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.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of Creative Commons Attribution 4.0 International (CC BY 4.0) License. For more information see our license.

23/07/2019
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


Reactome database release: 69

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


Editions

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007-11-29</td>
<td>Edited</td>
<td>D'Eustachio, P.</td>
</tr>
<tr>
<td>2007-11-29</td>
<td>Authored</td>
<td>Johansson, HE.</td>
</tr>
<tr>
<td>2008-01-28</td>
<td>Reviewed</td>
<td>Jassal, B.</td>
</tr>
</tbody>
</table>
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

DHPS tetramer synthesizes Dhp-K50-EIF5A from EIF5A and spermidine. Cytosolic deoxyhypusine synthase (DHPS) tetramer catalyzes the reaction of EIF5A protein, spermidine (SPM), and NAD+ to convert lysine 50 of EIF5A to deoxyhypusine (Dhp), generating 1,3 diaminopropene, 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


Editions

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007-11-29</td>
<td>Edited</td>
<td>D'Eustachio, P.</td>
</tr>
<tr>
<td>2007-11-29</td>
<td>Authored</td>
<td>Johansson, HE.</td>
</tr>
<tr>
<td>2008-01-28</td>
<td>Reviewed</td>
<td>Jassal, B.</td>
</tr>
</tbody>
</table>
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**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007-11-29</td>
<td>Edited</td>
<td>D'Eustachio, P.</td>
</tr>
<tr>
<td>2007-11-29</td>
<td>Authored</td>
<td>Johansson, HE.</td>
</tr>
<tr>
<td>2008-01-28</td>
<td>Reviewed</td>
<td>Jassal, B.</td>
</tr>
</tbody>
</table>
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**


**Editions**

2007-11-29 Edited D'Eustachio, P.

2007-11-29 Authored Johansson, HE.

2008-01-28 Reviewed Jassal, B.
# Table of Contents

- **Introduction** 1

  - Hypusine synthesis from eIF5A-lysine 2
    - DHPS tetramer synthesizes Dhp-K50-EIF5A from EIF5A and spermidine 3
    - DHPS tetramer synthesizes EIF5A and spermidine from Dhp-K50-EIF5A 4
    - DOHH:Fe2+ hydroxylates Dhp-K50-EIF5A to form Hyp-K50-EIF5A 5

Table of Contents 6