

Nucleoside

Overview: Nucleoside transporters are divided into two families, the sodium-dependent, solute carrier family 28 (SLC28) and the equilibrative, solute carrier family 29 (SLC29), where the endogenous substrates are nucleosides. The SLC28 family members have 13 transmembrane segments with cytoplasmic N-termini and extracellular C-termini.

Nomenclature	CNT1	CNT2	CNT3
Systematic Nomenclature	SLC28A1	SLC28A2	SLC28A3
Other names	N2/ <i>cit</i>	N1/ <i>cif</i> , SPNT	N3/ <i>cib</i>
Ensembl ID	ENSG00000156222	ENSG00000137860	ENSG00000099118
Endogenous substrates	Uridine, cytidine, thymidine, adenosine	Adenosine, guanosine, inosine, thymidine	Uridine, cytidine, thymidine, adenosine, guanosine, inosine
Synthetic substrates	AZT, zalcitabine, gemcitabine	Formycin B, cladribine, fludarabine, vidarabine, didanosine	AZT, zalcitabine, didanosine, formycin B, 5-fluorouridine, 5-fluoro-2'-deoxyuridine, zebularine, gemcitabine, cladribine, fludarabine
Predicted stoichiometry	1:1 Na ⁺	1:1 Na ⁺	1:2 Na ⁺

A further two Na⁺-dependent (1:1 Na⁺ stoichiometry) nucleoside transporters have been defined on the basis of substrate and inhibitor selectivity: CNT4 (N4/*cit*, which transports uridine, thymidine and guanosine) and CNT5 (N5/*csg*, which transports guanosine and adenosine, and may be inhibited by NBTI).

SLC29 family members appear to be composed of 11 transmembrane segments with cytoplasmic N-termini and extracellular C-termini.

Nomenclature	ENT1	ENT2
Systematic nomenclature	SLC29A1	SLC29A2
Other names	<i>es</i> , NBTI-sensitive	<i>ei</i> , NBTI-insensitive
Ensembl ID	ENSG00000112759	ENSG00000174669
Endogenous substrates	Adenosine, guanosine, inosine, uridine, thymidine, cytidine	Adenosine, guanosine, inosine, uridine, thymidine, hypoxanthine
Synthetic substrates	2-Chloroadenosine, dideoxyinosine, formycin B, tubercidin, vidarabine, cytarabine, AZT, cladribine, pentostatin, zalcitabine, didanosine, floxidine, gemcitabine	2-Chloroadenosine, formycin B, tubercidin, cytarabine, cladribine, vidarabine, gemcitabine
Selective inhibitors	NBTI (9.7), draflazine (9.5), KF24345 (9.4, Hammond & Archer, 2004), NBTGR (9.3), dilazep (9), dipyrindamole (8.5)	–
Probes	[³ H]-NBTI (0.5 nM)	–
Predicted stoichiometry	Equilibrative	Equilibrative

Additional members of the family have been identified [including ENT3 (SLC29A3, ENSG00000156604) and ENT4 (SLC29A4, ENSG00000164638)]. ENT3 has been reported to be intracellular purine nucleoside transporters (Baldwin *et al.*, 2005), and ENT4 is an organic cation carrier that transports adenosine at acidic pH (Barnes *et al.*, 2006; Zhou *et al.*, 2007).

The affinities of draflazine, dilazep, KF24345 and dipyrindamole at ENT1 transporters are species-dependent, exhibiting lower affinity at rat transporters than at human transporters (Sundaram *et al.*, 1998; Hammond & Archer, 2004).

Abbreviations: AZT, 3'-azido-3'-deoxythymidine; NBTI, nitrobenzylthioinosine (also known as NBMPR); NBTGR, nitrobenzylthioguanosine; KF24345, 3-(1-[6,7-diethoxy-2-morpholinoquinazolin-4-yl]piperidin-4-yl)-1,6-dimethyl-2,4(1*H*,3*H*)-quinazolinedione hydrochloride

Further Reading

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King AE, Ackley MA, Cass CE, Young JD, Baldwin SA (2006). Nucleoside transporters: from scavengers to novel therapeutic targets. *Trends Pharmacol Sci* **27**: 416–425.

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