FRONTAGE
YOUR DRUG DEVELOPMENT PARTNER

DRUG TRANSPORTER SERVICES

Drug transporters can be major determinants of pharmacokinetics, drug-drug interactions, safety and efficacy of drugs

At Frontage, we have extensive experience in drug transporter research. We offer comprehensive transporter services to support projects from discovery to development including screening, and full characterization of both uptake and efflux transporters.

Transporters	Substrates	Test Systems
P-gp	Digoxin, vinblastine, quinidine	Caco-2, transfected MDCK cells
BCRP	Prazosin, E-3-S, cladribine, topotecan	Transfected MDCK cells
OATP1B1	E-3-S, pravastatin, E-17b-G, rosuvastatin	Hepatocytes, transfected HEK293 cells
OATP1B3	CCK-8, telmisartan, E-17b-G, rosuvastatin	Hepatocytes, transfected HEK293 cells
OAT1	p-Aminohippurate, furosemide	Transfected HEK293 cells
OAT3	Estrone 3-sulfate, furosemide	Transfected HEK293 cells
OCT2	MPP+, metformin	Transfected HEK293 cells
MATE1	MPP+, metformin	Transfected HEK293 cells
MATE2K	MPP+, metformin	Transfected HEK293 cells
BSEP	Glycocholate, taurocholate	Hepatocytes, membrane-vesicles
MDR3	d9-phosphatidylecholine	Hepatocytes
MRP2	Bilirubin-G, E-17b-G, coproporphyrin-1	Hepatocytes, membrane-vesicles
NTCP	Taurocholate	Transfected HEK293 cells
OATP2B2, 1A2	Estrone 3-sulfate	Transfected HEK293 cells
OAT2	cGMP	Transfected HEK293 cells
OAT3, OAT4	Estrone 3-sulfate, furosemide	Transfected HEK293 cells
OCT1, OCT2	MPP+, metformin	Transfected HEK293 cells

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WE PROVIDE INNOVATIVE SOLUTIONS TO BETTER UNDERSTAND THE IMPLICATION OF TRANSPORTERS IN DRUG-INDUCED LIVER INJURY (DILI)

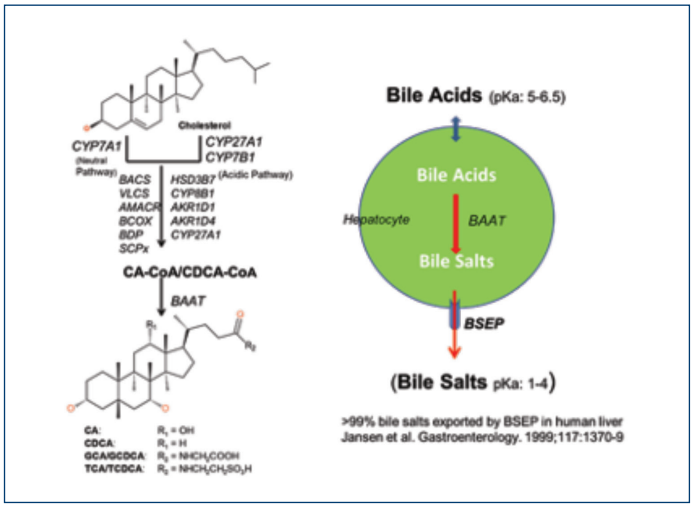
Hepatic transporters help facilitate bile production by exporting bile salts and phosphatidylcholine (PC) from hepatocytes. In humans, inhibition of bile salt export protein (BSEP, ABCB11) and/or multidrug resistance protein 3 (MDR3, ABCB4) transporters can lead to potentially serious DILI. Drug candidates can be screened for inhibition of BSEP and/or MDR3 to assess DILI risk.

BSEPcyte® and MDR3cyte® assays detect the potential of drug candidates to inhibit BSEP and MDR3, respectively. Both approaches utilize a hepatocyte suspension platform, which offers several advantages over other *in vitro* techniques:

- Hepatocytes are more physiologically relevant compared to vesicles and transfected cell lines
- *In situ* metabolism capability is present in hepatocytes
- Suspension studies save cell culturing time and allows quicker data generation
- Assay is accurate, robust, reproducible, and customizable
- Assay allows for cross species comparison
- Specific LC-MS/MS determination of exported bile salts

BSEP*cyte*®

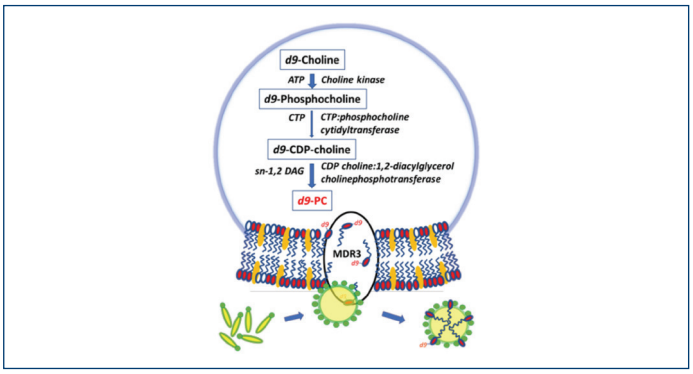
BSEP is responsible for biliary secretion of bile salts, which is the primary driving force for enterohepatic recirculation of bile salts and maintaining bile flow. Inhibition of BSEP by a diverse range of drugs or therapeutic agents is associated with DILI. At Frontage, we have developed a novel assay, BSEPcyte®, that accurately measures BSEP inhibition.



BSEPcyte® is protected by patent US 9,772,325

MDR3*cyte*®

MDR3 is primarily expressed in the canalicular membrane of hepatocytes and is responsible for the biliary secretion of PC. PC combined with bile salts forms mixed micelles in bile that solubilize cholesterol and prevent highly concentrated bile salts from damaging biliary canaliculi epithelial cells. Mutations in the human MDR3 gene are associated with progressive familial intrahepatic cholestasis, primary biliary cirrhosis, cholangiocarcinoma, and DILI. The novel MDR3cyte® assay platform at Frontage can provide accurate assessment of MDR3 inhibition by drug candidates and new chemical entities.



MDR3cyte® is protected by patent US 10,280,401

Frontage Laboratories, Inc. is a contract research organization (CRO) that provides integrated, science-driven, product development services throughout the drug discovery and development process to enable pharmaceutical and biotechnology companies to achieve their development goals. Comprehensive services include drug metabolism and pharmacokinetics, analytical testing and formulation development, preclinical and clinical trial material manufacturing, bioanalysis, preclinical safety and toxicology assessment and early phase clinical studies. Frontage has enabled many biotechnology companies and leading pharmaceutical companies of varying sizes to advance a myriad of molecules through development and file regulatory submissions in the United States, China, and other countries.

FOR MORE INFORMATION, CONTACT US AT: *sales@frontagelab.com* **OR VISIT US AT:** *frontagelab.com*

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