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editorial

Bile Acid Disposition and Drug Pharmacokinetic Implications

Numerous transporters translocate bile acids across membranes in gut, liver, and biliary tissues to support gut and hepatobiliary functioning. These transporters often work in concert with metabolic enzymes to coordinate bile acid absorption, distribution, metabolism, and excretion. The expression and functionality of bile acid transporters has implications for disease, as well as implications for potential underlying mechanisms for targeted drug delivery and drug interactions.

This special issue "Bile Acid Disposition and Drug Pharmacokinetic Implications" highlights molecular features of bile acid transport in the gut and liver, through several contextual reviews and articles. The reviews "Role of Nuclear Receptors in the Adaptive Response to Bile Acids and Cholestasis: Pathogenetic and Therapeutic Considerations" (Zollner et al.) and "Coordinate Regulation of Hepatic Bile Acid Oxidation and Conjugation by Nuclear Receptors" (Trottier et al.) each summarize aspects of nuclear receptor involvement in bile acid synthesis, metabolism, and transport, including nuclear receptors as drug targets. In "Methods To Evaluate Biliary Excretion of Drugs in Humans: An Updated Review", Ghibellini et al. discuss recent advances in in vivo methods to estimate human biliary excretion and in vitro methods to probe for molecular features of biliary excretion. The review "Apical Sodium Dependent Bile Acid Transporter (ASBT, SLC10A2): A Potential Prodrug Target" (Balakrishnan and Polli) summarizes current progress in utilizing hASBT as a drug delivery target.

Contributed articles include two that investigate the interaction of drugs and substrates with bile salt export pump (Hirano et al.) and ASBT (Balakrishnan et al.) and that have implications for adverse drug reactions and targeted drug delivery. Rose et al. establish methodologies to culture dog and monkey hepatocytes with optimal bile canalicular formation and function and report differences that may reflect in vivo differences between species. Caron et al. report a simple method to purify and quantify analytical standards of several bile acid glucuronides. Additionally, given the importance of clarifying substrate specificities, two articles discuss compounds that are not substrates of Mrp3 and ABCG2 (Sakamoto et al.; Vaidya and Gerk).

Bile acid disposition is complex, requiring a full complement of laboratory tools and clinical study designs to push the area forward. I hope this special issue of *Molecular Pharmaceutics* provides contemporary insights from ongoing efforts, as well as inspiring new lines of research. While much is known about proteins that translocate and metabolize bile acids, further progress is needed to better understand mechanisms that control bile acid disposition, from system level organization to the understanding of substrate requirements of individual transporters and enzymes. Such advances will unveil novel therapeutic targets, allow for the anticipation and avoidance of drug interactions, and lead to new molecular-based strategies to target gut and liver.

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