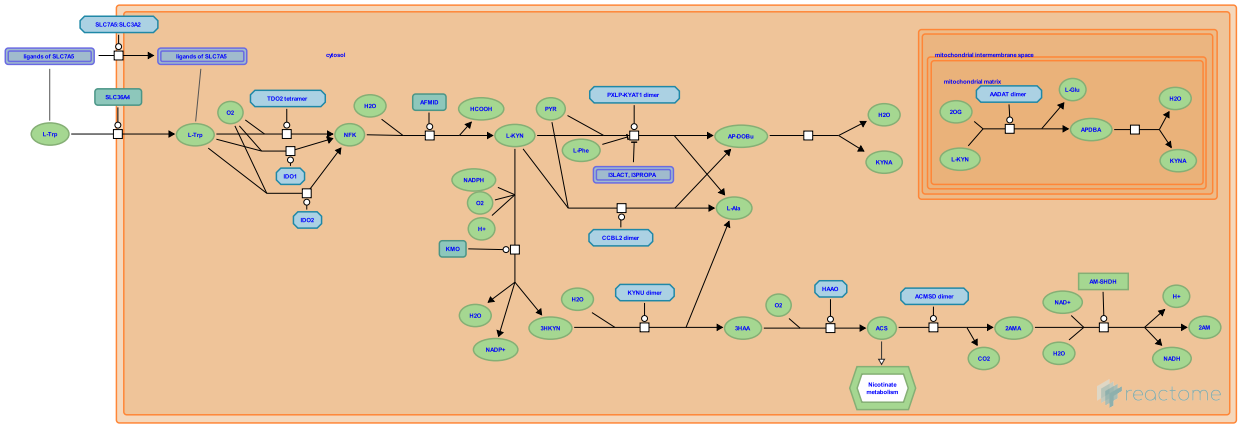
# Tryptophan catabolism

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26/04/2024

# 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. ↗

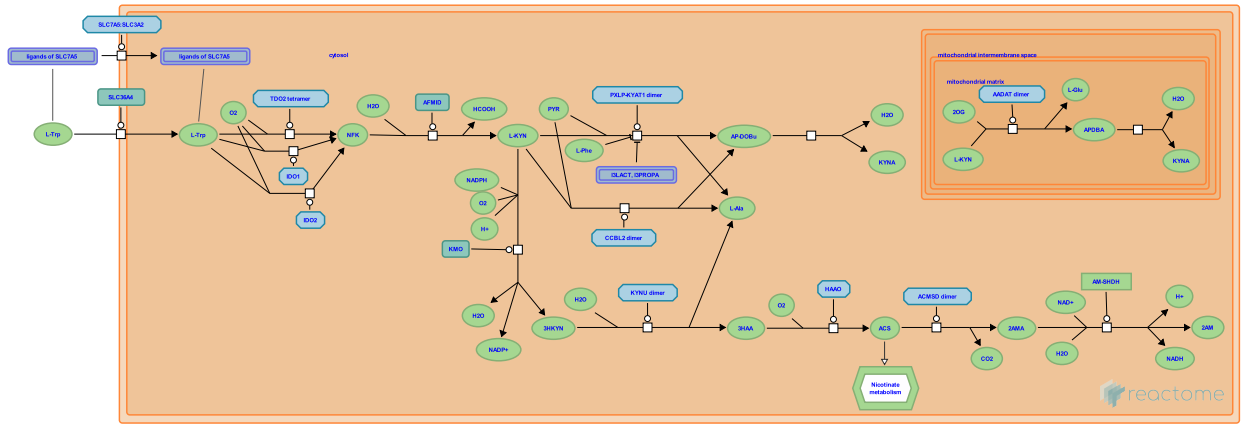
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

## Tryptophan catabolism ↗

**Stable identifier:** R-HSA-71240

**Compartments:** cytosol




Tryptophan is catabolized in seven steps to yield aminomuconate. Intermediates in this process are also used in the synthesis of serotonin and kynurenine (Peters 1991).

## Literature references


Peters, JC. (1991). Tryptophan nutrition and metabolism: an overview. *Adv Exp Med Biol, 294*, 345-58. ↗


## Editions

| | | |
|---|---|---|
| 2005-07-20 | Authored, Edited | D'Eustachio, P. |

## SLC7A5:SLC3A2 transports neutral amino acids from extracellular region to cytosol

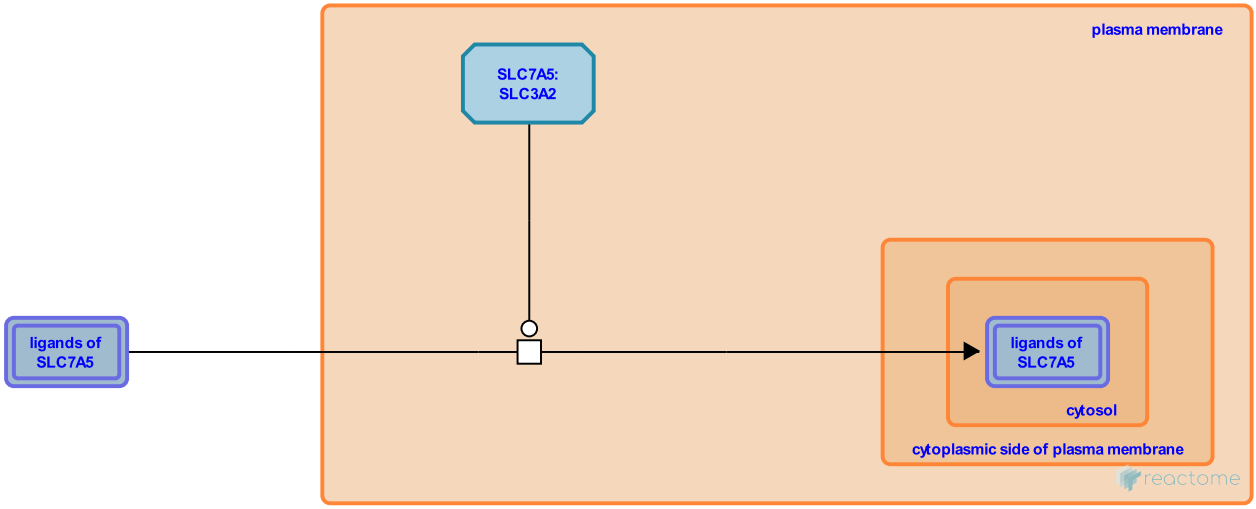
↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-352232

**Type:** transition

**Compartments:** plasma membrane




SLC7A5, complexed with SLC3A2 in the plasma membrane, mediates the uptake of neutral amino acids. The process is Na+-independent and not coupled to H+ transport. As measured by Northern blotting SLC7A5 is widely expressed in the body. In situ hybridization studies indicate that the gene product is widely expressed in the body but not in the kidney (Pineda et al. 1999; Prasad et al. 1999).

**Followed by:** IDO2 dioxygenates L-Trp to NFK, TDO tetramer dioxygenates L-Trp to NFK, IDO1 dioxygenates L-Trp to NFK

## Literature references


Palacin, M., Torrents, D., Zorzano, A., Lloberas, J., López, C., Fernández, E. et al. (1999). Identification of a membrane protein, LAT-2, that Co-expresses with 4F2 heavy chain, an L-type amino acid transport activity with broad specificity for small and large zwitterionic amino acids. *J Biol Chem, 274*, 19738-44. ↗

Leibach, FH., Ganapathy, V., Huang, W., Rajan, DP., Prasad, PD., Kekuda, R. et al. (1999). Human LAT1, a subunit of system L amino acid transporter: molecular cloning and transport function. *Biochem Biophys Res Commun, 255*, 283-8. ↗


## Editions

| | | |
|---|---|---|
| 2008-06-03 | Authored, Edited | D'Eustachio, P. |
| 2008-06-03 | Reviewed | Jassal, B. |

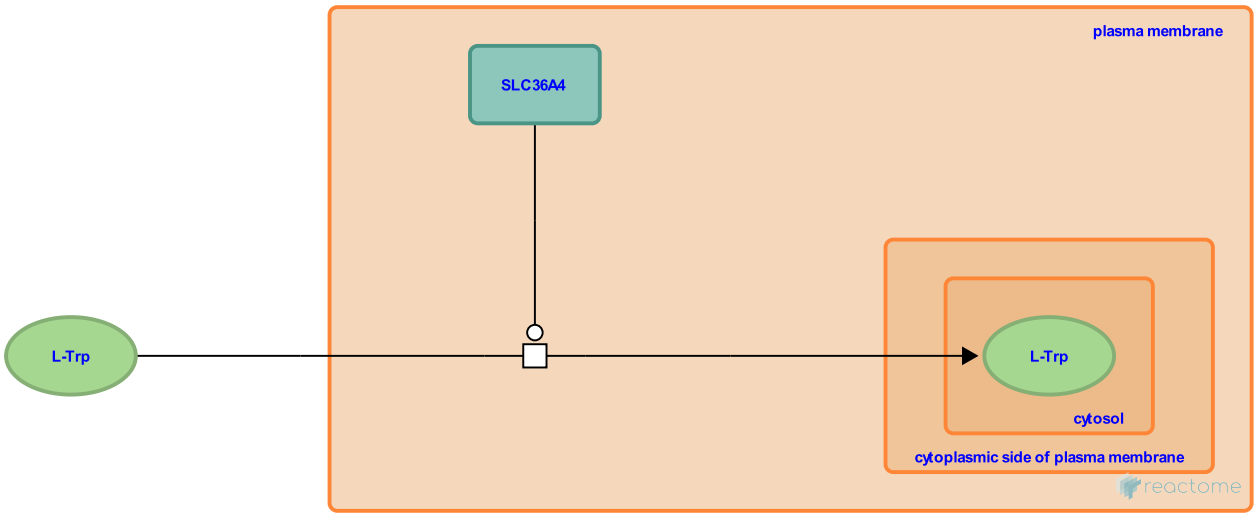
## SLC36A4 transports L-Trp from extracellular region to cytosol ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-8870352

**Type:** transition

**Compartments:** plasma membrane, extracellular region, cytosol




Plasma membrane-associated SLC36A4 (solute carrier family 36 member 4, also known as PAT4 - Proton-coupled amino acid transporter 4) mediates the uptake of extracellular L-Trp (L-tryptophan) (Pillai & Meredith 2011).

**Followed by:** IDO2 dioxygenates L-Trp to NFK, TDO tetramer dioxygenates L-Trp to NFK, IDO1 dioxygenates L-Trp to NFK

## Literature references

Pillai, SM., Meredith, D. (2011). SLC36A4 (hPAT4) is a high affinity amino acid transporter when expressed in Xenopus laevis oocytes. *J. Biol. Chem., 286*, 2455-60. ↗

## Editions

| | | |
|---|---|---|
| 2016-05-09 | Authored, Edited | D'Eustachio, P. |
| 2016-12-23 | Reviewed | Jassal, B. |

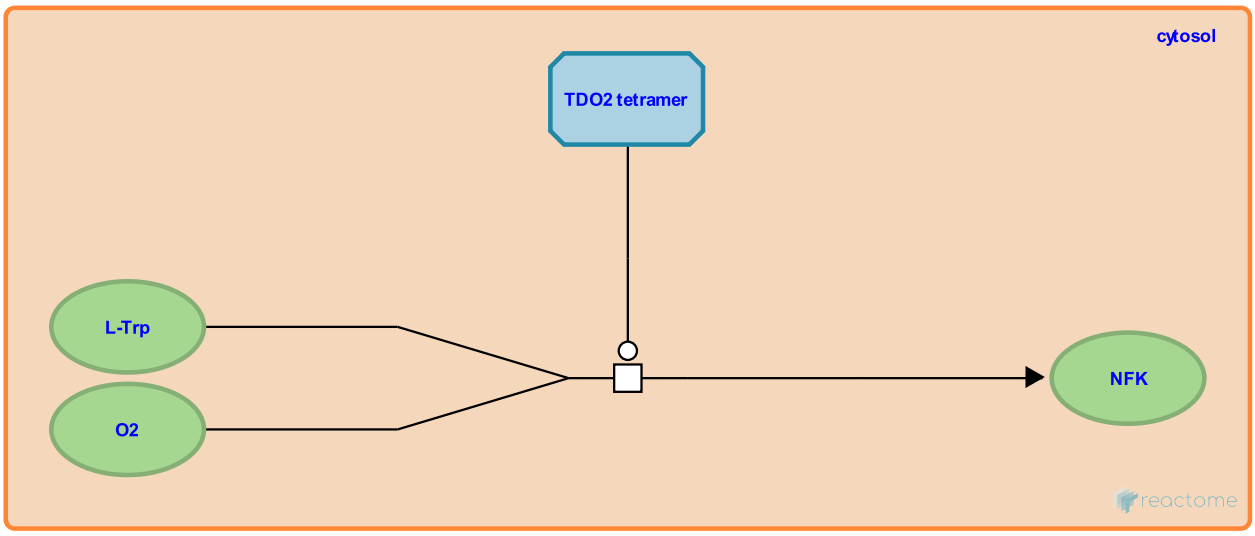
## TDO tetramer dioxygenates L-Trp to NFK ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-71188

**Type:** transition

**Compartments:** cytosol




Cytosolic tryptophan 2,3-dioxygenase (TDO) tetramer catalyzes the conversion of L-tryptophan and oxygen to formylkynurenine. The structure and catalytic properties of the human enzyme are inferred from the close similarity of its predicted amino acid sequence (Comings et al. 1995) to that of the well-studied rat enzyme (Dick et al. 2001). In the body, TDO is found predominantly in the liver and is induced by metabolites such as tryptophan and histidine, and by glucocorticoids. These properties, together with TDO's narrow substrate specificity, are consistent with the hypothesis that the enzyme functions functions primarily in tryptophan catabolism and NAD biosynthesis (Taylor and Feng 1991).

**Preceded by:** SLC7A5:SLC3A2 transports neutral amino acids from extracellular region to cytosol, SLC36A4 transports L-Trp from extracellular region to cytosol

**Followed by:** AFMID hydrolyses NFK to L-KYN

## Literature references

Comings, DE., Forest, GL., Dietz, G., Muhleman, D., Sherman, M. (1995). Sequence of human tryptophan 2,3-dioxygenase (TDO2): presence of a glucocorticoid response-like element composed of a GTT repeat and an intronic CCCCT repeat. *Genomics, 29*, 390-396. ↗

## Editions

| | | |
|---|---|---|
| 2005-07-20 | Authored, Edited | D'Eustachio, P. |

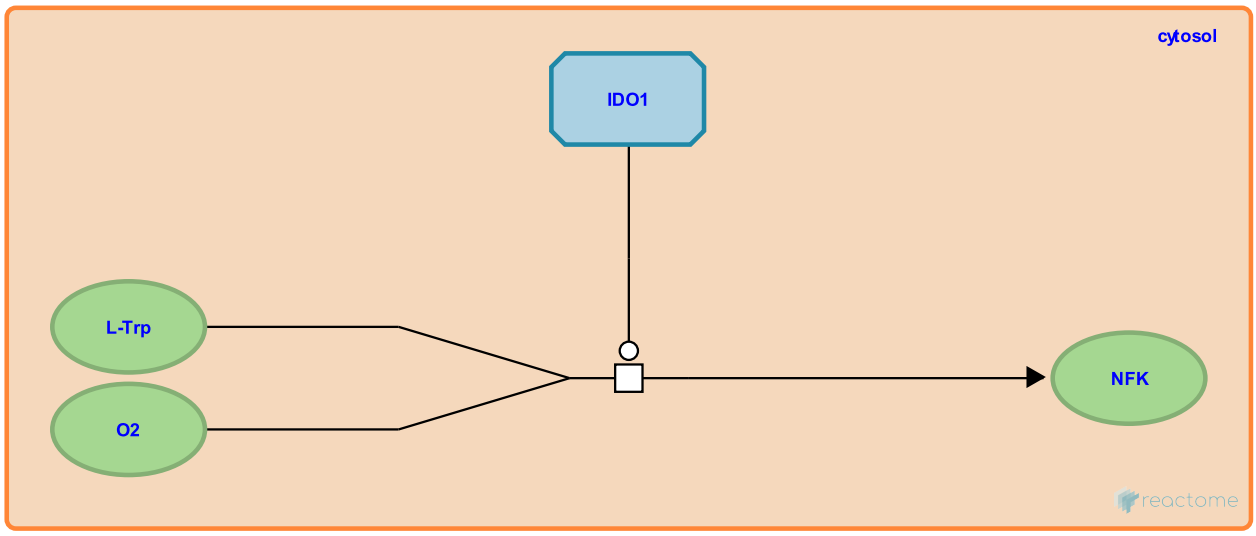
## IDO1 dioxygenates L-Trp to NFK ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-198563

**Type:** transition

**Compartments:** cytosol




Cytosolic indoleamine 2,3-dioxygenase (IDO) catalyzes the conversion of L-tryptophan and oxygen to formylkynurenine. The structure and catalytic properties of the human enzyme have been analyzed directly (Sugimoto et al. 2006); the subcellular location and monomeric state of the active form of the enzyme are inferred from the properties of its rabbit ortholog (Shimizu et al. 1976). In the body, IDO is ubiquitously expressed and is induced by interferon. These properties, together with IDO's broad substrate specificity, are consistent with the hypothesis that the enzyme functions functions in anti bacterial and inflammatory processes (Taylor and Feng 1991).

**Preceded by:** SLC7A5:SLC3A2 transports neutral amino acids from extracellular region to cytosol, SLC36A4 transports L-Trp from extracellular region to cytosol

**Followed by:** AFMID hydrolyses NFK to L-KYN

## Literature references

Shiro, Y., Hino, T., Yoshida, T., Otsuki, T., Sugimoto, H., Oda, SI. (2006). Crystal structure of human indoleamine 2,3-dioxygenase: catalytic mechanism of O2 incorporation by a heme-containing dioxygenase. *Proc Natl Acad Sci USA , 103,* 2611-2616. ↗

## Editions

| | | |
|---|---|---|
| 2007-06-22 | Authored, Edited | D'Eustachio, P. |

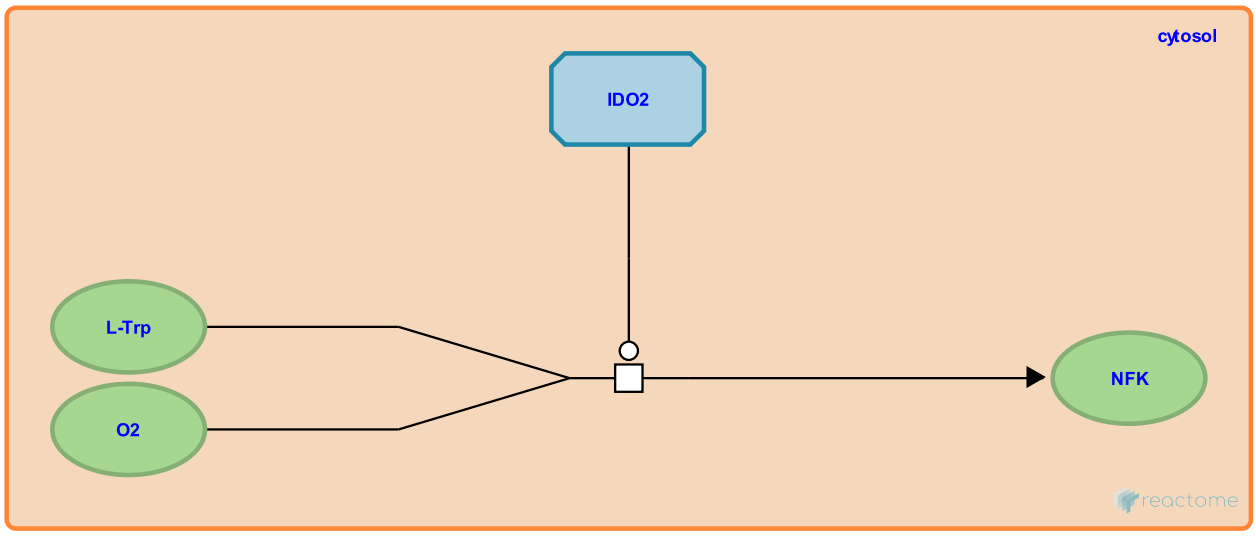
## IDO2 dioxygenates L-Trp to NFK ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-888614

**Type:** transition

**Compartments:** cytosol




Cytosolic indoleamine 2,3-dioxygenase 2 (IDO2) catalyzes the conversion of L-tryptophan and oxygen to formylkynurenine. The catalytic properties of the human enzyme have been analyzed directly; the subcellular location and monomeric state of the active form of the enzyme are inferred from the properties of its rabbit ortholog. In the body, IDO2 mRNA can be detected in a variety of cells, including dendritic cells, consistent with a normal role in immune function and a pathological one in tumor progression. Two IDO2 variants common in human populations encode enzymatically inactive protiens, suggesting that absence of IDO2 activity may be common in humans (Metz et al. 2007).

**Preceded by:** SLC7A5:SLC3A2 transports neutral amino acids from extracellular region to cytosol, SLC36A4 transports L-Trp from extracellular region to cytosol

## Literature references

Prendergast, GC., Kamasani, U., Muller, AJ., DuHadaway, JB., Metz, R., Laury-Kleintop, L. (2007). Novel tryptophan catabolic enzyme IDO2 is the preferred biochemical target of the antitumor indoleamine 2,3-dioxygenase inhibitory compound D-1-methyl-tryptophan. *Cancer Res, 67*, 7082-7. ↗

## Editions

| | | |
|---|---|---|
| 2010-07-02 | Authored, Edited | D'Eustachio, P. |

## AFMID hydrolyses NFK to L-KYN ↗

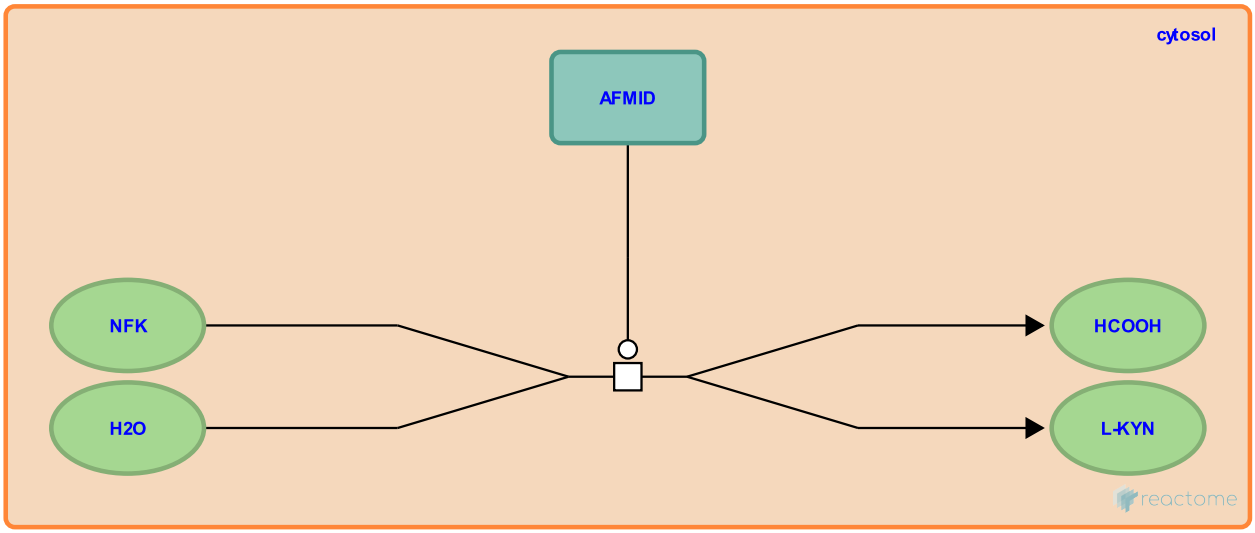
**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-71189

**Type:** transition

**Compartments:** cytosol

**Inferred from:** N-formylkynurenine + H2O => kynurenine + formate [mouse] (Mus musculus)




Cytosolic arylformamidase (AFMID) catalyzes the hydrolysis of formylkynurenine to yield formate and L-kynurenine. Human AFMID has been identified only as an open reading frame; its activity is inferred from that of its well-characterized mouse homologue (Pabarcus and Casida 2002).

**Preceded by:** TDO tetramer dioxygenates L-Trp to NFK, IDO1 dioxygenates L-Trp to NFK

**Followed by:** PXLP-KYAT1 dimer transaminates L-KYN to AP-DOBu, kynurenine + pyruvate => 4-(2-aminophenyl)-2,4-dioxobutanoic acid + alanine [CCBL2], kynurenine + O2 + NADPH + H+ => 3-hydroxykynurenine + NADP+ + H2O

## Literature references

Casida, JE., Pabarcus, MK. (2002). Kynurenine formamidase: determination of primary structure and modeling-based prediction of tertiary structure and catalytic triad. *Biochim Biophys Acta, 1596*, 201-11. ↗

## Editions

| | | |
|---|---|---|
| 2005-07-20 | Authored, Edited | D'Eustachio, P. |

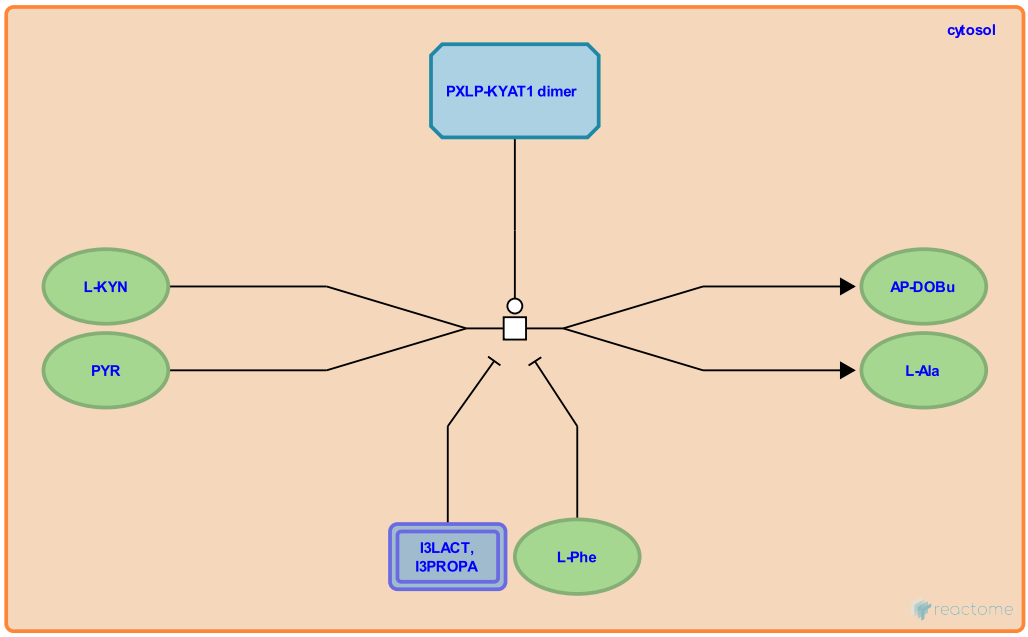
## PXLP-KYAT1 dimer transaminates L-KYN to AP-DOBu ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-893596

**Type:** transition

**Compartments:** cytosol




Kynurenine-oxoglutarate transaminase 1 (KYAT1, aka CCBL1, KAT1) catalyzes the reaction of kynurenine (L-KYN) and pyruvate (PYR) to form 4-(2-aminophenyl)-2,4-dioxobutanoate (AP-DOBu) and alanine (L-Ala). The active form of KYAT1 is a homodimer with one molecule of pyridoxal phosphate (PXLP) bound to each monomer (Baran et al. 1994, Han et al. 2009, Rossi et al. 2004). The enzyme's cytosolic localization is inferred from recombinant protein overexpressed in transfected cells (Perry et al. 1995). The pH optimum observed for KYAT1 in vitro is 9.5 - 10.0, so its role in kynurenine metabolism in vivo is not clear (Baran et al. 1994).

Biochemical studies of KYAT1 activity in vitro (e.g. Baren et al. 1994) invariably measure kynurenic acid as the reaction product, not AP-DOBu, the product to be expected from transamination of kynurenine. The condensation of AP-DOBu and elimination of a water molecule to form kynurenic acid has not been demonstrated directly. As noted by Miller et al. (1953) discussing their characterization of a bacterial form of the enzyme, "The keto acid assumed to be formed prior to ring closure in the conversion of kynurenine to kynurenic acid has not yet been detected. In principle, such detection should be possible, since it is sufficiently stable to have been synthesized. It also remains to be established whether ring closure is spontaneous, enzymatic, or both. The formation of kynurenic acid from L-kynurenine by the L-amino acid oxidase of Neurospora suggests, however, that ring closure can be spontaneous, unless the somewhat improbable assumption is made that Neurospora filtrate contained the ring-closing enzyme."

The alpha keto acids indole-3-propionic acid (I3PROPA) and indole-3-lactic acid (I3LACT) are potent inhibitors of KYAT1 (Han et al. 2009). Phenylalanine is an effective competitive inhibitor of kinurenine aminotransferase 1 (Han et al. 2004).

**Preceded by:** AFMID hydrolyses NFK to L-KYN

**Followed by:** 4-(2-aminophenyl)-2,4-dioxobutanoate => kynurenic acid + H2O [cytosolic]

## Literature references

Baran, H., Kido, R., Okuno, E., Schwarcz, R. (1994). Purification and characterization of kynurenine aminotransferase I from human brain. *J Neurochem, 62,* 730-8. ↗

Li, J., Li, J., Rizzi, M., Han, Q., Rossi, F. (2004). Crystal structure of human kynurenine aminotransferase I. *J Biol Chem, 279,* 50214-20. ↗

Scholfield, C., Perry, S., King, L., Harries, H., Goldfarb, P., Gibson, G. et al. (1995). Molecular cloning and expression of a cDNA for human kidney cysteine conjugate beta-lyase. *FEBS Lett, 360*, 277-80. ↗

Cai, T., Robinson, H., Li, J., Tagle, DA., Han, Q. (2009). Structural insight into the inhibition of human kynurenine aminotransferase I/glutamine transaminase K. *J Med Chem, 52*, 2786-93. ↗

Miller, IL., Adelberg, EA., Tsuchida, M. (1953). The transamination of kynurenine. *J Biol Chem, 203*, 205-11. ↗

## Editions

| | | |
|---|---|---|
| 2010-07-02 | Authored, Edited | D'Eustachio, P. |
| 2010-11-09 | Reviewed | Jassal, B. |

## kynurenine + pyruvate => 4-(2-aminophenyl)-2,4-dioxobutanoic acid + alanine [CCBL2]

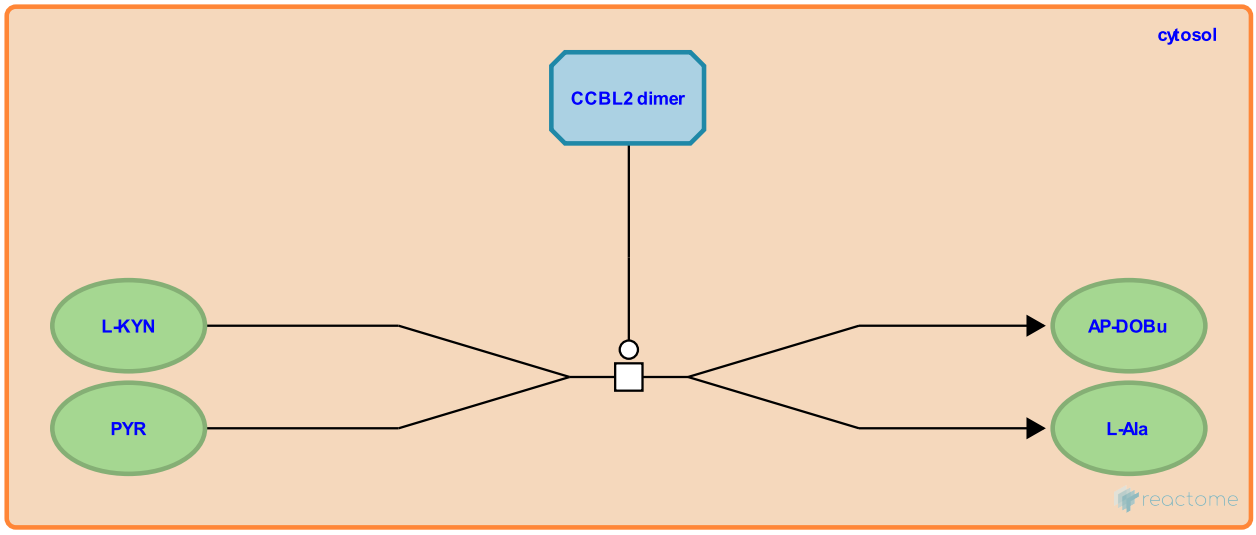
**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-901097

**Type:** transition

**Compartments:** cytosol

**Inferred from:** PXLP-KYAT1 dimer transaminates L-KYN to AP-DOBu (Homo sapiens)




CCBL2 (KAT 3) catalyzes the reaction of kynurenine and pyruvate to form 4-(2-aminophenyl)-2,4-dioxobutanoate and alanine. CCBL2 is known only as the predicted protein product of a cloned human gene closely homologous to CCBL1 (Yu et al. 2006) and all of the structural and catalytic properties annotated here are inferred from those of CCBL1.

**Preceded by:** AFMID hydrolyses NFK to L-KYN

**Followed by:** 4-(2-aminophenyl)-2,4-dioxobutanoate => kynurenic acid + H2O [cytosolic]

### Literature references

Cai, T., Zhang, L., Tagle, DA., Yu, P., Li, Z. (2006). Characterization of kynurenine aminotransferase III, a novel member of a phylogenetically conserved KAT family. *Gene, 365*, 111-8.

### Editions

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| 2010-11-09 | Reviewed | Jassal, B. |

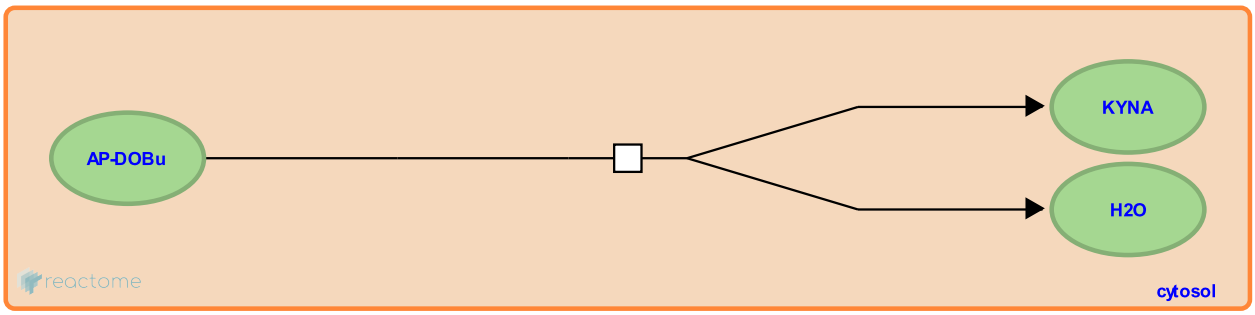
## 4-(2-aminophenyl)-2,4-dioxobutanoate => kynurenic acid + H2O [cytosolic] ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-893609

**Type:** transition

**Compartments:** cytosol




Cytosolic 4-(2-aminophenyl)-2,4-dioxobutanoate is thought to spontaneously condense with the elimination of water to form kynurenic acid (kynurenate).

Biochemical studies of kynurenine transamination in vitro invariably measure kynurenic acid, not 4-(2-aminophenyl)-2,4-dioxobutanoate, the expected transamination product. The reaction annotated here has not been demonstrated directly. As noted by Miller et al. (1953), "The keto acid assumed to be formed prior to ring closure in the conversion of kynurenine to kynurenic acid has not yet been detected. In principle, such detection should be possible, since it is sufficiently stable to have been synthesized. It also remains to be established whether ring closure is spontaneous, enzymatic, or both. The formation of kynurenic acid from L-kynurenine by the L-amino acid oxidase of Neurospora suggests, however, that ring closure can be spontaneous, unless the somewhat improbable assumption is made that Neurospora filtrate contained the ring-closing enzyme."

**Preceded by:** kynurenine + pyruvate => 4-(2-aminophenyl)-2,4-dioxobutanoic acid + alanine [CCBL2], PXLP-KYAT1 dimer transaminates L-KYN to AP-DOBu

### Literature references

Miller, IL., Adelberg, EA., Tsuchida, M. (1953). The transamination of kynurenine. *J Biol Chem, 203*, 205-11. ↗

### Editions

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| 2010-07-02 | Authored, Edited | D'Eustachio, P. |
| 2010-11-09 | Reviewed | Jassal, B. |

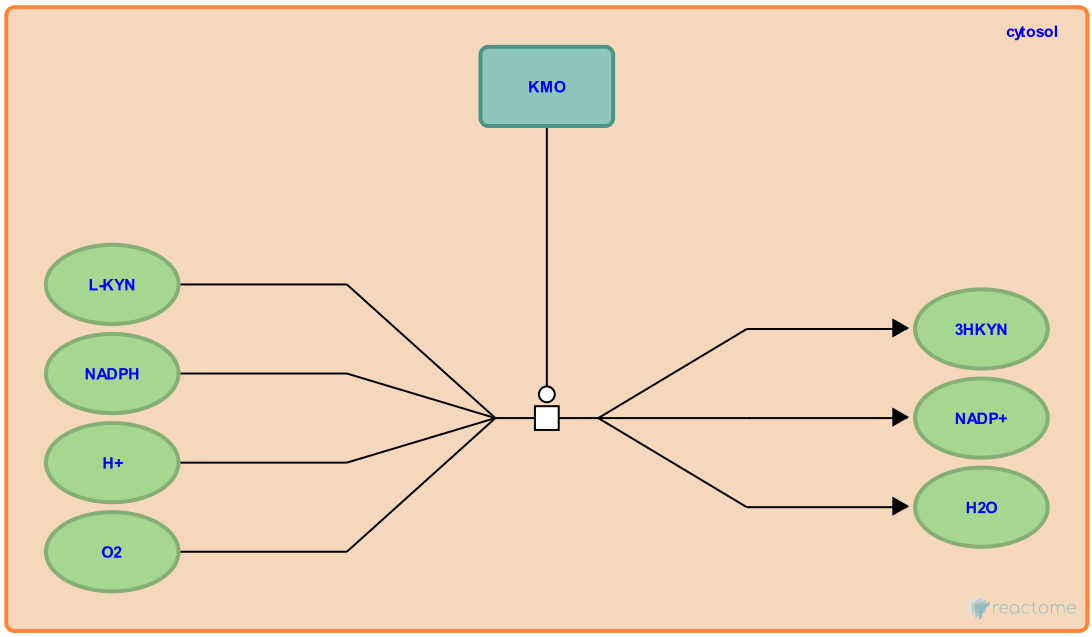
## kynurenine + O2 + NADPH + H+ => 3-hydroxykynurenine + NADP+ + H2O ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-71200

**Type:** transition

**Compartments:** cytosol




Cytosolic kynurenine 3-monooxygenase catalyzes the reaction of L-kynurenine, NADPH + H+, and O2 to form 3-hydroxy-L-kynurenine, NADP+, and H2O.

**Preceded by:** AFMID hydrolyses NFK to L-KYN

**Followed by:** 3-hydroxykynurenine + H2O => 3-hydroxyanthranilate + alanine

## Literature references

Covini, N., Avanzi, N., Cozzi, L., Magagnin, S., Breton, J., Isacchi, A. et al. (2000). Functional characterization and mechanism of action of recombinant human kynurenine 3-hydroxylase. *Eur J Biochem, 267,* 1092-1099. ↗

## Editions

| | | |
|---|---|---|
| 2005-07-20 | Authored, Edited | D'Eustachio, P. |

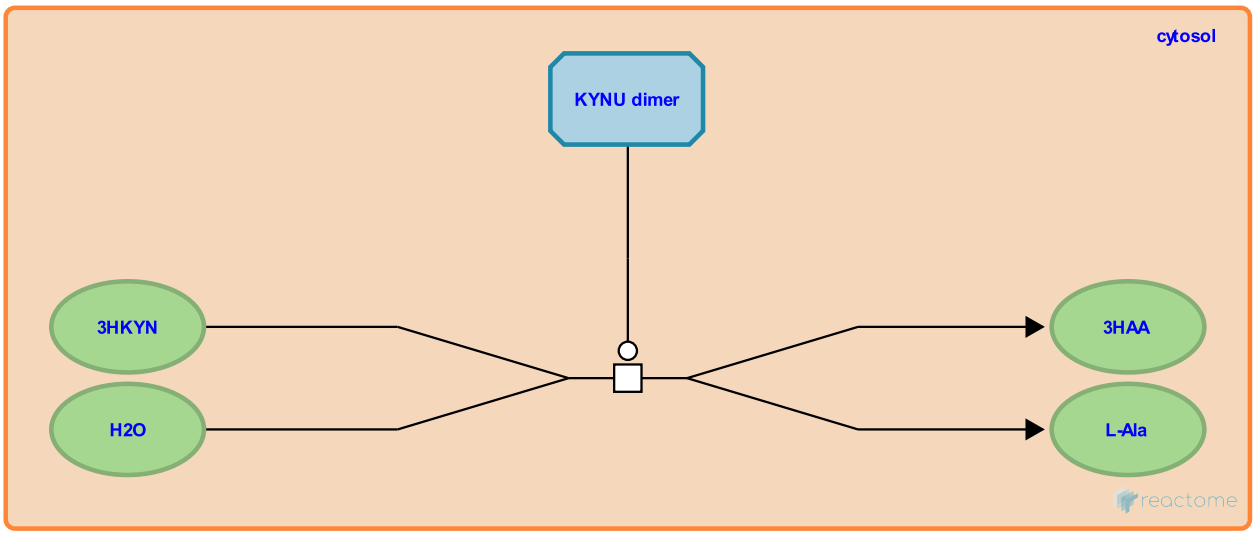
## 3-hydroxykynurenine + H2O => 3-hydroxyanthranilate + alanine ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-71217

**Type:** transition

**Compartments:** cytosol




Cytosolic kynureninase catalyzes the hydrolysis of 3-hydroxy-L-kynurenine to form L-alanine and 3-hydroxyanthranilate.

**Preceded by:** kynurenine + O2 + NADPH + H+ => 3-hydroxykynurenine + NADP+ + H2O

**Followed by:** 3-hydroxyanthranilate + O2 => 2-amino-3-carboxymuconate semialdehyde

## Literature references

Gatti, S., Benatti, L., Speciale, C., Mostardini, M., Avanzi, N., Cozzi, L. et al. (1997). Cloning and recombinant expression of rat and human kynureninase. *FEBS Lett, 408*, 5-10. ↗

## Editions

| | | |
|---|---|---|
| 2005-07-20 | Authored, Edited | D'Eustachio, P. |

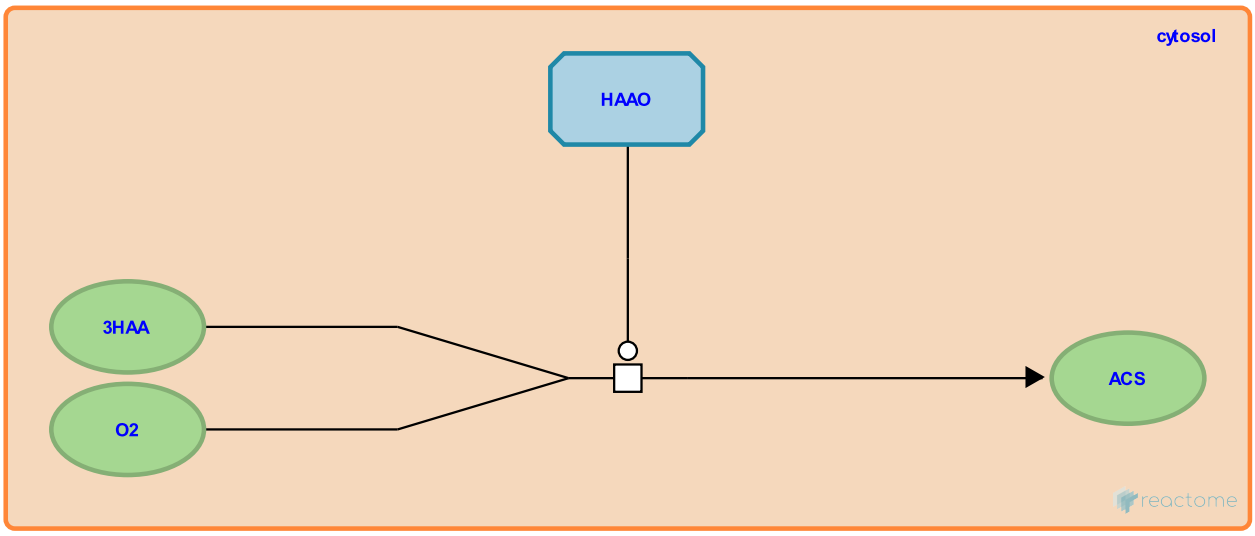
## 3-hydroxyanthranilate + O2 => 2-amino-3-carboxymuconate semialdehyde ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-71218

**Type:** transition

**Compartments:** cytosol




Cytosolic 3-hydroxyanthranilate oxygenase catalyzes the reaction of 3-hydroxyanthranilate and O2 to form 2-amino-3-carboxymuconate semialdehyde.

**Preceded by:** 3-hydroxykynurenine + H2O => 3-hydroxyanthranilate + alanine

**Followed by:** 2-amino-3-carboxymuconate semialdehyde => 2-aminomuconate semialdehyde + CO2

## Literature references

Lahm, HW., Cesura, AM., Kiefer, V., Schwarcz, R., Da Prada, M., Köhler, C. et al. (1994). Molecular cloning and functional expression of human 3-hydroxyanthranilic-acid dioxygenase. *J Biol Chem, 269*, 13792-7. ↗

## Editions

| | | |
|---|---|---|
| 2005-07-20 | Authored, Edited | D'Eustachio, P. |

## 2-amino-3-carboxymuconate semialdehyde => 2-aminomuconate semialdehyde + CO2 ↗

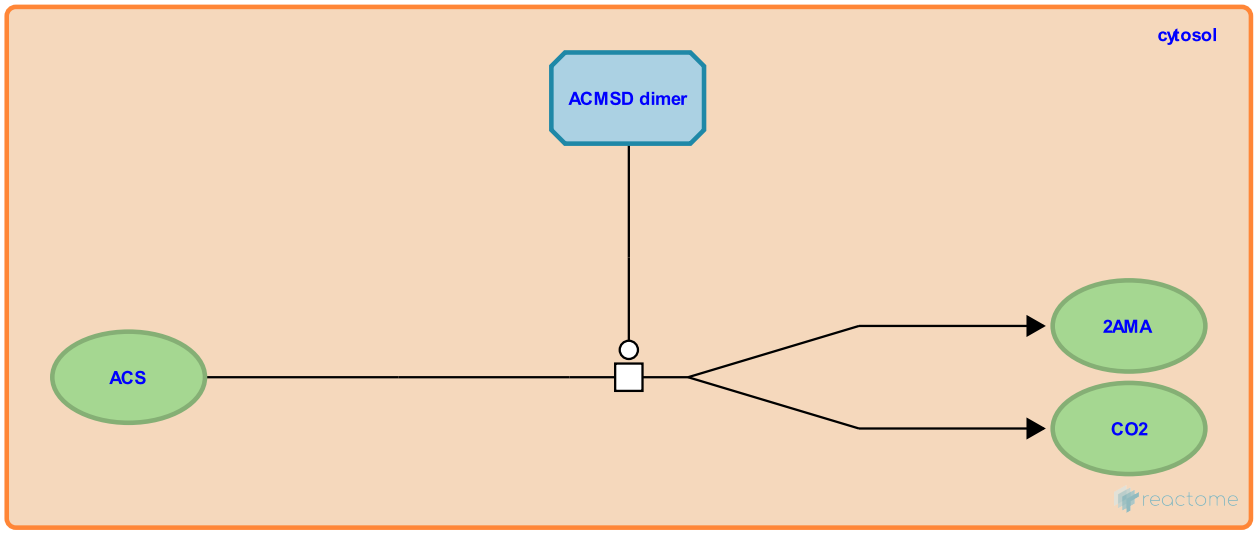
**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-71223

**Type:** transition

**Compartments:** cytosol

**Inferred from:** 2-amino-3-carboxymuconate semialdehyde => 2-aminomuconate semialdehyde + CO2 [rat] (Rattus norvegicus)




At the beginning of this reaction, 1 molecule of '2-Amino-3-carboxymuconate semialdehyde' is present. At the end of this reaction, 1 molecule of 'CO2', and 1 molecule of '2-Aminomuconate semialdehyde' are present.

This reaction takes place in the 'cytoplasm' and is mediated by the 'carboxy-lyase activity' of '2-amino-3-carboxymuconate-6-semialdehyde decarboxylase homodimer'.

**Preceded by:** 3-hydroxyanthranilate + O2 => 2-amino-3-carboxymuconate semialdehyde

**Followed by:** 2-aminomuconate semialdehyde + NAD+ + H2O => aminomuconate + NADH + H+

### Literature references

Fukuoka, S., Shibata, K., Tanabe, A., Egashira, Y., Yanagihara, K., Ishiguro, K. et al. (2002). Identification and expression of a cDNA encoding human alpha-amino-beta-carboxymuconate-epsilon-semialdehyde decarboxylase (ACMSD). A key enzyme for the tryptophan-niacine pathway and "quinolinate hypothesis". *J Biol Chem, 277*, 35162-7. ↗

### Editions

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|---|---|---|
| 2005-07-20 | Authored, Edited | D'Eustachio, P. |

## 2-aminomuconate semialdehyde + NAD+ + H2O => aminomuconate + NADH + H+ ↗

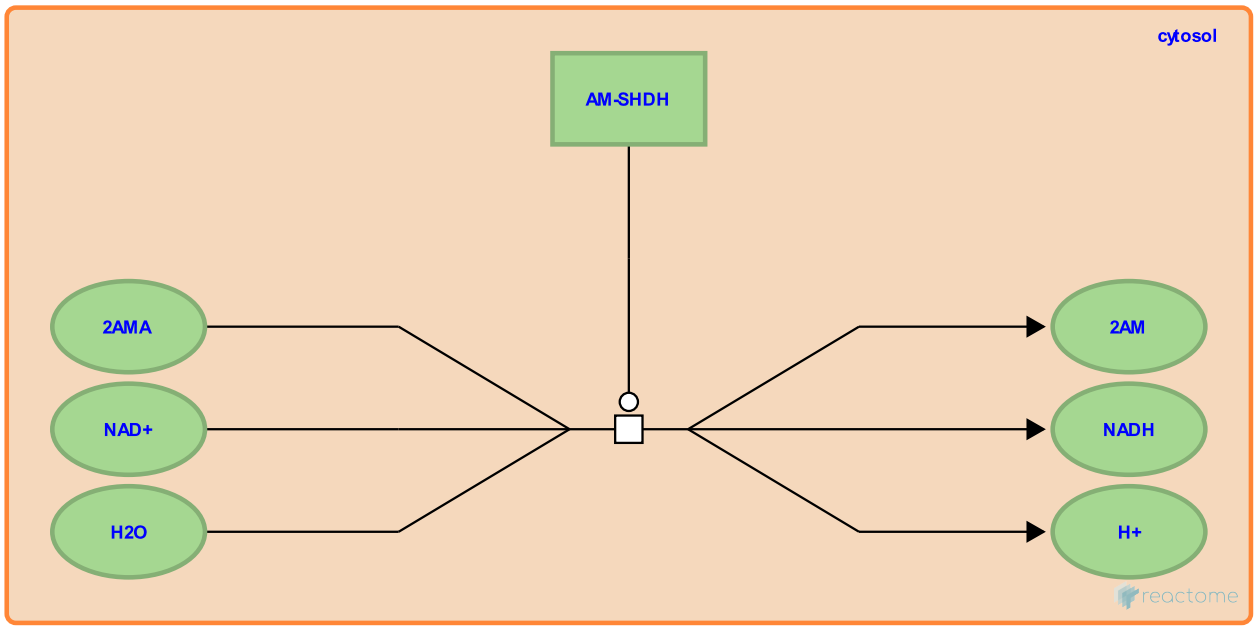
**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-71239

**Type:** transition

**Compartments:** cytosol

**Inferred from:** 2-aminomuconate semialdehyde + NAD+ + H2O => aminomuconate + NADH + H+ (Felis catus)




This reaction has been characterized in vitro using enzyme partially purified from cat liver (Ichiyama et al. 1965). The human event is inferred from the cat one. Neither the cat nor the human protein has been fully purified or sequenced.

**Preceded by:** 2-amino-3-carboxymuconate semialdehyde => 2-aminomuconate semialdehyde + CO2

## Literature references

Nishizuka, Y., Honjo, T., Hayaishi, O., Ichiyama, A., Kawai, H., Senoh, S. et al. (1965). Studies on the metabolism of the benzene ring of tryptophan in mammalian tissues. II. Enzymatic formation of alpha-muconic acid from 2-hydroxyanthranilic acid. *J Biol Chem, 240*, 740-9. ↗

## Editions

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|---|---|---|
| 2005-07-20 | Authored, Edited | D'Eustachio, P. |

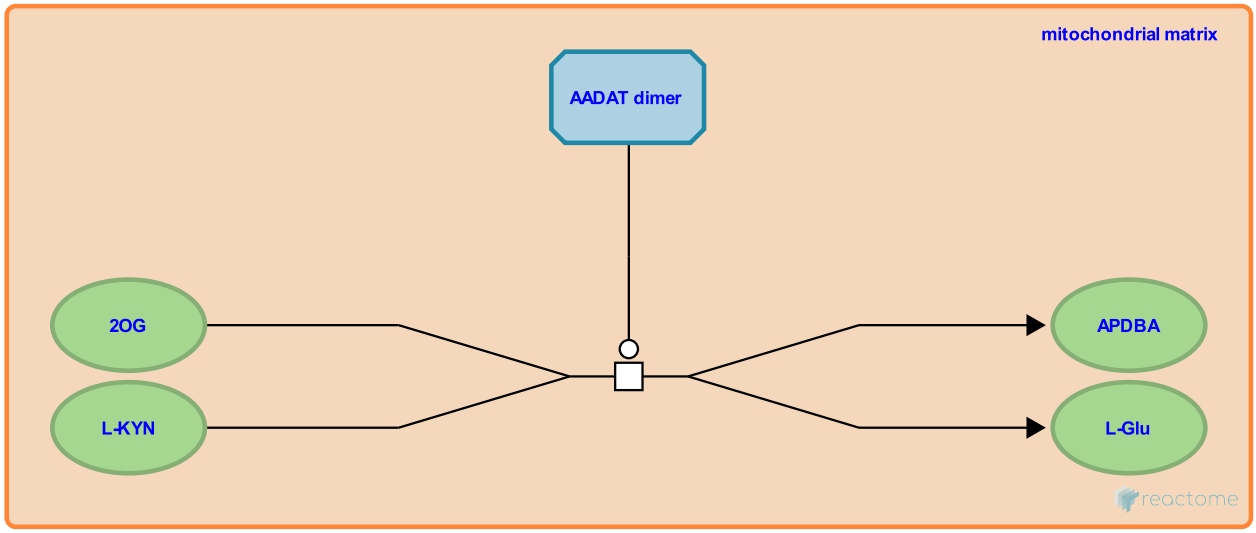
## kynurenine + 2-oxoglutarate => 4-(2-aminophenyl)-2,4-dioxobutanoic acid + glutamate ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-893583

**Type:** transition

**Compartments:** mitochondrial matrix




AADAT dimer localized in the mitochondrial matrix catalyzes the reaction of kynurenine and 2-oxoglutarate to form 4-(2-aminophenyl)-2,4-dioxobutanoate and glutamate (Han et al. 2008). Biochemical studies of kynurenine transamination in vitro invariably measure kynurenic acid, not 4-(2-aminophenyl)-2,4-dioxobutanoate, the expected transamination product. As noted by Miller et al. (1953), "The keto acid assumed to be formed prior to ring closure in the conversion of kynurenine to kynurenic acid has not yet been detected. In principle, such detection should be possible, since it is sufficiently stable to have been synthesized. It also remains to be established whether ring closure is spontaneous, enzymatic, or both. The formation of kynurenic acid from L-kynurenine by the L-amino acid oxidase of Neurospora suggests, however, that ring closure can be spontaneous, unless the somewhat improbable assumption is made that Neurospora filtrate contained the ring-closing enzyme."

**Followed by:** 4-(2-aminophenyl)-2,4-dioxobutanoate => kynurenic acid + H2O [mitochondrial]

### Literature references

Robinson, H., Li, J., Han, Q. (2008). Crystal structure of human kynurenine aminotransferase II. *J Biol Chem, 283*, 3567-73. ↗

Miller, IL., Adelberg, EA., Tsuchida, M. (1953). The transamination of kynurenine. *J Biol Chem, 203*, 205-11. ↗

### Editions

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|---|---|---|
| 2005-07-20 | Authored, Edited | D'Eustachio, P. |
| 2010-11-09 | Reviewed | Jassal, B. |

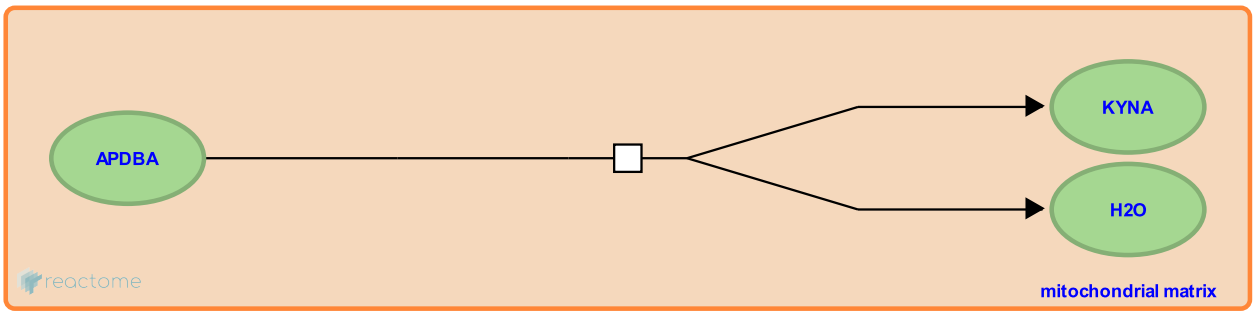
## 4-(2-aminophenyl)-2,4-dioxobutanoate => kynurenic acid + H2O [mitochondrial] ↗

**Location:** Tryptophan catabolism

**Stable identifier:** R-HSA-893597

**Type:** transition

**Compartments:** mitochondrial matrix




Mitochondrial 4-(2-aminophenyl)-2,4-dioxobutanoate is thought to spontaneously condense with the elimination of water to form kynurenic acid (kynurenate).

Biochemical studies of kynurenine transamination in vitro invariably measure kynurenic acid, not 4-(2-aminophenyl)-2,4-dioxobutanoate, the expected transamination product. The reaction annotated here has not been demonstrated directly. As noted by Miller et al. (1953), "The keto acid assumed to be formed prior to ring closure in the conversion of kynurenine to kynurenic acid has not yet been detected. In principle, such detection should be possible, since it is sufficiently stable to have been synthesized. It also remains to be established whether ring closure is spontaneous, enzymatic, or both. The formation of kynurenic acid from L-kynurenine by the L-amino acid oxidase of Neurospora suggests, however, that ring closure can be spontaneous, unless the somewhat improbable assumption is made that Neurospora filtrate contained the ring-closing enzyme."

**Preceded by:** kynurenine + 2-oxoglutarate => 4-(2-aminophenyl)-2,4-dioxobutanoic acid + glutamate

### Literature references

Miller, IL., Adelberg, EA., Tsuchida, M. (1953). The transamination of kynurenine. *J Biol Chem, 203*, 205-11. ↗

### Editions

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|---|---|---|
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