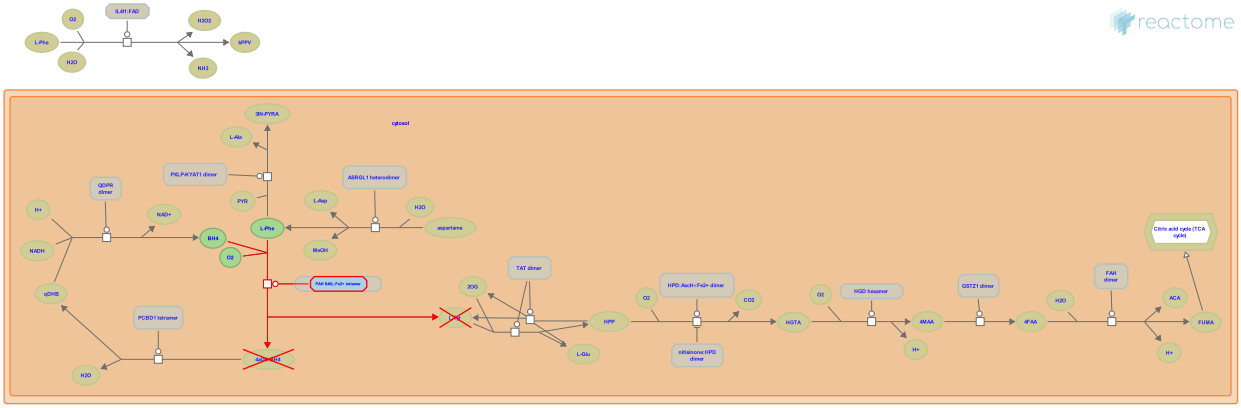
Phenylketonuria



D'Eustachio, P., Jassal, B.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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.

09/05/2024

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.

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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. ↗

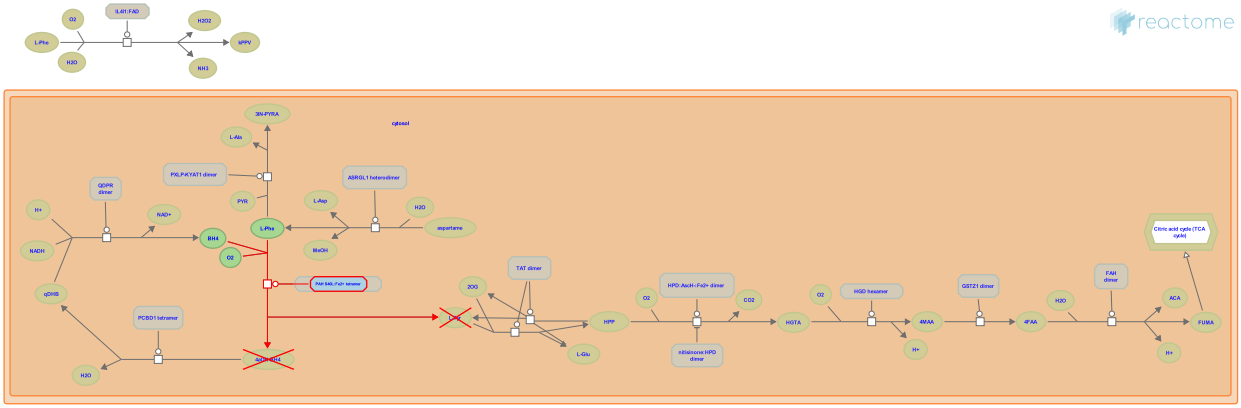
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Phenylketonuria ↗

Stable identifier: R-HSA-2160456

Diseases: phenylketonuria



Phenylalanine hydroxylase (PAH) normally catalyzes the conversion of phenylalanine to tyrosine. In the absence of functional PAH, phenylalanine accumulates to high levels in the blood and is converted to phenylpyruvate and phenyllactate (Clemens et al. 1990; Langenbeck et al. 1992; Mitchell et al. 2011). The extent of these conversions is modulated by genetic factors distinct from PAH, as siblings with the identical PAH defect can produce different amounts of them (Treacy et al. 1996).

Both L-amino acid oxidase (Boulland et al. 2004) and Kynurenine--oxoglutarate transaminase 3 (Han et al. 2004) can catalyze the conversion of phenylalanine to phenylpyruvate and lactate dehydrogenase can catalyze the conversion of the latter molecule to phenyllactate (Meister 1950), in reactions not annotated here.

Literature references

Lasoudris, F., Guiter, C., Moller, P., Marquet, J., Boulland, ML., Baia, M. et al. (2007). Human IL4I1 is a secreted L-phenylalanine oxidase expressed by mature dendritic cells that inhibits T-lymphocyte proliferation. *Blood, 110*, 220-7. ↗

Hoffmann, GF., Clemens, PC., Kohlschutter, A., Schunemann, MH. (1990). Plasma concentrations of phenyllactic acid in phenylketonuria. *J Inherit Metab Dis, 13*, 227-8. ↗

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Scriver, CR., Trakadis, YJ., Mitchell, JJ. (2011). Phenylalanine hydroxylase deficiency. *Genet. Med., 13*, 697-707. ↗

Seller, K., Cotton, RG., Treacy, E., Ramus, S., Pitt, JJ., Thompson, GN. (1996). In vivo disposal of phenylalanine in phenylketonuria: a study of two siblings. *J Inherit Metab Dis, 19*, 595-602. ↗

Editions

2012-03-05	Authored	D'Eustachio, P.
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2012-03-16	Reviewed	Jassal, B.
2015-01-28	Revised	Jassal, B.

Defective PAH does not hydroxylate L-Phe to L-Tyr ↗

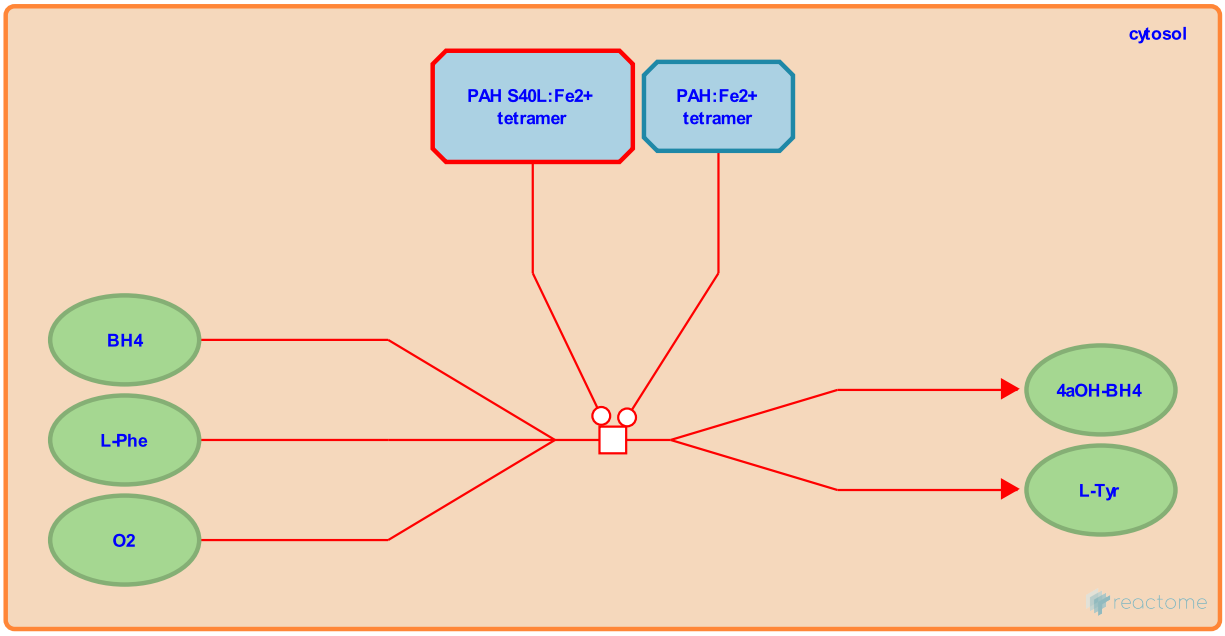
Location: Phenylketonuria

Stable identifier: R-HSA-5649483

Type: transition

Compartments: cytosol

Diseases: phenylketonuria



Inactivating mutations of cytosolic phenylalanine hydroxylase (PAH) block the normal reaction of phenylalanine, molecular oxygen and tetrahydrobiopterin to form tyrosine, water, and 4 alpha-hydroxytetrahydrobiopterin. Excess phenylalanine accumulates as a result, driving the formation of abnormally high levels of phenylpyruvate, and phenyllactate (Guldberg et al. 1996; Mitchell et al. 2011) in reactions not annotated here.

Literature references

Mallmann, R., Güttler, F., Henriksen, KF., Guldberg, P. (1996). Phenylalanine hydroxylase deficiency in a population in Germany: mutational profile and nine novel mutations. *Hum Mutat, 8*, 276-9. ↗

Scriver, CR., Trakadis, YJ., Mitchell, JJ. (2011). Phenylalanine hydroxylase deficiency. *Genet. Med., 13*, 697-707. ↗

Editions

2014-12-08	Authored, Edited	Jassal, B.
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