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Summary

INTEGRATING MUCOSAL TRANSCRIPTOMIC AND MICROBIAL SIGNATURES TO DEFINE COMPREHENSIVE DISEASE CONTROL IN ULCERATIVE COLITIS AT MOLECULAR RESOLUTION

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Comprehensive disease control in ulcerative colitis, defined by combined clinical, endoscopic, histological, and biomarker remission, corresponds to a distinct molecular and microbial signature predictive of excellent two-year outcomes without hospitalization or surgery.

KEY POINTS

- Among 173 UC patients, 31 achieved comprehensive disease control (CDC), defined as concurrent clinical remission (Partial Mayo Score 0-1), endoscopic remission (Mayo Score 0), histological remission (Nancy Index 0-1), and biomarker remission (CRP <5 mg/dL, leukocytes 2.5-9/nL); none required IBD-related hospitalization or surgery over two years.
- A random forest classifier identified 19 transcriptomic markers predictive of CDC with AUC 0.856, including known IBD-associated genes (CXCL1, KRT7, SLC6A14, ESRRA, FGFR3, ITPKA) and 13 novel markers.
- CDC patients showed enrichment of fatty acid metabolism, suppression of immune programs, and differential abundance of IBD-associated taxa Lachnoclostridium and Lachnospiraceae FC020 on mucosal 16S rRNA profiling.
- A subset of patients not meeting all CDC clinical criteria displayed a similar transcriptomic and microbial profile to CDC patients, suggesting the molecular signature may identify molecularly inactive disease even when clinical criteria are incomplete.
- The molecular gradient between CDC and non-CDC patients suggests a continuum of mucosal healing; external validation is needed to determine prognostic value for long-term clinical outcomes.

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