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Summary

BEYOND CLINICAL SCORES: IDENTIFYING ULCERATIVE COLITIS PROGNOSTIC DISEASE STATES BIOMARKERS THROUGH UNSUPERVISED MULTI-OMICS TRAJECTORY MAPPING

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An unsupervised multi-omics trajectory analysis of 193 UC patients from the VARSITY trial identified eight distinct molecular disease states and 22 novel candidate serum biomarkers predictive of early treatment response trajectories.

KEY POINTS

- Eight distinct transcriptomic disease states were identified using longitudinal data from 579 biopsies and 386 serum samples at baseline, week 14, and week 52.
- Four molecular endotypes existed at baseline despite comparable clinical indices (Mayo, Robarts, Geboes scores), indicating that active disease has multiple molecular definitions.
- Among 42 patients who transitioned to a different state by week 14, 39 followed trajectories of clinical and/or histology improvement.
- Early improvement trajectories were associated with changes in serum proteins including previously reported UC-related proteins (OSM, MMP10, CXCL9) and 22 novel candidate prognostic biomarkers.
- Each disease state was associated with specific biological pathways including immune regulation, inflammation, tissue remodeling, and gut barrier function, with active states showing enrichment in TNF, interferon gamma, and ECM markers.
- The data-driven approach reversed traditional biomarker discovery by defining patient states from tissue transcriptomics first without clinical labels, then mapping transitions and identifying circulating protein markers.

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