

Hypusine synthesis from eIF5A-lysine



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the <u>Reactome Textbook</u>.

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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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This document contains 1 pathway and 3 reactions (see Table of Contents)

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. ↗

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DHPS tetramer synthesizes Dhp-K50-EIF5A from EIF5A and spermidine 7

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

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- Folk, JE., Wolff, EC., Park, MH. (1997). Enzyme-substrate intermediate formation at lysine 329 of human deoxyhypusine synthase. J Biol Chem, 272, 15865-71. 🛪
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DHPS tetramer synthesizes EIF5A and spermidine from Dhp-K50-EIF5A **7**

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. ↗

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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. ↗
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