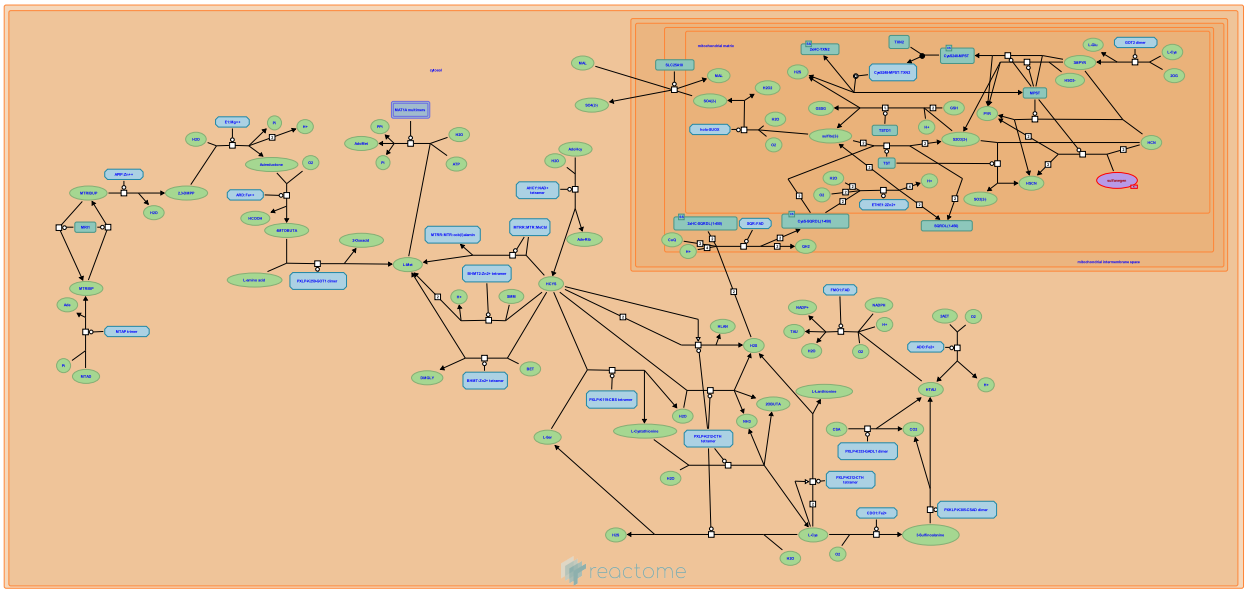
Sulfur amino acid metabolism



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

29/04/2024

Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

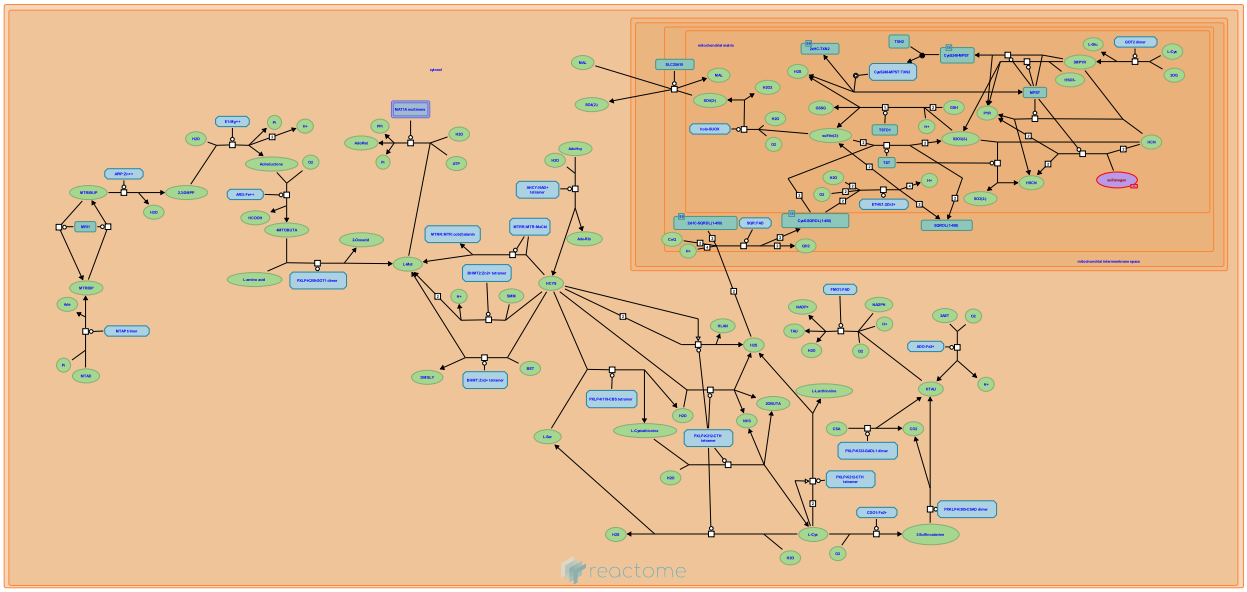
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Reactome database release: 88

This document contains 4 pathways and 5 reactions (see Table of Contents)

Sulfur amino acid metabolism ↗

Stable identifier: R-HSA-1614635



The main sulfur amino acids are methionine, cysteine, homocysteine and taurine. Of these, the first two are proteinogenic.

This group of reactions contains all processes that 1) break down sulfur amino acids, 2) interconvert between them, and 3) synthesize them from solved sulfide which comes from sulfate assimilation and reduction. Only plants and microorganisms employ all processes. Humans cannot de novo synthesize any sulfur amino acid, nor convert cysteine to methionine (Brosnan & Brosnan, 2006).

Literature references

Brosnan, JT., Brosnan, ME. (2006). The sulfur-containing amino acids: an overview. *J Nutr, 136*, 1636S-1640S. ↗

Editions

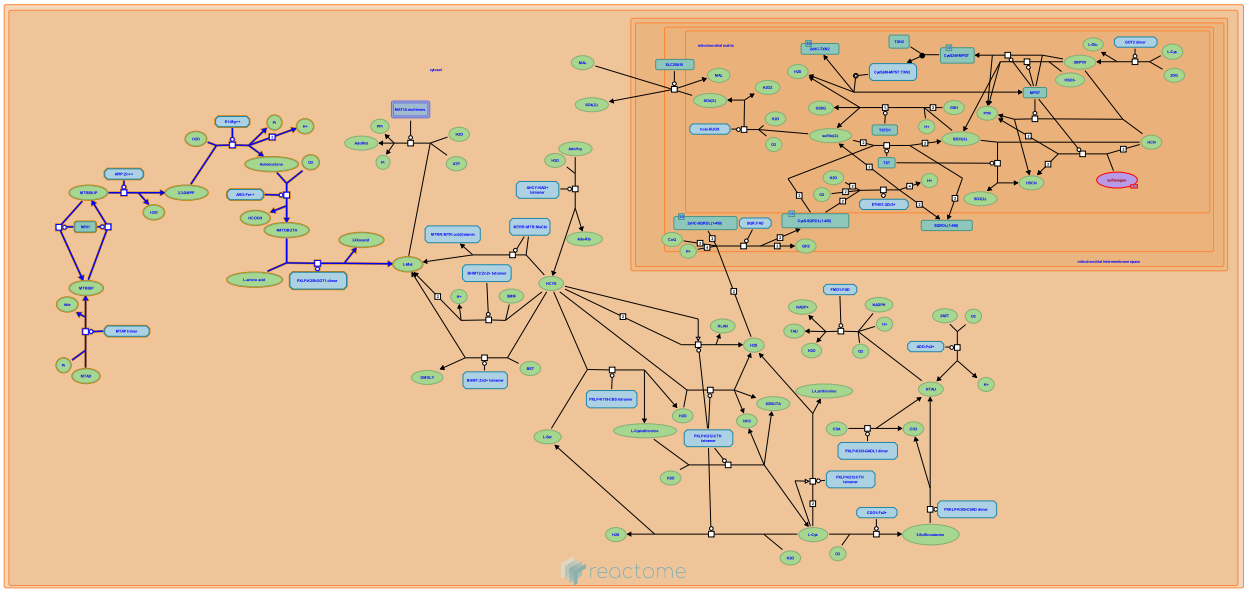
2010-10-24	Authored	Stephan, R.
2011-09-29	Edited	Jassal, B.
2011-10-13	Reviewed	D'Eustachio, P.

Methionine salvage pathway ↗

Location: Sulfur amino acid metabolism

Stable identifier: R-HSA-1237112

Compartments: cytosol



Methionine salvage is a sequential pathway of six reactions that create methionine from 5'-methylthioadenosine (MTA) which is a byproduct of polyamine biosynthesis in nearly all organisms. The process happens completely in the cytosol. It is important in humans for recycling of sulphur that has to be assimilated using energy. (Pirkov et al, 2008; Albers, 2009)

Literature references

Albers, E. (2009). Metabolic characteristics and importance of the universal methionine salvage pathway recycling methionine from 5'-methylthioadenosine. *IUBMB Life, 61*, 1132-42. ↗

Gustafsson, L., Pirkov, I., Norbeck, J., Albers, E. (2008). A complete inventory of all enzymes in the eukaryotic methionine salvage pathway. *FEBS J, 275*, 4111-20. ↗

Editions

2010-10-24	Authored	Stephan, R.
2011-03-30	Edited	Jassal, B.
2011-05-23	Reviewed	D'Eustachio, P.

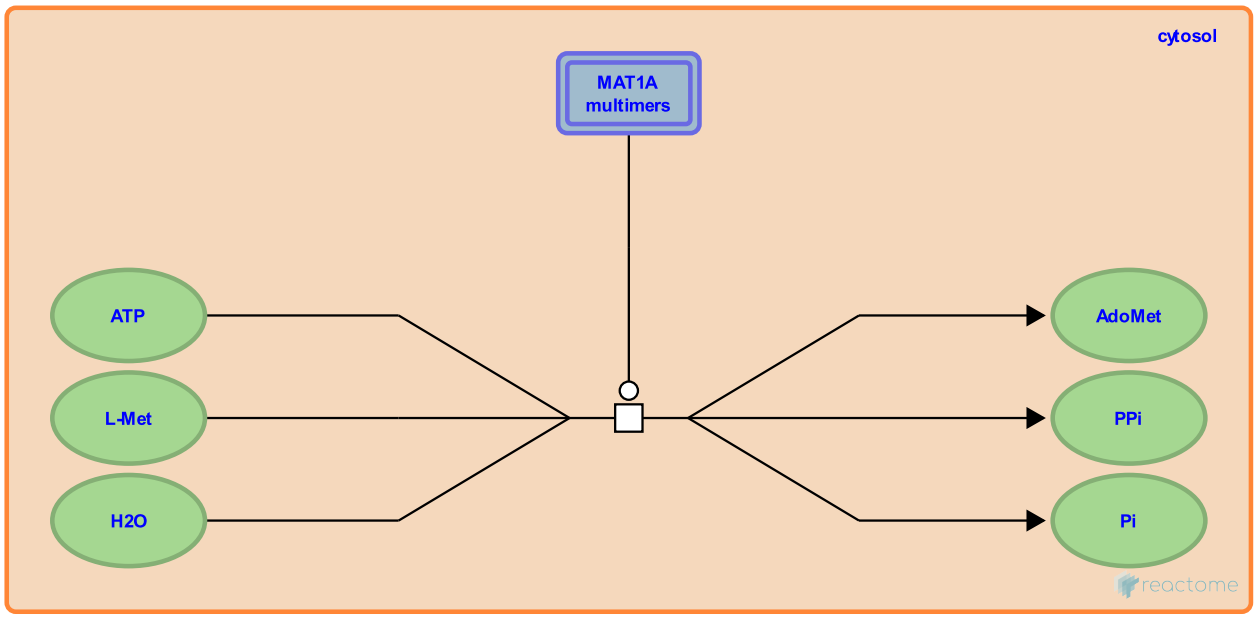
MAT1A multimers transfer Ado from ATP to L-Met ↗

Location: Sulfur amino acid metabolism

Stable identifier: R-HSA-174391

Type: transition

Compartments: cytosol



S-adenosylmethionine (AdoMet, SAM) is an essential metabolite in all cells. AdoMet is a precursor in the synthesis of polyamines. Methionine adenosyltransferases (MAT) catalyse the only known AdoMet biosynthetic reaction from methionine (L-Met) and ATP. In mammalian tissues, three different forms of MAT (MAT I, MAT III and MAT II) have been identified that are the product of two different genes (MAT1A and MAT2A). MAT1A binds 1 K+ and 2 Mg2+ (or Co2+, not shown here) in tetrameric or dimeric form (Corrales et al. 2002, Mato et al. 1997).

Literature references

Castro, C., Ruiz, F., García-Trevijano, ER., Latasa, U., Martinez-Cruz, A., Sánchez Del Pino, MM. et al. (2002). Regulation of mammalian liver methionine adenosyltransferase. *J Nutr, 132*, 2377S-2381S. ↗

Ortiz, P., Alvarez, L., Pajares, MA., Mato, JM. (1997). S-adenosylmethionine synthesis: molecular mechanisms and clinical implications. *Pharmacol Ther, 73*, 265-80. ↗

Editions

2006-04-27	Edited	Gopinathrao, G.
2008-05-21	Authored	Gopinathrao, G.
2008-06-12	Reviewed	D'Eustachio, P.
2014-06-23	Revised	Jassal, B.

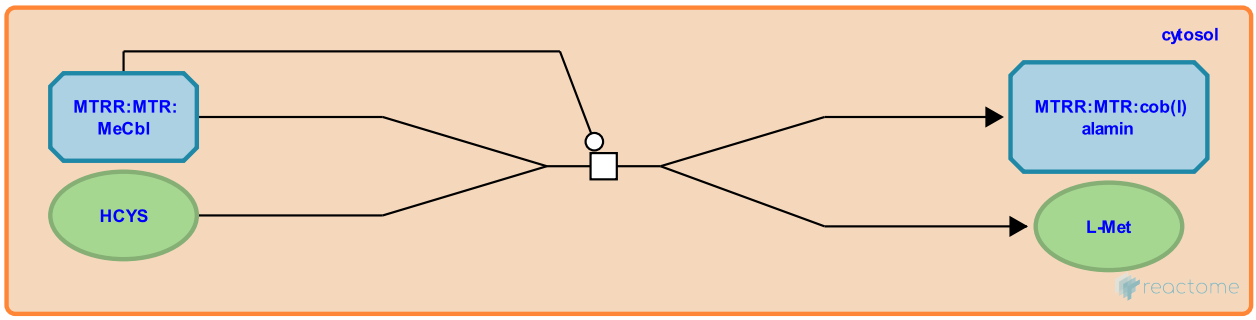
MTR transfers CH3 from MeCbl to HCYS ↗

Location: Sulfur amino acid metabolism

Stable identifier: R-HSA-174374

Type: transition

Compartments: cytosol



Methionine synthase (MTR) mediates the continuous shuttling of cobalamin (Cbl) between two forms, cob(I)alamin and MeCbl. In this half reaction, the methyl group from MeCbl is transferred to homocysteine (HYCS) to form methionine and regenerate cob(I)alamin (Hall et al. 2000; Leclerc et al. 1996).

Preceded by: AHCY:NAD+ tetramer hydrolyses AdoHcy

Literature references

Ross, M., Adjalla, CE., Eydoux, P., Gravel, RA., Rosenblatt, DS., Christensen, B. et al. (1996). Human methionine synthase: cDNA cloning and identification of mutations in patients of the cblG complementation group of folate/cobalamin disorders. *Hum Mol Genet, 5*, 1867-74. ↗

Jordan-Starck, TC., Ludwig, ML., Loo, RO., Hall, DA., Matthews, RG. (2000). Interaction of flavodoxin with cobalamin-dependent methionine synthase. *Biochemistry, 39*, 10711-9. ↗

Editions

2006-02-17	Edited	Jassal, B.
2007-04-24	Authored	Jassal, B.
2008-05-28	Reviewed	D'Eustachio, P.
2013-02-21	Revised	Jassal, B.

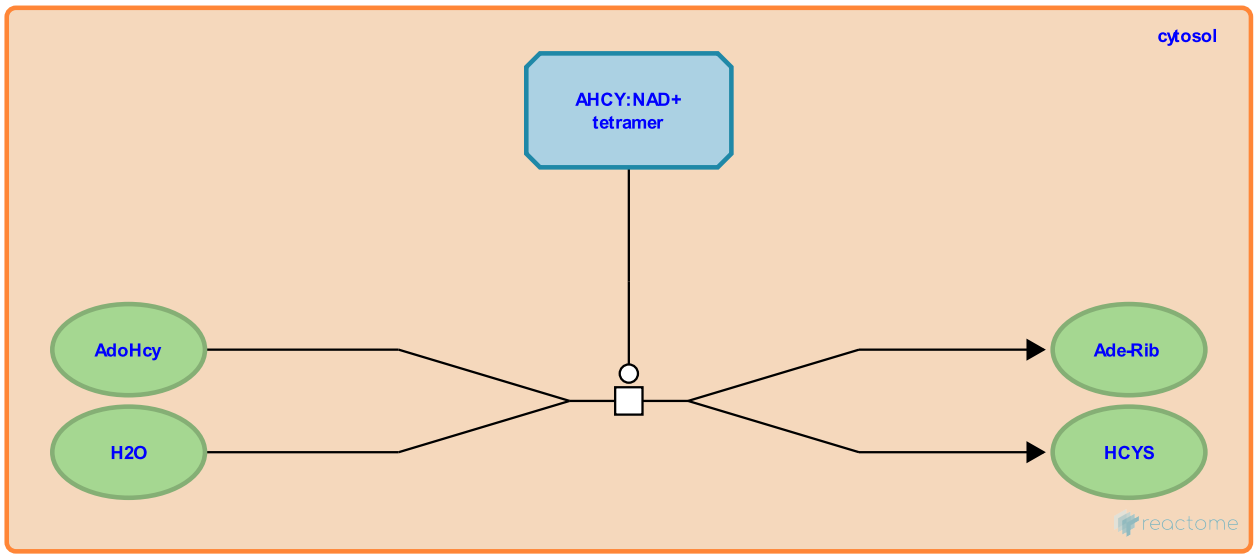
AHCY:NAD+ tetramer hydrolyses AdoHcy ↗

Location: Sulfur amino acid metabolism

Stable identifier: R-HSA-174401

Type: transition

Compartments: cytosol



Adenosylhomocysteinase (AHCY) is a tetrameric, NAD+-bound, cytosolic protein that regulates all adenosylmethionine-(AdoMet) dependent transmethylations by hydrolysing the feedback inhibitor adenosylhomocysteine (AdoHcy) to homocysteine (HCYS) and adenosine (Ade-Rib) (Turner et al. 1998, Yang et al. 2003).

Followed by: BHMT tetramer transfers CH3 group from BET to HCYS to form DMGLY, MTR transfers CH3 from MeCbl to HCYS

Literature references

Borchardt, RT., Kuczera, K., Howell, PL., Turner, MA., Yin, DH., Yang, X. et al. (2003). Catalytic strategy of S-adenosyl-L-homocysteine hydrolase: transition-state stabilization and the avoidance of abortive reactions. *Biochemistry, 42*, 1900-9. ↗

Turner, MA., Hershfield, MS., Howell, PL., Borchardt, RT., Yuan, CS., Smith, GD. (1998). Structure determination of selenomethionyl S-adenosylhomocysteine hydrolase using data at a single wavelength. *Nat. Struct. Biol., 5*, 369-76 . ↗

Editions

2008-05-28	Reviewed	D'Eustachio, P.

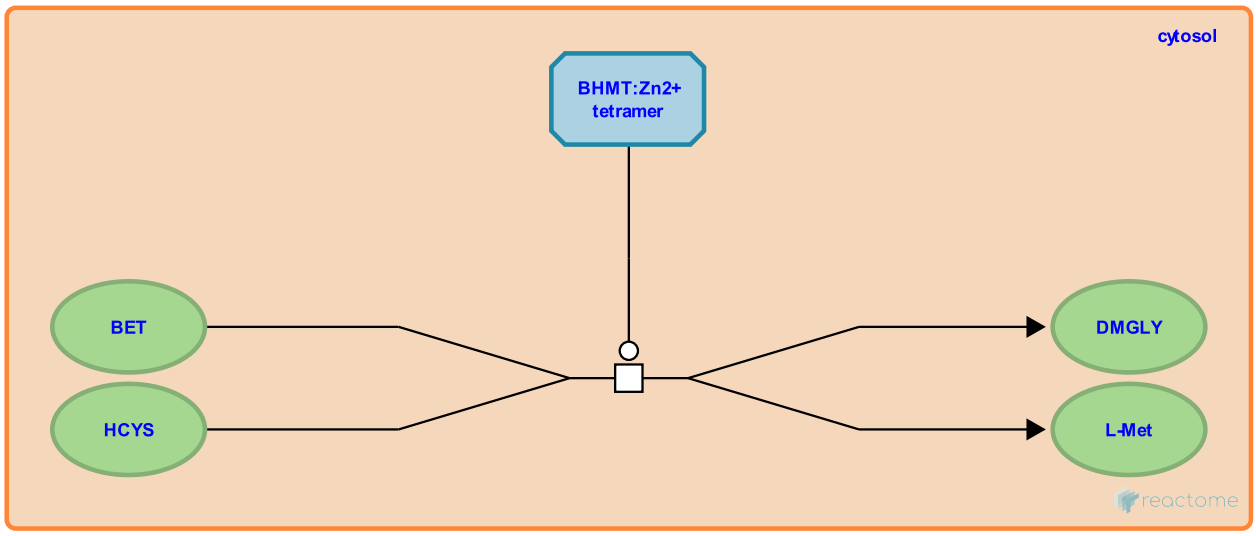
BHMT tetramer transfers CH3 group from BET to HCYS to form DMGLY ↗

Location: Sulfur amino acid metabolism

Stable identifier: R-HSA-1614654

Type: transition

Compartments: cytosol



Remethylation of homocysteine (HCYS) to methionine (L-Met) can also proceed by using betaine (BET) as a methyl donor, which is oxidised to dimethylglycine (DMGLY). This reaction is also part of choline catabolism, thereby providing a link to folate-dependent, one-carbon metabolism (Li et al. 2008).

Preceded by: AHCY:NAD+ tetramer hydrolyses AdoHcy

Literature references

Weinshilboum, RM., Eckloff, BW., Feng, Q., Li, F., Moon, I., Pelleymounter, LL. et al. (2008). Human betaine-homocysteine methyltransferase (BHMT) and BHMT2: common gene sequence variation and functional characterization. *Mol Genet Metab, 94*, 326-35. ↗

Editions

2010-10-24	Authored	Stephan, R.
2011-09-29	Edited	Jassal, B.
2011-10-13	Reviewed	D'Eustachio, P.

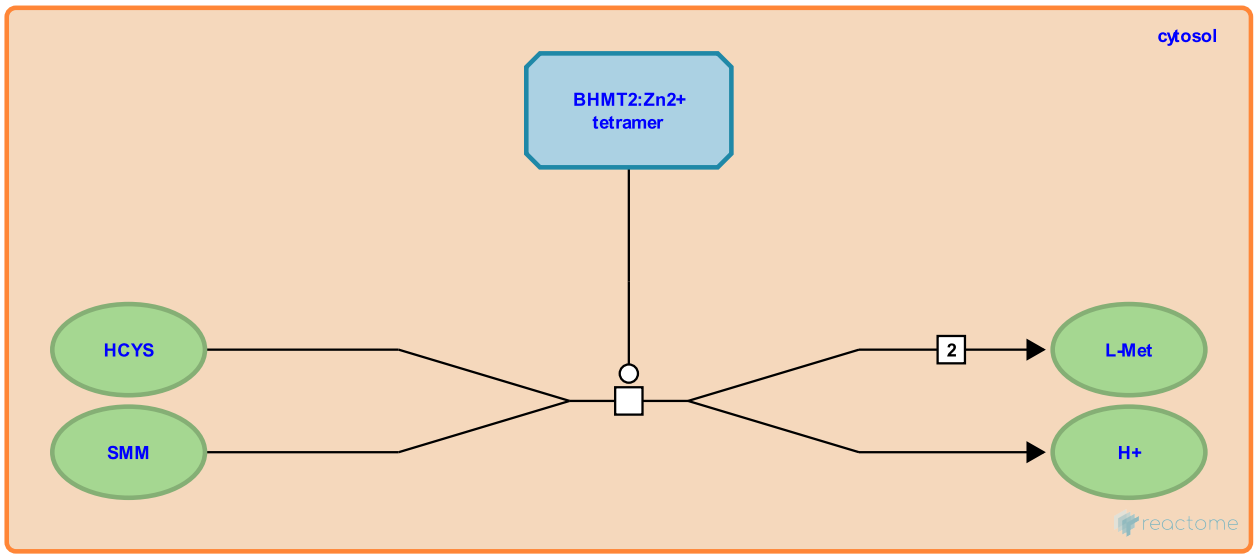
BHMT2 tetramer transfers CH3 group from SMM to LHCYS ↗

Location: Sulfur amino acid metabolism

Stable identifier: R-HSA-5696838

Type: transition

Compartments: cytosol



L-homocysteine (LHCYS) is derived from L-methionine (L-Met) and can either be remethylated to reform L-Met or take part in cysteine biosynthesis via the trans-sulfuration pathway. LHCYS remethylation can occur by the action of two enzymes; cobalamin-dependent methionine synthase and betaine-homocysteine methyltransferase, using methyltetrahydrofolate and betaine respectively as methyl donors. A third enzyme, S-methylmethionine-homocysteine S-methyltransferase (BHMT2), can use S-methylmethionine (SMM) as the methyl donor to methylate LHCYS and reform L-Met. BHMT2 is a tetrameric, cytosolic enzyme that requires one Zn2+ ion per subunit as cofactor (Szegedi et al. 2008).

Literature references

Koutmos, M., Castro, CC., Garrow, TA., Szegedi, SS. (2008). Betaine-homocysteine S-methyltransferase-2 is an S-methylmethionine-homocysteine methyltransferase. *J. Biol. Chem., 283*, 8939-45. ↗

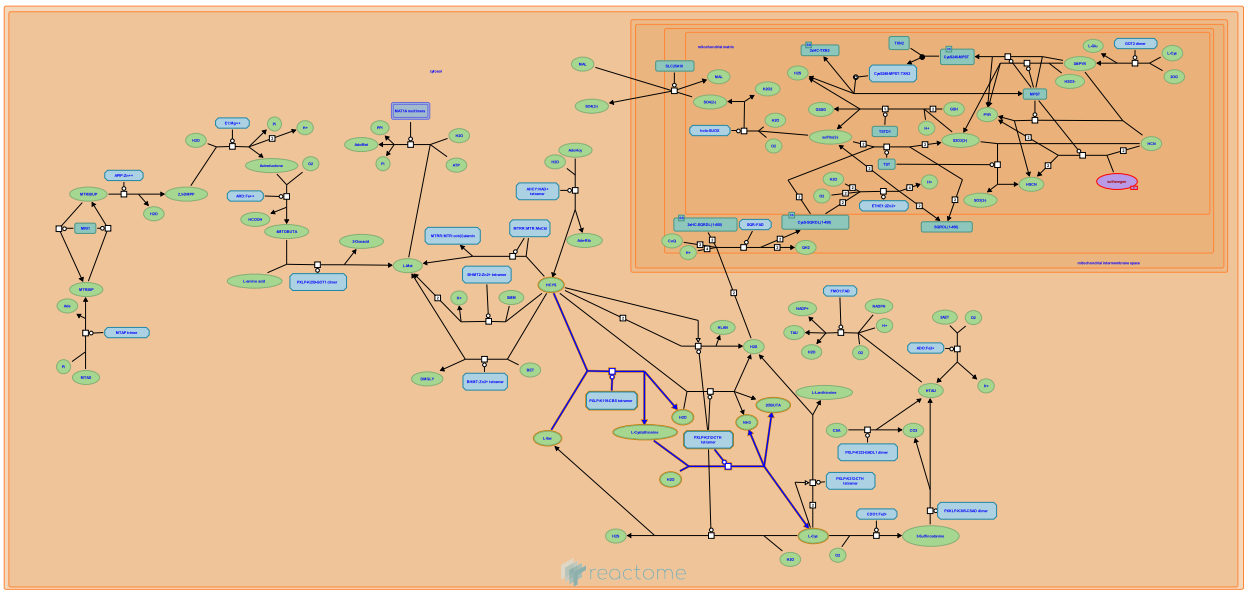
Editions

2015-06-01	Authored, Edited	Jassal, B.
2015-06-26	Reviewed	D'Eustachio, P.

Cysteine formation from homocysteine ↗

Location: Sulfur amino acid metabolism

Stable identifier: R-HSA-1614603



Transsulfuration is the interconversion of homocysteine and cysteine, and it fully takes place in bacteria and some plants and fungi. Animals however have only one direction of this bidirectional path, the synthesis of cysteine from homocysteine via cystathionine. Because excess cysteine is degraded to hydrogen sulfide, which is now known as a neuromodulator and smooth muscle relaxant, this pathway is also the main source of its production, which takes place in the cytosol, as well as in extracellular space (Dominy & Stipanuk 2004, Bearden et al. 2010).

Literature references

Beard RS, Jr., Bearden, SE., Pfau, JC. (2010). Extracellular transsulfuration generates hydrogen sulfide from homocysteine and protects endothelium from redox stress. *Am J Physiol Heart Circ Physiol, 299*, H1568-76. ↗

Dominy, JE., Stipanuk, MH. (2004). New roles for cysteine and transsulfuration enzymes: production of H2S, a neuromodulator and smooth muscle relaxant. *Nutr Rev, 62*, 348-53. ↗

Editions

2010-10-24	Authored	Stephan, R.
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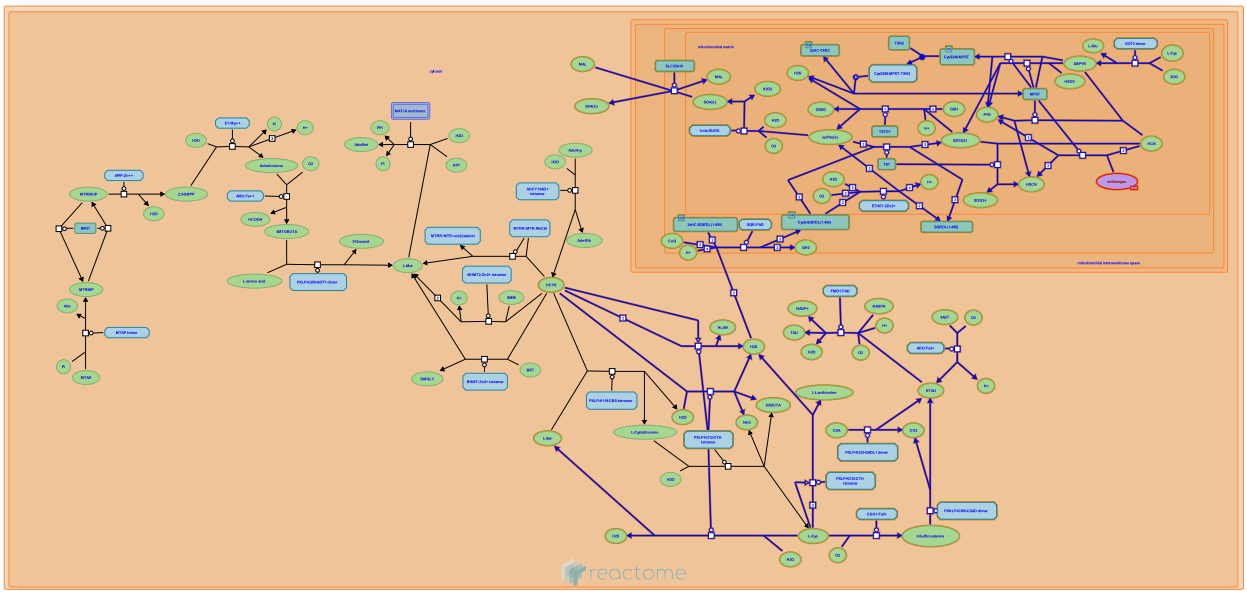
Degradation of cysteine and homocysteine ↗

Location: Sulfur amino acid metabolism

Stable identifier: R-HSA-1614558



While in humans excess methionine is converted to homocysteine, homocysteine and its transsulfuration product cysteine can be degraded to several end products, two of which, taurine and hydrogen sulfide, have uses in other biological processes (Stipanuk & Ueki 2011).

Literature references

Ueki, I., Stipanuk, MH. (2011). Dealing with methionine/homocysteine sulfur: cysteine metabolism to taurine and inorganic sulfur. *J Inherit Metab Dis, 34*, 17-32. ↗

Editions

2010-10-24	Authored	Stephan, R.
2011-09-29	Edited	Jassal, B.
2011-10-13	Reviewed	D'Eustachio, P.

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