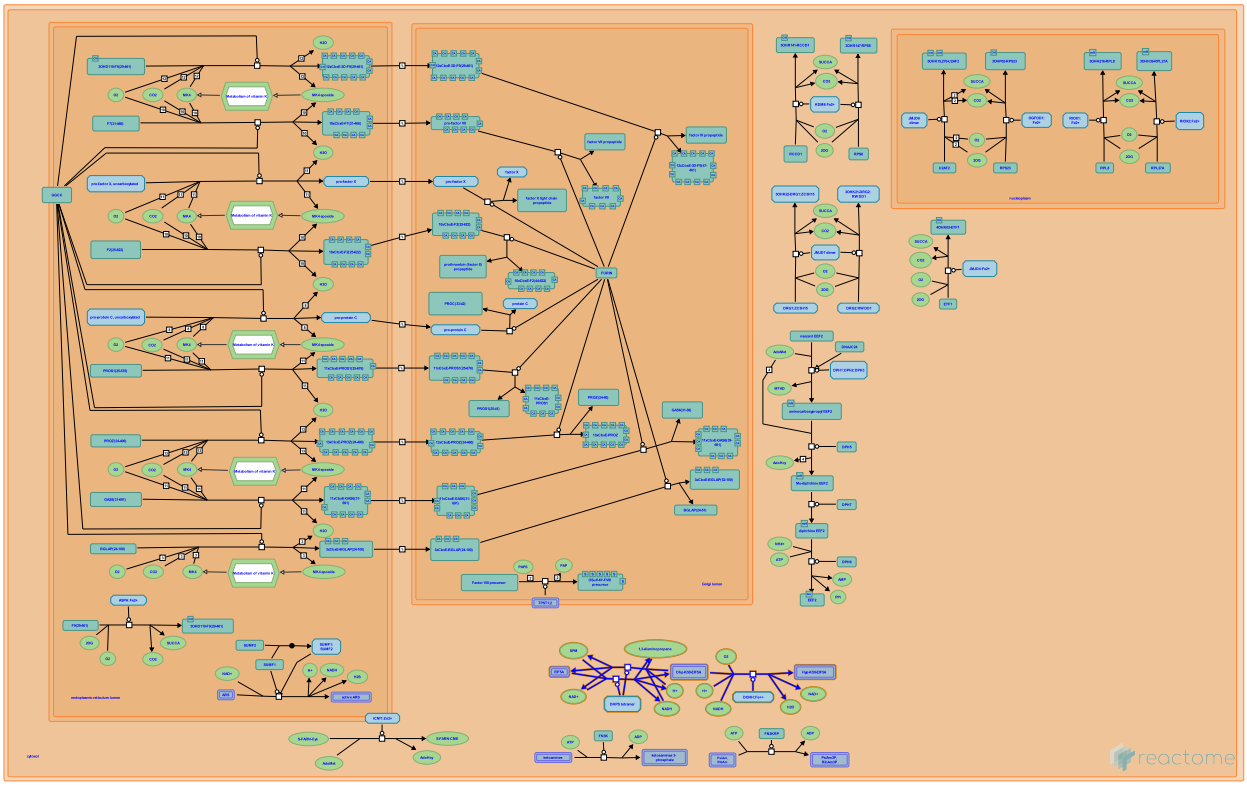
Hypusine synthesis from eIF5A-lysine



D'Eustachio, P., Jassal, B., Johansson, HE.

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.

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. ↗

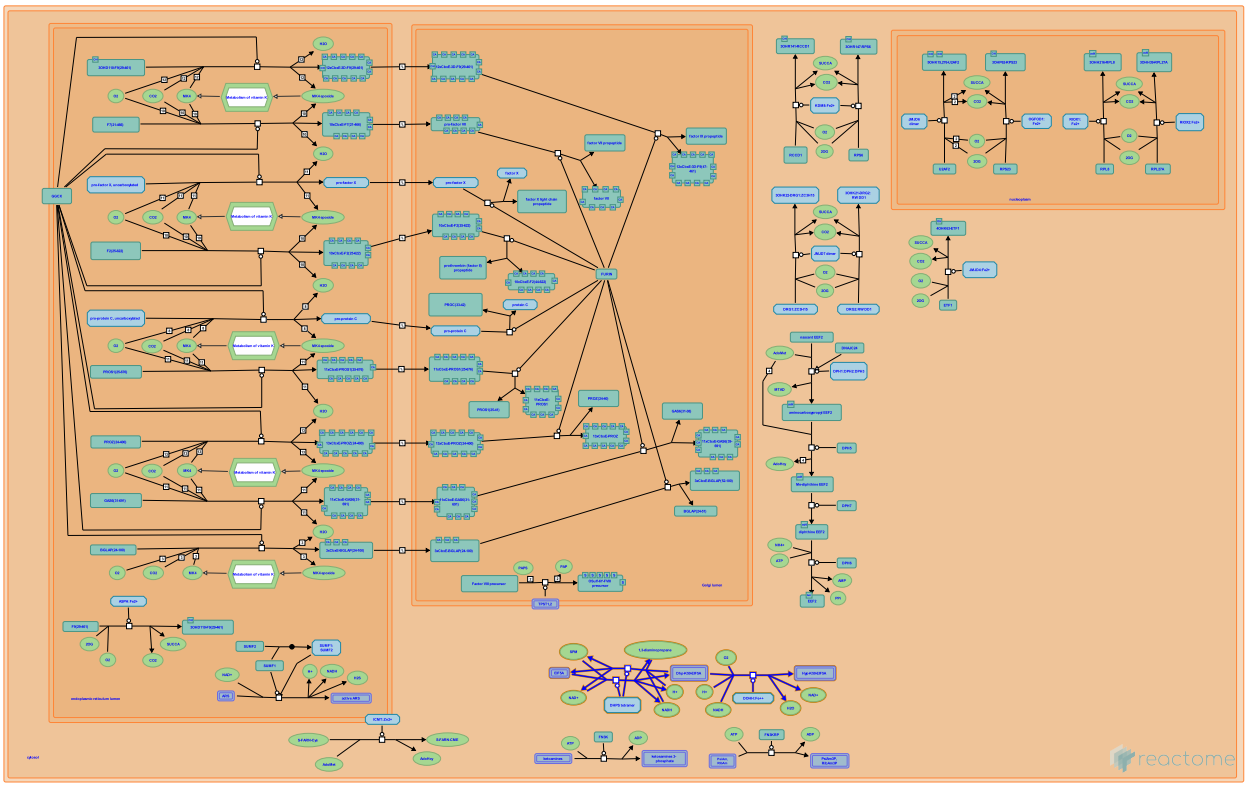
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Hypusine synthesis from eIF5A-lysine ↗

Stable identifier: R-HSA-204626

Compartments: cytosol



Cytosolic eukaryotic translation initiation factor 5A (eIF5A) undergoes a unique two-step post-translational modification at Lys 50 via deoxyhypusine (Dhp) to hypusine (Hyp). In the first step deoxyhypusine synthase transfers the aminobutyl group of spermidine to the epsilon-amino group of lysine 50, using NAD+ as a cofactor. Hydroxylation of the C2 of the newly added moiety in the second step is catalyzed by deoxyhypusine hydroxylase/monooxygenase with molecular oxygen as the source. The molecular function of eIF5A is unknown, but the protein is required for viability in eukaryotic cells and its normal function requires hypusinylation. eIF5A is the only protein known to undergo hypusinylation (Park 2006).

Literature references

Park, MH. (2006). The post-translational synthesis of a polyamine-derived amino acid, hypusine, in the eukaryotic translation initiation factor 5A (eIF5A). *J Biochem (Tokyo), 139*, 161-9. ↗

Editions

2007-11-29	Edited	D'Eustachio, P.
2007-11-29	Authored	Johansson, HE.
2008-01-28	Reviewed	Jassal, B.

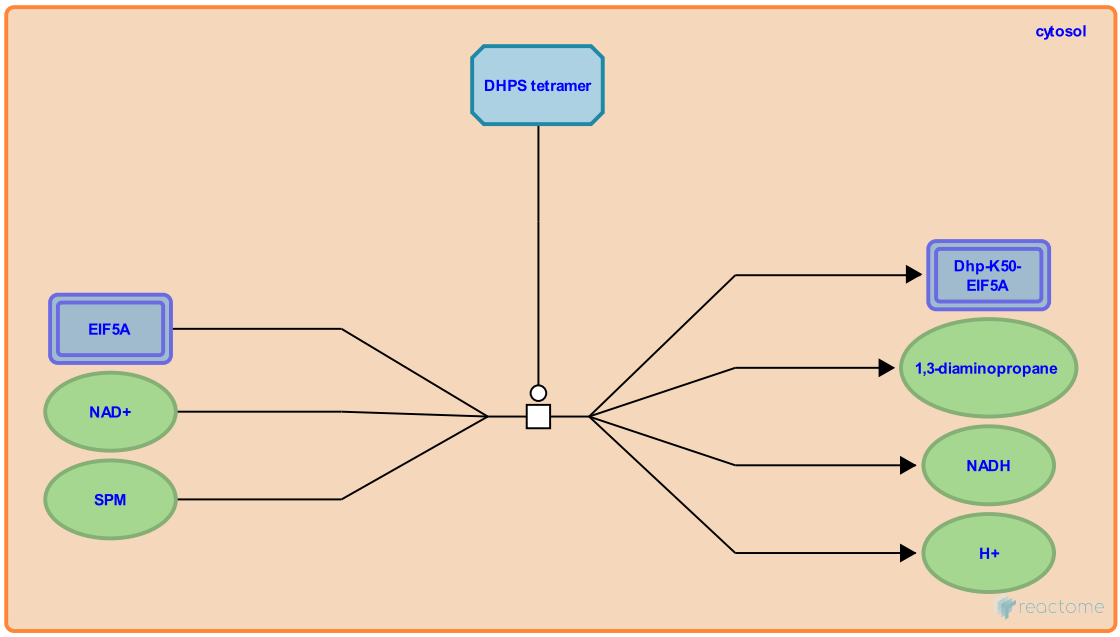
DHPS tetramer synthesizes Dhp-K50-EIF5A from EIF5A and spermidine ↗

Location: Hypusine synthesis from eIF5A-lysine

Stable identifier: R-HSA-204647

Type: transition

Compartments: cytosol



Cytosolic deoxyhypusine synthase (DHPS) tetramer catalyzes the reaction of of EIF5A protein, spermidine (SPM), and NAD+ to convert lysine 50 of EIF5A to deoxyhypusine (Dhp), generating 1,3 diaminopropane, NADH and H+ in the process (Clement et al. 2003; Joe et al. 1995; Park 2006; Wolff et al. 1997). Although the reaction is reversible, the reverse reaction is probably minimized under physiological conditions by the rapid, irreversible conversion of EIF5A Dhp residues to hypusine.

Followed by: DOHH:Fe2+ hydroxylates Dhp-K50-EIF5A to form Hyp-K50-EIF5A

Literature references

Folk, JE., Wolff, EC., Park, MH. (1997). Enzyme-substrate intermediate formation at lysine 329 of human deoxyhypusine synthase. *J Biol Chem, 272*, 15865-71. ↗

Wolff, EC., Park, MH., Joe, YA. (1995). Cloning and expression of human deoxyhypusine synthase cDNA. Structure-function studies with the recombinant enzyme and mutant proteins. *J Biol Chem, 270*, 22386-92. ↗

Wolff, EC., Henderson, CA., Park, MH., Johansson, HE., Hershey, JW., Clement, PM. et al. (2003). Identification and characterization of eukaryotic initiation factor 5A-2. *Eur J Biochem, 270*, 4254-63. ↗

Park, MH. (2006). The post-translational synthesis of a polyamine-derived amino acid, hypusine, in the eukaryotic translation initiation factor 5A (eIF5A). *J Biochem (Tokyo), 139*, 161-9. ↗

Editions

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2007-11-29	Authored	Johansson, HE.
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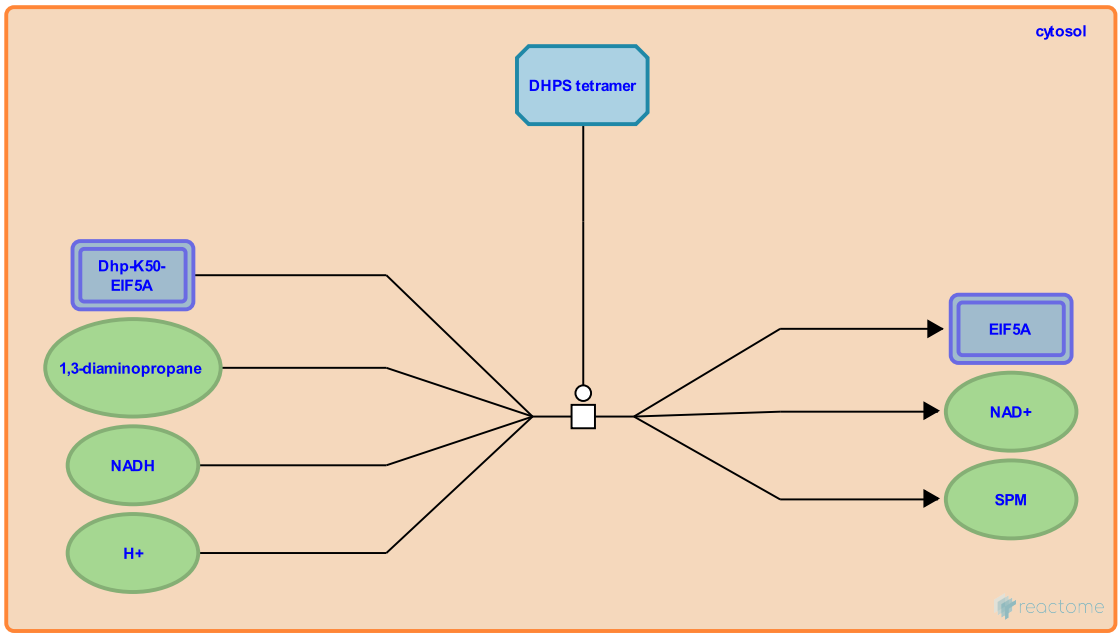
DHPS tetramer synthesizes EIF5A and spermidine from Dhp-K50-EIF5A ↗

Location: Hypusine synthesis from eIF5A-lysine

Stable identifier: R-HSA-204617

Type: transition

Compartments: cytosol



Cytosolic deoxyhypusine synthase (DHPS) tetramer catalyzes the reaction of the deoxyhypusine (Dhp) residue in EIF5A protein (Dhp-K50-EIF5A) with 1,3 diaminopropane, NADH and H+ to form EIF5A, spermidine (SPM), and NAD+ (Park et al. 2003; Park 2006). While this reaction is readily observed in vitro, it is probably minimized by the rapid, irreversible conversion of EIF5A Dhp residues to hypusine.

Literature references

Folk, JE., Wolff, EC., Park, MH., Park, JH. (2003). Reversal of the deoxyhypusine synthesis reaction. Generation of spermidine or homospermidine from deoxyhypusine by deoxyhypusine synthase. *J. Biol. Chem., 278*, 32683-91. ↗

Park, MH. (2006). The post-translational synthesis of a polyamine-derived amino acid, hypusine, in the eukaryotic translation initiation factor 5A (eIF5A). *J Biochem (Tokyo), 139*, 161-9. ↗

Editions

2007-11-29	Edited	D'Eustachio, P.
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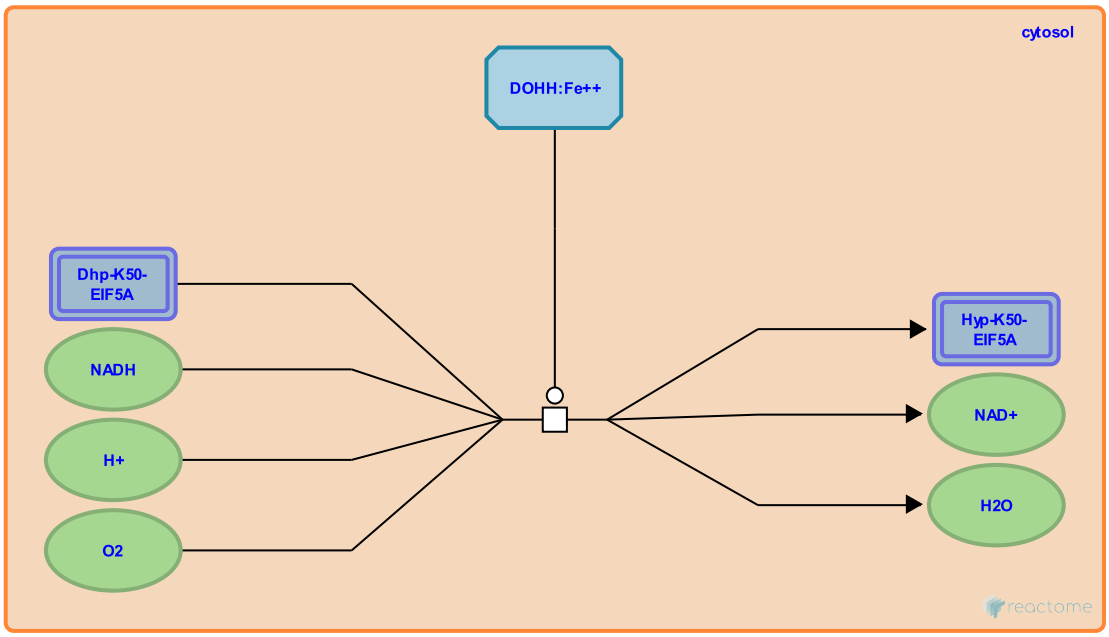
DOHH:Fe2+ hydroxylates Dhp-K50-EIF5A to form Hyp-K50-EIF5A ↗

Location: Hypusine synthesis from eIF5A-lysine

Stable identifier: R-HSA-204662

Type: transition

Compartments: cytosol



Cytosolic deoxyhypusine hydroxylase (DOHH) complexed with Fe2+ catalyzes the irreversible hydroxylation of peptidyl deoxyhypusine (Dhp-K50-EIF5A) to peptidyl hypusine (Hyp-K50-EIF5A) using molecular oxygen. The only known substrate for this enzyme is the modified lysine at residue 50 of the two isoforms of eIF5A (Clement et al. 2003; Kang et al. 2007; Kim et al. 2006).

Preceded by: DHPS tetramer synthesizes Dhp-K50-EIF5A from EIF5A and spermidine

Literature references

Wolff, EC., Park, MH., Kim, YS., Bell, JK., McPhie, P., Kang, KR. (2006). Deoxyhypusine hydroxylase is a Fe(II)-dependent, HEAT-repeat enzyme. Identification of amino acid residues critical for Fe(II) binding and catalysis [corrected]. *J Biol Chem, 281*, 13217-25. ↗

Wolff, EC., Henderson, CA., Park, MH., Johansson, HE., Hershey, JW., Clement, PM. et al. (2003). Identification and characterization of eukaryotic initiation factor 5A-2. *Eur J Biochem, 270*, 4254-63. ↗

Wolff, EC., Park, MH., Kim, YS., Kang, KR. (2007). Specificity of the deoxyhypusine hydroxylase-eukaryotic translation initiation factor (eIF5A) interaction: identification of amino acid residues of the enzyme required for binding of its substrate, deoxyhypusine-containing eIF5A. *J Biol Chem, 282*, 8300-8. ↗

Editions

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2008-01-28	Reviewed	Jassal, B.

Table of Contents