Synthesis of IP2, IP, and Ins in the cytosol

D'Eustachio, P., Jassal, B., Orlic-Milacic, M., Rush, MG., Williams, MG., Wundenberg, T.

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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 Reactome Textbook.

16/11/2022
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: 82

This document contains 1 pathway and 14 reactions (see Table of Contents)
Inositol phosphates IP2, IP and the six-carbon cyclic alcohol inositol (Ins) are produced by various phosphatases and the inositol-3-phosphate synthase 1 (ISYNA1) (Ju et al. 2004, Ohnishi et al. 2007, Irvine & Schell 2001, Bunney & Katan 2010).

**Literature references**


**Editions**

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I(1,4,5)P3 is dephosphorylated to I(1,4)P2 by INPP5(4) in the cytosol

Location: Synthesis of IP2, IP, and Ins in the cytosol

Stable identifier: R-HSA-1855174

Type: transition

Compartments: cytosol

A group of inositol phosphatases dephosphorylate inositol 1,4,5-trisphosphate (I(1,4,5)P3) to inositol 1,4-bisphosphate (I(1,4)P2). The group of inositol phosphatases involved are: inositol polyphosphate 5-phosphatase OCRL-1 (OCRL), phosphatidylinositol 4,5-bisphosphate 5-phosphatase A (INPP5J), and synaptic inositol-1,4,5-trisphosphate 5-phosphatase 1 (SYNJ1).

The following lists the above proteins with their corresponding literature references: OCRL (Zhang et al. 1995, Zhang et al. 1998, Schmid et al. 2004); INPP5J (Mochizuki & Thompson 1999); SYNJ1 (Schmid et al. 2004).

Followed by: I(1,4)P2 is dephosphorylated to I4P by INPP1 in the cytosol

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I(1,4,5)P3 is dephosphorylated to I(1,4)P2 by INPP5A/B at the plasma membrane

**Location:** Synthesis of IP2, IP, and Ins in the cytosol

**Stable identifier:** R-HSA-1855222

**Type:** transition

**Compartments:** plasma membrane, cytosol

Type I inositol-1,4,5-trisphosphate 5-phosphatase (INPP5A) and the Type II phosphatase (INPP5B) are isoprenylated to the plasma membrane and act as a lipid anchor. Here they dephosphorylate inositol 1,4,5-trisphosphate (I(1,4,5)P3) to inositol 1,4-bisphosphate I(1,4)P2.

The following lists the above proteins with their corresponding literature references: INPP5A (Laxminarayan et al. 1994); INPP5B (Jefferson & Majerus 1995, Ross et al. 1991, Schmid et al. 2004).

**Followed by:** I(1,4)P2 is dephosphorylated to I4P by INPP1 in the cytosol

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I(1,4)P2 is dephosphorylated to I4P by INPP1 in the cytosol

Location: Synthesis of IP2, IP, and Ins in the cytosol

Stable identifier: R-HSA-1855208

Type: transition

Compartments: cytosol

Inositol polyphosphate 1-phosphatase (INPP1) dephosphorylates inositol 1,4-bisphosphate (I(1,4)P2) to inositol 4-phosphate (I4P) (York et al. 1993).

Preceded by: I(1,4,5)P3 is dephosphorylated to I(1,4)P2 by INPP5A/B at the plasma membrane, I(1,4,5)P3 is dephosphorylated to I(1,4)P2 by INPP5(4) in the cytosol

Followed by: I4P is dephosphorylated to Ins by IMPA1/2 in the cytosol

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I4P is dephosphorylated to Ins by IMPA1/2 in the cytosol

Location: Synthesis of IP2, IP, and Ins in the cytosol

Stable identifier: R-HSA-1855211

Type: transition

Compartments: cytosol

Inositol monophosphatase 1 (IMPA1) and 2 (IMPA2) homodimers dephosphorylate inositol 4-phosphate (I4P) to inositol (Ins). In vitro, IMPA1 and 2 differ in their pH optima and IMPA1 has a significantly greater activity on IP4 than does IMPA2 (Ohnishi et al. 2007).

Preceded by: I(1,4)P2 is dephosphorylated to I4P by INPP1 in the cytosol

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I1P is dephosphorylated to Ins by IMPA1/2 in the cytosol

**Location:** Synthesis of IP2, IP, and Ins in the cytosol

**Stable identifier:** R-HSA-1855154

**Type:** transition

**Compartments:** cytosol

Inositol monophosphatase 1 (IMPA1) and 2 (IMPA2) homodimers dephosphorylate inositol 1-phosphate (I1P) to inositol (Ins). In vitro, IMPA1 and 2 differ in their pH optima and IMPA1 has a significantly greater activity on IP4 than does IMPA2 (McAllister et al. 1992, Ohnishi et al. 2007).

**Literature references**


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I(1,3,4)P3 is dephosphorylated to I(1,3)P2 by INPP4A/B in the cytosol

Location: Synthesis of IP2, IP, and Ins in the cytosol

Stable identifier: R-HSA-1855180

Type: transition

Compartments: cytosol

Type I (INPP4A) and type II inositol-3,4-bisphosphate 4-phosphatase (INPP4B) dephosphorylate inositol 1,3,4-trisphosphate (I(1,3,4)P3) to inositol 1,3-bisphosphate (I(1,3)P2) (Norris et al. 1995, Norris et al. 1997).

Literature references


Atkins, RC., Majerus, PW., Norris, FA. (1997). The cDNA cloning and characterization of inositol polyphosphate 4-phosphatase type II. Evidence for conserved alternative splicing in the 4-phosphatase family. J Biol Chem, 272, 23859-64.

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I(1,3,4)P3 is dephosphorylated to I(3,4)P2 by INPP1 in the cytosol

Location: Synthesis of IP2, IP, and Ins in the cytosol

Stable identifier: R-HSA-1855232

Type: transition

Compartments: cytosol

Inositol polyphosphate 1-phosphatase (INPP1) dephosphorylates inositol 1,3,4-trisphosphate (I(1,3,4)P3) to inositol 3,4-bisphosphate (I(3,4)P2) (York et al. 1993).

Followed by: I(3,4)P2 is dephosphorylated to I3P by INPP4A/B in the cytosol

Literature references


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I(3,4)P2 is dephosphorylated to I3P by INPP4A/B in the cytosol

**Location:** Synthesis of IP2, IP, and Ins in the cytosol

**Stable identifier:** R-HSA-1855202

**Type:** transition

**Compartments:** cytosol

Type I (INPP4A) and type II inositol-3,4-bisphosphate 4-phosphatase (INPP4B) dephosphorylate inositol 3,4-bisphosphate (I(3,4)P2) to inositol 3-phosphate (I3P) (Norris et al. 1995, Norris et al. 1997).

**Preceded by:** I(1,3,4)P3 is dephosphorylated to I(3,4)P2 by INPP1 in the cytosol

**Followed by:** I3P is dephosphorylated to Ins by IMPA1/2 in the cytosol

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https://reactome.org
Inositol-3-phosphate synthase 1 (ISYNA1) aka hIPS isomerises glucose 6-phosphate (Glc6P) to inositol 3-phosphate (I3P) (Ju et al. 2004).

**Followed by:** I3P is dephosphorylated to Ins by IMPA1/2 in the cytosol

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https://reactome.org
**I3P is dephosphorylated to Ins by IMPA1/2 in the cytosol**

**Location:** Synthesis of IP2, IP, and Ins in the cytosol

**Stable identifier:** R-HSA-1855210

**Type:** transition

**Compartments:** cytosol

Inositol monophosphatase 1 (IMPA1) and 2 (IMPA2) homodimers dephosphorylate inositol 3-phosphate (I3P) to inositol (Ins). In vitro, IMPA1 and 2 differ in their pH optima and IMPA1 has a significantly greater activity on IP4 than does IMPA2 (Ohnishi et al. 2007).

**Preceded by:** I(3,4)P2 is dephosphorylated to I3P by INPP4A/B in the cytosol, Glc6P is isomerised to I3P by ISYNA1 in the cytosol

**Followed by:** MIOX oxidises Ins to GlcA

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Inositol oxidase (MIOX) catalyses the oxidation of inositol (Ins) to glucuronic acid (GlcA). MIOX binds two Fe2+ ions as cofactor (Arner et al. 2004, Thorsell et al. 2008).

**Preceded by:** I3P is dephosphorylated to Ins by IMPA1/2 in the cytosol

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https://reactome.org
I(1,3)P2 is dephosphorylated into I1P by MTMR7

Location: Synthesis of IP2, IP, and Ins in the cytosol

Stable identifier: R-HSA-6809561

Type: transition

Compartments: cytosol

Inferred from: I(1,3)P2 is dephosphorylated into I1P by Mtmr7 (Mus musculus)

MTMR7 dephosphorylates inositol-1,3-bisphosphate, I(1,3)P2, acting as an inositol-1,3-bisphosphate 3-phosphatase (Mochizuki and Majerus 2003).

Literature references


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MTMR7 binds MTMR9

**Location:** Synthesis of IP₂, IP, and Ins in the cytosol

**Stable identifier:** R-HSA-6809238

**Type:** binding

**Compartments:** cytosol

**Inferred from:** Mtmr7 binds Mtmr9 (Mus musculus)

MTMR7 binds to MTMR9, an enzymatically inactive myotubularin family member, which results in increased enzymatic activity of MTMR7. Almost all MTMR7 in the cell is present in the complex with MTMR9 (Mochizuki and Majerus 2003).

**Followed by:** I(1,3)P₂ is dephosphorylated into I1P by MTMR7:MTMR9

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I(1,3)P2 is dephosphorylated into I1P by MTMR7:MTMR9

**Location:** Synthesis of IP2, IP, and Ins in the cytosol

**Stable identifier:** R-HSA-6809565

**Type:** transition

**Compartments:** cytosol

**Inferred from:** I(1,3)P2 is dephosphorylated into I1P by Mtmr7:Mtmr9 (Mus musculus)

Formation of a complex with MTMR9 results in 2- to 5-fold increase in MTMR7 inositol-1,3-bisphosphate 3-phosphatase catalytic activity (Mochizuki and Majerus 2003).

**Preceded by:** MTMR7 binds MTMR9

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