Gentest® TransportoCells™

Cryopreserved Transporter Cells

GENTEST®
ADMET and Preclinical Solutions

Gentest® TransportoCells™ products are high-performance mammalian cells in a convenient, cryopreserved format that transiently overexpress a single human SLC transporter protein. The frozen cells deliver robust data, while eliminating the time required to culture and maintain stable cell lines.

Culturing and maintaining stable transporter cell lines can be expensive and time-consuming. In addition, it can take a week or more to prepare cells for assaying. Gentest TransportoCells products can be thawed, plated, and assayed in just two days with high uptake ratios.

Features

- Cryopreserved format provides flexibility for experimental planning
- Cells are readily available, can be stored onsite, and shipped globally
- Cells can be thawed, plated, and assayed in just two days
- Robust results with uptake ratios ≥10 fold
- Consistent with other mammalian cell-based models
- One vial contains 10 million cells and supports one 24-well plate, one 48-well plate, or one 96-well microplate
- Includes current USFDA, European Medicines Agency (EMA), and International Transporter Consortium (ITC) recommended SLC drug transporters

Convenient and Cost-efficient

Gentest TransportoCells products are a convenient, cost-efficient alternative to maintaining stable cell lines. They provide the utmost flexibility for experimental planning. The cells can be removed from storage one day and assayed the following day.

Robust and Validated

Gentest TransportoCells products deliver high performance and robust data with uptake ratios ≥10 fold. The model has been fully validated for substrate specificity, transporter kinetics and inhibition profiles to ensure data are consistent with existing transporter cell models.

Supports Regulatory Recommendations

Gentest TransportoCells products support USFDA, EMA, and ITC recommendations for identification of drug transporters and transporter drug-drug interaction studies critical in the development of new investigational drugs.

Contract Research Services Available

SLC Transporter Interaction Studies using Gentest TransportoCells products are available from Gentest℠ Contract Research Services. All assays are designed and built to meet regulatory agency recommendations.

Table 1. **Performance summary of Gentest® TransportoCells™ cryopreserved SLC transporter cells.** The post-thaw viability exceeds 80%. Uptake activity of HEK-293 cells transiently over-expressing a single SLC transporter protein as listed below, are evaluated by incubating the cells with listed prototypical substrates at indicated concentration. Uptake ratio is calculated by dividing uptake activity measured in the SLC transporter cells by that in control cells.

Transporters	Post-Thaw Viability	Probe Substrate	Incubation Time (min)	Uptake Activity in Transporter Cells (pmol/mg/min)	Uptake Activity in Control Cells (pmol/mg/min)	Uptake Ratio
OATP1B1*1a	90%	2 µM E17βG	5	72.2†	0.57†	127†
OATP1B1*1a	90%	5 µM F-MTX	10	676†	36†	18.8†
OATP1B1*5	90.90%	5 µM F-MTX	10	305†	36†	8.5†
OATP1B1*15	91.90%	5 µM F-MTX	10	228†	36†	6.3†
OATP1B3	91%	2 µM CCK-8	5	35.3†	0.17†	212†
OAT1	93%	3 µM PAH	10	141.0	0.38	372
OAT2	93.90%	2 µM C-GMP	2	293	4.69	62.4
OAT3	88%	2 µM E3S	5	121.1	0.91	133
OAT4	92.80%	2 µM E3S	5	42.5	1.49	28.5
OCT1	88%	30 µM TEA	10	253.0	4.8	53
OCT2	89%	30 µM TEA	10	171.5	4.8	36
MATE1	95%	30 µM TEA	2	1,166†	24.8†	47†
MATE2-K	92%	30 µM TEA	2	664†	15.1†	44†
PEPT1	94%	50 µM GlySar	5	617†	9.1†	68†
PEPT2	90%	50 µM GlySar	5	1,568†	13.4†	117†
OATP2B1	90%	2 µM E3S	5	36.9	1.54	24
OATP1A2	92%	2 µM E3S	5	54.6†	2.81†	19†
NTCP	94%	2 µM TCA	5	111†	1.1†	104†
OCTN2	91.60%	2 µM L-Carnitine	10	166	4.8	34.6
Rat Oatp1b2	91%	2 µM E17βG	5	66.7	1.26	53
Dog Oatp1b4	93%	2 µM E17βG	5	15.3	0.76	20
Monkey Oatp1b1	93.70%	2 µM E17βG	5	25.1	1	24.6

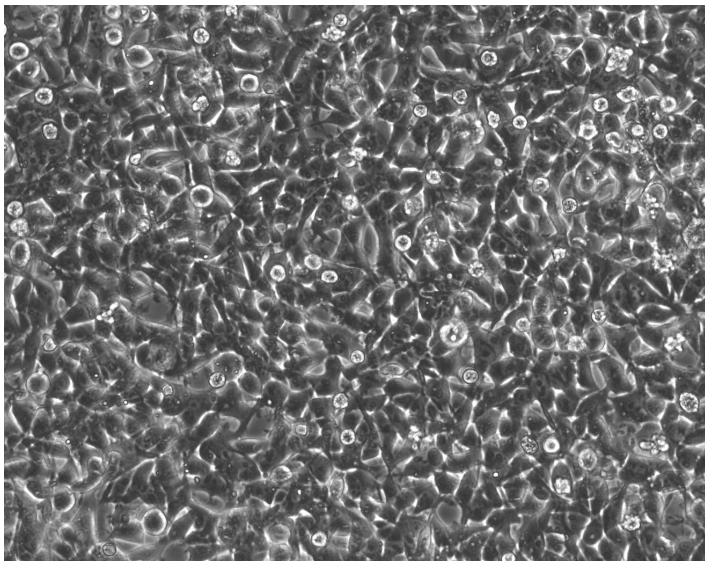
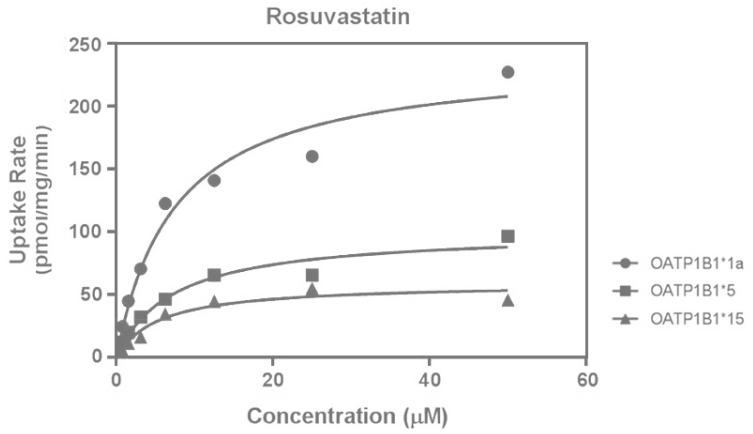


Figure 1. Cell morphology after 24 hours plating on poly-D-lysine plate. After 24 hours post-plating on the Poly-D-Lysine plate, the HEK-293 cells transiently over-expressing transporters formed a confluent monolayer. The image represents OATP1B1*1a cells.

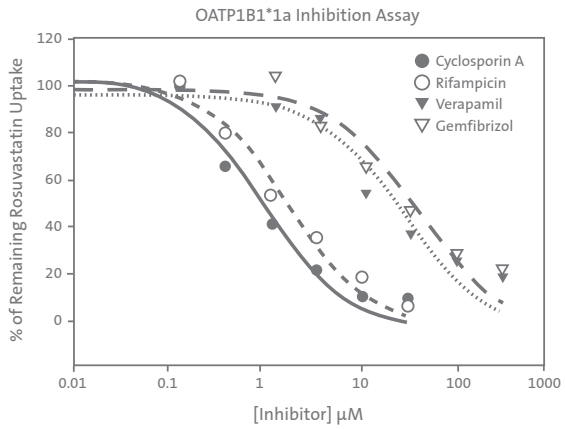


Gentest® SLC Transporter Cells

Transporter	Substrate	K_m (μM)	K_m (μM)	Literature Reference
OATP1B1*1a	Rosuvastatin	7.5	13.1	E. van de Steeg, et al. DMD (2013)
OATP1B3	CCK-8	20.2	16.5[a]	Poirier A, et al. J Pharmacokinet Pharmacodyn (2009)
OAT1	PAH	87.5	28	Ueo H, et al. Biochem Pharmacol (2005)
OAT2	cGMP	138	88	Cropp C, et al. Mol Pharmacol (2008)
OAT3	E3S	4.0	6.3	Ueo H, et al. Biochem Pharmacol (2005)
OAT4	E3S	8.9	20.9	Yamashita F, et al. J Pharmacy and Pharmacology (2006)
OCT1	TEA	713	566[b]	Iwai M, et al. Drug Metab Dispos (2009)
OCT2	TEA	401	431[c]	Gorboulev V, et al. DNA Cell Biol (1997)
MATE1	Metformin	282	227	Chen Y, et al. Pharmacogenomics J (2009)
MATE2-K	Metformin	824	1,050	Masuda S, et al. J Am Soc Nephrol (2006)
PEPT1	GlySar	970	1,100[d]	Knutter I, et al. Drug Metab Dispos (2009)
PEPT2	GlySar	78	140[e]	Knutter I, et al. Drug Metab Dispos (2009)
OATP2B1	E3S	9.3	10.2	Noé J, et al. Drug Metab Dispos (2007)
NTCP	TCA	14	7.5[f]	Ho R, et al. J Biol Chem (2004)
OCTN2	L-Carnitine	16.9	4.3	Tamai I, et al. J Biol Chem (1998)

[a]Tested in CHO-stable cell line; [b]Tested in S2-stable cell line; [c]Tested in Oocytes; [d]Tested in Caco-2 cells; [e]Tested in SKPT

Figure 2. SLC transporter cells kinetic assay. Concentration-dependent uptake of prototypical substrates in the listed SLC transporter cells are determined. The solid line represents the nonlinear fit of the uptake into the transporter cells minus the uptake in the control cells. K_m values of the listed prototypical substrates are comparable to those published in the literature. Testing system is HEK-293 stable cell line, except where noted.



Gentest SLC Transporter Cells

Transporter	Substrate	Inhibitor	IC_{50} (μM)	IC_{50} (μM)	Test System	Literature Reference
OATP1B1*1a	Rosuvastatin	Cyclosporin A	0.9	0.31	Hela	Ho RH, et al. Gastroenterology (2006)
OATP1B3	Rosuvastatin	Cyclosporin A	0.3	0.06	Hela	Ho RH, et al. Gastroenterology (2006)
OAT1	PAH	Probenecid	7.2	6.5	CHO	Ho ES, et al. J Am Soc Nephrol (2001)
OAT3	E3S	Probenecid	8.8	9	S2	Takeda M, et al. Eur J Pharmacol (2001)
OCT1	TEA	Decynium-22	2.2	2.7	Hela	Zhang L, et al. JPET (1998)
OCT2	TEA	Decynium-22	7	13.8	Oocytes	Okuda M, et al. Biochim Biophys Acta (1999)
MATE1	Metformin	Verapamil	15	27.5	HEK	Tsuda M, et al. JPET (2009)

Figure 3. SLC transporter cells inhibition assay. IC_{50} values for the indicated transporter modulators are determined by incubating the cells with the prototypical substrate at a fixed concentration with the selected modulator at a range of concentration. The IC_{50} values generated using TransportoCells products are comparable to that published in the literature.

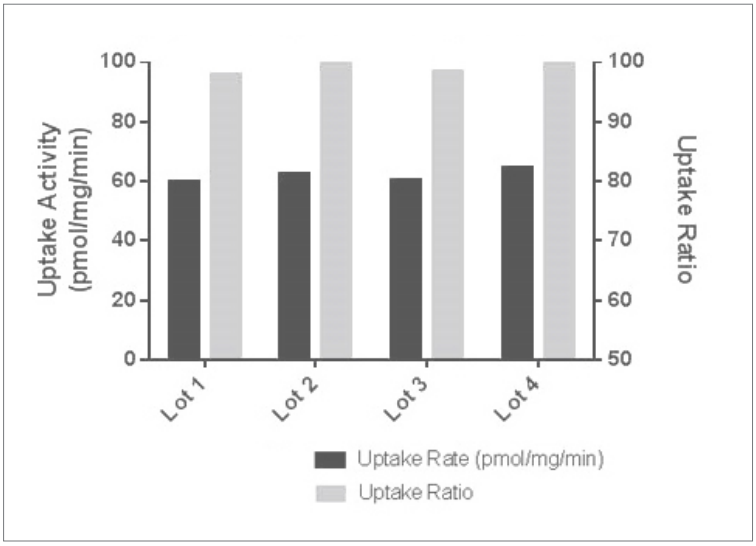


Figure 4. Gentest® TransportoCells™ lot-to-lot consistency. Four lots of OATP1B1*1a cells were plated at the same time at 200K per well in a 48-well PDL-coated plate. Cells were refed with fresh media supplemented with 2 mM sodium butyrate at 3 to 4 hours post-plating and assayed at 24 hours post-plating by incubating with 2 µM estradiol-17β-glucuronide for 5 minutes. Average uptake activity of the four lots is 62 pmol/mg/min with CV of 3.5%.

Ordering Information

Gentest TransportoCells Cryopreserved SLC Transporter Cells

Cat. No. Cells	Description	Full Name	Gene Accession Number	Number of
354851	OATP1B3/SLCO1B3	Organic anion-transporting polypeptide 1B3	NM_019844	≥10 million
354852	OCT1/SLC22A1	Organic cation transporter 1	NM_003057	≥10 million
354853	OCT2/SLC22A2	Organic cation transporter 2	NM_003058	≥10 million
354854	Vector Control	N/A	N/A	≥10 million
354855	MATE1/SLC47A1	Multidrug and Toxin Extrusion transporter 1	NM_018242	≥10 million
354856	MATE2-K/SLC47A2	Multidrug and Toxin Extrusion transporter 2-K	NM_001099646	≥10 million
354857	OAT1/SLC22A6	Organic anion transporter 1	NM_004790	≥10 million
354858	OAT3/SLC22A8	Organic anion transporter 3	NM_004254	≥10 million
354859	OATP1B1*1a/SLCO1B1*1a	Organic anion-transporting polypeptide 1B1, Wild Type (388A)	NM_006446.4	≥10 million
354860	PEPT1/SLC15A1	Peptide transporter 1	NM_005073	≥10 million
354861	PEPT2/SLC15A2	Peptide transporter 2	NM_021082	≥10 million
354862	OATP2B1/SLCO2B1	Organic anion-transporting polypeptide 2B1	NM_007256	≥10 million
354863	OATP1A2/SLCO1A2	Organic anion-transporting polypeptide 1A2	NM_021094	≥10 million
354864	NTCP/SLC10A1	Na^+-taurocholate cotransporting polypeptide	NM_003049	≥10 million
354866	OCTN2	Organic cation/carnitine transporter 2	NM_003060	≥10 million
354867	OAT2	Organic anion transporter 2	NM_006672	≥10 million
354868	OAT4	Organic anion transporter 4	NM_018484	≥10 million
354841	Rat Oatp1b2	Rat organic anion-transporting polypeptide 1b2	NM_031650	≥10 million
354842	Dog Oatp1b4	Dog organic anion-transporting polypeptide 1b4	GQ497899	≥10 million
354843	Monkey Oatp1b1	Monkey organic anion-transporting polypeptide 1b1	JX866725	≥10 million
354878	OATP1B1*5	Organic anion-transporting polypeptide 1B1 SNP (521T>C)	NM_006446.4 with 521T>C	≥10 million
354879	OATP1B1*15	Organic anion-transporting polypeptide 1B1 SNPs (388A>G, 521T>C)	NM_006446.4 with 388A>G, 521T>C	≥10 million

Related Products and Contract Research Services

- ABC human and animal transporter membranes and vesicles
- ATPase assay kit
- BCRP/MRP and BSEP vesicle assay kits
- MDR1 LLC-PK1 (P-gp) cell line
- Transporter-qualified hepatocytes
- Gentest® media, buffers, and supplements (DMEM, FBS, non-essential amino acids, HBSS)
- Transwell® permeable supports
- Corning, Falcon®, and BioCoat™ microplates
- Caco-2 5-day assay system
- Gentest℠ Contract Research Services – assays designed and built to meet regulatory agency recommendations
  - ABC transporter interaction studies in cell lines and vesicles
  - SLC transporter interaction studies in Gentest TransportoCells cryopreserved transporter cells
  - Transporter models include: Caco-2, transfected cell lines, vesicles, membranes, hepatocytes
  - Other *in vitro* drug-drug Interaction studies, including enzyme induction and enzyme inhibition

Use of Genetically Modified Microorganisms (GMM)
Information for European Customers: These products are genetically modified as described in Discovery Life Sciences technical literature. As a condition of sale, use of this product must be in accordance with all applicable local guidelines on the contained use of genetically modified microorganisms, including the Directive 2009/41/EC of the European Parliament and of the Council.

For additional product or technical information, visit **www.dls.com** or call 866.838.2798. Outside the United States, call +359.2.870.2117 or contact your local Gentest sales representative.

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