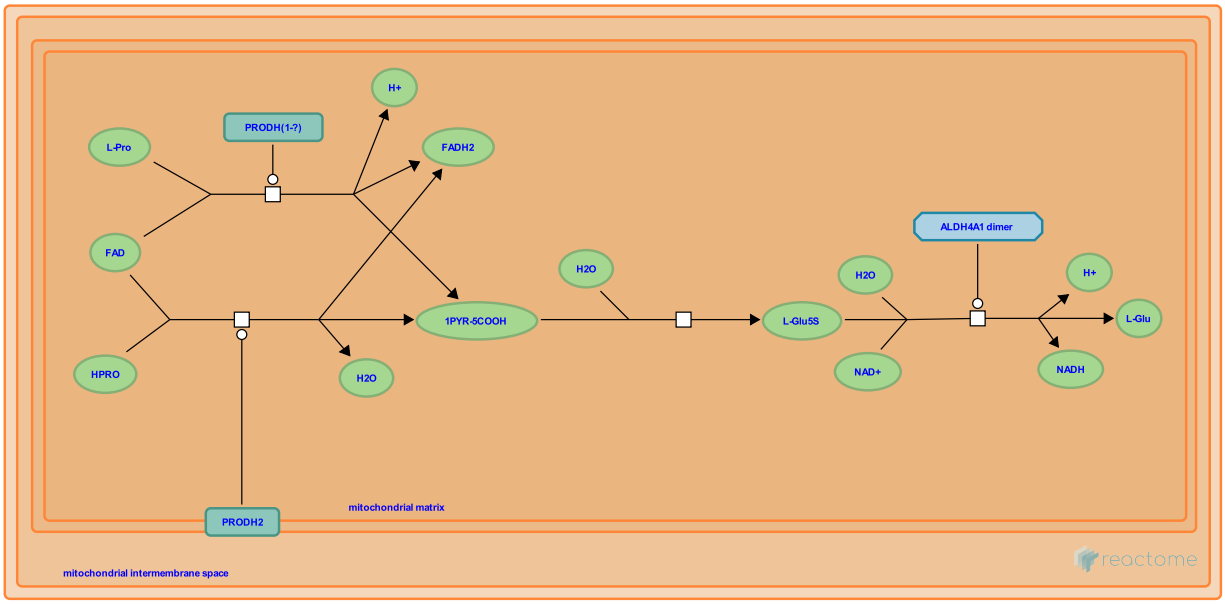
Proline catabolism



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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. ↗

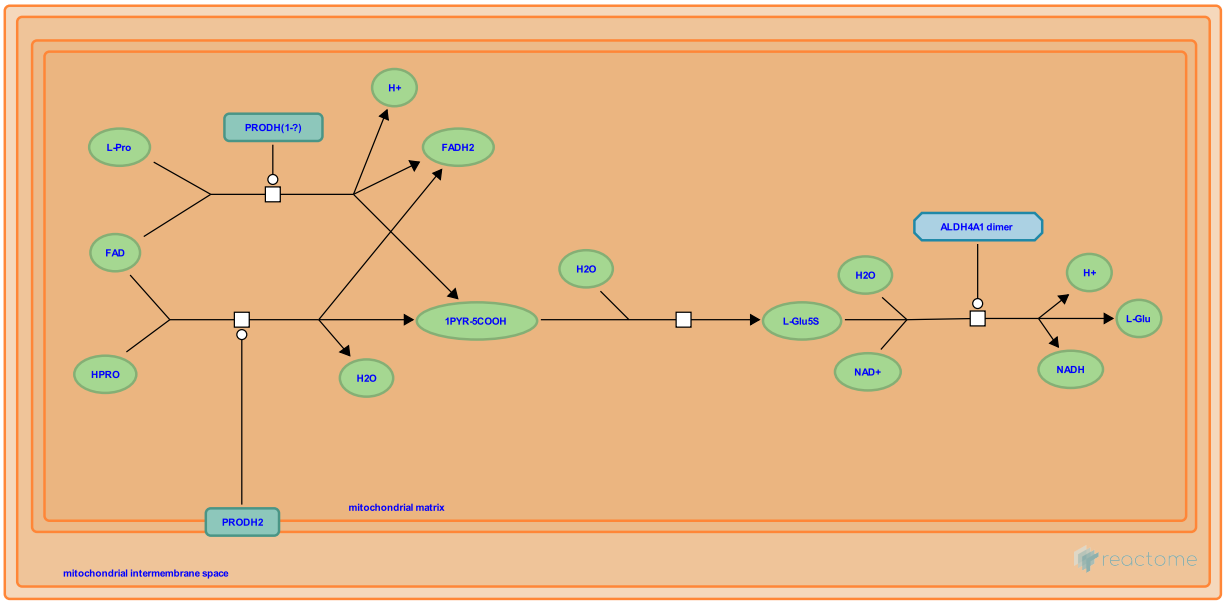
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Proline catabolism ↗

Stable identifier: R-HSA-70688

Compartments: mitochondrion



Proline is catabolized in two steps to yield L-glutamate gamma-semialdehyde, which can react further with glutamate to yield ornithine and alpha-ketoglutarate (annotated as a reaction of amino acid synthesis and interconversion) or with NAD+ to yield glutamate and NADH + H+ (Phang et al. 2001).

Literature references

Beaudet, AL., Scriver, CR., Sly, WS., Valle, D. (2001). Disorders of proline and hydroxyproline metabolism, The Metabolic and Molecular Bases of Inherited Disease, 8th ed. *McGraw Hill*, 1821-1838.

Editions

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

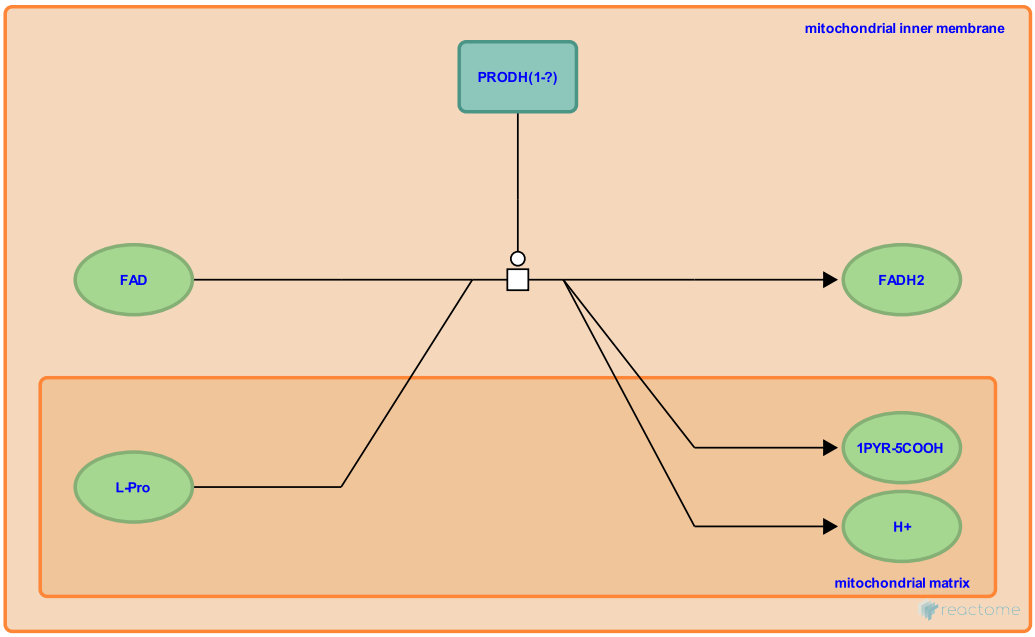
PRODH oxidises L-Pro to 1PYR-5COOH ↗

Location: Proline catabolism

Stable identifier: R-HSA-70670

Type: transition

Compartments: mitochondrial inner membrane, mitochondrial matrix



The dehydrogenation (oxidation) of proline to L-1-pyrroline-5-carboxylate coupled to the conversion of FAD to FADH2 is the first step in proline breakdown (Bender et al. 2005). Proline dehydrogenase (PRODH), the enzyme that catalyzes this reaction, is found in liver, kidney, and brain cells, where it is tightly bound to the inner mitochondrial membrane.

Followed by: 1PYR-5COOH spontaneously hydrolyses to L-GluSS

Literature references

Lin, WW., Willis, A., Valle, D., Pulver, A., Bender, HU., Steel, G. et al. (2005). Functional consequences of PRODH missense mutations. *Am J Hum Genet, 76*, 409-20. ↗

Editions

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

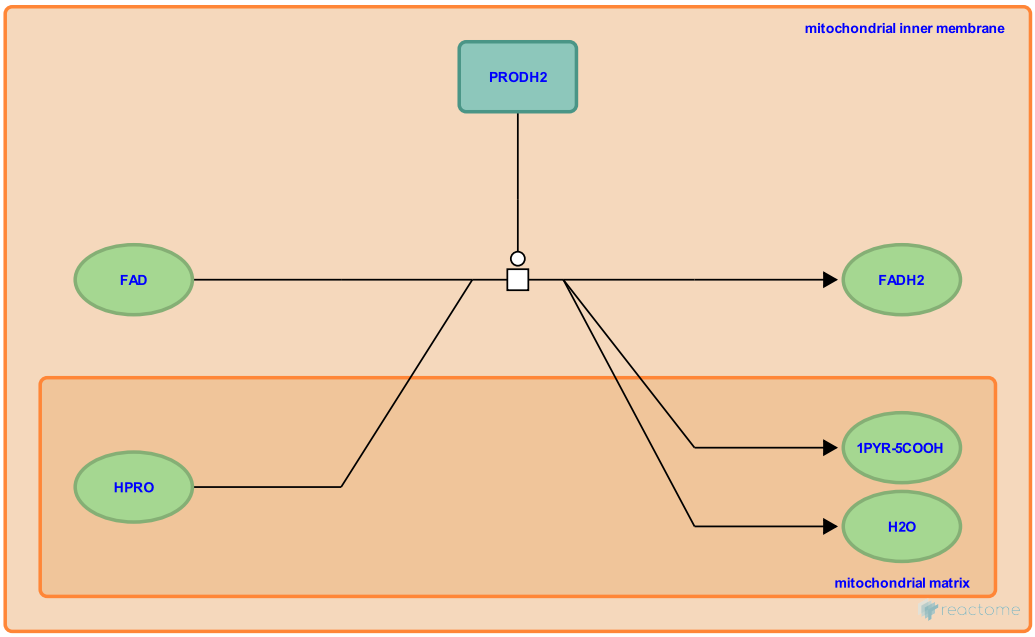
PRODH2 oxidises HPRO to 1PYR-5COOH ↗

Location: Proline catabolism

Stable identifier: R-HSA-8955817

Type: transition

Compartments: mitochondrial inner membrane, mitochondrial matrix



The catabolism of trans-4-hydroxy-L-proline (HPRO) and proline (L-Pro) (from endogenous and dietary sources of collagen) makes a significant contribution to the glyoxylate pool in humans. The dehydrogenation (oxidation) of HPRO/L-Pro to L-1-pyrroline-5-carboxylate (1PYR-5COOH) coupled to the conversion of FAD to FADH2 is the first step in proline catabolism. Proline dehydrogenases (PRODHs), located at the inner mitochondrial membrane mediate this reaction. Whereas PRODH prefers L-Pro as substrate, PRODH2 has a clear preference for HPRO (Summitt et al. 2015).

Followed by: 1PYR-5COOH spontaneously hydrolyses to L-GluSS

Literature references

Holmes, RP., Johnson, LC., Summitt, CB., Parsonage, D., Lowther, WT., Jönsson, TJ. (2015). Proline dehydrogenase 2 (PRODH2) is a hydroxyproline dehydrogenase (HYPDH) and molecular target for treating primary hyperoxaluria . *Biochem. J., 466*, 273-81. ↗

Editions

2017-01-13	Authored, Edited	Jassal, B.
2017-01-30	Reviewed	D'Eustachio, P.

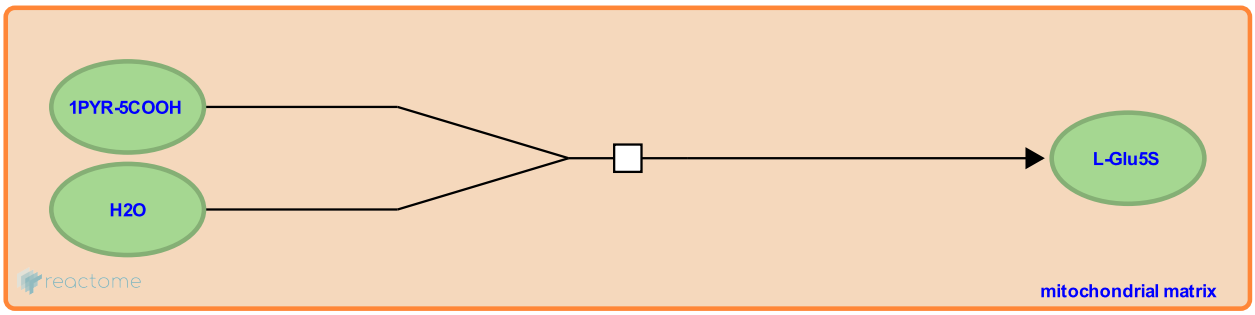
1PYR-5COOH spontaneously hydrolyses to L-GluSS ↗

Location: Proline catabolism

Stable identifier: R-HSA-70667

Type: transition

Compartments: mitochondrial matrix



The interconversion of (S)-1-pyrroline-5-carboxylate (1PYR-5COOH) glutamate 5-semialdehyde (L-GluSS) is a spontaneous reaction (Scriver et al. 2001).

Preceded by: PRODH oxidises L-Pro to 1PYR-5COOH, PRODH2 oxidises HPRO to 1PYR-5COOH

Followed by: ALDH4A1 oxidises L-GluSS to Glu

Literature references

Beaudet, AL., Scriver, CR., Sly, WS., Valle, D. (2001). The hyperornithinemias, The Metabolic and Molecular Bases of Inherited Disease, 8th ed. *McGraw Hill*, 1857-1895.

Editions

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

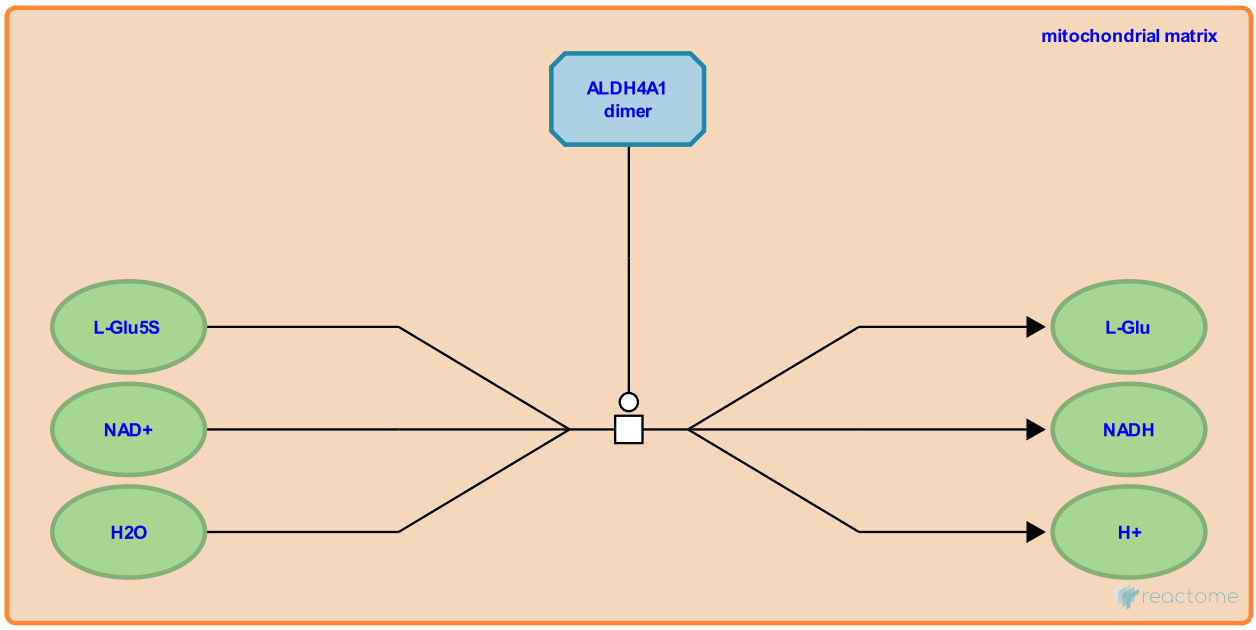
ALDH4A1 oxidises L-GluSS to Glu ↗

Location: Proline catabolism

Stable identifier: R-HSA-70679

Type: transition

Compartments: mitochondrial matrix



Mitochondrial delta-1-pyrroline-5-carboxylate dehydrogenase (ALDH4A1) catalyzes the reaction of L-glutamate gamma-semialdehyde and NAD+ to form glutamate and NADH + H+ (Hu et al. 1996). The enzyme is a dimer (Forte-McRobbie and Pietruszko 1986). ALDH4A1 mutations cause type II hyperprolinemia in vivo (Geraghty et al. 1998).

Preceded by: 1PYR-5COOH spontaneously hydrolyses to L-GluSS

Literature references

Jimenez-Sanchez, G., Flynn, MP., Nicholson, AJ., Obie, C., Lin, WW., Geraghty, MT. et al. (1998). Mutations in the Delta1-pyrroline 5-carboxylate dehydrogenase gene cause type II hyperprolinemia. *Hum Mol Genet, 7*, 1411-5. ↗

Forte-McRobbie, CM., Pietruszko, R. (1986). Purification and characterization of human liver "high Km" aldehyde dehydrogenase and its identification as glutamic gamma-semialdehyde dehydrogenase. *J Biol Chem, 261*, 2154-63. ↗

Editions

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

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