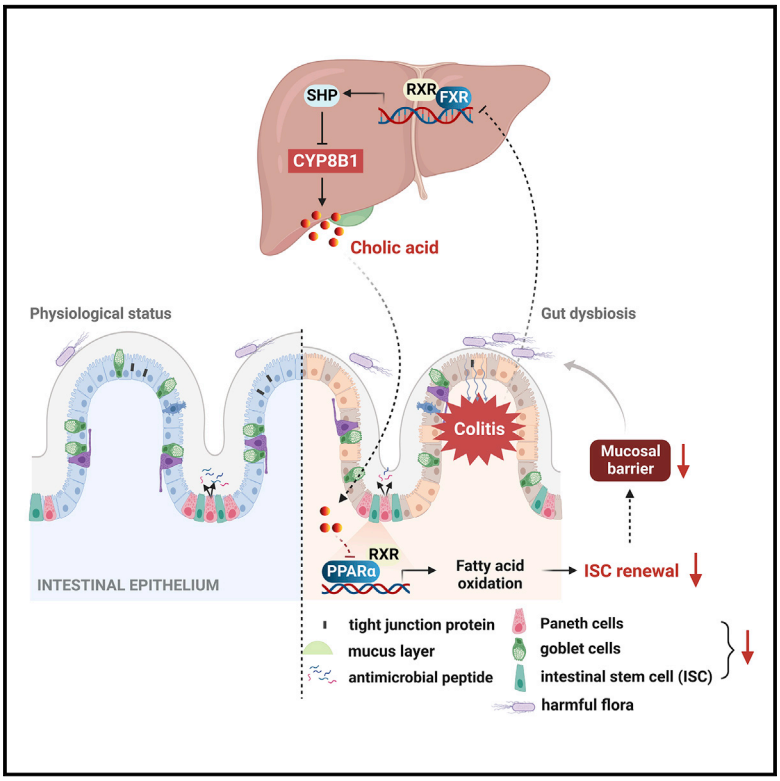
Cell Stem Cell

Article

Hepatic cytochrome P450 8B1 and cholic acid potentiate intestinal epithelial injury in colitis by suppressing intestinal stem cell renewal

Graphical abstract



Highlights

- CA accumulates in the gut during colitis because of activation of hepatic CYP8B1
- Exogenous CA or liver CYP8B1 overexpression potentiates intestinal injury
- Excessive CA triggers Lgr5^{+} ISCs dysfunction by suppressing PPARα-mediated FAO
- Activation of liver FXR and ablation of CYP8B1 expression alleviate colitis

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In brief

Xie and colleagues propose a regulatory mechanism of hepatic bile acid metabolism in colitis pathogenesis. They find that the hepatic CYP8B1-cholic acid metabolic axis impairs Lgr5^{+} intestinal stem cell renewal by repressing PPARα, thus exacerbating intestinal injury. Hepatic FXR activation or CYP8B1 knockout restores damaged epithelial barrier and alleviates colitis.

Chen et al., 2022, Cell Stem Cell *29*, 1366–1381
September 1, 2022 Published by Elsevier Inc.
https://doi.org/10.1016/j.stem.2022.08.008