S1 Box | SLC: Solute Carrier Family Transporters and their role in drug uptake

Notes on Evidence

The evidence has been grouped into broad types according to the experiment that supports the claim of drug uptake via transporters.

- 'Direct assay' refers to the physical detection of the substrate (i.e. radiotracer) on the opposite side of the membrane
- 'Indirect assay' refers to the detection of the substrate on the opposite side of the membrane by some known consequence of its presence (e.g. cytotoxicity).
- 'Transporter Operation Assay' refers to an assay that correlates the presence of a transporter substrate with the observation of transporter operation, typically via a change in membrane potential.
- 'Transfected cells' are cells (perhaps *Xenopus* oocytes) in which the transporter has been introduced. Untransfected cells provide the background level of transport
- 'Differentially expressing cell lines' are cell lines in which the transporter has been shown to be expressed at different levels. Typically evidence supporting the role of the transporter in substrate transport is supported by evidence from competition assays.
- 'Differentially expressing tissues' are tissues in which the transporter has been shown to be expressed at different levels. Typically evidence supporting the role of the transporter in substrate transport is supported by evidence from competition assays.
- 'Transporter Operation Assay' refers to an assay of transporter operation (such as a patch clamp experiment) that is associated with the substrate. An example would be the change in membrane potential associated with exchanging ions to drive uptake against a gradient.

Competition assays are only considered where the presence of the query substrate can be demonstrated on the opposite side of the membrane and transport is reduced in the presence of a known substrate (denoted 'Direct Competition Assay'). Indirect competition assays, where known substrate transport is shown to reduce in the presence of the query substrate, are not considered as only native substrate transport inhibition is implied and there is no proof of the actual transport of query substrate.

DATC: Direct Assay in Transfected/Mutant Cells

A direct assay of transport in cells in which transporter expression has been induced. Also includes mutant forms of cells where the mutation knocks out transporter function.

DADC: Direct Assay in Differentially Expressing Cell Lines

IADC: Indirect Assay in Differentially Expressing Cell Lines

DADT: Direct Assay in Differentially Expressing Tissues

IATC: Indirect Assay in Transfected/Mutant Cells

DCA: Direct Competition Assay

Refers to a competition assay in which the presence of the query substrate is demonstrated on the opposite side of the membrane in a manner that is altered by competition with a known transporter substrate.

TOATC: Transporter Operation Assay linked to substrate in Transfected Cells

TOAVC: Transporter Operation Assay linked to substrate under varying known transporter-required conditions (such as sodium ion absence/presence)

Caveat: some evidence for transport derives from expression of close homologues.

SLC Family	HUGO Symbol + Synonyms	Description	Substrate	References	Code
1 (Ref 1)	*SLC1A1; EAAC1; EAAT3*	Neuronal/epithelial high affinity glutamate transporter	*cis*-1-aminocyclobutane-1,3-dicarboxylate	2	TOATC
			L-trans-2,4-pyrrolidine-2,4-dicarboxylate	2	TOATC
	SLC1A2; EAAT2	Glial high affinity glutamate transporter	*cis*-1-aminocyclobutane-1,3-dicarboxylate	2	TOATC
			L-trans-2,4-pyrrolidine-2,4-dicarboxylate	2	TOATC
	SLC1A3; GLAST; EAAT1	Glial high affinity glutamate transporter	*cis*-1-aminocyclobutane-1,3-dicarboxylate	2	TOATC
			L-trans-2,4-pyrrolidine-2,4-dicarboxylate	2	TOATC
	SLC1A4; SATT; ASCT1	Glutamate/neutral amino acid transporter	hydroxyproline	3	DATC
2 (Ref 4)	*SLC2A1; GLUT1*	Facilitated glucose transporter	dehydroascorbic acid	5	DADC
				6	DADC
			3-O-D-methylglucose	5	DADC
			2-deoxyglucose	5	DADC
	SLC2A2; GLUT2	Facilitated glucose transporter	3-O-D-methylglucose	7	DADT
	SLC2A3; GLUT3	Facilitated glucose transporter	3-O-D-methylglucose	5	DADC
			dehydroascorbic acid	5	DADC
			3-O-methyl-D-glucose	7	DADT
5 (Ref 8)	*SLC5A4; SGLT3; SAAT1*	Low affinity glucose co-transporter	β-D-glucosylisophosphoramide	9	DATC
	SLC5A7; CHT1	Choline transporter	NONI (a nicotinium quaternary ammonium analog, see reference)	10	DCA
	SLC5A8; AIT; SMCT1	Na^+/ monocarboxylate transporter	propionate	11	DATC
			nicotinate	11	DATC
			β-D-hydroxybutyrate	12	DATC
			acetoacetate	12	DATC
			α-ketoisocaproate	12	DATC
6 (Ref 13)	*SLC6A2; NET*	Neurotransmitter transporter (noradrenalin)	1-methyl-4-tetrahydropyridinium	14	DADC
			MDMA	15	DATC
	SLC6A3; DAT	Neurotransmitter transporter (dopamine)	MDMA	15	DATC
	SLC6A4; SERT	Neurotransmitter transporter (serotonin)	MDMA	15	DATC
	SLC6A14; ATB$^{0,+}$	Amino acid transporter	D-serine	16	DATC
			α-carboxyl esters of neutral amino acids	17	DCA
			valacyclovir	17	DCA
			valganciclovir	17	DCA
7 (Ref 18) NB: Note SLC7s	*SLC7A5; LAT1*	Cationic amino acid transporter, y+ system), member 5	methylmercury-L-cysteine complex	20	DATC
			L-dopa	21	DATC
				22	DATC

frequently form complexes with 4F2hc (SLC3A2) (Ref 19)			triiodothyronine	23	DATC
			thyroxine	23	DATC
			melphalan	24	DATC
			D-leucine	25	DATC
			D-phenylalanine	25	DATC
	SLC7A8; LAT2	Cationic amino acid transporter, y+ system	methylmercury-L-cysteine complex	20	DATC
			L-dopa	21	DADC
	SLC7A10; Asc1	Neutral amino acid transporter, y+ system	α-(methylamino) isobutyric acid	26	DATC
	SLC7A11; xCT	Cationic amino acid transporter, y+ system	L-alanosine	27	IADC
	SLC7?; Undetermined	An undetermined LAT transporter	gabapentin	28	DATC
			pregabalin	28	DATC
10 (Ref 29)	*SLC10A1; NTCP*	Sodium/bile acid cotransporter	cis-diammine-chloro-cholylglycinate-platinum(II)	30	DATC
			cis-diammine-bisursodeoxycholate-platinum(II)	30	DATC
			taurocholate	31	DATC
			chlorambucil-taurocholate	32	DATC
			rosuvastatin	33	DATC
			estrone-3-sulfate	34	DATC
			taurochenodeoxycholate	34	DATC
			glycocholate	34	DATC
			tauroursodeoxycholate	34	DATC
	SLC10A2; ASBT	Sodium/bile acid cotransporter	acyclovir valylchenodeoxycholate	35	DATC
	SLC10A6; SOAT	Sodium/bile acid cotransporter	estrone-3-sulfate	36	DATC
			dehydroepiandrosterone sulfate	36	DATC
			pregnelone sulfate	36	DATC
15 (Ref 37)	*SLC15A1; PEPT1*	Oligopeptide transporter	L-dopa-L-Phe	38	DATC
			cefalexin	39	DATC
			delta-aminolevulinic acid	40	DATC
				41	DATC
			N-acetyl-Asp-Glu	41	DATC
			bestatin	41	DATC
				42	DATC
			glycylsarcosine	43	DATC
			amoxicillin	41	DATC
				44	DADC
			ampicillin	41	DATC
			cefaclor	44	DADC
			cefadroxil	45	DATC
				41	DATC
			cefixime	45	DATC
			ceftibuten	46	DCA
			temocapril	47	DATC
			temocaprilate	47	DATC

			enalapril	47	DATC
			midodrine	48	DATC
			valacyclovir	43	DATC
			valganciclovir	49	DATC
	SLC15A2; PEPT2	H+/peptide transporter	amoxicillin	44	DADC
			cefaclor	44	DADC
			cefadroxil	50	DADT
			bestatin	42	DATC
			delta-aminolevulinic acid	40	DATC
			beta-Ala-Lys-Nepsilon-AMCA	51	DATC
			glycylsarcosine	52	DATC
			valganciclovir	49	DATC
16 (Ref 53)	*SLC16A1; MCT1*	Monocarboxylic acid transporter	carindacillin	54	DCA
			phenethicillin	55	DCA
			pravastatin	56	DCA
			DL-2-hydroxy-(4-methylthio)butanoic acid	57	TOAVC
			benzoic acid	58	DADC
	SLC16A3; MCT4	Monocarboxylic acid transporter	nicotinate	59	DCA
	Unspecified MCT	Monocarboxylic acid transporter	salicylic acid	60	DCA
	SLC16A10; TAT1	Aromatic amino acid transporter	L-DOPA	61	DATC
			D-phenylalanine	61	DATC
19 (Ref 62)	*SLC19A1; RFT*	Folate transporter	methotrexate	63	DADC
22 (Ref 64)	*SLC22A1; OCT1*	Organic cation transporter	1-methyl-4-phenylpyridinium	65	DATC
			tetraethylammonium	65	DATC
			choline	65	DATC
			tributylmethylammonium	66	DATC
			N-methylquinidine	66	DATC
			N-methylquinine	66	DATC
			azidoprocainamide methoiodide	66	DATC
			acyclovir	67	DATC
			ganciclovir	67	DATC
			metformin	68	DATC
			prostaglandin $F_{2\alpha}$	69	DATC
			prostaglandin E_2	69	DATC
			agmatine	70	DATC
			cimetidine	68	DATC
	SLC22A2; OCT2	Organic cation transporter	1-methyl-4-phenylpyridinium	65	DATC
			tetraethylammonium	65	DATC
			dopamine	65	DATC
			histamine	65	DATC
			adrenaline	71	DATC
			noradrenaline	71	DATC
			5-hydroxytryptamine	71	DATC

			(serotonin)		
			N-methylnicotinamide	72	DATC
			amantadine	73	TOATC
			memantine	73	DATC
			norepinephrine	73	DATC
			metformin	74	DATC
			propanolol	75	DATC
			cimetidine	65	DATC
			guanidine	76	DATC
			zidovudine	76	DATC
			agmatine	70	DATC
			choline	72	TOATC
			D-tubocurarine	72	TOATC
			pancuronium	72	TOATC
			cyanine863	72	TOATC
			prostaglandin $F_{2\alpha}$	69	DATC
			prostaglandin E_2	69	DATC
			quinine	72	TOATC
	SLC22A3; OCT3; EMT	Extraneuronal monoamine transporter	1-methyl-4-phenylpyridinium	65	DATC
			cimetidine	65	DATC
			agmatine	70	DATC
			tetraethylammonium	77	DATC
			tyramine	78	DATC
	SLC22A4; OCTN1	Organic cation transporter	tetraethylammonium	79	DATC
			quinidine	80	DATC
			pyrilamine	80	DATC
			verapamil	80	DATC
			carnitine	80	DATC
	SLC22A5; OCTN2	Organic cation transporter	tetraethylammonium	81	DATC
			quinidine	81	DATC
			pyrilamine	81	DATC
			verapamil	81	DATC
			L-carnitine	81	DATC
			D-carnitine	81	DATC
			valproate	81	DATC
			acetyl-L-carnitine	81	DATC
			1-methyl-4-phenylpyridinium	81	DATC
			cephaloridine	82	DATC
	SLC22A6; OAT1	Organic anion transporter	ρ-aminohippurate	44	DADC
			adefovir	83	DATC
			cidofovir	83	DATC
			acyclovir	84	DATC
			9-(2-phosphonylmethoxyethyl)guanine	85	DATC
			9-(2-phosphonylmethoxyethyl)diaminopurine	85	DATC
			zalcitabine	84	DATC
			didanosine	84	DATC
			stavudine	84	DATC

			trifluridine	84	DATC
			ganciclovir	67	DATC
			lamivudine	84	DATC
			zidovudine	84	DATC
			methotrexate	86	DATC
			cAMP	86	DATC
			cGMP	86	DATC
			urate	86	DATC
			alpha-ketoglutarate	86	DATC
			[((S)-1-2-hydroxy-2-oxo-1,4,2-dioxaphosphorinan-5-yl)methyl]-cytosine (cyclic prodrug of cidofovir)	83	DATC
			6-carboxyfluorescein	83	DATC
			ketoprofen (low uptake)	87	DATC
			ibuprofen (low uptake)	87	DATC
			ochratoxin A	88	DADT
			zidovudine	67	DATC
			prostaglandin $F_{2\alpha}$	69	DATC
			prostaglandin E_2	86	DATC
			cimetidine	89	DATC
			N-acetyl-cysteinyl mercury	90	DATC
			tetracycline	91	DATC
			ellagic acid	92	DATC
			cephaloridine	93	IATC
	SLC22A7; OAT2	Organic anion transporter	zidovudine	67	DATC
			tetracycline	91	DATC
			salicylate	94	DATC
			methotrexate	95	DATC
			tetracycline	91	DATC
			zidovudine	67	DATC
			prostaglandin $F_{2\alpha}$	69	DATC
			prostaglandin E_2	69	DATC
			erythromycin	96	DATC
			theophyline	96	DATC
	SLC22A8; OAT3	Organic anion transporter	p-aminohippurate	97	DATC
			valacyclovir	67	DATC
			zidovudine	67	DATC
			methotrexate	97	DATC
			urate	97	DATC
			taurocholate	97	DATC
			salicylate	97	DATC
			ochratoxin A	97	DATC
			estrone sulphate	97	DATC
			estradiol-17β-glucuronide	97	DATC
			dehydroepiandrosterone-3-sulfate	97	DATC
			cimetidine	97	DATC
			tetracycline	91	DATC
			zidovudine	67	DATC

			prostaglandin $F_{2\alpha}$	69	DATC
			prostaglandin E_2	69	DATC
			cephaloridine	93	IATC
			indoxyl sulphate	98	DATC
			tetraethylammonium	98	DATC
	SLC22A11; OAT4	Organic anion/cation transporter	zidovudine	67	DATC
			tetracycline	91	DATC
			zidovudine	67	DATC
			prostaglandin $F_{2\alpha}$	69	DATC
			prostaglandin E_2	69	DATC
			ochratoxin A	99	DATC
			cephaloridine	93	IATC
			indoxyl sulphate	98	DATC
			ellagic acid	92	DATC
	SLC22A16; CT2	Organic cation transporter	carnitine	100	DATC
23 (ref 101)	*SLC23A1; SVCT1*	Nucleobase transporter	vitamin C	102	DATC
			6-bromo-6-deoxy-L-ascorbic acid	103	DATC
			vitamin C	102	DATC
			6-bromo-6-deoxy-L-ascorbic acid	103	DATC
28 (Ref 104)	*SLC28A1; CNT1*	Sodium-coupled nucleoside transporter	zidovudine	105	TOATC
			gemcitabine	106	DATC
			stavudine	105	TOATC
	SLC28A3; CNT2	Sodium-coupled nucleoside transporter	cladribine	107	DATC
			inosine	107	DATC
			2-chloroadenosine	107	DATC
			2'-deoxyadenosine	107	DATC
			adenosine-arabinoside	107	DATC
			fludarabine	107	DATC
			ribavirin	108	DATC
	SLC28A3; CNT3	Sodium-coupled nucleoside transporter	adenosine	109	DATC
			cladribine	109	DATC
			fludarabine	109	DATC
			inosine	109	DATC
			thymidine	109	DATC
29 (Ref 110)	*SLC29A1; ENT1*	Nucleoside transporter	gemcitabine	111	DADC
			uridine	111	DADC
			zalcitabine	112	DATC
			didanosine	112	DATC
	SLC29A2; ENT2	Nucleoside transporter	zalcitabine	112	DATC
			gemcitabine	106	DATC
			zidovudine	112	DATC
			didanosine	112	DATC
31 (Ref 113)	*SLC31A1; CTR1*	Copper transporter	cisplatin	114	DADC
			carboplatin	115	DATC
			oxaliplatin	115	DATC
34 (Ref 116)	*SLC34A1; NaPi-1*	Sodium phosphate transporter	uranyl phosphate	117	DATC
36 (Ref 118)	*SLC36A1; PAT1*	Proton/amino acid symporter	isonipecotic acid	119	IAVC
			D,L-β-aminobutyric acid	119	IAVC

			3-amino-1-propanesulphonic acid	119	IAVC
			α-(methylamino)isobutyric acid	120	DATC
			L-azetidine-2-carboxylic acid	121	DATC
			cis-4-hydroxy-L-proline	121	DATC
			cis-4-hydroxy-D-proline	121	DATC
			trans-4-hydroxy-L-proline	121	DATC
			D-proline	121	DATC
			vigabatrin	122	TOA
			trans-4-aminocrotonic acid	122	TOATC
			guvacine	122	TOATC
			nipecotic acid	119	TOAVC
			GABA	119	TOAVC
	SLC36A2; PAT2; TRAMD1	Proton/amino acid symporter	2-azetidine-carboxylate	123	TOATC
			D-cycloserine	123	TOATC
			L-cycloserine	123	TOATC
SLCO (Ref 124)	*SLCO1A2; OATP; OATP-A; OATP1A2*	Organic anion transporter	fexofenadine	125	TOATC
			ouabain (neutral)	126	DATC
			BQ-123	127	DATC
			D-penicillamine-2,5-enkephalin	127	DATC
			bromosulfophthalein	127	DATC
			taurocholate	32	DATC
			glycocholate	127	DATC
			estrone-3-sulfate (anionic)	126	DATC
			estradiol-17β-glucuronide	127	DATC
			dehydroepiandrosterone sulfate	127	DATC
			N-methyl quinine	127	DATC
			N-methyl quinidine	128	DATC
			prostaglandin E_2	127	DATC
			APD-ajmalinium (cationic)	126	DATC
			thyroxin (T4)	127	DATC
			triiodothyronine (T3)	127	DATC
			chlorambuciltaurocholate	32	DATC
			cholate	129	DATC
			cis-diammine-chloro-cholylglycinate-platinum(II)	30	DATC
			cis-diammine-bisursodeoxycholate-platinum(II)	30	DATC
			Gd-B20790	130	DATC
			Deltorphin II	127	DATC
			Microcystin-LR	131	DATC
			rocuronium	128	DATC

			taurochenodeoxycholate	129	DATC
			tauroursodeoxycholate	129	DATC
			enalapril	132	DATC
			temocaprilat	133	DATC
			unoprostone carboxylate metabolite M1	134	DATC
			rosuvastatin	33	DATC
	SLCO1B1; OATP-C; LST1; OATP1B1; OATP2	Organic anion transporter	benzylpenicillin	135	DATC
			pravastatin	136	DATC
			rifampicin	137	DATC
			bromosulfophthalein	127	DATC
			taurocholate	127	DATC
			glycocholate	127	DATC
			estrone-3-sulfate	127	DATC
			estradiol-17β-glucuronide	127	DATC
			dehydroepiandrosterone sulfate	127	DATC
			prostaglandin E_2	127	DATC
			triiodothyronine	127	DATC
			thyroxine	127	DATC
			D-penicillamine-2,5-enkephalin	127	DATC
			BQ-123	127	DATC
			atorvastatin	138	DATC
			capsofungin	139	DATC
			cerivastatin	138	DATC
			fexofenadine	125	DATC
			thromboxane B_2	140	DATC
			demethylphalloin	141	DATC
			methotrexate	142	IATC
			benzylpenicillin	135	DATC
			leukotriene C_4	127	DATC
			DADLE	143	DATC
			ACU-154	144	DATC
			PKI166	144	DATC
			bilirubin	145	DATC
			bisglucuronosyl bilirubin	145	DATC
			cholate	145	DATC
			Bamet-UD2	30	DATC
			Bamet-R2	30	DATC
			fluvastatin	146	DATC
			glycocholate	127	DATC
			leukotriene E_4	140	DATC
			Microcystin-LR	140	DATC
			Monoglucuronosyl bilirubin	145	DATC
			pitavastatin	147	DATC
	SLCO1B3; LST-2; OATP1B3; OATP8	Organic anion transporter	leukotriene C_4	127	DATC
			estradiol-17β-glucuronide	127	DATC
			bromosulfophthalein	127	DATC
			taurocholate	127	DATC

			glycocholate	127	DATC
			estrone-3-sulfate	127	DATC
			dehydroepiandrosterone -3-sulfate	127	DATC
			triiodothyronine	127	DATC
			thyroxine	127	DATC
			ouabain	127	DATC
			digoxin	127	DATC
			deltorphin II	127	DATC
			BQ-123	127	DATC
			DPDPE	127	DATC
			demethylphalloin	148	DATC
			methotrexate	142	IATC
			rifampicin	137	DATC
			cholecystokinin-8	149	DATC
			bilirubin	150	DATC
			fexofenadine	151	DATC
			fluvastatin	146	DATC
			microcystin-LR	140	DATC
			monoglucuronosyl bilirubin	145	DATC
			pitavastatin	147	DATC
			rosuvastatin	33	DATC
	SLCO1C1; OATP-F; OATP1C1; OATP1	Organic anion transporter	bromosulfophthalein	152	DATC
			estrone-3-sulfate	152	DATC
			estradiol-17β-glucuronide	152	DATC
			thyroxine	152	DATC
			triiodothyronine	152	DATC
			rT_3 (thyroid hormone)	152	DATC
	SLCO2A1; OATP2A1; PGT	Organic anion transporter; Prostaglandin transporter	prostaglandin E_1	153	DATC
			prostaglandin E_2	153	DATC
			prostaglandin D2	153	DATC
			prostaglandin $F_{2\alpha}$	153	DATC
			thromboxane B_2	153	DATC
	SLCO2B1; OATP2B1; OATP-B	Organic anion transporter	estrone sulphate	127	DATC
			pravastatin	154	DATC
			bromosulfophthalein	127	DATC
			prostaglandin E_2	135	DATC
			dehydroepiandrosterone -3-sulfate	127	DATC
			7-ethyl-10-hydroxycamptothecin	155	DATC
			glibenclamide	156	DATC
			unoprostone carboxylate metabolite M1	134	DATC
			atorvastatin	157	DATC
			benzylpenicillin	135	DATC
			fluvastatin	146	DATC
			rosuvastatin	33	DATC
	SLCO3A1; OATPD; OATP3A1	Organic anion transporter	prostaglandin E_2	158	DATC
			estrone-3-sulfate	135	DATC
			benzylpenicillin	135	DATC

			prostaglandin $F_{2\alpha}$	158	DATC
			prostaglandin E_1	158	DATC
	SLCO4A1; OATP-E; OATP4A1	Organic anion transporter	prostaglandin E_2	135	DATC
			estrone-3-sulfate	135	DATC
			estradiol-17β-glucuronide	135	DATC
			benzylpenicillin	135	DATC
			triiodothyronine	159	DATC
			thyroxine	159	DATC
			rT3	159	DATC
			taurocholate	159	DATC
			unoprostone carboxylate metabolite M1	134	DATC
	SLCO4C1; OATP4C1	Organic anion transporter	triiodothyronine	160	DATC
			thyroxine	160	DATC
			methotrexate	160	DATC
			ouabain	160	DATC
			digoxin	160	DATC

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