Table S1. Summary of endogenous metabolites, which are substrates of OATP1B1 and have been evaluated as OATP1B1-mediated drug-drug interaction biomarkers. This table summarizes the metabolites and their evidence (i) as substrates of different influx and efflux transporters; (ii) in clinical OATP1B1-mediated drug-drug interactions (human, preclinical studies); (iii) from human genetic studies with OATP1B1-Val174Ala or knockout mice; and (iv) from disease associations.

Metabolite Class	Metabolite and Transporter Substrate and Inhibitor Profile	Fold increase (if available) by OATP1B1 inhibitor	Fold increase by other transporter inhibitor (species)	Human genetic polymorphism; knockout mice; human disease	References
Porphyrin (arising from heme synthesis)	Coproporphyrin I (CP-I) Substrate: OATP1B1, OATP1B3, MRP2, MRP3 Inhibitor: OATP2B1, OCT1, OCT2, OAT1, OAT3, NTCP	**Rifampicin**: AUC, 4-fold (human) **Rifampicin**: C_{max}, 5.7-fold (human) **Rifampicin**: AUC, 2.7-fold (monkey) **Cyclosporine**: AUC, 2.6-fold (monkey) **Various OATP1B1 inhibitors:** AUC 1.4-fold (mild inhibitor), AUC, 2-3-fold (moderate inhibitor) ≥5-fold (strong inhibitor) **GDC-0810 (weak inhibitor)**: AUC 1.5-fold	NA	**Mice**: Oatp1a/1b(-/-) increased CPs in plasma and urine (>7-fold) **Human**: (this paper) **Human disease**: Dubin Johnson	1-6
Porphyrin (arising from heme synthesis)	Coproporphyrin III (CP-III) Substrate: OATP1B1, OATP1B3, OATP2B1, MRP2, MRP3 Inhibitor: OCT1, OCT2, OAT1, OAT3, NTCP	**Rifampicin**: AUC, 3.3-fold (human) **Rifampicin:** C_{max}, 5.4-fold (human) **Rifampicin**: AUC, 3.6-fold (monkey) **Cyclosporin:** AUC, 5.2-fold (monkey) **Various OATP1B1 inhibitors**: AUC, 2-3-fold (moderate inhibitor) ≥5-fold (strong inhibitor) **GDC-0810 (weak inhibitor)**: AUC 1.5 fold	NA	No (this paper) **Human disease**: Dubin Johnson	1-4
Heme (degradation product of heme)	Bilirubin Substrate: OATP1B1, OATP1B3, MRP2 Inhibitor: none characterized	**Rifampicin**: AUC increased (rat, human)	NA	**Mice**: Oatp1a/1b(-/-) increased total bilirubin and bilirubin glucuronides in plasma and/or urine **Human**: Yes **Human disease**: Rotor syndrome, a rare, benign hereditary conjugated hyperbilirubinemia	7-12
Dicarboxylic acid	Tetradecanedioic acid (TDA) Substrate: OATP1B1, OAT1, OAT3 Not substrate of: OATP1B3, OATP2B1, NTCP. Not inhibitor of: P-gp, MRP2, BCRP, BSEP	**Rifampicin**: AUC, 3.2-fold (human) **Rifampicin**: C_{max}, 2.2-fold (human) **CSA:** 30 min after CSA (GCDCA-G) (human)	**Probenecid**: AUC, 2.8-fold (monkey) **Probenecid**: C_{max}, 2.3-fold (monkey)	**Human GWAS**: Significant with $p<5x10^{-8}$ **Human disease**: Not known	13-19
Dicarboxylic acid	Hexadecanedioic acid (HDA)	**Rifampicin**: AUC, 3.2-fold (human) **Rifampicin**: Cmax, 2.2-fold (human)	**Probenecid**: AUC, 1.9 fold (monkey)	**Human GWAS**: Significant with $p<5x10^{-8}$	13-21

	Substrate: OATP1B1, OAT1, OAT3 Not substrate of: OATP1B3, OATP2B1, NTCP. Not inhibitor of: P-gp, MRP2, BCRP, BSEP	**CSA:** 30 min after CSA (GCDCA-G) (human)	**Probenecid**: C_{max}, 2.0-fold (n.s) (monkey)	**Human disease**: Association with blood pressure	
Bile acid glucuronide	• Chenodeoxycholate-3-glucuronide (CDCA-3G) • Chenodeoxycholate-24-glucuronide (CDCA-24G) • Glycochenodeoxycholate glucuronide (GCDCA-G) Substrate: OATP1B1, OATP1B3, NTCP, MRP2, MRP3, OAT3 Inhibitor: none characterized	**Rifampicin**: CDCA-3G and CDCA-24G are not detectable at baseline and increased with rifampicin (human) **CSA**: 30 min after CSA (GCDCA-G) (human)	NA	**Human GWAS** (GCDCA-G): Significant with $p<5x10^{-8}$ **Human disease**: Not known	8,13,16-18,22-26
Bile acid sulfates	• Cholic acid 3-O-sulfate (CA-S) • Chenodeoxycholic acid 3-O-sulfate (CDCA-S) • Deoxycholic acid 3-O-sulfate (DCA-S) • Glycocholic acid 3-O-sulfate (GCA-S) • Glycochenodeoxycholic acid 3-O-sulfate (GCDCA-S) • Glycolithocholic acid 3-O-sulfate (GLCA-S) • Glycoursodeoxycholic acid 3-O-sulfate (GUDCA-S) • Lithocholic acid 3-O-sulfate (LCA-S) • Taurocholic acid 3-O-sulfate (TCA-S) • Taurochenodeoxycholic acid 3-O-sulfate (TCDCA-S) • Taurodeoxycholic acid 3-O-sulfate (TDCA-S) • Taurolithocholic acid 3-O-sulfate (TLCA-S) • Tauroursodeoxycholic	**Rifampicin**: AUC, 20.3-fold (GCDCA-S) (human) **Rifampicin**: C_{max} and AUC, 10-30-fold (LCA-S, GLCA-S, TLCA-S, UDCA-S); 50-100-fold (GCDCA-S, TCDCA-S, DCA-S, GDCA-S, TDCA-S) (monkey) **CSA**: 30 min after CSA (GCDCA-S, GDCA-S, TLCA-S) (human)	**Probenecid**: renal clearance reduced ($p<0.05$), plasma levels (n.s) (GCDCA-S) (human)	**Human GWAS** (GDCA-S): Significant with $p<5x10^{-8}$ **Human GWAS** (TLCA-S, GCDCA-S): Significant with $p<1x10^{-4}$ **Human disease**: Not known	13,14,16,17,22-24

	acid 3-O-sulfate (TUDCA-S) • Ursodeoxycholic acid 3-O-sulfate (UDCA-S) Substrate: OATP1B1, OATP1B3, NTCP, OAT3 (GCDCA-S), BSEP Inhibitor:None characterized				
Unsulfated bile acids	• Cholic acid (CA) Chenodeoxycholic acid (CDCA) • Deoxycholic acid (DCA) • Glycocholic acid (GCA) • Glycochenodeoxycholic acid (GCDCA) • Glycodeoxycholic acid (GDCA) • Glycoursodeoxycholic acid (GUDCA) • Lithocholic acid (LCA) • Taurocholic acid (TCA) • Taurochenode-oxycholic acid (TCDCA) • Taurodeoxycholic acid (TDCA) • Taurohyodeoxycholic acid/tauroursodeoxycholic acid (THDCA/TUDCA) • Ursodeoxycholic acid/hyodeoxycholic acid (UDCA/HDCA) Substrate: OATP1B1, OATP1B3, NTCP, OAT3, BSEP	**Rifampicin**: AUC, 2-7-fold (GDCA,TDCA,GCA,GCDCA) (human) **Rifampicin**: AUC, 1.8-5.9-fold (TUDCA, GCA, CA, TCA, GCDCA, GDCA, TCDCA, TDCA, CDCA) (human) **Rifampicin**: C_{max} and AUC, 2-5-fold (UDCA, GDCA, TUDCA, CDCA, GCDCA, TCDCA, DCA, GDCA, TDCA) (monkey) **Rifampicin**: AUC (total bile acids) (rat)	NA	**Human disease**: Not known	11,14,16,17,24,27-30
Steroid sulfates	• Dehydroepiandrosterone Sulfate (DHEAS) Substrate: OATP1B1, OATP1B3, OAT3, MRP3	**Rifampicin**: AUC (not significant) (DHEAS) (human)	NA	Yes **Human disease**: Not known	14,16,26,31

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