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Summary

SINGLE-CELL RNA SEQUENCING REVEALS TRANSCRIPTIONAL REMODELLING OF IL-23R^{+} CELLS FOLLOWING IL-23–TARGETED THERAPY IN PATIENTS WITH CROHN'S DISEASE AFTER ILEOCAECAL RESECTION

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Single-cell RNA sequencing of post-resection Crohn's disease patients identifies ILC3s as the primary IL-23-responsive cell population whose baseline transcriptional signature predicts response to anti-IL-23 biologics.

KEY POINTS

- Four major IL-23 receptor-expressing cell types were identified (Th17 cells, MAIT cells, Tregs, and ILC3s), with ILC3s showing the most significant transcriptional changes following treatment with anti-p19 (Risankizumab, N=6) or anti-p40 (Ustekinumab, N=6) antibodies while MAIT cells and Tregs showed no significant changes.
- Inflamed ILC3 subsets at baseline displayed elevated expression of GNLY, TNFSF4, and ITGAX compared to post-treatment samples, demonstrating that both therapies drive transcriptional and phenotypic remodeling in ILC3s.
- An expanded set of previously underappreciated IL-23-associated genes was identified in ILCs prior to treatment, including VDR, BATF, FURIN, and ZNRF1.
- At baseline, ILC3s from responders showed reduced CCR7 expression and increased LTB and ZFP36L1 expression compared to non-responders, while no significant baseline differences were observed in other IL-23R-positive populations.
- The study used FACS-based enrichment for IL-23R-expressing populations on intestinal biopsies from patients with endoscopic recurrence at 6 months post-ileocecal resection, with follow-up biopsies approximately 4 months after treatment initiation.

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