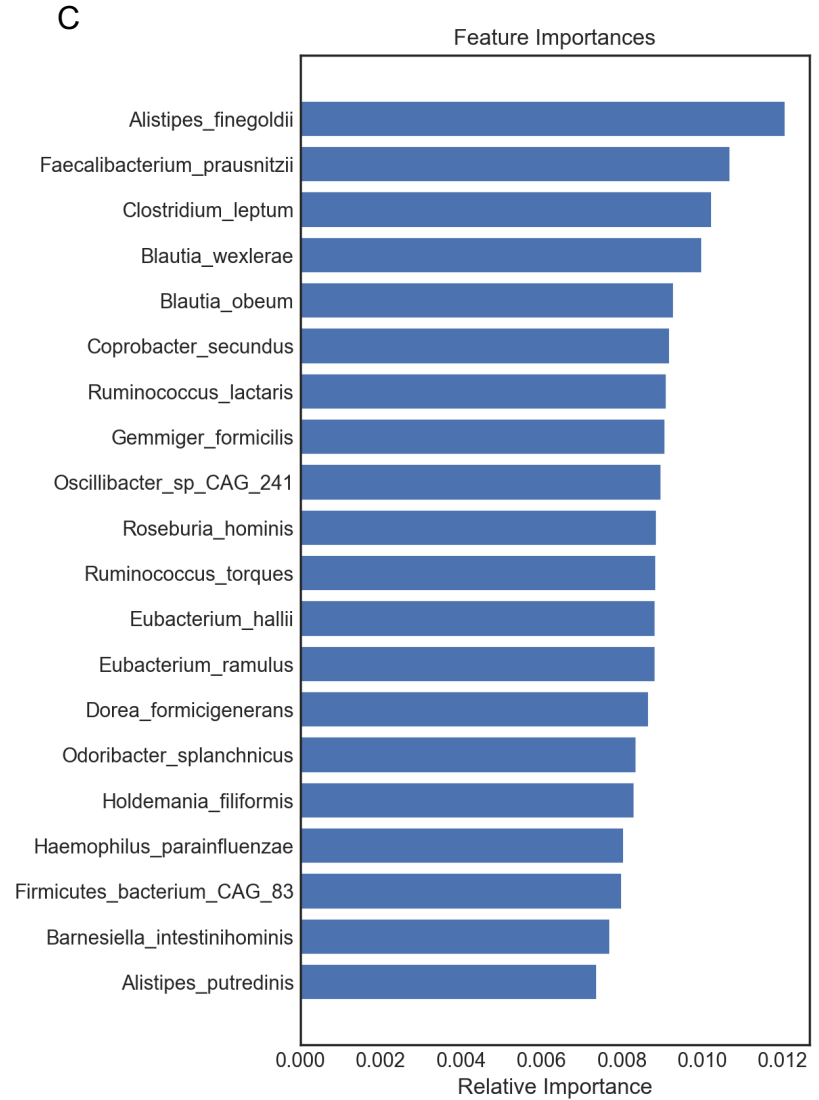
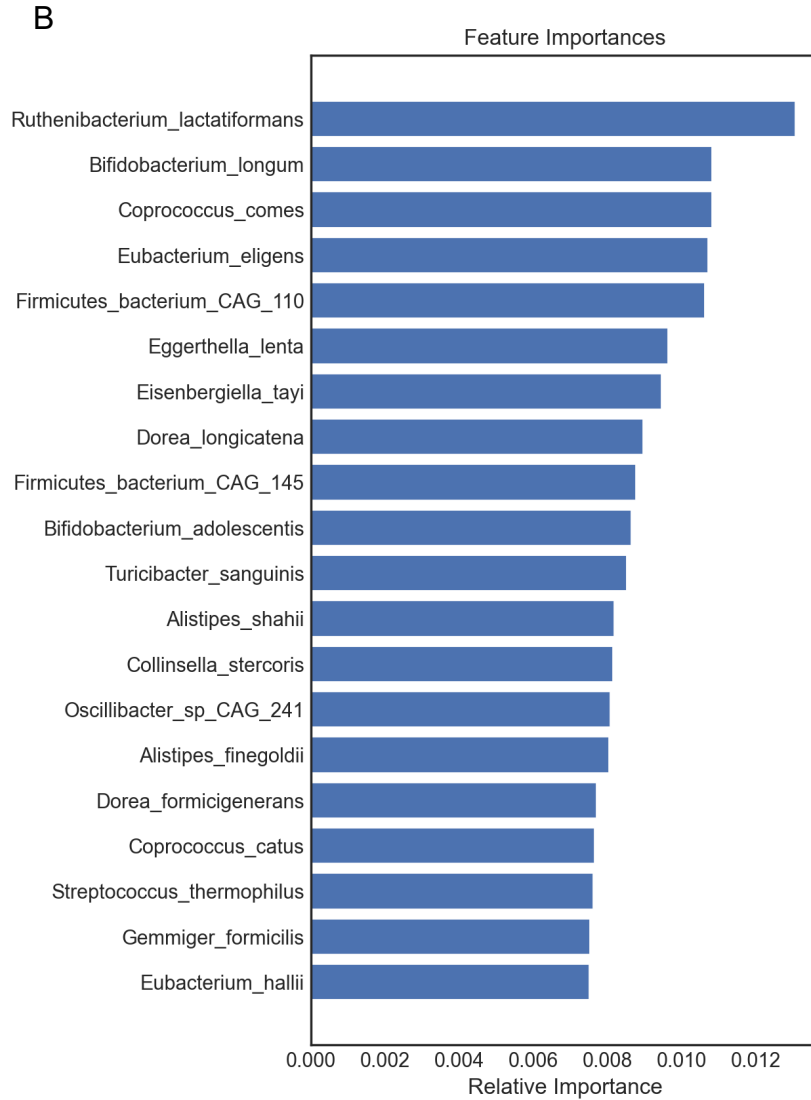
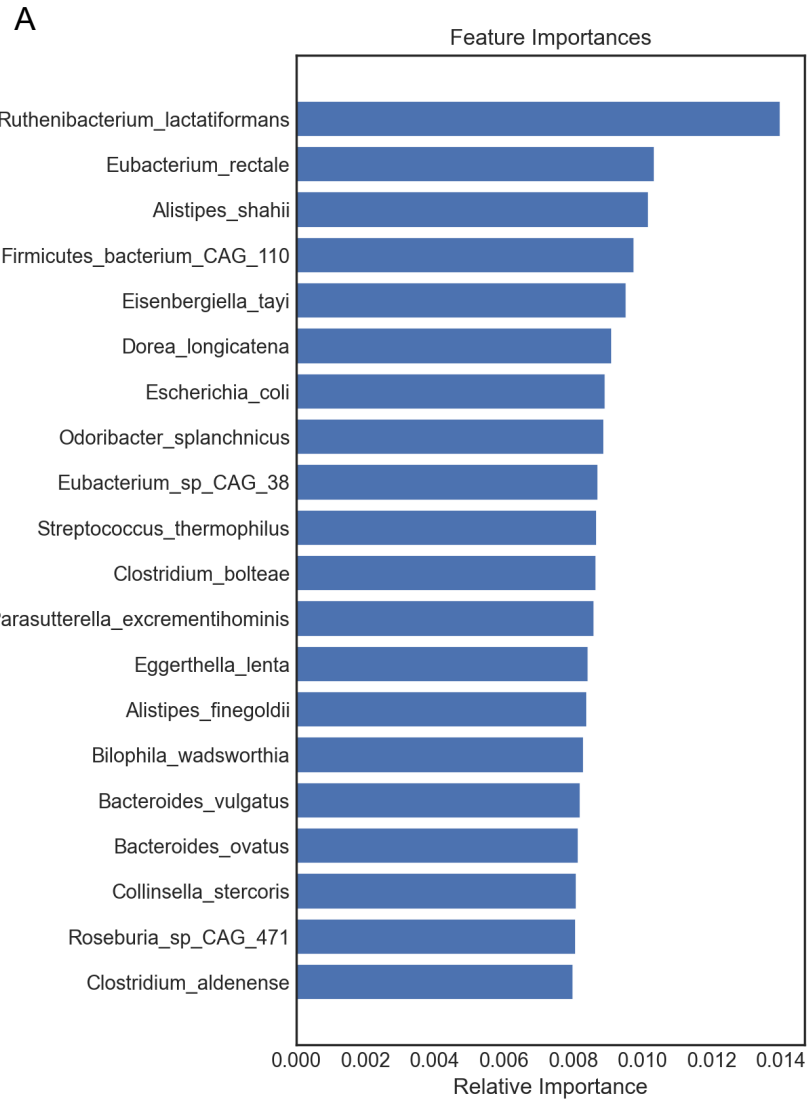
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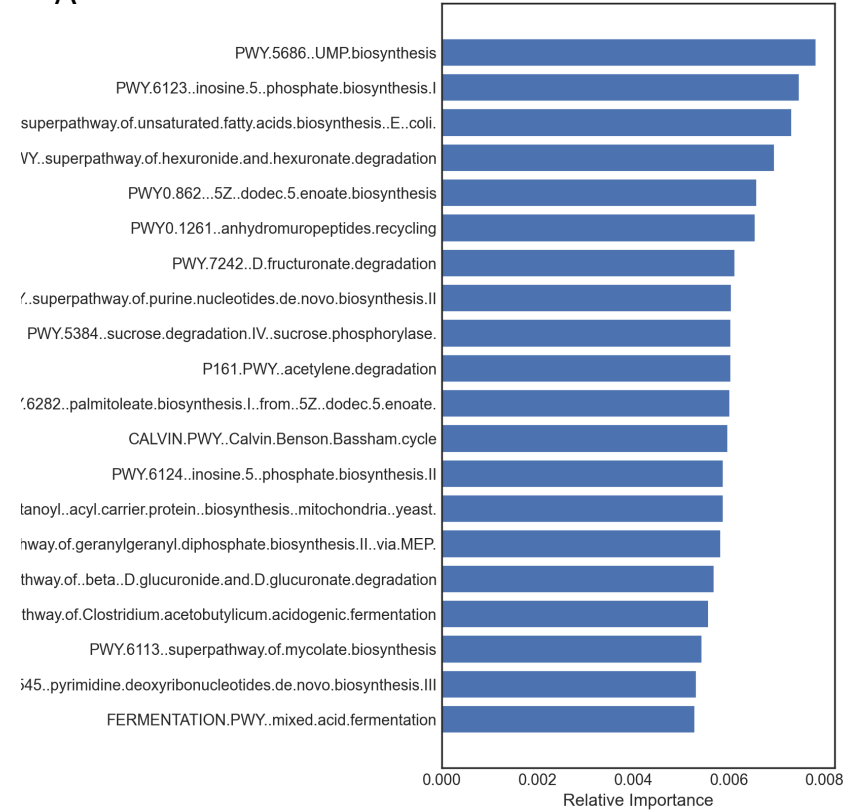
Supplementary Figure 6. Associations between gene families contributed by *Coprococcus comes* and IBS-C. Logistic regression model was adjusted for age and sex. *p-value<0.05, **p-value<0.01, ***p-value<0.001; Q: p-value adjusted for Benjamini-Hochberg method.



Supplementary Figure 7. Gut microbial taxa with top 20 feature importance in distinguishing (A) IBS-C, (B) IBS-D, and (C) IBS-M.

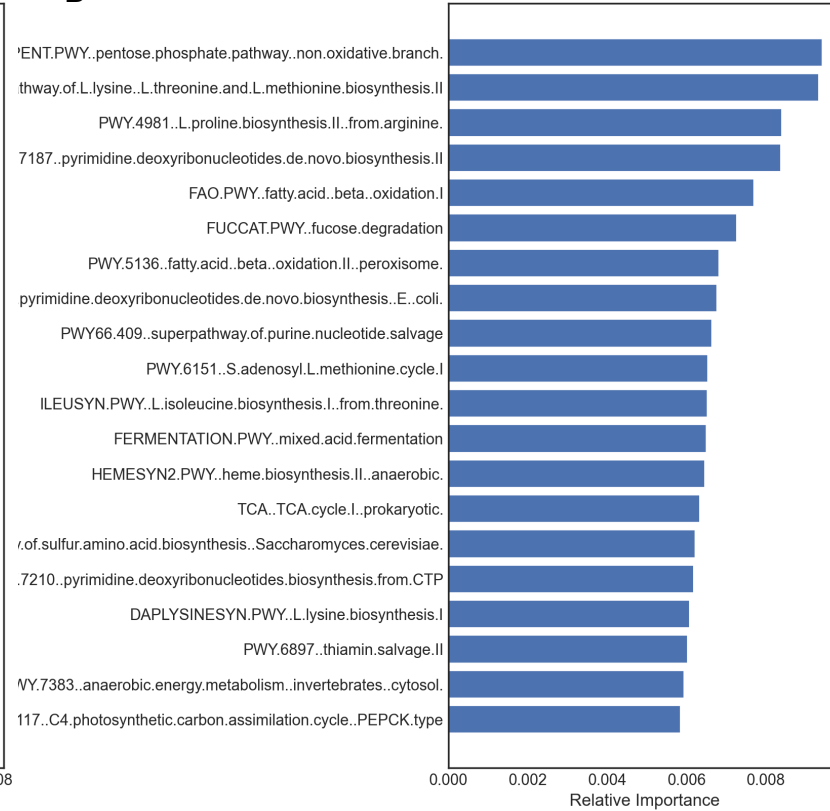
A

Feature Importances



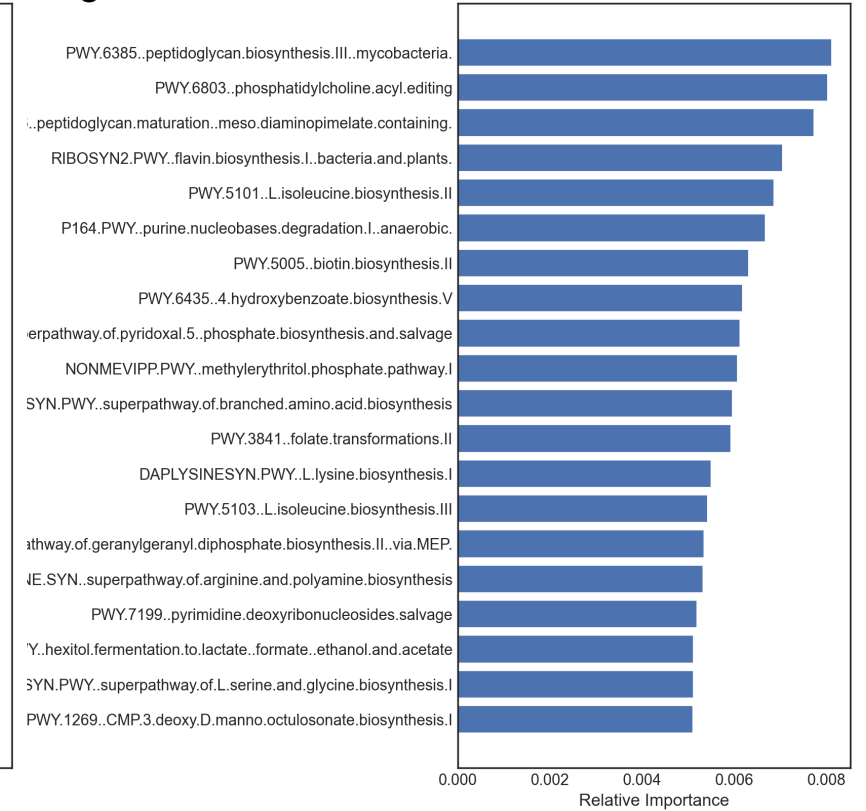
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Feature Importances

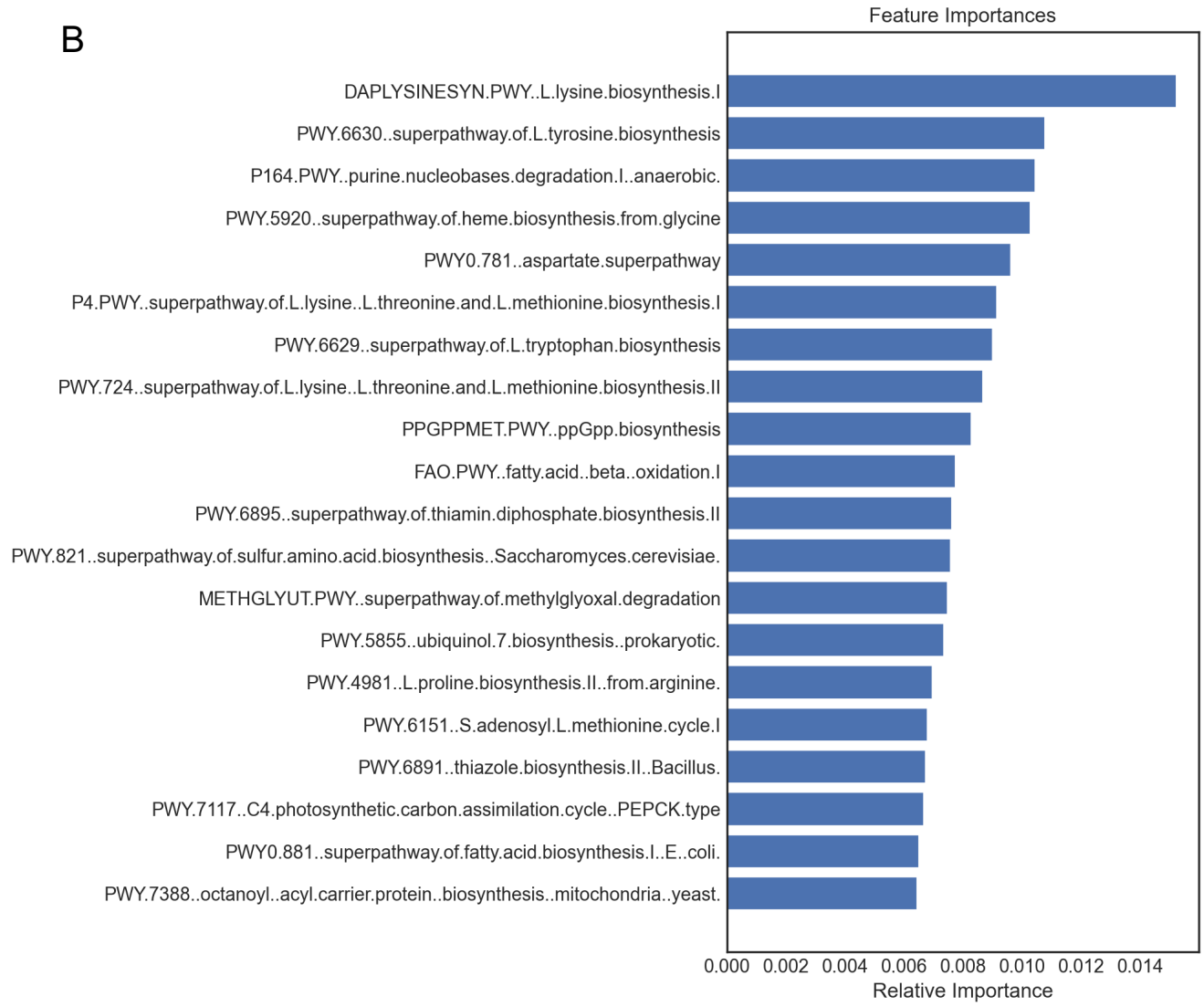
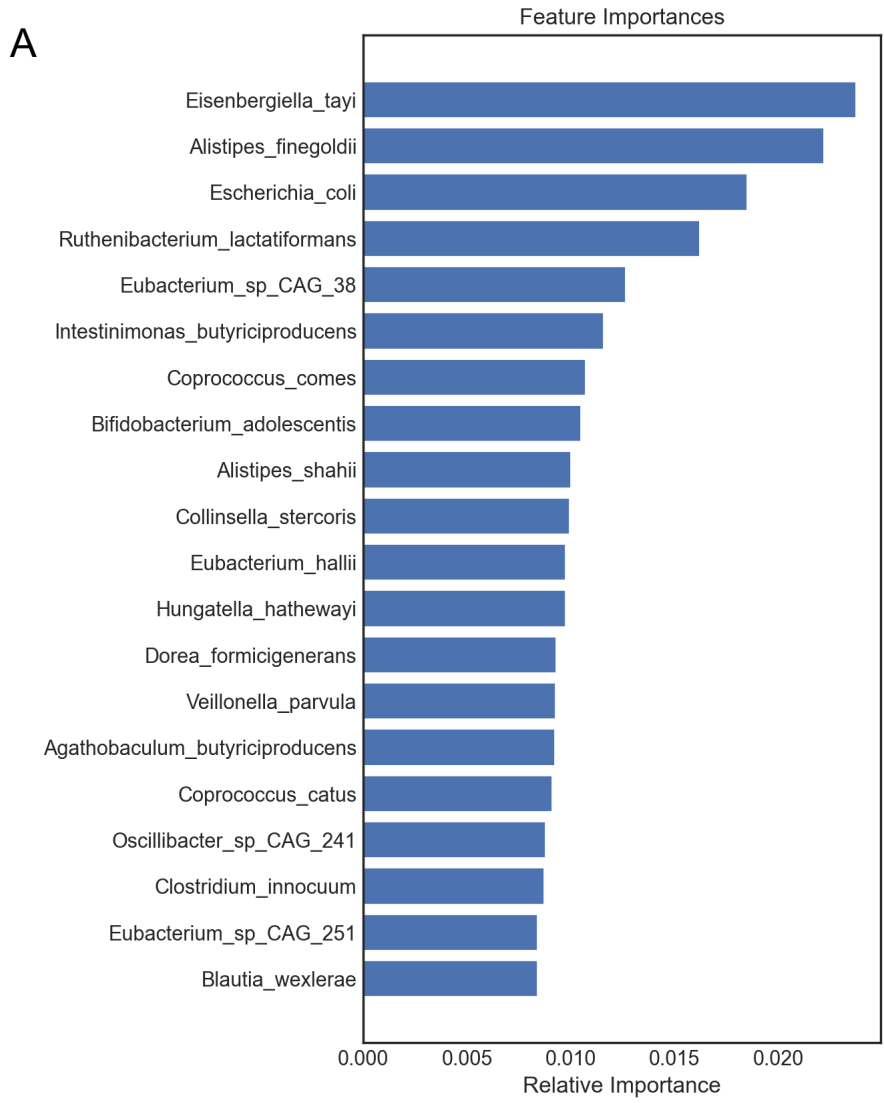


C

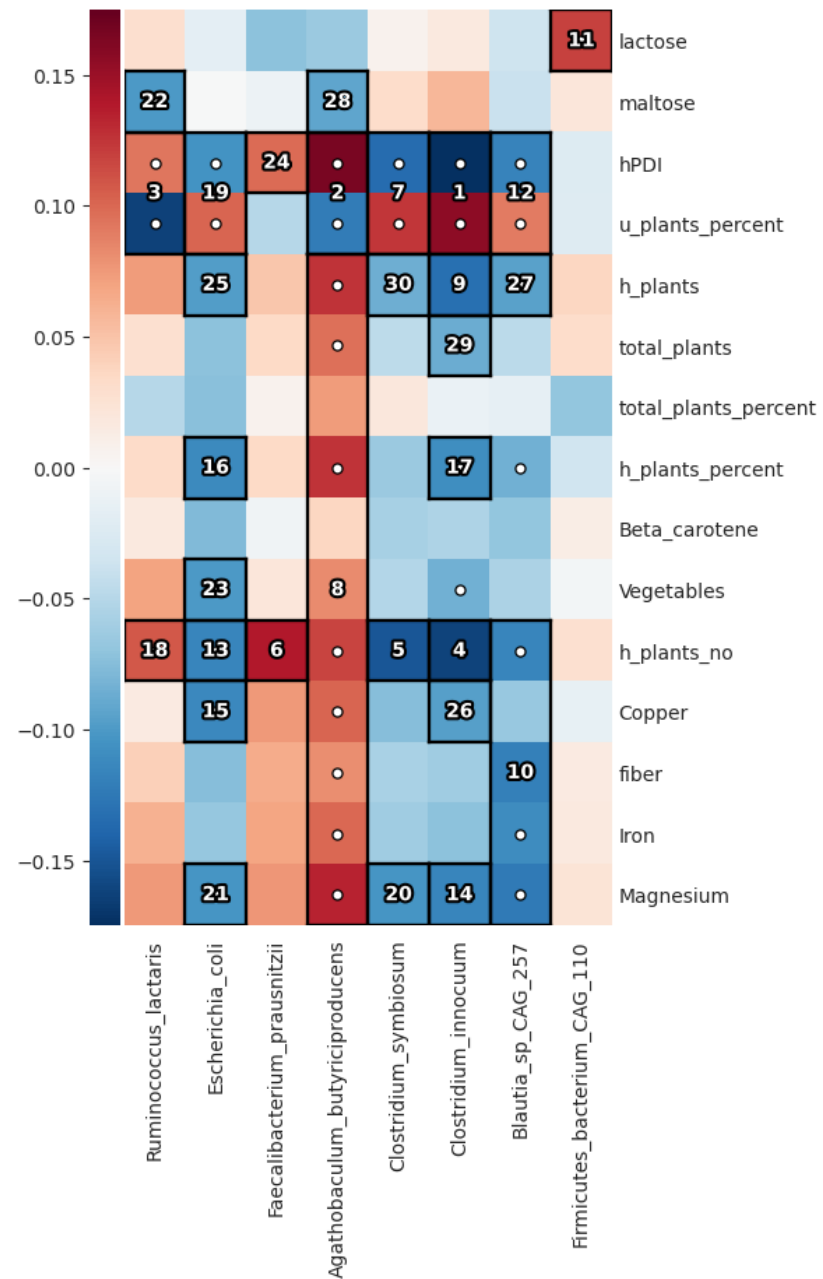
Feature Importances



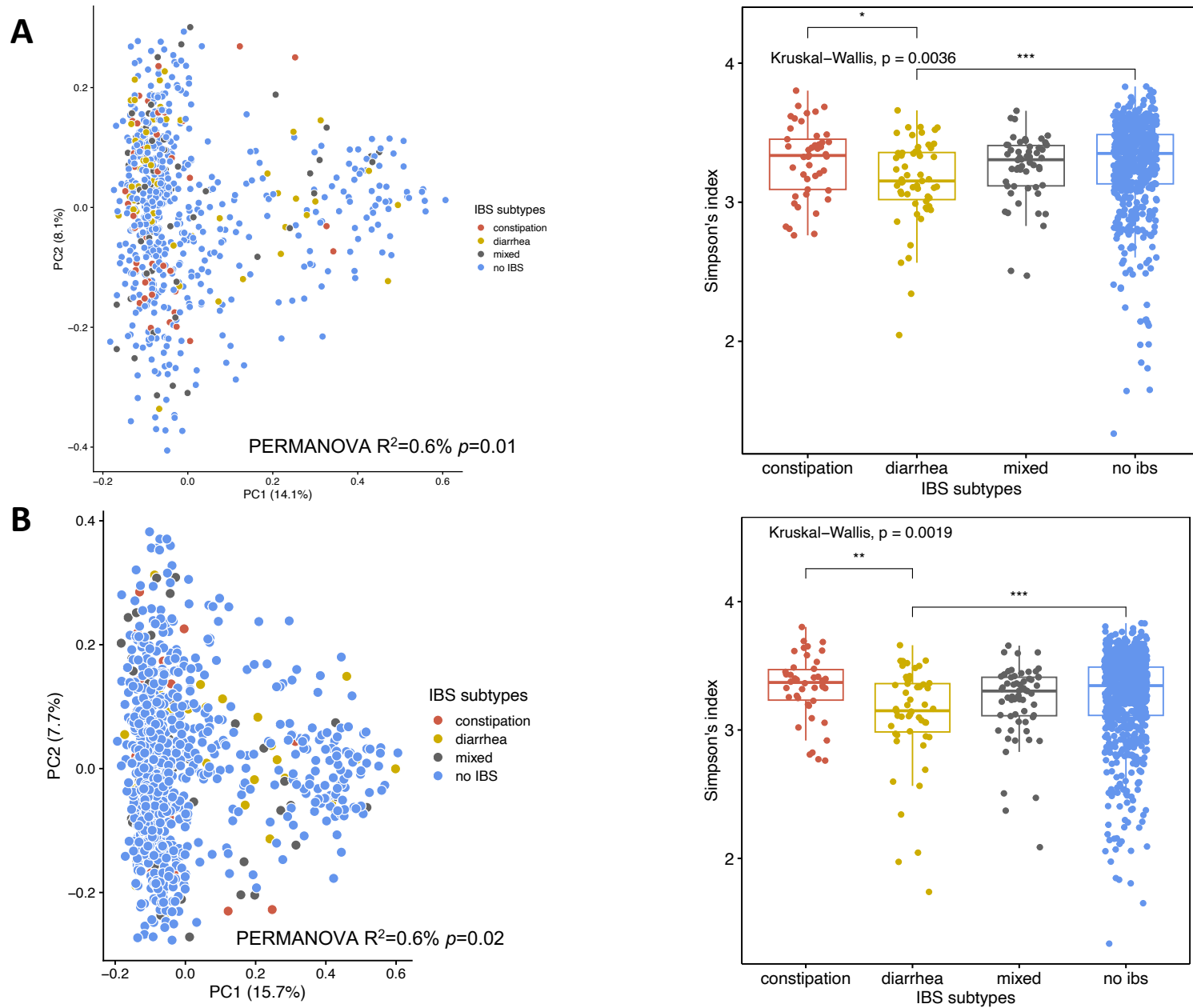
Supplementary Figure 8. Gut microbial functional pathways with top 20 feature importance in distinguishing IBS subtype.



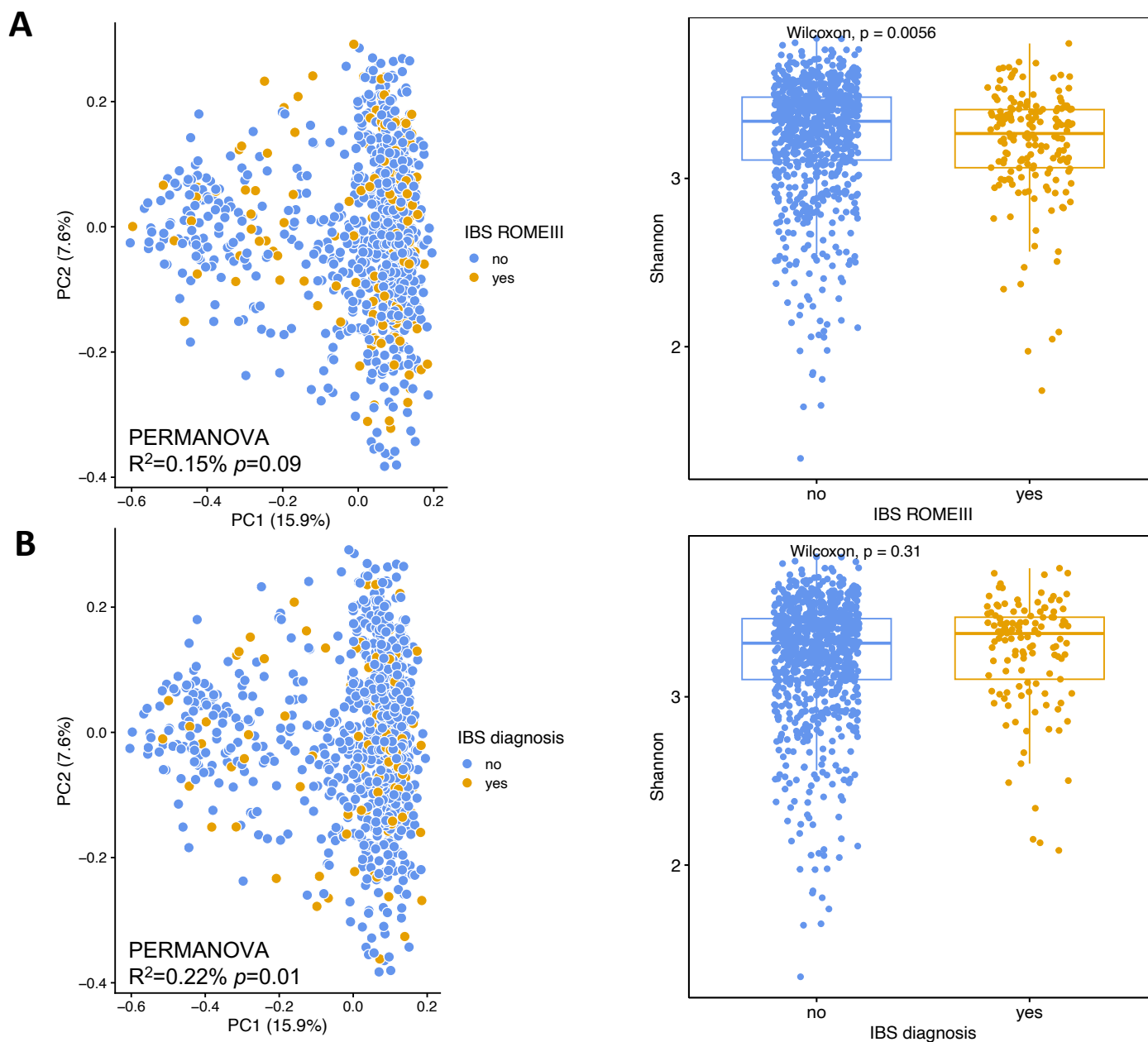
Supplementary Figure 9. Gut microbial taxa and functional pathways with top 20 feature importance in distinguishing IBS-C and IBS-D.



Supplementary Figure 10. Correlation between gut microbial taxa and dietary risk factors associated with IBS subtypes. Correlation was assessed using HALLA, a computational method for pattern discovery in high-dimensional datasets.



Supplementary Figure 11. The differences of gut microbial between-person diversity (beta-diversity) and within-person diversity (alpha-diversity) across IBS subtypes among (A) women and (B) participants without imputed dietary information. Between-person diversity was measured by Bray-Curtis dissimilarity and its difference by IBS was assessed using permutational multivariate analysis of variance (PERMANOVA). Figure shows the first two axes of principal coordinate analysis and numbers in parentheses represent the variance explained by each axis. Within-person diversity (alpha-diversity) was measured using Shannon index and its difference by IBS was assessed using Wilcoxon rank sum test. **, p -value<0.01; ***, p -value<0.001.



Supplementary Figure 12. The differences of gut microbial between-person diversity (beta-diversity) and within-person diversity (alpha-diversity) between participants with and without IBS according to (A) ROMEIII criteria and (B) physician diagnosis. Between-person diversity was measured by Bray-Curtis dissimilarity and its difference by IBS was assessed using permutational multivariate analysis of variance (PERMANOVA). Figure shows the first two axes of principal coordinate analysis and numbers in parentheses represent the variance explained by each axis. Within-person diversity (alpha-diversity) was measured using Shannon index and its difference by IBS was assessed using Wilcoxon rank sum test. **, p-value<0.01; ***, p-value<0.001.