LIVER

Fgf15 maintains bile acid homeostasis and is a key mediator of liver regeneration in mice

Fibroblast growth factor 15 (Fgf15, FGF19 in humans) is a key mediator of the growth-promoting effects of bile acids and is essential for the maintenance of bile acid homeostasis in a mouse model of liver regeneration, a new study in *Gut* finds.

Liver regeneration is complex and tightly regulated, but poorly understood. The authors explored whether Fgf15 and

bile acids have a role in the regenerative response after partial hepatectomy in *Fgf15*-knockout and wild-type mice.

After removal of 70% of the liver, *Fgf15*^{-/-} mice had very high mortality (only 31.9% survival) owing to toxic intrahepatic concentrations of bile acids. Delivery of Fgf15 reduced intrahepatic levels of bile acids and increased survival in these mice.

Survival also improved upon delivery of Fgf15 in wild-type mice after extensive (85% removal) liver resection.

Importantly, Fgf15 also had a crucial role in modulating the growth-promoting effects of bile acids in the liver. *Fgf15*^{-/-} mice had impaired bile-acid-induced liver growth and proliferation of liver epithelial cells, whilst *in vitro* studies showed that Fgf15 was a direct mitogen for hepatocytes and cholangiocytes.

“Our findings identify Fgf15/FGF19 as a growth factor potentially applicable in the management of cholestasis and the prevention of acute liver failure after extensive liver resection,” says author Matías Avila.

Katrina Ray

Fgf15 has a key role in liver regeneration. Images show liver tissue samples at 44 h posthepatectomy. Courtesy of M. Avila.

Original article Uriarte, I. *et al.* Identification of fibroblast growth factor 15 as a novel mediator of liver regeneration and its application in the prevention of post-resection liver failure in mice. *Gut* doi:10.1136/gutjnl-2012-302945