11β-Hydroxysteroid dehydrogenase-1 is involved in bile acid homeostasis by modulating fatty acid transport protein-5 in the liver of mice

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Author(s) Penno, Carlos A; Morgan, Stuart A; Rose, Adam J; Herzig, Stephan; Lavery, Gareth G; Odermatt, Alex
Author(s) at UniBasel Odermatt, Alex ;
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11β-Hydroxysteroid dehydrogenase-1 (11β-HSD1) plays a key role in glucocorticoid receptor (GR) activation. Besides, it metabolizes some oxysterols and bile acids (BAs). The GR regulates BA homeostasis; however, the impact of impaired 11β-HSD1 activity remained unknown. We profiled plasma and liver BAs in liver-specific and global 11β-HSD1-deficient mice. 11β-HSD1-deficiency resulted in elevated circulating unconjugated BAs, an effect more pronounced in global than liver-specific knockout mice. Gene expression analyses revealed decreased expression of the BA-CoA ligase Fatp5, suggesting impaired BA amidation. Reduced organic anion-transporting polypeptide-1A1 (Oatp1a1) and enhanced organic solute-transporter-β (Ostb) mRNA expression were observed in livers from global 11β-HSD1-deficient mice. The impact of 11β-HSD1-deficiency on BA homeostasis seems to be GR-independent because intrahepatic corticosterone and GR target gene expression were not substantially decreased in livers from global knockout mice. Moreover, Fatp5 expression in livers from hepatocyte-specific GR knockout mice was unchanged. The results revealed a role for 11β-HSD1 in BA homeostasis.

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