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Supporting Information

Beyond nanoparticle-based oral drug delivery: transporter-mediated absorption and disease targeting

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Supplemental Table 1. A) Quantitative protein expression levels and B) relative mRNA expression levels of transporters/receptors in the human intestine[1, 2]

A) Quantitative protein expression levels of transporters (fmol/mg membrane protein)				
Transporter	**Duodenum**	**Jejunum**	**Ileum**	**Colon**
ABCB1	371	657	796	499
ABCC3	1115	577	711	2327
ASBT	35	196	1057	36
OATP2B1	436	511	411	667
OCT1	736	655	728	613
OCT3	78	58	64	91
PEPT1	2574	37220	4915	286

B) Relative mRNA expression levels of transporters			
Transporter	**Duodenum**	**Ileum**	**Colon**
ASBT	0.09	0.42	< 0.01
CNT1	0.06	0.06	< 0.01
CNT2	0.32	0.15	< 0.01
ENT2	< 0.01	< 0.01	0.09
OATP2B1	0.02	0.06	0.08
OCTN1	0.53	1.27	1.99
OCTN2	0.09	0.10	0.82
PEPT1	3.87	3.79	0.54
SERT	0.04	0.09	< 0.01

Supplemental Table 2. The solubility of substrate candidates for transporter/receptor-mediated oral drug delivery

Transporter	Slightly soluble (> 1 mg/mL)	Very slightly soluble or practically insoluble (< 1 mg/mL)
ASBT	Cholic acid sodium salt (150 mg/mL), deoxycholic acid sodium salt (330 mg/mL), glycolic acid sodium salt (200 mg/mL), taurocholic acid sodium salt (100 mg/mL)	Benzothiazepine (and derivatives)*, cholic acid (0.175 mg/mL), deoxycholic acid (0.044 mg/mL), naphthol derivates (0.74 mg/mL)
$ATB^{0,+}$	Carnitine (32 mg/mL), propionyl-L-carnitine (10 mg/mL in acidic pH)	Acetylcarnitine (0.355 mg/mL)
CNT2	Adenosine (7 mg/mL), cladribine (4.52 mg/mL), didanosine (27.3 mg/mL), floxuridine (49 mg/mL), formycin B (10 mg/mL), inosine (47 mg/mL), mizoribine (20 mg/mL), ribavirin (20 mg/mL), uridine (50 mg/mL), zidovudine (53 mg/mL)	Clofarabine*, fluoropyrimidine (0.467 mg/mL), guanosine*
ENT1	Adenosine (7 mg/mL), capecitabine (26 mg/mL), cladribine (4.52 mg/mL), cytosine (8 mg/mL), fialuridine (2 mg/mL), fludarabine (9.2 mg/mL), gemcitabine (19 mg/mL), ribavirin (20 mg/mL), uridine (50 mg/mL), thymidine (50 mg/mL), thymine (3.82 mg/mL)	Guanine*, guanosine*
GLUT2	Glucose (133 mg/mL)	-
GLUT5	Fructose (36 mg/mL)	-
MCT1	β-D-Hydroxybutyric acid (25 mg/mL in PBS), γ-hydroxybutyric acid (494 mg/mL), L-lactic acid (100 mg/mL), pyruvic acid (1g/mL), salicylates (2.24 mg/mL), valproic acid (1.3 mg/mL)	Nateglinide (0.0088 mg/mL)
OATP2B1	Aliskiren (100 mg/mL), fexofenadine (2 mg/mL)	Amiodarone (0.72 mg/mL), atorvastatin (0.0204 mg/mL), bosentan (0.01 mg/mL), DHEAS (0.0081 mg/mL), estrone-3-sulphate*, glibenclamide*, talinolol (0.0451 mg/mL), telmisartan*, L-thyroxine (0.105 mg/mL)
OCTN1	Acetylcholine (100 mg/mL), carnitine (32 mg/mL), doxorubicin hydrochloride (10 mg/mL), entecavir (2.4 mg/mL), ergothioneine (50 mg/mL), gabapentin (10 mg/mL), imatinib (200 mg/mL), ipratropium (83 mg/mL), metformin (33 mg/mL), oxaliplatin (6 mg/mL), pregabalin (36 mg/mL), pyrilamine (80 mg/mL), verapamil (25 mg/mL)	Mitoxantrone (0.734 mg/mL), quinidine (0.14 mg/mL), tiotropium (0.0176 mg/mL)
OCTN2	Carnitine (32 mg/mL), cephaloridine (257.7 mg/mL), emetine (100 mg/mL), entecavir (2.4 mg/mL), imatinib (200 mg/mL), ipratropium (83 mg/mL), verapamil (25 mg/mL)	Etoposide*, spironolactone*, tiotropium (0.0176 mg/mL)
OSTα/β	Cholic acid sodium salt (150 mg/mL), deoxycholic acid sodium salt (330 mg/mL), glycolic acid sodium salt (200 mg/mL), PGE2 (1.05 mg/mL), taurocholic acid sodium salt (100 mg/mL)	Cholic acid (0.175 mg/mL), deoxycholic acid (0.044 mg/mL), DHEAS (0.0081 mg/mL), digoxin*
PAT1	Betaine (50 mg/mL), L-tryptophan (11.4 mg/mL)	-
PCFT	-	Folic acid (0.01 mg/mL), 5-Methyltetrahydrofolate*
PEPT1	5-Aminolevulinic acid (50 mg/mL), carnosine (125 mg/mL), cephalexin (10 mg/mL), penicillin G (benzylpenicillin) (100 mg/mL), D-Phe-Ala (14.11 mg/mL), valacyclovir (174 mg/mL)	Cefadroxil (0.399 mg/mL), glibenclamide*, nateglinide (0.0088 mg/mL)
SGLT1	Glucose (133 mg/mL), galactose (100 mg/mL)	-
SMVT1	Pantothenic acid (50 mg/mL)	Biotin (0.22 mg/mL), lipoic acid*
SVCT1	L-Ascorbic acid (10 mg/mL) (mg/mL)	-

* : water insoluble

Supplemental Table 3. The change in the expression level of GI transporters/receptors in the status of disease[3-25].

Transporter	Disease	Species/cell line	mRNA	Protein
ASBT	Diabetes	Rat	Ileum ↑	-
	IBD (UC)	Human	Colon (2.8-fold ↓)	-
	IBD (CD)	Human	-	31 % ↓
	Obesity	Rat	Ileum ↑	Ileum (3.0-fold ↓)
	Obstructive cholestasis	Human	Duodenum (4.0-fold ↓)	-
FcRn	Infection	IPEC-J2		↑
FRα	Colorectal cancer	Human		Colorectal Cancer ↑
FRβ	IBD	Human		Macrophage cc
GLUT2	Diabetes	Human	Duodenum (3-fold ↑)	-
GLUT5	Diabetes	Human (T2DM)	Duodenum (3-fold ↑)	2.5-fold ↑
	IBD (CD)	Mouse	Small intestine ↓	
Mannose receptor	IBD	Human		Macrophage ↑ Dendritic cell ↑
MCT1	Alzheimer disease	APP/PS1 Mouse	-	Small intestine (1.9-fold ↓)
	IBD (CD)	Human	Colon (2.0-fold ↓)	Colon (3.9-fold ↓)
	IBD (UC)	Human	Colon (3.0-fold ↓)	-
OATP2B1	Cushing syndrome	Human (T2DM)	Duodenum (1.3-fold ↑)	-
	IBD (CD)	Human	Ileum (7-fold ↑)	-
	IBD (UC)	Human	Ileum (4-fold ↑) Colon (13-fold ↑)	-
OCTN2	IBD (CD)	Human	Ileum (50.0-fold ↓)	-
	IBD (UC)	Human		Colon ↓
OSTα	IBD (UC)	Human	Colon (5.0-fold ↓)	-
	Cholestasis	BDL-C57BL/6	-	Ileum (1.7-fold ↓)
OSTβ	Cholestasis	BDL-C57BL/6	-	Ileum (5.0-fold ↓)
	IBD (UC)	Human	Colon (3.4-fold ↓)	-
PCFT	Diabetes	Rat	Jejunum (12.3-fold ↑)	-
PEPT1	Cushing syndrome	Caco-2	-	Membrane (1.8-fold ↑)
	Hyperthyroidism	Caco-2	4.0-fold ↓	3.5-fold ↓
	Hyperthyroidism	Rat	1.4-fold ↓	1.4-fold ↓
	IBD	Human	-	Colon ↑
	Obesity	Caco-2	-	Membrane (2.2-fold ↑) Intracellular (2.0-fold ↓)
SGLT1	Diabetes	Human	Duodenum (3-fold ↑)	-
SMVT	IBD (UC)	Mouse	-	Colon (4.0-fold ↓)
SVCT1	IBD (UC)	Human	2.94-fold ↓	-
SVCT2	IBD (CD)	Human	Ileum (7-fold ↑) Colon (8-fold ↑)	-
Transferrin receptor	IBD (CD)	Rat	-	Colon (1.4-fold ↑)

* IBD, inflammatory disease; CD, Crohn's disease; UC, Ulcerative colitis; T2DM, Type 2 diabetes mellitus; BDL, bile duct ligation

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