

SLC28 and SLC29 families of nucleoside transporters (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

James R. Hammond¹

1. University of Alberta, Canada

Abstract

Nucleoside transporters are divided into two families, the sodium-dependent, concentrative solute carrier family 28 (SLC28) and the equilibrative, solute carrier family 29 (SLC29). The endogenous substrates are typically nucleosides, although some family members can also transport nucleobases and organic cations.

Contents

This is a citation summary for SLC28 and SLC29 families of nucleoside transporters in the [Guide to Pharmacology](#) database (GtoPdb). It exists purely as an adjunct to the database to facilitate the recognition of citations to and from the database by citation analyzers. Readers will almost certainly want to visit the relevant sections of the database which are given here under database links.

[GtoPdb](#) is an expert-driven guide to pharmacological targets and the substances that act on them. GtoPdb is a reference work which is most usefully represented as an on-line database. As in any publication this work should be appropriately cited, and the papers it cites should also be recognized. This document provides a citation for the relevant parts of the database, and also provides a reference list for the research cited by those parts.

Please note that the database version for the citations given in GtoPdb are to the most recent preceding version in which the family or its subfamilies and targets were substantially changed. The links below are to the current version. If you need to consult the cited version, rather than the most recent version, please contact the GtoPdb curators.

Database links

[SLC28 and SLC29 families of nucleoside transporters](#)

<http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=149>

[SLC28 family](#)

<http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=215>

Transporters

[CNT1\(Sodium/nucleoside cotransporter 1\)](#)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1114>

[CNT2\(Sodium/nucleoside cotransporter 2\)](#)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1115>

[CNT3\(Solute carrier family 28 member 3\)](#)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1116>

SLC29 family

<http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=216>

Transporters

ENT1(Equilibrative nucleoside transporter 1)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1117>

ENT2(Equilibrative nucleoside transporter 2)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1118>

ENT3(Equilibrative nucleoside transporter 3)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1119>

PMAT(Plasma membrane monoamine transporter)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1120>

References

1. Armstrong D, Summers C, Ewart L, Nylander S, Sidaway JE and van Giezen JJ. (2014) Characterization of the adenosine pharmacology of ticagrelor reveals therapeutically relevant inhibition of equilibrative nucleoside transporter 1. *J. Cardiovasc. Pharmacol. Ther.* **19**: 209-19 [PMID:24414167]
2. Baldwin SA, Yao SY, Hyde RJ, Ng AM, Foppolo S, Barnes K, Ritzel MW, Cass CE and Young JD. (2005) Functional characterization of novel human and mouse equilibrative nucleoside transporters (hENT3 and mENT3) located in intracellular membranes. *J. Biol. Chem.* **280**: 15880-7 [PMID:15701636]
3. Barnes K, Dobrzynski H, Foppolo S, Beal PR, Ismat F, Scullion ER, Sun L, Tellez J, Ritzel MW and Claycomb WC *et al.*. (2006) Distribution and functional characterization of equilibrative nucleoside transporter-4, a novel cardiac adenosine transporter activated at acidic pH. *Circ. Res.* **99**: 510-9 [PMID:16873718]
4. Choi MK. (2012) Variability of gemcitabine accumulation and its relationship to expression of nucleoside transporters in peripheral blood mononuclear cells. *Arch. Pharm. Res.* **35**: 921-7 [PMID:22644860]
5. Choi MK, Kim MH, Maeng HJ and Song IS. (2015) Contribution of CNT1 and ENT1 to ribavirin uptake in human hepatocytes. *Arch. Pharm. Res.* **38**: 904-13 [PMID:25011570]
6. Daniels G, Ballif BA, Helias V, Saison C, Grimsley S, Mannessier L, Hustinx H, Lee E, Cartron JP and Peyrard T *et al.*. (2015) Lack of the nucleoside transporter ENT1 results in the Augustine-null blood type and ectopic mineralization. *Blood* **125**: 3651-4 [PMID:25896650]
7. Engel K and Wang J. (2005) Interaction of organic cations with a newly identified plasma membrane monoamine transporter. *Mol. Pharmacol.* **68**: 1397-407 [PMID:16099839]
8. Gupte A and Buolamwini JK. (2009) Synthesis and biological evaluation of phloridzin analogs as human concentrative nucleoside transporter 3 (hCNT3) inhibitors. *Bioorg. Med. Chem. Lett.* **19**: 917-21 [PMID:19097778]
9. Hammond JR. (2000) Interaction of a series of draflazine analogues with equilibrative nucleoside transporters: species differences and transporter subtype selectivity. *Naunyn Schmiedebergs Arch. Pharmacol.* **361**: 373-82 [PMID:10763851]
10. Hammond JR and Archer RG. (2004) Interaction of the novel adenosine uptake inhibitor 3-[1-(6,7-diethoxy-2-morpholinoquinazolin-4-yl)piperidin-4-yl]-1,6-dimethyl-2,4(1H,3H)-quinazolin-2-one hydrochloride (KF24345) with the es and ei subtypes of equilibrative nucleoside transporters. *J. Pharmacol. Exp. Ther.* **308**: 1083-93 [PMID:14634039]
11. Ho HT, Pan Y, Cui Z, Duan H, Swaan PW and Wang J. (2011) Molecular analysis and structure-activity relationship modeling of the substrate/inhibitor interaction site of plasma membrane monoamine transporter. *J. Pharmacol. Exp. Ther.* **339**: 376-85 [PMID:21816955]
12. Hsu CL, Lin W, Seshasayee D, Chen YH, Ding X, Lin Z, Suto E, Huang Z, Lee WP and Park H *et al.*. (2012) Equilibrative nucleoside transporter 3 deficiency perturbs lysosome function and macrophage homeostasis. *Science* **335**: 89-92 [PMID:22174130]
13. Kang N, Jun AH, Bhutia YD, Kannan N, Unadkat JD and Govindarajan R. (2010) Human equilibrative

- nucleoside transporter-3 (hENT3) spectrum disorder mutations impair nucleoside transport, protein localization, and stability. *J. Biol. Chem.* **285**: 28343-52 [PMID:20595384]
14. Larráyoiz IM, Fernández-Nistal A, Garcés A, Gorraitz E and Lostao MP. (2006) Characterization of the rat Na⁺/nucleoside cotransporter 2 and transport of nucleoside-derived drugs using electrophysiological methods. *Am. J. Physiol., Cell Physiol.* **291**: C1395-404 [PMID:16837649]
 15. Owen RP, Badagnani I and Giacomini KM. (2006) Molecular determinants of specificity for synthetic nucleoside analogs in the concentrative nucleoside transporter, CNT2. *J. Biol. Chem.* **281**: 26675-82 [PMID:16840788]
 16. Sundaram M, Yao SY, Ng AM, Griffiths M, Cass CE, Baldwin SA and Young JD. (1998) Chimeric constructs between human and rat equilibrative nucleoside transporters (hENT1 and rENT1) reveal hENT1 structural domains interacting with coronary vasoactive drugs. *J. Biol. Chem.* **273**: 21519-25 [PMID:9705281]
 17. Tatani K, Hiratochi M, Nonaka Y, Isaji M and Shuto S. (2015) Identification of 8-aminoadenosine derivatives as a new class of human concentrative nucleoside transporter 2 inhibitors. *ACS Med Chem Lett* **6**: 244-8 [PMID:25815140]
 18. Wang C, Lin W, Playa H, Sun S, Cameron K and Buolamwini JK. (2013) Dipyridamole analogs as pharmacological inhibitors of equilibrative nucleoside transporters. Identification of novel potent and selective inhibitors of the adenosine transporter function of human equilibrative nucleoside transporter 4 (hENT4). *Biochem. Pharmacol.* **86**: 1531-40 [PMID:24021350]
 19. Wang J. (2016) The plasma membrane monoamine transporter (PMAT): Structure, function, and role in organic cation disposition. *Clin. Pharmacol. Ther.* **100**: 489-499 [PMID:27506881]
 20. Warraich S, Bone DB, Quinonez D, Li H, Choi DS, Holdsworth DW, Drangova M, Dixon SJ, Séguin CA and Hammond JR. (2013) Loss of equilibrative nucleoside transporter 1 in mice leads to progressive ectopic mineralization of spinal tissues resembling diffuse idiopathic skeletal hyperostosis in humans. *J. Bone Miner. Res.* **28**: 1135-49 [PMID:23184610]
 21. Yao SY, Ng AM, Cass CE, Baldwin SA and Young JD. (2011) Nucleobase transport by human equilibrative nucleoside transporter 1 (hENT1). *J. Biol. Chem.* **286**: 32552-62 [PMID:21795683]
 22. Zhou M, Xia L and Wang J. (2007) Metformin transport by a newly cloned proton-stimulated organic cation transporter (plasma membrane monoamine transporter) expressed in human intestine. *Drug Metab. Dispos.* **35**: 1956-62 [PMID:17600084]