SINGLE-CELL AND SPATIAL ANALYSIS REVEAL MAS-DRIVEN PRO-INFLAMMATORY MICROENVIRONMENT IN ACETAMINOPHEN-INDUCED LIVER INJURY

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Multi-omic study identifies myeloid-Mas signaling as a critical driver of immunometabolic landscape in acetaminophen-induced liver injury, with potential implications for targeted therapeutic strategies and diagnostic models.

KEY POINTS

- Myeloid-Mas signaling was identified as the critical driver of immunometabolic landscape in the progression of acetaminophen-induced liver injury using multiple cell-specific Mas1-knockout mice and multi-omic analysis.
- The AILI-imprinted immunometabolic landscape consists of CD31+MYC+CD63+ endothelial cells, F4/80+MMP12+ macrophages and monocytes, firstly visualized by hour-long intravital imaging in living mice.
- The myeloid-Mas driven landscape established in mouse AILI was mapped and enriched in human AILI, with the human landscape consisting of MYC+ endothelial cells, MMP12+ macrophages and CD14+ monocytes.
- Unsupervised clustering using k-means algorithm suggests 83% probability to identify advanced AILI by microenvironmental characteristics, showing potential for clinical transformation into diagnostic models.
- The study combines single-cell RNA sequencing, spatial transcriptomics and intravital imaging to provide a paradigm for studying cellular interactions in complex pathophysiological microenvironments.

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