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FXR REGULATE LIVER REPAIR AFTER CCL4 INDUCED INJURY

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Farnesoid X Receptor (FXR, NR1H4) is a member of the nuclear hormone receptor superfamily. It plays a key role in regulating liver metabolism, particularly bile acid homeostasis. Previously we have shown that FXR is required for normal liver regeneration after 70% partial hepatectomy. In the present study, we demonstrate that FXR is essential for regulating liver repair after toxic injury by carbon tetrachloride (CCL4) treatment. We compared the response of liver repair in age-matched wild type and FXR-/− mice after exposure to a single hepatotoxic dose of CCL4. The results indicate that FXR-null mice had severe defect in liver repair after injury. Compared with the wild type controls, FXR-/− mice displayed increased mortality rate, enhanced hepatocyte death and decreased peak of regenerative DNA synthesis. Induced expression of genes involved in liver cell cycle progression including Cyclin D1 and FoxM1b were significantly reduced in FXR-/− liver. The FXR-/− mice showed strongly decreased phosphorylation and DNA binding activity of liver STAT3 in FXR-/− mice. In contrast, AP1 gene expression and NFκB activities were comparable between FXR-/− livers and the wild type controls. Exogenous expression of a constitutively active STAT3 protein in FXR-/− liver effectively suppressed hepatocyte death after CCL4 treatment. These results indicate that FXR is required for regulating liver repair after toxin induced liver injury via modulating pathways in both hepatocyte survival and liver regeneration 1-11.

Further reading &

References:


