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Title

Impaired paracrine FGF signalling in the insulin resistant liver: implications for chronic injury repair and epithelial remodelling.

Chronic liver disease in obese and diabetic patients represents a burgeoning healthcare problem. In response to chronic injury, parenchymal hepatocytes can dedifferentiate to bipotent epithelial progenitor cells that expand and are capable of re-differentiating to maintain liver function. Our research investigates the impact of insulin resistance on the chronic liver injury response, with particular focus on the behaviour of progenitor cells and their ability to differentiate back to hepatocytes. We present the novel finding that FGFR2 IIIb (FGF7 receptor) expression is regulated in progenitors by insulin/IRS2 signalling. Hence, we propose that insulin resistance blocks the paracrine communication between fibrotic niche cells and epithelial progenitors in periportal tracts. These findings may have profound implications for our understanding of the mechanistic link between metabolic disease and chronic liver disease.

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