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Summary

# CELL SIGNALLING IN COLITIS-ASSOCIATED COLON CANCER

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**Spatial transcriptomics of colitis-associated carcinoma identifies SPP1-expressing macrophages and an immunosuppressive microenvironment with regulatory T cells and metabolically impaired CD8+ T cells.**

KEY POINTS

- Immunology gene expression profiling and spatial transcriptomics on FFPE tissue from 40 IBD and CAC patients revealed robust upregulation of SPP1 (osteopontin) and FN1 in CAC compared to ulcerative colitis and Crohn's disease.
- SPP1 was primarily expressed by CD68+ macrophages in CAC and showed spatial mutual exclusion with CD8+ T cells, validated by confocal microscopy.
- Ligand-receptor analysis identified SPP1 as a key macrophage signal engaging CD44 and integrin receptors on T cells.
- CD4+ T cells in CAC showed upregulation of FOXP3 and CTLA4 indicating a regulatory phenotype, while CD8+ T cells displayed upregulation of GZMK, downregulated JAK-STAT signalling, and upregulated LDHA, hypoxia and glycolysis pathways indicating metabolic reprogramming and functional impairment.
- The authors conclude these features define a CAC-specific immune landscape and propose the gene signature has potential to detect pre-malignant changes in inflammatory bowel disease.

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