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E-mail: info@primacyt.com, Tel.: +49 (0) 385-3993-600, Fax: +49 (0) 385-3993-602

Organic anion transporting polypeptides (OATPs)

Introduction: Organic anion transporting polypeptides (OATPs, gene family: SLCO) are expressed in a variety of different tissue and mediate the uptake of a broad range of substrates. Some of them are organ specific like OATP1B1 and OATP1B3, which are only expressed in the liver. Others like OATP1A2, which is localized in brain, kidney and small intestine are ubiquitous expressed. Because of their wide tissue distribution and broad substrate spectrum, altered transport kinetics can contribute to the interindividual variability of drug effects.

Methods: A cell platform using stable transfected HEK293 cells expressing OATP1B1, OATP1B3 and OATP1A2, respectively, was generated. The uptake functions of OATP1B1 and OATP1B3 were analyzed with Fluorescein methotrexate (FMTX) and Cholyl-Lysyl-Fluorescein (CLF). HEK-OATP1A2 was characterized with Rhodamine. The uptake was inhibited by addition of the reference inhibitor Rifampicin.

OATP1B1

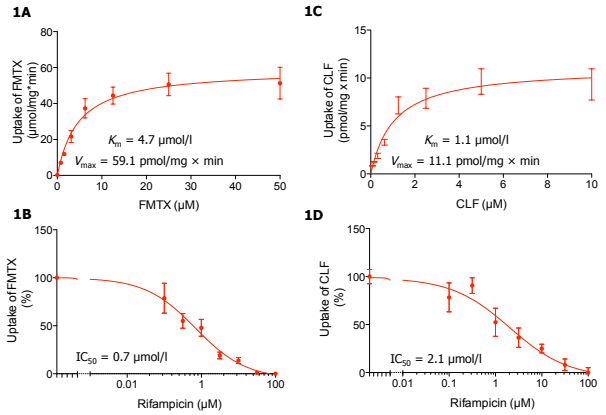

Figure 1: Concentration dependent uptake of FMTX (1A) and CLF (1C) mediated by OATP1B1. Rifampicin inhibited OATP1B1 mediated uptake of FMTX (1B) and CLF (1D)

OATP1B3

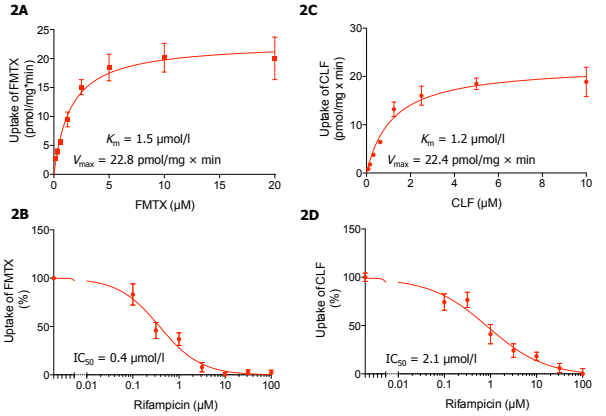

Figure 2: Concentration dependent uptake of FMTX (2A) and CLF (2C) mediated by OATP1B3. Rifampicin inhibited OATP1B3 mediated uptake of FMTX (2B) and CLF (2D)

OATP1A2

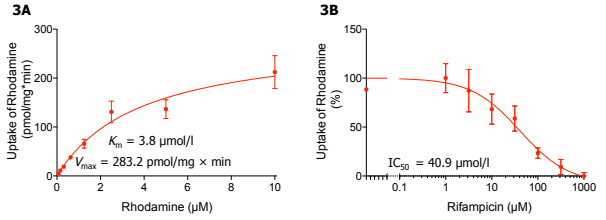

Figure 3: OATP1A2 mediated concentration dependent uptake of Rhodamine (3A). Inhibition of OATP1A2 mediated Rhodamine uptake by Rifampicin (3B)

OATP1B1

Substrate	Inhibitor	Kinetic parameter	Literature
FMTX	-	K_m = 4.7 µmol/l	K_m = 3.8 µmol/l (Gui C, 2010)
FMTX	Rifampicin	IC_{50} = 0,7 µmol/l	IC50 = 1.5 µmol/l (Gui C, 2010)

OATP1B3

Substrate	Inhibitor	Kinetic parameter	Literature
FMTX	-	K_m = 1.5 µmol/l	K_m = 7.9 µmol/l (Gui C, 2010)
FMTX	Rifampicin	IC_{50} = 0.4 µmol/l	IC_{50} = 1.5 µmol/l (Gui C, 2010)
CLF	-	K_m = 1.2 µmol/l	K_m = 4.6 µmol/l (de Waart DR, 2010)

Notes: PRIMACYT is a registered trademark of PRIMACYT Cell Culture Technology GmbH

Literature:

Gui C, Obaidat A, Chaguturu R, Hagenbuch B. *Development of a cell-based high-throughput assay to screen for inhibitors of organic anion transporting polypeptides 1B1 and 1B3*. Curr Chem Genomics. 2010, 4: 1-8

de Waart DR, Häusler S, Vlaming ML, Kunne C, Hänggi E, Gruss HJ, Oude Elferink RP, Stieger B. *Hepatic transport mechanisms of cholyl-L-lysyl-fluorescein*. J Pharmacol Exp Ther. 2010, 334(1):78-86