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Summary

BLOCKADE OF PLATELET ACTIVATING FACTOR RECEPTOR PATHWAY WITH A LIGAND ANTAGONIST BN-52021 REDUCES LIVER DAMAGE AND PROINFLAMMATORY GENE EXPRESSION IN CIRRHOTIC MICE

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The platelet-activating factor receptor pathway is activated in experimental cirrhosis and its blockade with antagonist BN-52021 reduces liver damage and inflammation in mice.

KEY POINTS

- PAFR is hypomethylated and significantly upregulated in hepatic macrophages of cirrhotic mice, with increased PAF ligand detected in serum due to altered synthesis and degradation enzyme expression.
- In vitro stimulation of immortalized Kupffer cells with PAF induces proinflammatory polarization, increasing cytokines TNF, IL1β, and TGFβ1 and chemokines CCL3, CCL20, CXCL15, and CXCL16, while reducing anti-inflammatory cytokines IL4, IL10, and IL-13.
- Treatment of cirrhotic mice with PAF receptor antagonist BN-52021 ameliorated fibrosis and liver damage measured by sirius red, aSMA, and vimentin staining, improved biochemical markers, and reduced proinflammatory and profibrogenic gene expression.
- The authors suggest that blocking the PAF/PAF-R pathway may have value in reducing experimental cirrhosis progression and represents a potential therapeutic target.

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