METABOLITE CLUSTERS AND IBD SEVERITY

Exploring Metabolite-Based Cluster Patterns Associated with Severity in Inflammatory Bowel Disease

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Background and Aims

Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), is a chronic immune-mediated disorder with a heterogeneous clinical course increasingly investigated through metabolomics. This study examined whether serum metabolite profiles obtained from patients sampled around IBD diagnosis associate with IBD severity.

Methods

- Untargeted LC–MS serum metabolomics in the PREDICT cohort linked to the Danish National Biobank and Danish National Patient Register.
- Five machine learning algorithms trained for classification of severe versus non-severe IBD using metabolite cluster scores.
- Separate feature selection, biomarker correlation, and biological interpretation of key metabolite clusters.

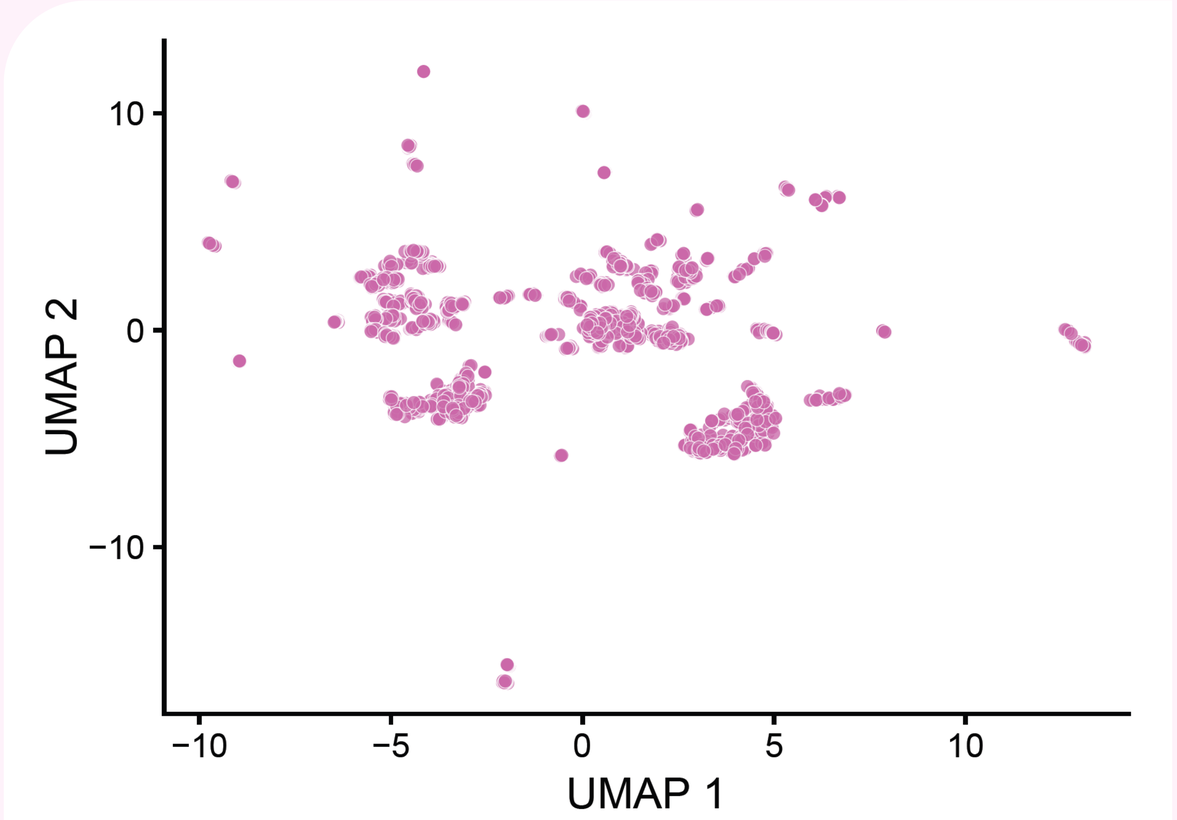

Figure 1: UMAP embedding of raw metabolomic data (N = 2,909 metabolites, prior to unsupervised clustering).

Model Performance Summary

Evaluation metrics for top-performing CD and UC classification models

Model	AUC	95% CI	Accuracy	Brier Score	RMSE	Diagnosis
RF	0.714	[0.592, 0.828]	0.687	0.217	0.465	CD
SVC	0.562	[0.451, 0.671]	0.504	0.261	0.511	UC

Results

- 60 stable metabolite clusters (2,458 metabolites) were identified.
- Random Forest showed the best performance for CD severity classification.
- Hippurate, indole-3-propionic acid, secondary bile acids, and γ-glutamyl peptides were linked to non-severe disease; glycerophosphocholines to severe CD but non-severe UC.

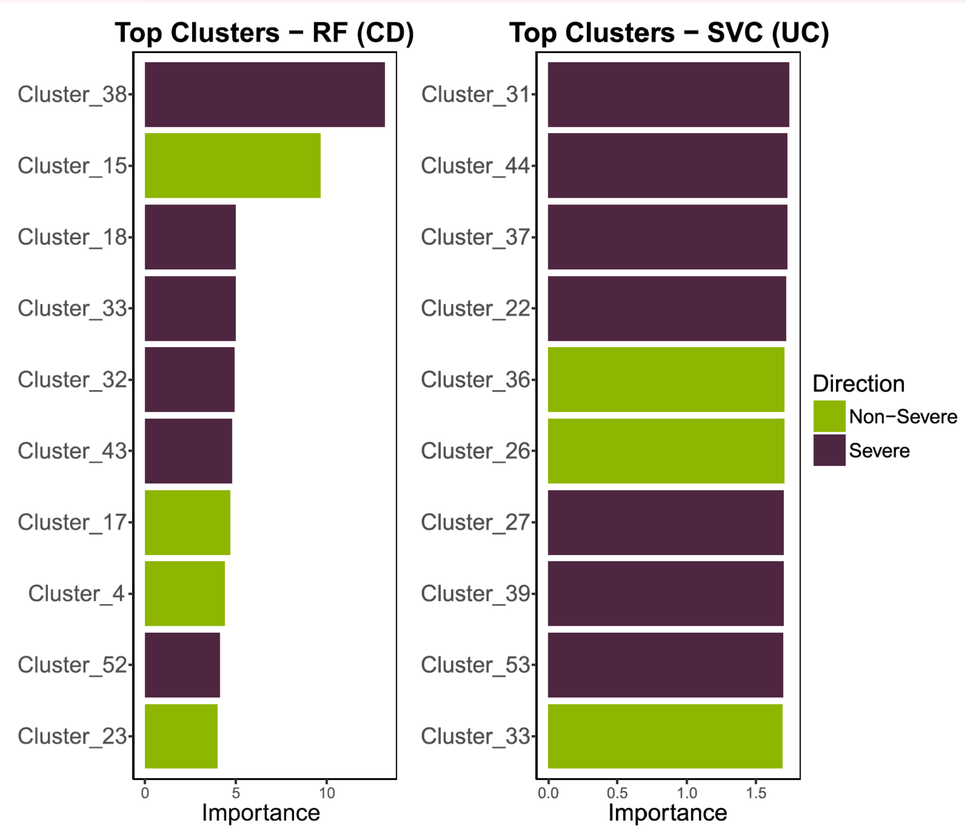

Figure 2: Feature importance for top clusters in CD and UC. Colours denote correlation direction with predicted severity probability.

Conclusions

This study presents a metabolite cluster framework for IBD severity stratification, highlighting subtype-specific patterns and biologically relevant pathways underlying disease progression.

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