

LEVERAGING SPATIAL MULTI-OMICS TO UNCOVER THE ROLE OF DUCTULAR REACTION IN THE PROGRESSION OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Multi-omics spatial profiling identified pro-inflammatory hepatic progenitor cell signatures that predict fibrosis progression in MASLD patients.

KEY POINTS

- In a dual biopsy cohort, hepatic progenitor cell presence in the parenchyma at baseline was significantly associated with progression of at least 1 fibrosis stage and predicted fibrosis progression in a binary logistic regression model.
- High-throughput transcriptomics of the hepatic progenitor cell niche identified 3,282 differentially expressed genes enriched in pro-inflammatory cytokines (CXCL6, CCL19, CCL2, CCL5, CCL21, SPP1), inflammatory cell markers (CCR2, CD48, CD8a, CD96, CXCR3, S100A4), and antigen presenting genes.
- Spatial transcriptomics uncovered distinct ductular reaction subsets: SPP1+CCL2- cells localised predominantly in the parenchyma and peri-portal region, while CCL2+SPP1- cells were confined mainly to the portal tract.
- The hepatic progenitor cell gene signature stratified 206 MASLD biopsies into clusters characterised by steatohepatitis, high disease activity, fibrosis and elevated AST levels.
- Spatial proteomics identified CD48 and HLA-DR-expressing macrophages as key immune cells of the hepatic progenitor cell niche, with neighbourhood analysis highlighting antigen-presenting cells and IGHA1+IGHG1+ plasma cells in close proximity to ductular reaction.

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