Adenosine metabolising enzymes

Overview: Adenosine is a multifunctional, ubiquitous molecule that acts at cell-surface 7TM 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 metabolism may be produced by cytosolic 5′-nucleotidases or through S-adenosylhomocysteine hydrolase (also producing homocysteine).

Nomenclature	Adenosine deaminase	Adenosine kinase	Ecto-5′-nucleotidase	S-adenosylhomocysteine hydrolase
E.C.	3.5.4.4	2.7.1.20	3.1.3.5	3.3.1.1
Preferred abbreviation	ADA	ADK	NT5E	SAHH
Other names	Adenosine aminohydrolase	–	CD73, 5′-NT	Adenosylhomocysteinase
Ensembl ID	ENSG00000196839	ENSG00000156110	ENSG00000135318	ENSG00000101444
Rank order of affinity	2′-Deoxyadenosine ≥ adenosine	Adenosine	5′-AMP, 5′-GMP, 5′-IMP, 5′-UMP > 5′-dAMP, 5′-dGMP	S-Adenosylhomocysteine
Products	2′-Deoxyinosine, inosine	5′-AMP	Adenosine, guanine, inosine, uridine	Adenosine
Selective inhibitors	EHNA, 2′-deoxycoformycin	A134974 (pIC$_{50}$ 10.2, McGaraughty *et al*., 2001), ABT702 (pIC$_{50}$ 8.8, Jarvis *et al*., 2000)	$\alpha\beta$-methyleneADP	–

Other forms of adenosine deaminase act on ribonucleic acids and may be divided into two families: ADAT1 (ENSG00000065457) deaminates transfer RNA; ADAR (EC 3.5.4.-, also known as 136 kDa double-stranded RNA-binding protein, P136, K88DSRBP, Interferon-inducible protein 4, ENSG00000160710); ADARB1 (EC 3.5.-.-, also known as dsRNA adenosine deaminase, ENSG00000197381) and ADARB2 (EC 3.5.-.-, also known as dsRNA adenosine deaminase B2, RNA-dependent adenosine deaminase 3, ENSG00000185736) act on double-stranded RNA. Particular polymorphisms of the ADA gene result in loss-of-function and severe combined immunodeficiency syndrome. Adenosine deaminase is able to complex with dipeptidyl peptidase IV (EC 3.4.14.5, also known as T-cell activation antigen CD26, TP103, adenosine deaminase complexing protein 2, ENSG00000197635) to form a cell-surface activity (Kameoka *et al*., 1993).

Cytosolic 5′-nucleotidase may be divided into IA (NT5C1A, ENSG00000116981), IB (NT5C1B, ENSG00000185013), II (NT5C2, ENSG00000076685), III (NT5C3, ENSG00000122643) and 5′(3′)-nucleotidases (NT5C, ENSG00000125458), together with a mitochondrial isoform (NT5M, ENSG00000205309).

Abbreviations: **5′-AMP**, adenosine 5′-monophosphate; **5′NT**, 5′-nucleotidase; **A134974**, N^7-[(1′R,2′S,3′R,4′S)-2′,3′-dihydroxy-4′-aminocyclopentyl]-4-amino-5-iodopyrrolopyrimidine; **ABT702**, 4-amino-5-(3-bromophenyl)-7-(6-morpholinopyridin-3-yl)pyrido[2,3-d]pyrimidine; **ADA**, adenosine deaminase; **ADK**, adenosine kinase, **EHNA**, *erythro*-9-(2-hydroxy-3-nonyl)adenine hydrochloride

Further Reading

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