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Summary

DEFINING THE CELLULAR GUT MUCOSAL ORIGINS OF PRECLINICAL CIRCULATING PROTEIN SIGNATURES IN INFLAMMATORY BOWEL DISEASE

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Single-cell RNA sequencing reveals that circulating protein signatures associated with preclinical IBD originate predominantly from gut mucosal immune cells in established disease, with several showing inflammation-associated expression differences.

KEY POINTS

- Genes encoding previously reported CD and UC circulating protein signatures were mapped onto single-cell RNA-sequencing datasets from intestinal biopsies (CD: 159 ileal biopsies from 151 patients; UC: 78 colonic biopsies from 53 patients).
- In CD, six of nine biomarkers (CXCL9, IL6, DNER, MDK, GPNMB, MMP10) showed significant differential expression between inflamed and non-inflamed tissue, with strongest associations for IL6 in inflammatory macrophages (adjusted P=2.15x10^-14) and CXCL9 in activated dendritic cells (P=1.03x10^-4).
- In UC, nine of twelve biomarkers (STAMBP, SCAMP3, ADAM8, GZMB, ABL1, CCL11, CD5, CDKN1A, CXCL9) showed significant inflammation-associated differences, with strongest associations for CCL11 in WNT2B+Fos-lo1 fibroblasts (P=9.87x10^-47) and CDKN1A in inflammatory monocytes (P=3.50x10^-11).
- In IBD, biomarker expression was distributed across immune subsets including Th17 tissue-resident memory cells, activated dendritic cells, inflammatory macrophages, cycling T- and B-cells, and natural killer cells; in healthy controls, expression was mainly localized to stromal subsets.
- Sample processing was performed by Takeda.

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