Mice lacking Mrp3 (Abcc3) have normal bile salt transport, but altered hepatic transport of endogenous glucuronides

Background/Aim: Multidrug Resistance Protein 3 (MRP3) transports bile salts and glucuronide conjugates in vitro and is postulated to protect the liver in cholestasis. Whether the absence of Mrp3 affects these processes in vivo is tested.

Methods: Mrp3-deficient mice were generated and the contribution of Mrp3 to bile salt and glucuronide conjugate transport was tested in (1): an Ussing-chamber set-up with ileal explants (2), the liver during bile-duct ligation (3), liver perfusion experiments, and (4) in vitro vesicular uptake experiments. Results: The Mrp3(−/−) mice show no overt phenotype. No differences between WT and Mrp3-deficient mice were found in the trans-ileal transport of taurocholate. After bile-duct ligation, there were no differences in histological liver damage and serum bile salt levels between Mrp3(−/−) and WT mice, but Mrp3-deficient mice had lower serum bilirubin glucuronide concentrations. Glucuronide conjugates of hyocholate and hyodeoxycholate are substrates of MRP3 in vitro and in livers that lack Mrp3, there is reduced sinusoidal secretion of hyodeoxycholate-glucuronide after perfusion with hyodeoxycholate. Conclusions: Mrp3 does not have a major role in bile salt physiology, but is involved in the transport of glucuronidated compounds, which could include glucuronidated bile salts in humans.

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