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Summary

SINGLE-CELL DISSECTION OF PERIPHERAL CD3⁺ T CELL REPERTOIRE REMODELING INDUCED BY ADVANCED COMBINATION TREATMENT IN INFLAMMATORY BOWEL DISEASE

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Single-cell RNA and TCR sequencing in six Crohn's disease patients achieving clinical response to advanced combination treatment revealed mechanistically distinct T cell remodeling patterns: anti-TNF plus anti-integrin α4β7 produced a diversified, polyclonal repertoire, while anti-TNF plus anti-IL-23 drove focused oligoclonal expansion.

KEY POINTS

- Four patients received anti-TNF plus anti-integrin α4β7 and two received anti-TNF plus anti-IL-23; all six patients with difficult-to-treat Crohn's disease achieved clinical response.
- Anti-TNF plus anti-integrin α4β7 treatment was associated with marked enrichment of CD4+ tissue central memory and CD4+ naïve T cells, greater TCR diversity, reduced clonal dominance, and enhanced repertoire evenness.
- Anti-TNF plus anti-IL-23 treatment showed marked enrichment of CD8+ naïve T cells, reduced TCR diversity, and pronounced oligoclonal expansion with greater dominance of highly expanded clones.
- The divergent T cell signatures indicate mechanistically distinct pathways of immune reprogramming and suggest that advanced combination treatment does not induce uniform effects on the T cell compartment.
- The study provides proof of concept that single-cell RNA sequencing and TCR profiling can serve as molecular readouts of remission and may inform rational selection of biologic combinations in inflammatory bowel disease.

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