

## Adenosine turnover (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

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### Abstract

A multifunctional, ubiquitous molecule, [adenosine](#) acts at cell-surface G protein-coupled receptors, as well as numerous enzymes, including protein kinases and adenylyl cyclase. Extracellular adenosine is thought to be produced either by export or by metabolism, predominantly through ecto-5'-nucleotidase activity (also producing inorganic phosphate). It is inactivated either by extracellular metabolism *via* adenosine deaminase (also producing ammonia) or, following uptake by nucleoside transporters, *via* adenosine deaminase or adenosine kinase (requiring [ATP](#) as co-substrate). Intracellular adenosine may be produced by cytosolic 5'-nucleotidases or through S-adenosylhomocysteine hydrolase (also producing [L-homocysteine](#)).

### Contents

This is a citation summary for Adenosine turnover 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

#### Adenosine turnover

<http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=248>

Enzymes

[ADA\(Adenosine deaminase\)](#)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1230>

[ADK\(Adenosine kinase\)](#)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1231>

NT5E(Ecto-5'-Nucleotidase)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1232>

SAHH(S-Adenosylhomocysteine hydrolase)

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1233>

5'-nucleotidase IA

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1234>

5'-nucleotidase IB

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1235>

5'-nucleotidase II

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1236>

5'-nucleotidase III

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1237>

5'(3')-nucleotidase

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1238>

Mitochondrial 5'-nucleotidase

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1239>

## References

1. Agarwal RP, Spector T and Parks Jr RE. (1977) Tight-binding inhibitors--IV. Inhibition of adenosine deaminases by various inhibitors. *Biochem. Pharmacol.* **26**: 359-67 [PMID:849330]
2. Antonioli L, Pacher P, Vizi ES and Haskó G. (2013) CD39 and CD73 in immunity and inflammation. *Trends Mol Med* **19**: 355-67 [PMID:23601906]
3. Baqi Y, Lee SY, Iqbal J, Ripphausen P, Lehr A, Scheiff AB, Zimmermann H, Bajorath J and Müller CE. (2010) Development of potent and selective inhibitors of ecto-5'-nucleotidase based on an anthraquinone scaffold. *J. Med. Chem.* **53**: 2076-86 [PMID:20146483]
4. Bastid J, Cottalorda-Regairaz A, Alberici G, Bonnefoy N, Eliaou JF and Bensussan A. (2013) ENTPD1/CD39 is a promising therapeutic target in oncology. *Oncogene* **32**: 1743-51 [PMID:22751118]
5. Boison D. (2013) Adenosine kinase: exploitation for therapeutic gain. *Pharmacol. Rev.* **65**: 906-43 [PMID:23592612]
6. Burger RM and Lowenstein JM. (1975) 5'-Nucleotidase from smooth muscle of small intestine and from brain. Inhibition of nucleotides. *Biochemistry* **14**: 2362-6 [PMID:1169962]
7. Cortés A, Gracia E, Moreno E, Mallol J, Lluís C, Canela EI and Casadó V. (2015) Moonlighting adenosine deaminase: a target protein for drug development. *Med Res Rev* **35**: 85-125 [PMID:24933472]
8. Geoghegan JC, Diedrich G, Lu X, Rosenthal K, Sachsenmeier KF, Wu H, Dall'Acqua WF and Damschroder MM. (2016) Inhibition of CD73 AMP hydrolysis by a therapeutic antibody with a dual, non-competitive mechanism of action. *MAbs* **8**: 454-67 [PMID:26854859]
9. Glazer RI, Hartman KD, Knode MC, Richard MM, Chiang PK, Tseng CK and Marquez VE. (1986) 3-Deazaneplanocin: a new and potent inhibitor of S-adenosylhomocysteine hydrolase and its effects on human promyelocytic leukemia cell line HL-60. *Biochem. Biophys. Res. Commun.* **135**: 688-94 [PMID:3457563]
10. Guranowski A, Montgomery JA, Cantoni GL and Chiang PK. (1981) Adenosine analogues as substrates and inhibitors of S-adenosylhomocysteine hydrolase. *Biochemistry* **20**: 110-5 [PMID:7470463]
11. Häusler SF, Del Barrio IM, Diessner J, Stein RG, Strohschein J, Hönig A, Dietl J and Wischhusen J. (2014) Anti-CD39 and anti-CD73 antibodies A1 and 7G2 improve targeted therapy in ovarian cancer by blocking adenosine-dependent immune evasion. *Am J Transl Res* **6**: 129-39 [PMID:24489992]
12. Jarvis MF, Yu H, Kohlhaas K, Alexander K, Lee CH, Jiang M, Bhagwat SS, Williams M and Kowaluk EA. (2000) ABT-702 (4-amino-5-(3-bromophenyl)-7-(6-morpholinopyridin-3-yl)pyrido[2, 3-d]pyrimidine), a novel orally effective adenosine kinase inhibitor with analgesic and anti-inflammatory properties: I. In vitro characterization and acute antinociceptive effects in the mouse. *J. Pharmacol. Exp. Ther.* **295**: 1156-64

[PMID:11082453]

13. Kameoka J, Tanaka T, Nojima Y, Schlossman SF and Morimoto C. (1993) Direct association of adenosine deaminase with a T cell activation antigen, CD26. *Science* **261**: 466-9 [PMID:8101391]
14. Leclerc BG, Charlebois R, Chouinard G, Allard B, Pommey S, Saad F and Stagg J. (2016) CD73 Expression Is an Independent Prognostic Factor in Prostate Cancer. *Clin. Cancer Res.* **22**: 158-66 [PMID:26253870]
15. Loi S, Pommey S, Haibe-Kains B, Beavis PA, Darcy PK, Smyth MJ and Stagg J. (2013) CD73 promotes anthracycline resistance and poor prognosis in triple negative breast cancer. *Proc. Natl. Acad. Sci. U.S.A.* **110**: 11091-6 [PMID:23776241]
16. Lu XX, Chen YT, Feng B, Mao XB, Yu B and Chu XY. (2013) Expression and clinical significance of CD73 and hypoxia-inducible factor-1 $\alpha$  in gastric carcinoma. *World J. Gastroenterol.* **19**: 1912-8 [PMID:23569336]
17. Maier SA, Galellis JR and McDermid HE. (2005) Phylogenetic analysis reveals a novel protein family closely related to adenosine deaminase. *J. Mol. Evol.* **61**: 776-94 [PMID:16245011]
18. McGaraughty S, Chu KL, Wismer CT, Mikusa J, Zhu CZ, Cowart M, Kowaluk EA and Jarvis MF. (2001) Effects of A-134974, a novel adenosine kinase inhibitor, on carrageenan-induced inflammatory hyperalgesia and locomotor activity in rats: evaluation of the sites of action. *J. Pharmacol. Exp. Ther.* **296**: 501-9 [PMID:11160637]
19. Ren ZH, Lin CZ, Cao W, Yang R, Lu W, Liu ZQ, Chen YM, Yang X, Tian Z and Wang LZ *et al.*. (2016) CD73 is associated with poor prognosis in HNSCC. *Oncotarget* **7**: 61690-61702 [PMID:27557512]
20. Roifman CM, Zhang J, Atkinson A, Grunebaum E and Mandel K. (2008) Adenosine deaminase deficiency can present with features of Omenn syndrome. *J. Allergy Clin. Immunol.* **121**: 1056-8 [PMID:18243287]
21. Stagg J. (2012) The double-edge sword effect of anti-CD73 cancer therapy. *Oncoimmunology* **1**: 217-218 [PMID:22720247]
22. Villa A, Notarangelo LD and Roifman CM. (2008) Omenn syndrome: inflammation in leaky severe combined immunodeficiency. *J. Allergy Clin. Immunol.* **122**: 1082-6 [PMID:18992930]
23. Wang H, Lee S, Nigro CL, Lattanzio L, Merlano M, Monteverde M, Matin R, Purdie K, Mladkova N and Bergamaschi D *et al.*. (2012) NT5E (CD73) is epigenetically regulated in malignant melanoma and associated with metastatic site specificity. *Br. J. Cancer* **106**: 1446-52 [PMID:22454080]
24. Wang L, Fan J, Thompson LF, Zhang Y, Shin T, Curiel TJ and Zhang B. (2011) CD73 has distinct roles in nonhematopoietic and hematopoietic cells to promote tumor growth in mice. *J. Clin. Invest.* **121**: 2371-82 [PMID:21537079]
25. Williams-Karnesky RL, Sandau US, Lusardi TA, Lytle NK, Farrell JM, Pritchard EM, Kaplan DL and Boison D. (2013) Epigenetic changes induced by adenosine augmentation therapy prevent epileptogenesis. *J. Clin. Invest.* **123**: 3552-63 [PMID:23863710]
26. Wu XR, He XS, Chen YF, Yuan RX, Zeng Y, Lian L, Zou YF, Lan N, Wu XJ and Lan P. (2012) High expression of CD73 as a poor prognostic biomarker in human colorectal cancer. *J Surg Oncol* **106**: 130-7 [PMID:22287455]
27. Zavialov AV, Yu X, Spillmann D, Lauvau G and Zavialov AV. (2010) Structural basis for the growth factor activity of human adenosine deaminase ADA2. *J. Biol. Chem.* **285**: 12367-77 [PMID:20147294]