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Summary

DOCTIS: A SINGLE CELL RNA-SEQ ATLAS OF DRUG RESPONSE TO TARGETED THERAPIES IN IMMUNE-MEDIATED INFLAMMATORY DISEASES

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Single-cell RNA sequencing of 360 PBMC samples from 176 patients across six immune-mediated inflammatory diseases including Crohn's disease and ulcerative colitis reveals that drug responses are largely disease-specific rather than shared across conditions treated with the same targeted therapy.

KEY POINTS

- The DoCTIS project analyzed more than two million peripheral immune cells from patients with six IMIDs (psoriasis, psoriatic arthritis, Crohn's disease, ulcerative colitis, rheumatoid arthritis, and systemic lupus erythematosus) treated with drugs targeting TNF, IL12p40, IL6R, BLySS, IL17, and JAK pathways at baseline and at the week of clinical response
- Ulcerative colitis and Crohn's disease showed more similar circulating immune cell profiles to each other than to other IMIDs, with identified differences in pDC, MAIT, NK CD16- and T CD4+ Memory subsets between the two diseases
- Strong regulatory differences were found in B and CD14+ monocyte compartments between UC and CD despite their highly shared genetic risk
- The impact of each drug was largely disease-specific, with different gene expression programs upregulated in UC versus Crohn's disease even when treated with the same targeted therapy
- The scRNA-seq atlas will be made available through an online application as a resource for understanding drug response and disease heterogeneity across immune-mediated inflammatory diseases

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