

Supplementary Information

Hepatic Transporter Alterations by Nuclear Receptor Agonist T0901317 in Sandwich-cultured Human Hepatocytes: Proteomic Analysis and PBPK Modeling to Evaluate Drug-Drug Interaction Risk

Katsuaki Ito, Noora Sjöstedt, Melina M. Malinen, Cen Guo and Kim L.R. Brouwer

Division of Pharmacotherapy and Experimental Therapeutics, UNC Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC (K.I., N.S., M.M.M., C.G., K.L.R.B.);

DMPK Research Department, Teijin Pharma Limited, Hino, Tokyo, Japan (K.I.)

Supplementary Table 1. Signature peptides selected for proteomic analysis of transporter proteins. Bold letters indicate amino acids labeled with stable isotope (¹³C and ¹⁵N).

Gene Symbol	Alias	Analyte or IS	Signature Peptide	Parent Ion	Product Ions				Peptide No.
					1	2	3	4	
<i>SLC Transporter</i>									
<i>SLC10A1</i>	NTCP	Analyte	GIYDGLK	440.7	710.3	547.3	260.2	432.2	-
		IS	GIYDGLK	444.7	718.3	555.3	268.2	440.3	
<i>SLC01B1</i>	OATP1B1	Analyte	NVTGFFQSFK	587.8	381.2	656.3	860.4	961.5	Peptide 1
		IS	NVTGFFQSFK	591.8	389.2	664.4	868.4	969.5	
		Analyte	YVEQQYGQPSSK	707.3	234.1	418.2	603.3	766.4	Peptide 2
		IS	YVEQQYGQPSSK	711.3	242.2	426.2	611.3	774.4	
<i>SLC01B3</i>	OATP1B3	Analyte	NVTGFFQSLK	570.8	826.4	927.5	347.2	622.4 ^a /769.4 ^b	-
		IS	NVTGFFQSLK	574.8	834.5	935.5	355.2	630.4 ^a /777.4 ^b	
<i>SLC02B1</i>	OATP2B1	Analyte	SSPAVEQQLLVSGPGK	798.9	544.3	445.2	358.2	301.2	-
		IS	SSPAVEQQLLVSGPGK	802.9	552.3	453.3	366.2	309.2	
<i>SLC22A1</i>	OCT1	Analyte	LSPSFADLFR	576.8	952.5	621.3	768.4	435.3	-
		IS	LSPSFADLFR	581.8	962.5	631.3	778.4	445.3	
<i>SLC22A3</i>	OCT3	Analyte	FLQGVFGK	448.3	635.4	507.3	351.2	204.1	-
		IS	FLQGVFGK	452.3	643.4	515.3	359.2	212.1	
<i>SLC22A7</i>	OAT2	Analyte	NVALLALPR	483.8	456.3	569.4	682.5	753.5	-
		IS	NVALLALPR	488.8	466.3	579.4	692.5	763.5	

SLC47A1	MATE1	Analyte	GGPEATLEVR	514.8	688.4	617.4	516.3	274.2	-
		IS	GGPEATLEVR	519.8	698.4	627.4	526.3	284.2	
SLC51A	OST α	Analyte	YTADLLEVLK	582.8	601.4	829.5	900.5	260.2	-
		IS	YTADLLEVLK	586.8	609.4	837.5	908.6	268.2	
SLC51B	OST β	Analyte	DVLSVFLPDVPETES	823.9	873.4	562.2	986.5	336.1	-
		IS	DVLSVFLPDVPETES	826.9	879.4	562.2	992.5	336.1	
ABC Transporter									
ABCB1	MDR1	Analyte	IATEAIENFR	582.3	749.4	678.4	565.3	979.5	-
		IS	IATEAIENFR	587.3	759.4	688.4	575.3	989.5	
ABCB4	MDR3	Analyte	IATEAIENIR	565.3	644.4	945.5	715.4	531.3	-
		IS	IATEAIENIR	570.3	654.4	955.5	725.4	541.3	
ABCB11	BSEP	Analyte	STALQLIQR	515.3	841.5	529.3	770.5	657.4	Peptide 1
		IS	STALQLIQR	520.3	851.5	539.4	780.5	667.4	
		Analyte	STSIQLLER	523.8	530.3	858.5	658.4	417.2	Peptide 2
		IS	STSIQLLER	528.8	540.3	868.5	668.4	427.3	
ABCC2	MRP2	Analyte	LTIIQDPILFSGSLR	885.5	666.4	1329.7	989.6	519.3	-
		IS	LTIIQDPILFSGSLR	890.5	676.4	1339.7	999.6	529.3	
ABCC3	MRP3	Analyte	ADGALTQEEK	531.3	634.3	747.4	875.4	533.3	Peptide 1
		IS	ADGALTQEEK	535.3	642.3	755.4	883.5	541.3	
		Analyte	AEGEISDPFR	560.8	419.2	920.4	175.1	621.3	Peptide 2
		IS	AEGEISDPFR	565.8	429.2	930.5	185.1	631.3	
ABCC4	MRP4	Analyte	AEEAALTETAK	538.3	875.5	733.4	662.4	549.3	-
		IS	AEEAALTETAK	542.3	883.5	741.4	670.4	557.3	

<i>ABCG2</i>	BCRP	Analyte	SSLLDVLAAR	522.8	644.4	757.5	529.3	430.3	Peptide 1
		IS	SSLLDVLAAR	527.8	654.4	767.5	539.4	440.3	
		Analyte	ENLQFSAALR	574.8	664.4	517.3	792.4	359.2	Peptide 2
		IS	ENLQFSAALR	579.8	674.4	527.3	802.4	369.2	

^aUsed for hepatocyte lot 1 and 3

^bUsed for hepatocyte lot 2

Supplementary Table 2.

Gradient condition for OCT1

Time (min)	Percent B
0	5
1	5
25	60
25.5	90
30	90
32	5
42	5

Gradient condition for the other transporters

Time (min)	Percent B
0	5
1	5
25	35
25.5	90
30	90
32	5
42	5