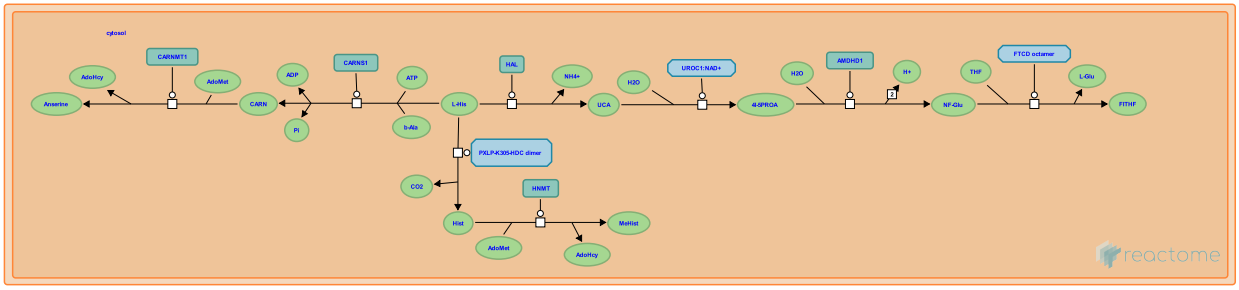
Histidine catabolism



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01/04/2024

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. ↗

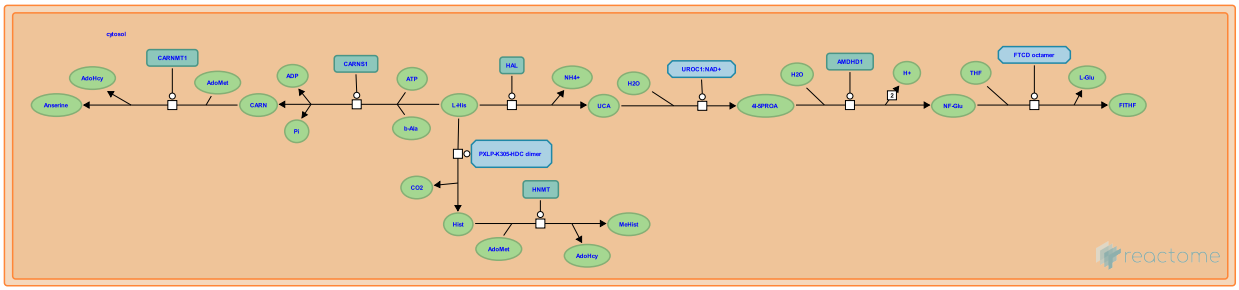
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Histidine catabolism ↗

Stable identifier: R-HSA-70921

Compartments: cytosol



The major pathway of histidine catabolism, annotated here, proceeds in four steps to yield glutamate and, in the process, convert one molecule of tetrahydrofolate to 5-formiminotetrahydrofolate (Morris et al. 1972). Histidine can also be decarboxylated to form histamine. Histidine can also be used to form carnosine (beta-alanyl-L-histidine), an abundant dipeptide in skeletal muscle and brain of most vertebrates.

Literature references

Lee, SC., Morris, ML., Harper, AE. (1972). Influence of differential induction of histidine catabolic enzymes on histidine degradation in vivo. *J Biol Chem, 247*, 5793-804. ↗

Editions

2003-06-24	Authored, Edited	D'Eustachio, P.
2010-02-18	Revised	D'Eustachio, P.

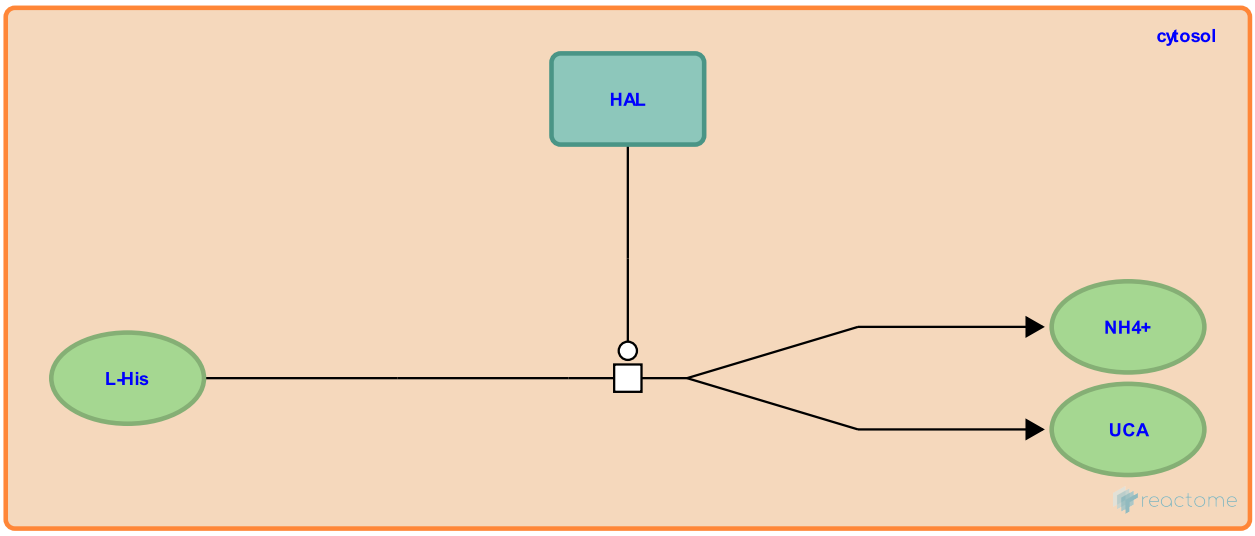
histidine => urocanate + NH4+ ↗

Location: Histidine catabolism

Stable identifier: R-HSA-70899

Type: transition

Compartments: cytosol



Cytosolic histidine ammonia lyase (HAL) catalyzes the reaction of histidine to form urocanate and NH4+ (Kawai et al. 2005).

Followed by: urocanate + H2O => 4-imidazolone-5-propionate

Literature references

Asai, K., Sumi, S., Coleman-Campbell, CM., Morishita, H., Moriyama, A., Kawai, Y. et al. (2005). Molecular characterization of histidinemia: identification of four missense mutations in the histidase gene. *Hum Genet, 116*, 340-6. ↗

Editions

2003-06-24	Authored, Edited	D'Eustachio, P.

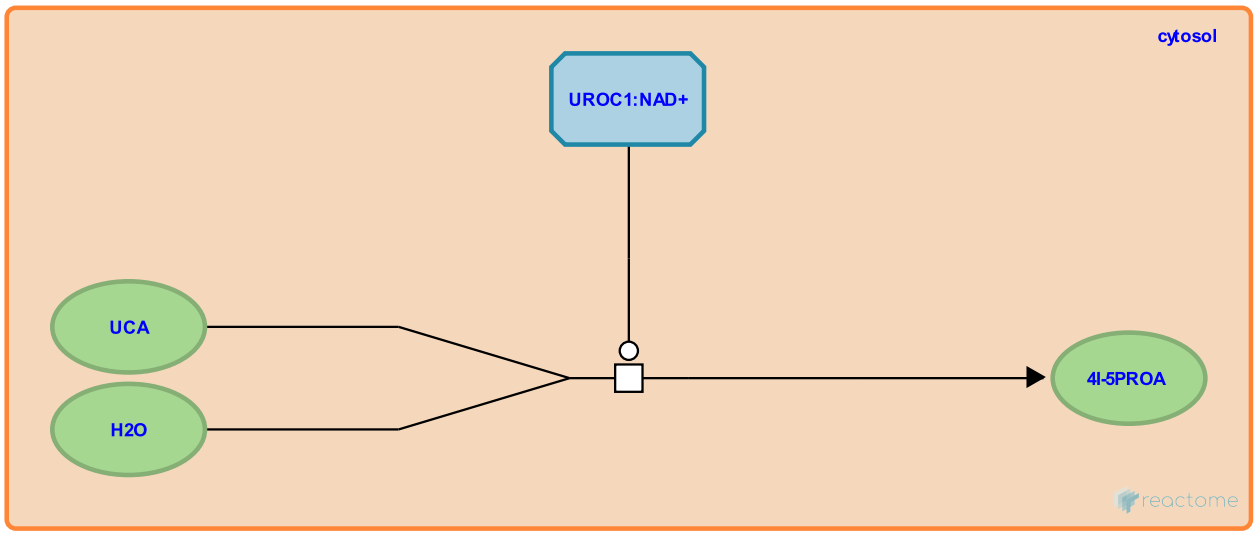
urocanate + H2O => 4-imidazolone-5-propionate ↗

Location: Histidine catabolism

Stable identifier: R-HSA-70903

Type: transition

Compartments: cytosol



Cytosolic urocanate hydratase (UROC1) catalyzes the hydrolysis of urocanate to form 4-imidazolone-5-propanoate. Human UROC1 was first identified in surveys of genes differentially expressed in hepatoblastoma (Yamamda et al. 2004). Recent biochemical and molecular studies of UROC1 protein and cDNA from a patient with urocanic aciduria has confirmed the function of UROC1 in vivo (Espinos et al. 2009).

Preceded by: histidine => urocanate + NH4+

Followed by: 4-imidazolone-5-propionate + H2O => N-formiminoglutamate + 2H+

Literature references

Vilaseca, MA., Palau, F., Espinós, C., Spaapen, LJ., Martinez-Rubio, D., Artuch, R. et al. (2009). Mutations in the urocanase gene UROC1 are associated with urocanic aciduria. *J Med Genet, 46*, 407-11. ↗

Kaneko, M., Yamada, S., Ohnuma, N., Suita, S., Suzuki, Y., Hirata, T. et al. (2004). Expression profiling and differential screening between hepatoblastomas and the corresponding normal livers: identification of high expression of the PLK1 oncogene as a poor-prognostic indicator of hepatoblastomas. *Oncogene, 23*, 5901-11. ↗

Editions

2003-06-24	Authored, Edited	D'Eustachio, P.

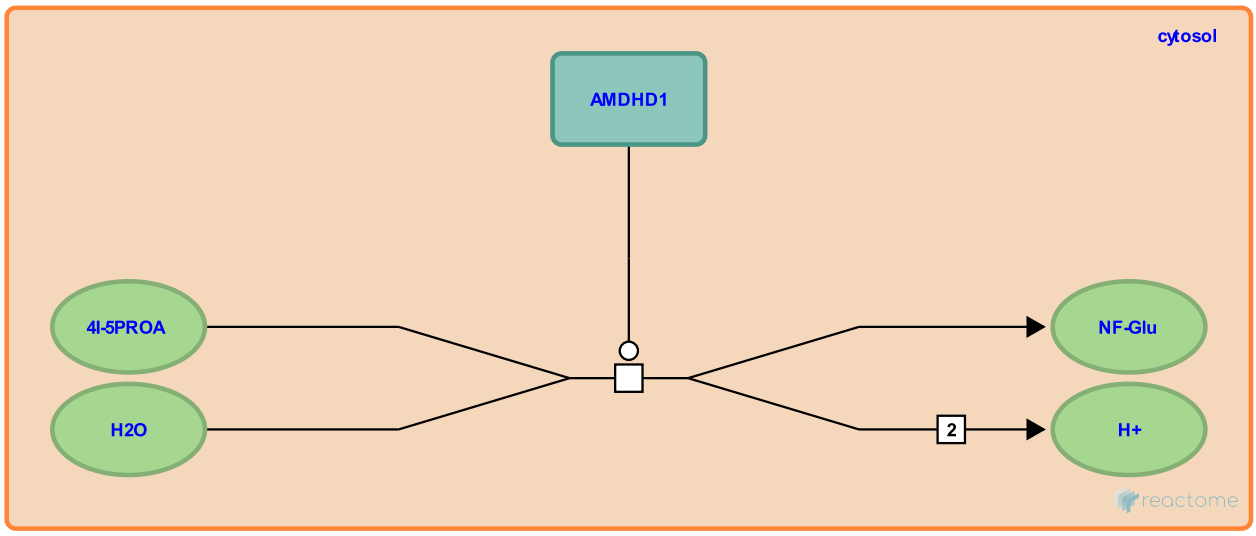
4-imidazolone-5-propionate + H2O => N-formiminoglutamate + 2H+ ↗

Location: Histidine catabolism

Stable identifier: R-HSA-70906

Type: transition

Compartments: cytosol



Cytosolic imidazolonepropionase catalyzes the hydrolysis of 4-imidazolone-5-propanoate to form N-Formimino-L-glutamate. While evidence from many experimental systems indicates that this reaction occurs, existence of the human enzyme is inferred only from high-throughput screening studies (e.g., Yamada et al. 2004).

Preceded by: urocanate + H2O => 4-imidazolone-5-propionate

Followed by: N-formiminoglutamate + tetrahydrofolate => glutamate + 5-formiminotetrahydrofolate

Literature references

Kaneko, M., Yamada, S., Ohnuma, N., Suita, S., Suzuki, Y., Hirata, T. et al. (2004). Expression profiling and differential screening between hepatoblastomas and the corresponding normal livers: identification of high expression of the PLK1 oncogene as a poor-prognostic indicator of hepatoblastomas. *Oncogene, 23*, 5901-11. ↗

Editions

2003-06-24	Authored, Edited	D'Eustachio, P.

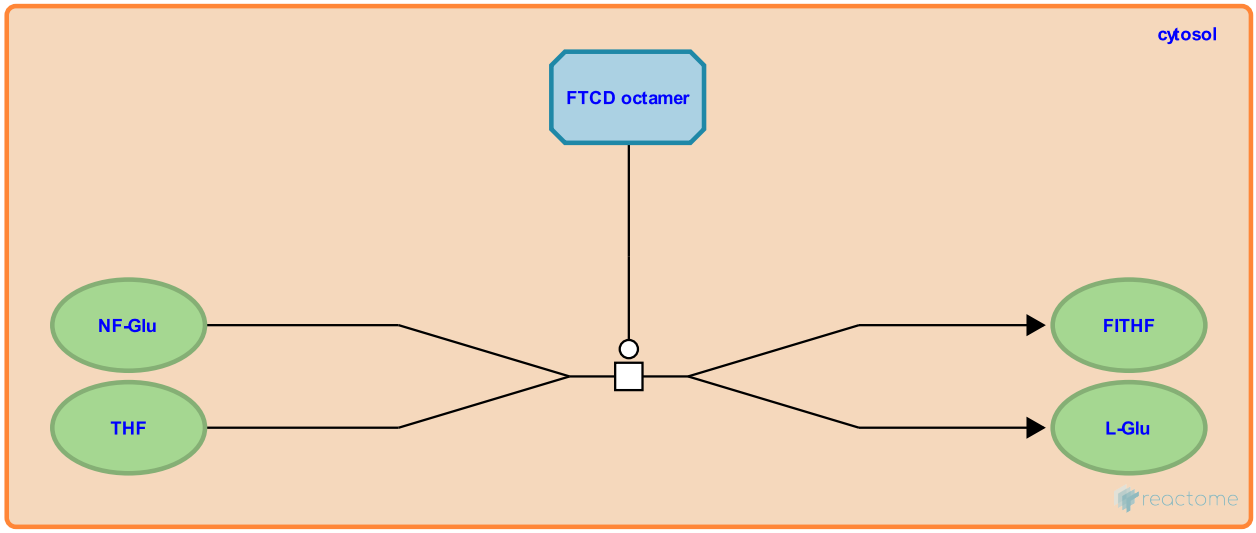
N-formiminoglutamate + tetrahydrofolate => glutamate + 5-formiminotetrahydrofolate ↗

Location: Histidine catabolism

Stable identifier: R-HSA-70920

Type: transition

Compartments: cytosol



Cytosolic formimidoyltransferase-cyclodeaminase (FTCD) catalyzes the reaction of N-formiminoglutamate and tetrahydrofolate to form glutamate and 5-formiminotetrahydrofolate. The gene encoding the human enzyme has beeen cloned and its sequence can encode a protein homologous the the biochemically characterized porcine protein (Solans et al. 2000; Murley et al. 1993). The function of FTCD in vivo was established by identification of missense mutations that reduce enzyme activity in patients with glutamate formiminotransferase deficiency (Hilton et al. 2003). Human FTCD is inferred to be an octamer by homology to the porcine enzyme (Murley et al. 1993).

Preceded by: 4-imidazolone-5-propionate + H2O => N-formiminoglutamate + 2H+

Literature references

Murley, LL., Mejia, NR., MacKenzie, RE. (1993). The nucleotide sequence of porcine formiminotransferase cyclodeaminase. Expression and purification from Escherichia coli. *J Biol Chem, 268*, 22820-4. ↗

Hudson, TJ., Rosenblatt, DS., Hilton, JF., de la Luna, S., Christensen, KE., Watkins, D. et al. (2003). The molecular basis of glutamate formiminotransferase deficiency. *Hum Mutat, 22*, 67-73. ↗

de la Luna, S., Solans, A., Estivill, X. (2000). Cloning and characterization of human FTCD on 21q22.3, a candidate gene for glutamate formiminotransferase deficiency. *Cytogenet Cell Genet, 88*, 43-9. ↗

Editions

2003-06-24	Authored, Edited	D'Eustachio, P.

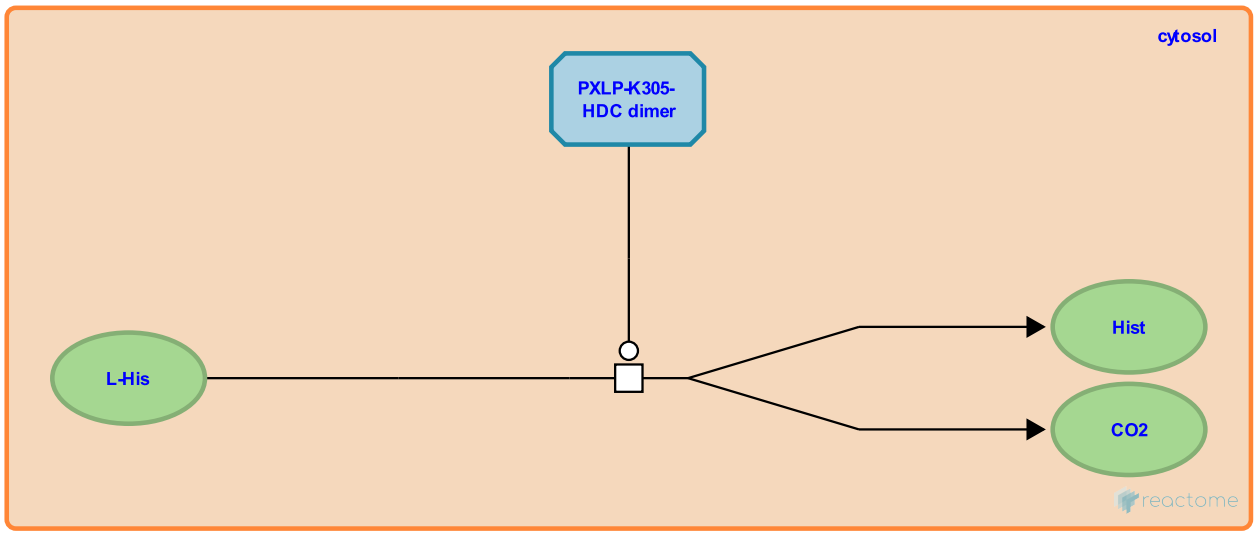
Histidine is decarboxylated to histamine ↗

Location: Histidine catabolism

Stable identifier: R-HSA-977301

Type: transition

Compartments: cytosol



Decarboxylation of L-Histidine happens analogously to other decarboxylations of amino acids. It uses the cofactor pyridoxal phosphate and is catalyzed by histidine decarboxylase (Mamune-Sato et al, 1992).

Followed by: HNMT transfers CH3 group from AdoMet to Hist

Literature references

Shibahara, S., Takishima, T., Maeyama, K., Yamauchi, K., Ohkawara, Y., Mamune-Sato, R. et al. (1992). Functional analysis of alternatively spliced transcripts of the human histidine decarboxylase gene and its expression in human tissues and basophilic leukemia cells. *Eur J Biochem, 209*, 533-9. ↗

Editions

2010-10-15	Authored	Stephan, R.
2010-10-18	Edited	Jassal, B.
2011-10-26	Reviewed	D'Eustachio, P.

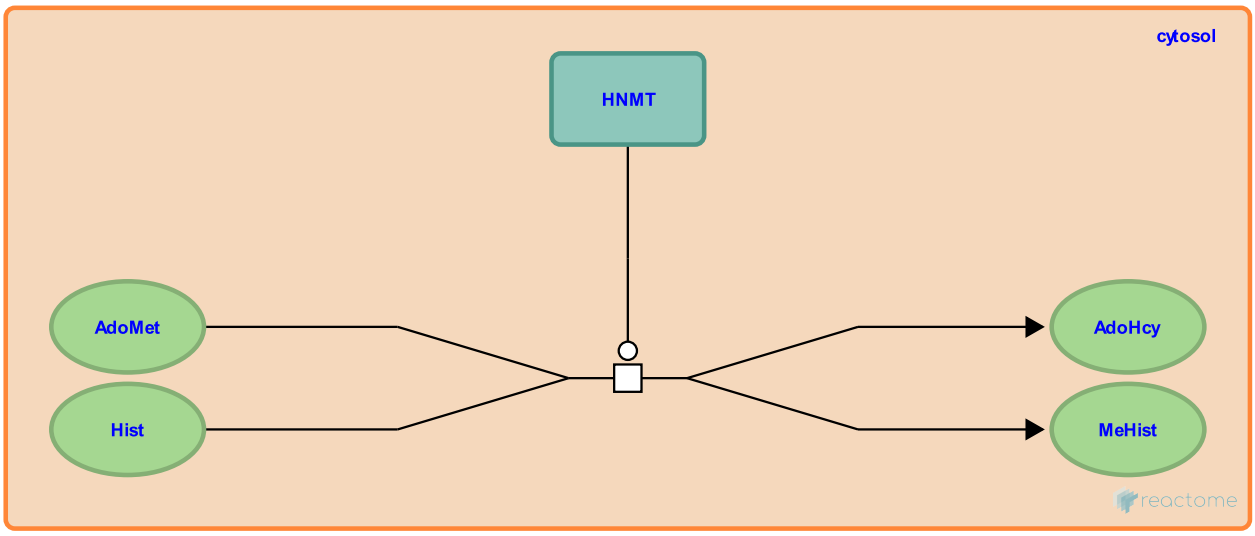
HNMT transfers CH3 group from AdoMet to Hist ↗

Location: Histidine catabolism

Stable identifier: R-HSA-175993

Type: transition

Compartments: cytosol



Histamine (Hist) plays important biological roles in cell-to-cell communication via by binding to histamine receptors and its local action is terminated primarily by methylation. Histamine is inactivated principally by two enzymes: histamine N-methyltransferase (HNMT) and diamine oxidase. HNMT uses the methyl donor AdoMet, methylates Hist to form methylhistamine (MetHist) (Yamauchi et al. 1994). The common polymorphism T105I correlates with high (T) or low (I) activity phenotypes (Horton et al. 2001, Rutherford et al. 2008).

Preceded by: Histidine is decarboxylated to histamine

Literature references

Rutherford, K., Parson, WW., Daggett, V. (2008). The histamine N-methyltransferase T105I polymorphism affects active site structure and dynamics. *Biochemistry, 47*, 893-901. ↗

Zhang, X., Cheng, X., Sawada, K., Horton, JR., Nishibori, M. (2001). Two polymorphic forms of human histamine methyltransferase: structural, thermal, and kinetic comparisons. *Structure, 9*, 837-49. ↗

Takemura, M., Sekizawa, K., Ohtsu, H., Shibahara, S., Yamauchi, K., Nakazawa, H. et al. (1994). Structure and function of human histamine N-methyltransferase: critical enzyme in histamine metabolism in airway. *Am. J. Physiol. , 267*, L342-9. ↗

Editions

2006-02-27	Authored	Jassal, B.
2015-06-18	Edited	Jassal, B.
2015-06-26	Reviewed	D'Eustachio, P.

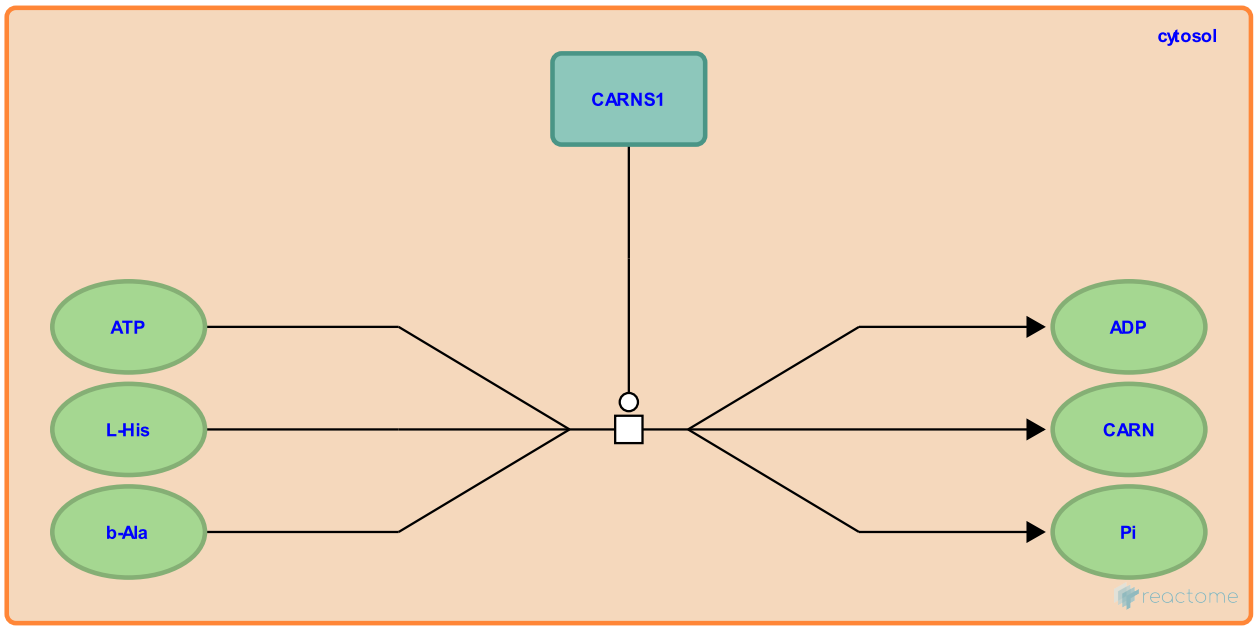
CARNS1 transforms ATP, L-His, b-Ala to CARN ↗

Location: Histidine catabolism

Stable identifier: R-HSA-6786245

Type: transition

Compartments: cytosol



Carnosine (beta-alanyl-L-histidine) and homocarnosine (gamma-aminobutyryl-L-histidine) are abundant dipeptides in skeletal muscle and brain of most vertebrates. Carnosine synthase 1 (CARNS1) transforms ATP, L-histidine (L-His) and beta-alanine (b-Ala) to carnosine (CARN) with much greater efficiency than synthesis of homocarnosine (Drozak et al. 2010).

Followed by: CARNMT1 methylates CARN to Anserine

Literature references

Stroobant, V., Vertommen, D., Veiga-da-Cunha, M., Drozak, J., Van Schaftingen, E. (2010). Molecular identification of carnosine synthase as ATP-grasp domain-containing protein 1 (ATPGD1). *J. Biol. Chem., 285*, 9346-56. ↗

Editions

2015-07-06	Authored, Edited	Jassal, B.
2015-09-14	Reviewed	D'Eustachio, P.

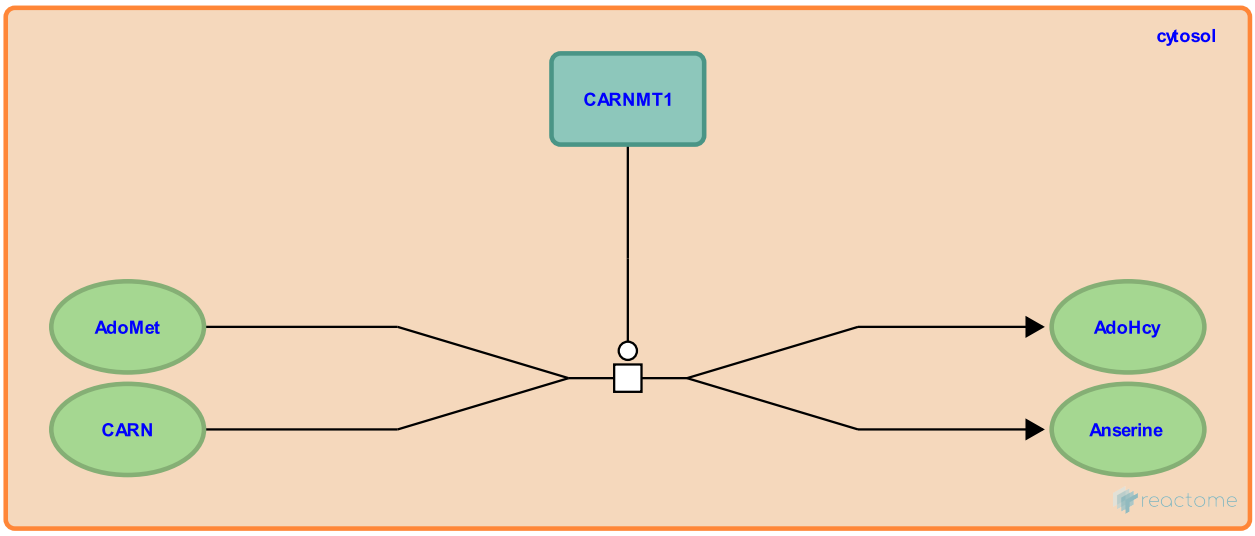
CARNMT1 methylates CARN to Anserine ↗

Location: Histidine catabolism

Stable identifier: R-HSA-8876789

Type: transition

Compartments: cytosol



Anserine (Beta-alanyl-N(Pi)-methyl-L-histidine) is a methylated derivative of carnosine (Beta-alanyl-L-histidine) and an abundant constituent of vertebrate skeletal muscles (Boldyrev et al. 2013). It has been suggested to serve as a proton buffer and radical scavenger. The formation of anserine is catalyzed by carnosine N-methyltransferase (CARNMT1), which transfers a methyl group from S-adenosyl-L-methionine (SAM) onto the nitrogen atom (Pi) of L-histidine residue in carnosine (Drozak et al. 2015). While CARNMT1 produces anserine in mammals, a similar reaction is catalysed by a different enzyme (carnosine N-methyltransferase 2) in birds and reptiles (Drozak et al. 2013).

Preceded by: CARNS1 transforms ATP, L-His, b-Ala to CARN

Literature references

Piecuch, M., Kozlowski, P., de Heer, E., Chrobok, L., Poleszak, O., Drozak, J. et al. (2015). UPF0586 Protein C9orf41 Homolog Is Anserine-producing Methyltransferase. *J. Biol. Chem., 290*, 17190-205. ↗

Editions

2016-06-16	Authored	Jupe, S.
2016-07-05	Edited	Jupe, S.
2016-07-12	Reviewed	Drozak, J.

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