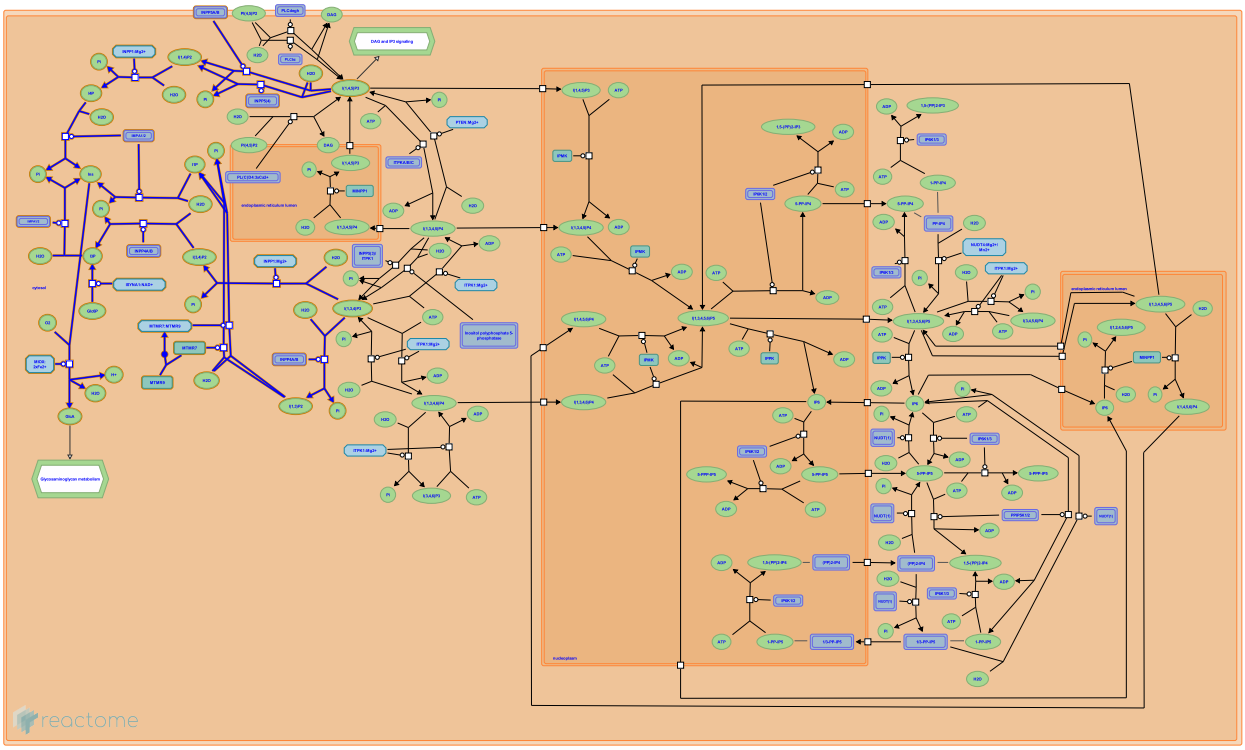
Synthesis of IP2, IP, and Ins in the cytosol



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

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

18/08/2021

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. ↗

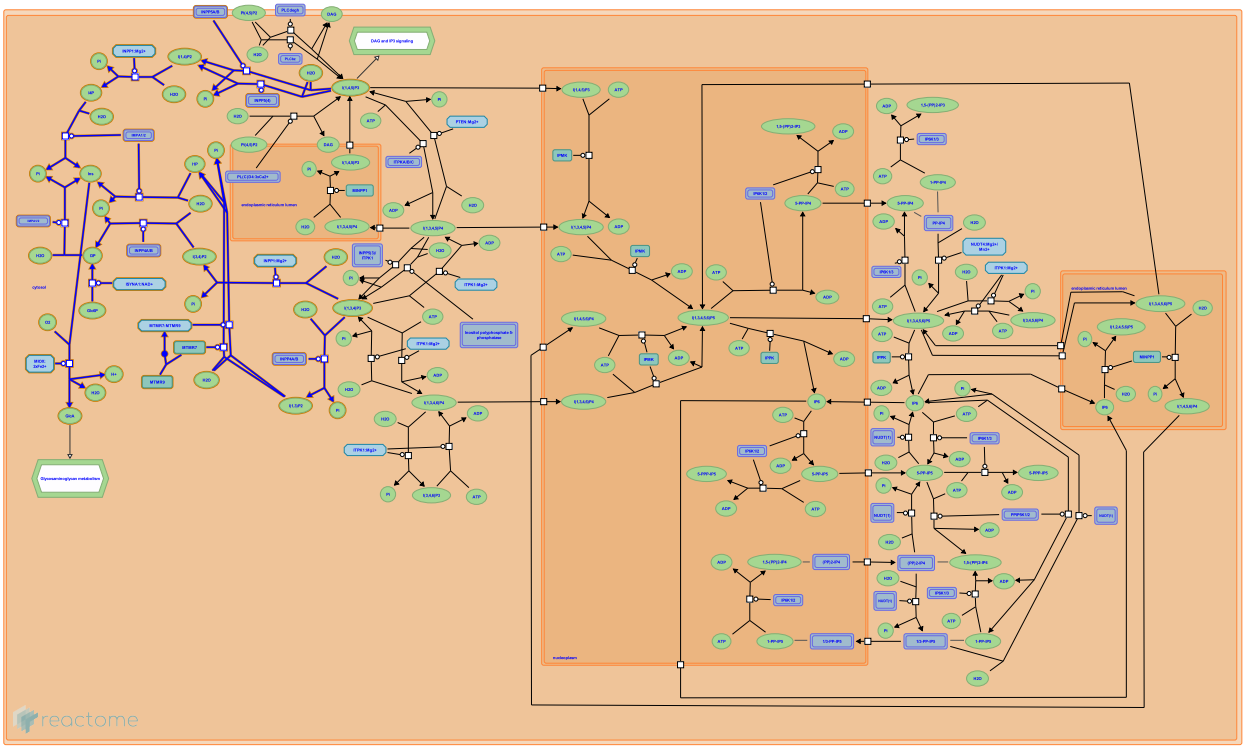
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Synthesis of IP2, IP, and Ins in the cytosol ↗

Stable identifier: R-HSA-1855183



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

Irvine, RF., Schell, MJ. (2001). Back in the water: the return of the inositol phosphates. *Nat Rev Mol Cell Biol, 2*, 327-38 . ↗

Bunney, TD., Katan, M. (2010). Phosphoinositide signalling in cancer: beyond PI3K and PTEN. *Nat Rev Cancer, 10*, 342-52. ↗

Ohnishi, T., Ohba, H., Seo, KC., Im, J., Sato, Y., Iwayama, Y. et al. (2007). Spatial expression patterns and biochemical properties distinguish a second myo-inositol monophosphatase IMPA2 from IMPA1. *J Biol Chem, 282*, 637-46. ↗

Ju, S., Shaltiel, G., Shamir, A., Agam, G., Greenberg, ML. (2004). Human 1-D-myo-inositol-3-phosphate synthase is functional in yeast. *J Biol Chem, 279*, 21759-65. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.
2017-02-24	Revised	Orlic-Milacic, M.

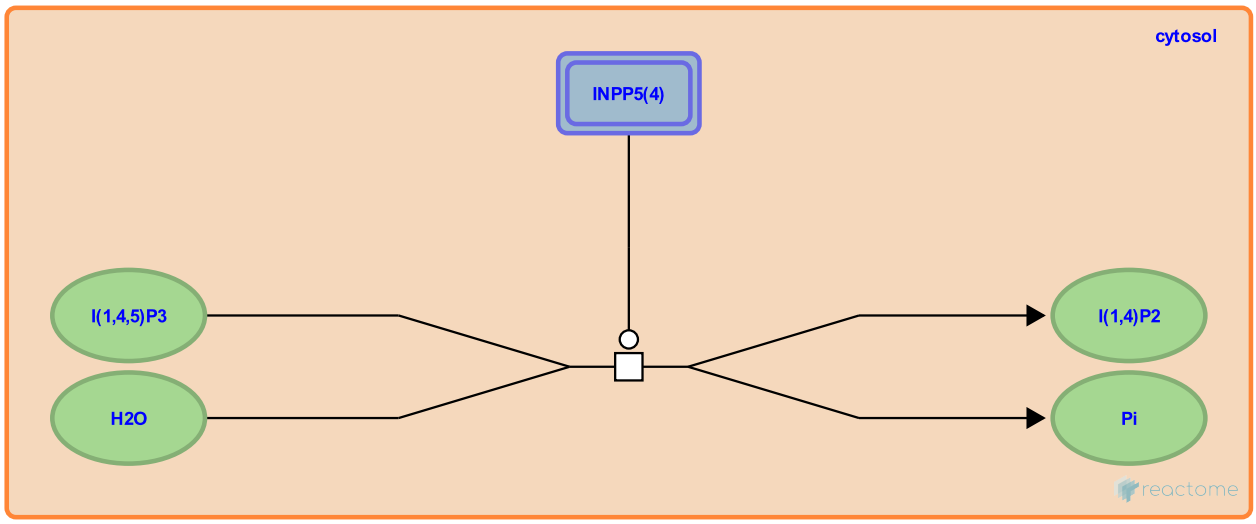
I(1,4,5)P3 is dephosphorylated to I(1,4)P2 by INPP5(4) in the cytosol ↗

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

Literature references

Schmid, AC., Wise, HM., Mitchell, CA., Nussbaum, R., Woscholski, R. (2004). Type II phosphoinositide 5-phosphatases have unique sensitivities towards fatty acid composition and head group phosphorylation. *FEBS Lett, 576*, 9-13. ↗

Mochizuki, Y., Takenawa, T. (1999). Novel inositol polyphosphate 5-phosphatase localizes at membrane ruffles. *J Biol Chem, 274*, 36790-5. ↗

Zhang, X., Jefferson, AB., Auethavekiat, V., Majerus, PW. (1995). The protein deficient in Lowe syndrome is a phosphatidylinositol-4,5-bisphosphate 5-phosphatase. *Proc Natl Acad Sci U S A, 92*, 4853-6. ↗

Zhang, X., Hartz, PA., Philip, E., Racusen, LC., Majerus, PW. (1998). Cell lines from kidney proximal tubules of a patient with Lowe syndrome lack OCRL inositol polyphosphate 5-phosphatase and accumulate phosphatidylinositol 4,5-bisphosphate. *J Biol Chem, 273*, 1574-82. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.

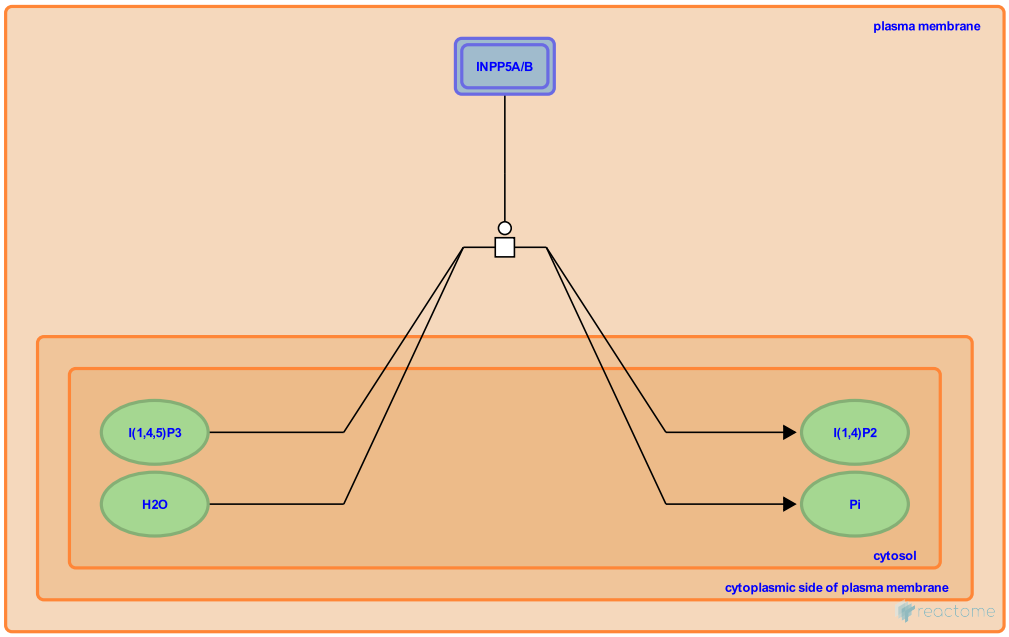
I(1,4,5)P3 is dephosphorylated to I(1,4)P2 by INPP5A/B at the plasma membrane ↗

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

Literature references

Laxminarayan, KM., Chan, BK., Tetaz, T., Bird, PI., Mitchell, CA. (1994). Characterization of a cDNA encoding the 43-kDa membrane-associated inositol-polyphosphate 5-phosphatase. *J Biol Chem, 269*, 17305-10. ↗

Jefferson, AB., Majerus, PW. (1995). Properties of type II inositol polyphosphate 5-phosphatase. *J Biol Chem, 270*, 9370-7. ↗

Ross, TS., Jefferson, AB., Mitchell, CA., Majerus, PW. (1991). Cloning and expression of human 75-kDa inositol polyphosphate-5-phosphatase. *J Biol Chem, 266*, 20283-9. ↗

Schmid, AC., Wise, HM., Mitchell, CA., Nussbaum, R., Woscholski, R. (2004). Type II phosphoinositide 5-phosphatases have unique sensitivities towards fatty acid composition and head group phosphorylation. *FEBS Lett, 576*, 9-13. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.

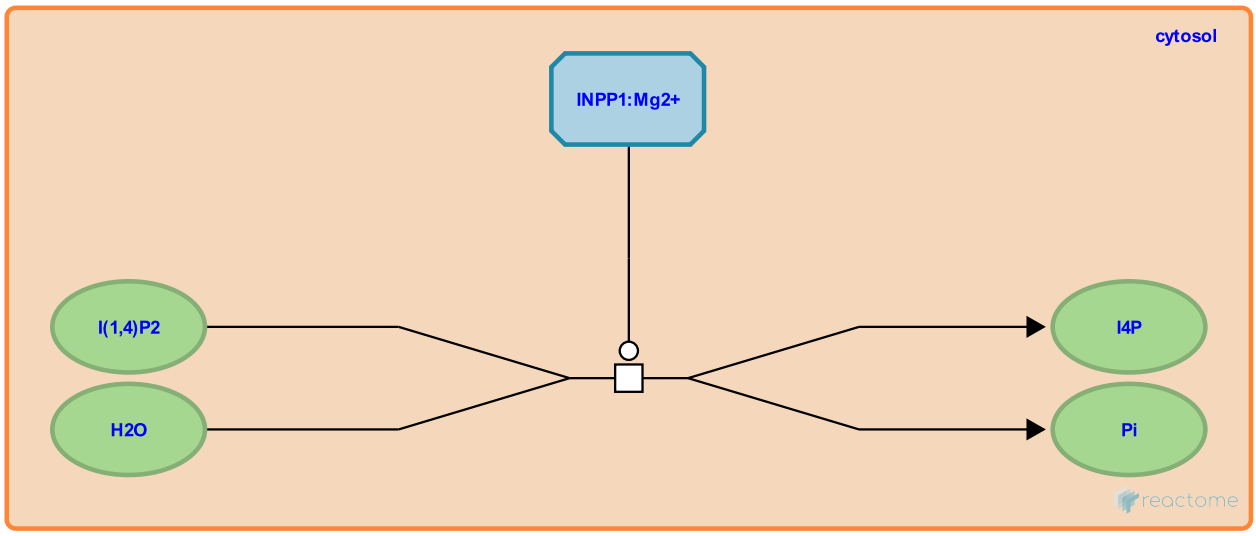
I(1,4)P2 is dephosphorylated to I4P by INPP1 in the cytosol ↗

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

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

Literature references

York, JD., Veile, RA., Donis-Keller, H., Majerus, PW. (1993). Cloning, heterologous expression, and chromosomal localization of human inositol polyphosphate 1-phosphatase. *Proc Natl Acad Sci U S A, 90,* 5833-7. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.

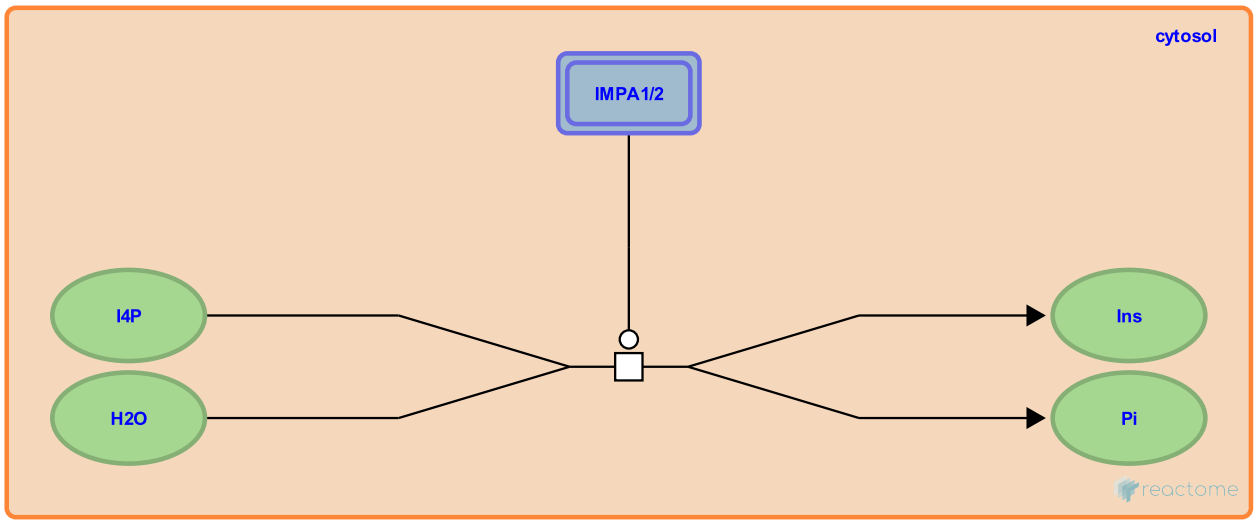
I4P is dephosphorylated to Ins by IMPA1/2 in the cytosol ↗

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

Literature references

Ohnishi, T., Ohba, H., Seo, KC., Im, J., Sato, Y., Iwayama, Y. et al. (2007). Spatial expression patterns and biochemical properties distinguish a second myo-inositol monophosphatase IMPA2 from IMPA1. *J Biol Chem, 282*, 637-46. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.

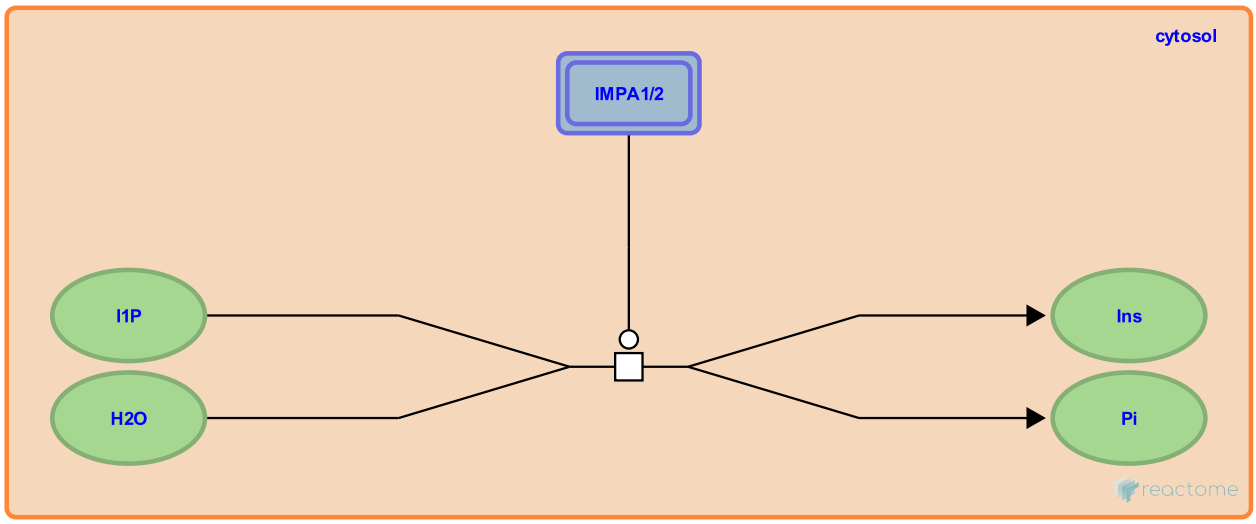
I1P is dephosphorylated to Ins by IMPA1/2 in the cytosol ↗

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

McAllister, G., Whiting, P., Hammond, EA., Knowles, MR., Atack, JR., Bailey, FJ. et al. (1992). cDNA cloning of human and rat brain myo-inositol monophosphatase. Expression and characterization of the human recombinant enzyme. *Biochem J, 284*, 749-54. ↗

Ohnishi, T., Ohba, H., Seo, KC., Im, J., Sato, Y., Iwayama, Y. et al. (2007). Spatial expression patterns and biochemical properties distinguish a second myo-inositol monophosphatase IMPA2 from IMPA1. *J Biol Chem, 282*, 637-46. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.

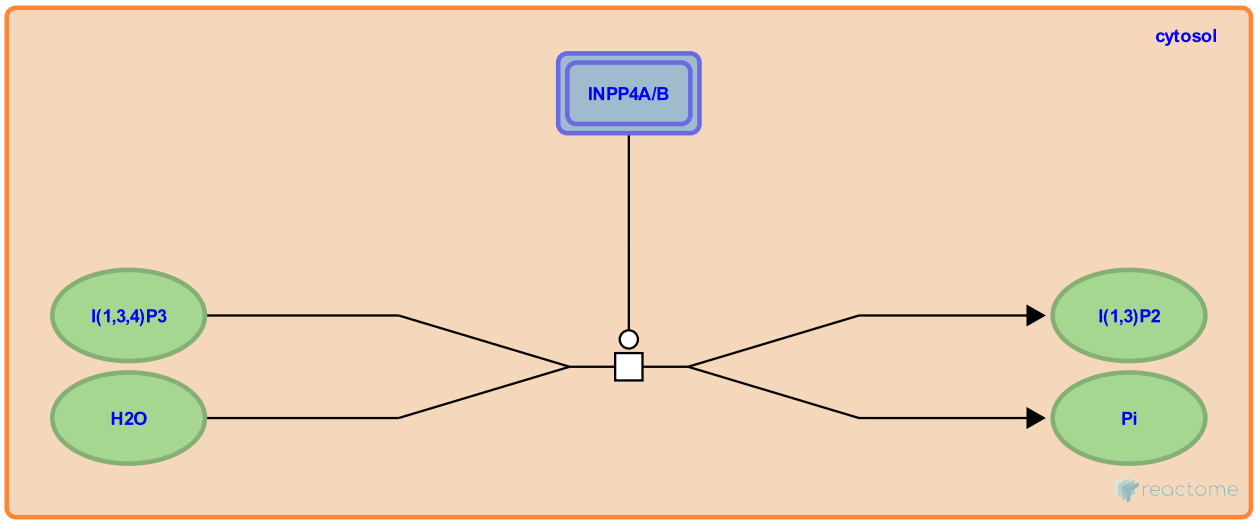
I(1,3,4)P3 is dephosphorylated to I(1,3)P2 by INPP4A/B in the cytosol ↗

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

Norris, FA., Auethavekiat, V., Majerus, PW. (1995). The isolation and characterization of cDNA encoding human and rat brain inositol polyphosphate 4-phosphatase. *J Biol Chem, 270*, 16128-33. ↗

Norris, FA., Atkins, RC., Majerus, PW. (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. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.

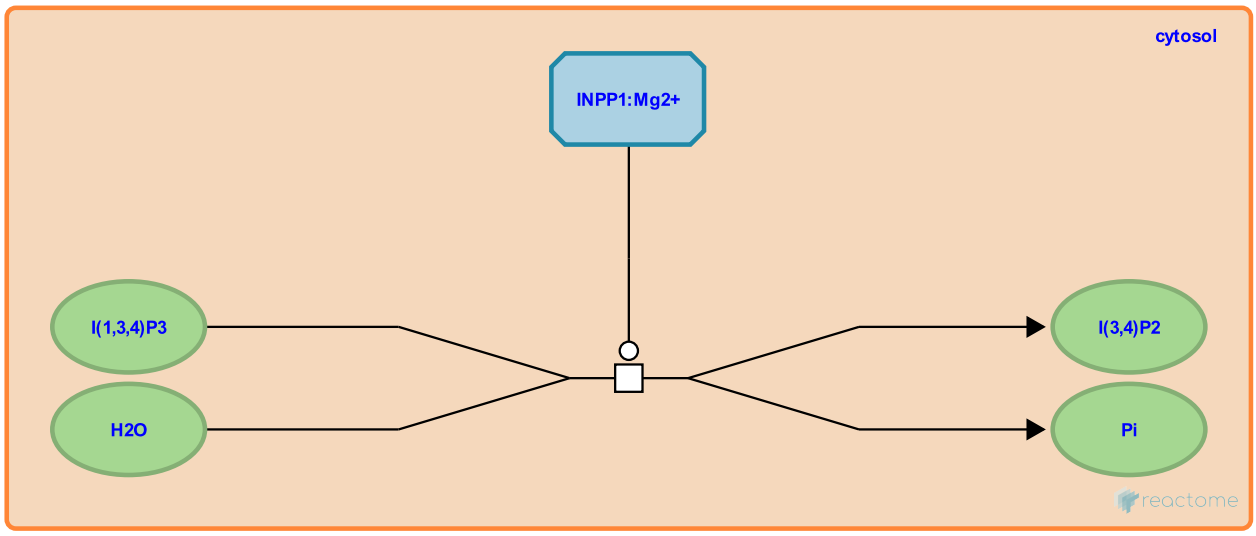
I(1,3,4)P3 is dephosphorylated to I(3,4)P2 by INPP1 in the cytosol ↗

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

York, JD., Veile, RA., Donis-Keller, H., Majerus, PW. (1993). Cloning, heterologous expression, and chromosomal localization of human inositol polyphosphate 1-phosphatase. *Proc Natl Acad Sci U S A, 90*, 5833-7. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.

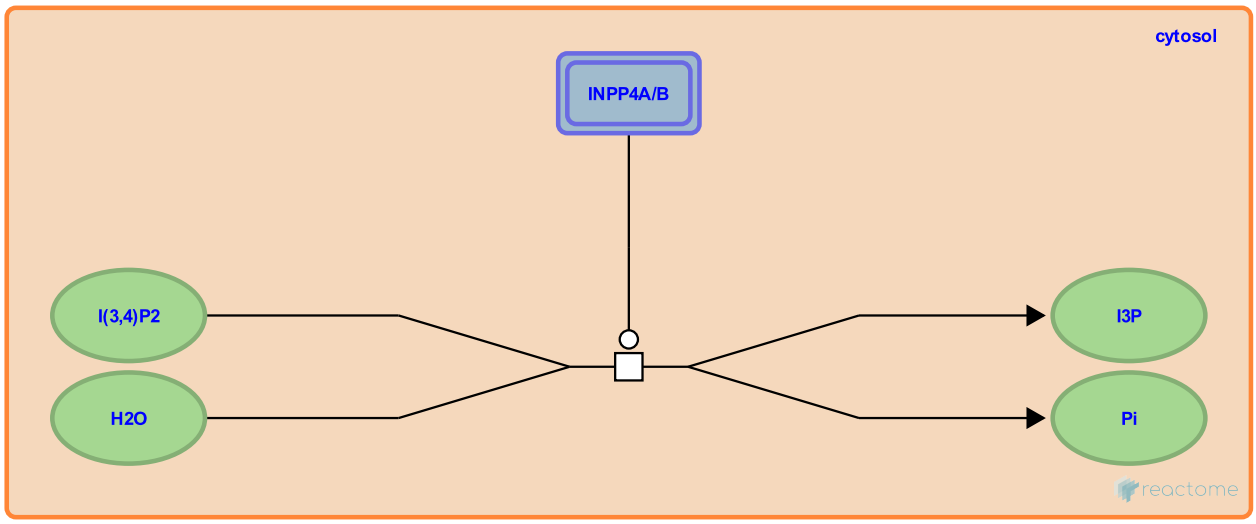
I(3,4)P2 is dephosphorylated to I3P by INPP4A/B in the cytosol ↗

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

Literature references

Norris, FA., Auethavekiat, V., Majerus, PW. (1995). The isolation and characterization of cDNA encoding human and rat brain inositol polyphosphate 4-phosphatase. *J Biol Chem, 270*, 16128-33. ↗

Norris, FA., Atkins, RC., Majerus, PW. (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. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.

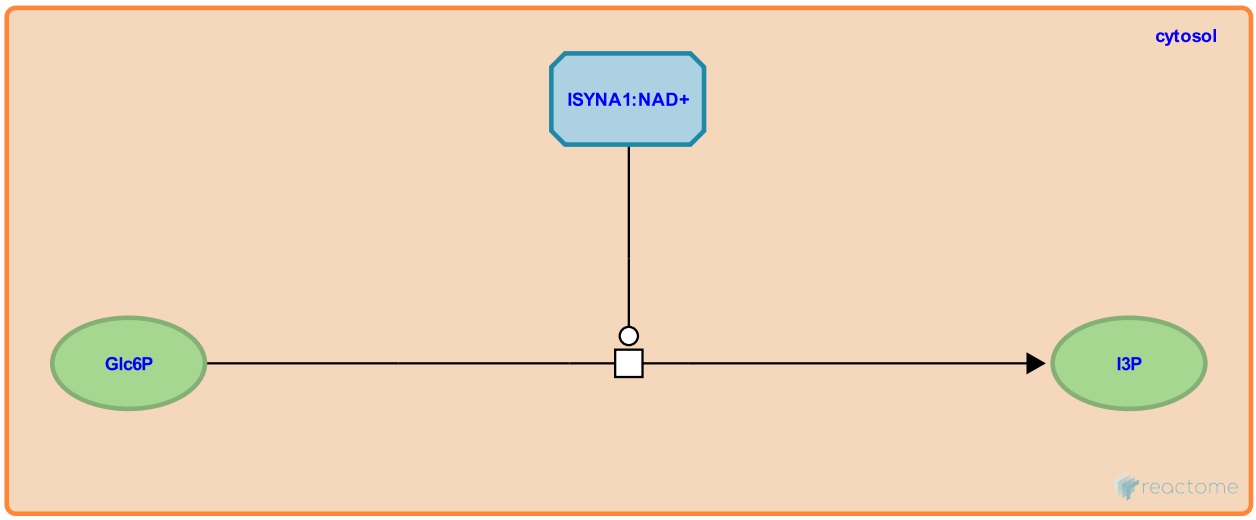
Glc6P is isomerised to I3P by ISYNA1 in the cytosol ↗

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

Stable identifier: R-HSA-1855178

Type: transition

Compartments: cytosol



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

Literature references

Ju, S., Shaltiel, G., Shamir, A., Agam, G., Greenberg, ML. (2004). Human 1-D-myo-inositol-3-phosphate synthase is functional in yeast. *J Biol Chem, 279*, 21759-65. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.

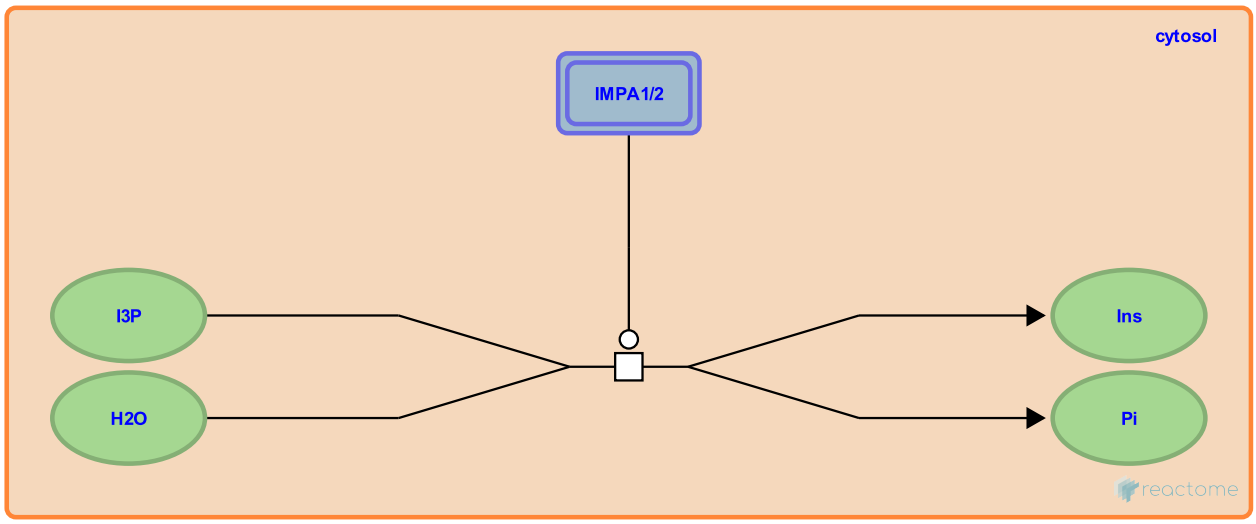
I3P is dephosphorylated to Ins by IMPA1/2 in the cytosol ↗

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

Literature references

Ohnishi, T., Ohba, H., Seo, KC., Im, J., Sato, Y., Iwayama, Y. et al. (2007). Spatial expression patterns and biochemical properties distinguish a second myo-inositol monophosphatase IMPA2 from IMPA1. *J Biol Chem, 282*, 637-46. ↗

Editions

2011-10-28	Authored, Edited	Williams, MG.
2012-11-07	Reviewed	Wundenberg, T.

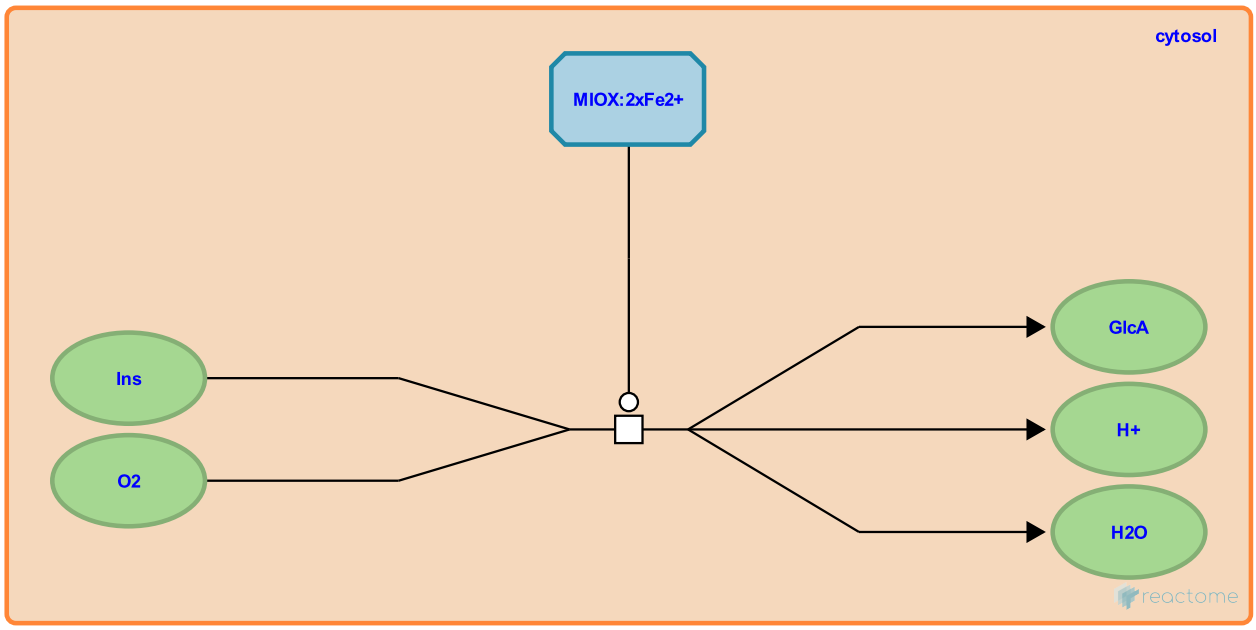
MIOX oxidises Ins to GlcA ↗

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

Stable identifier: R-HSA-5678327

Type: transition

Compartments: cytosol



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

Literature references

Arner, RJ., Prabhu, KS., Reddy, CC. (2004). Molecular cloning, expression, and characterization of myo-inositol oxygenase from mouse, rat, and human kidney. *Biochem. Biophys. Res. Commun., 324*, 1386-92. ↗

Thorsell, AG., Persson, C., Voevodskaya, N., Busam, RD., Hammarström, M., Gräslund, S. et al. (2008). Structural and biophysical characterization of human myo-inositol oxygenase. *J. Biol. Chem., 283*, 15209-16. ↗

Editions

2015-02-23	Authored, Edited	Jassal, B.
2017-01-11	Reviewed	D'Eustachio, P.

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

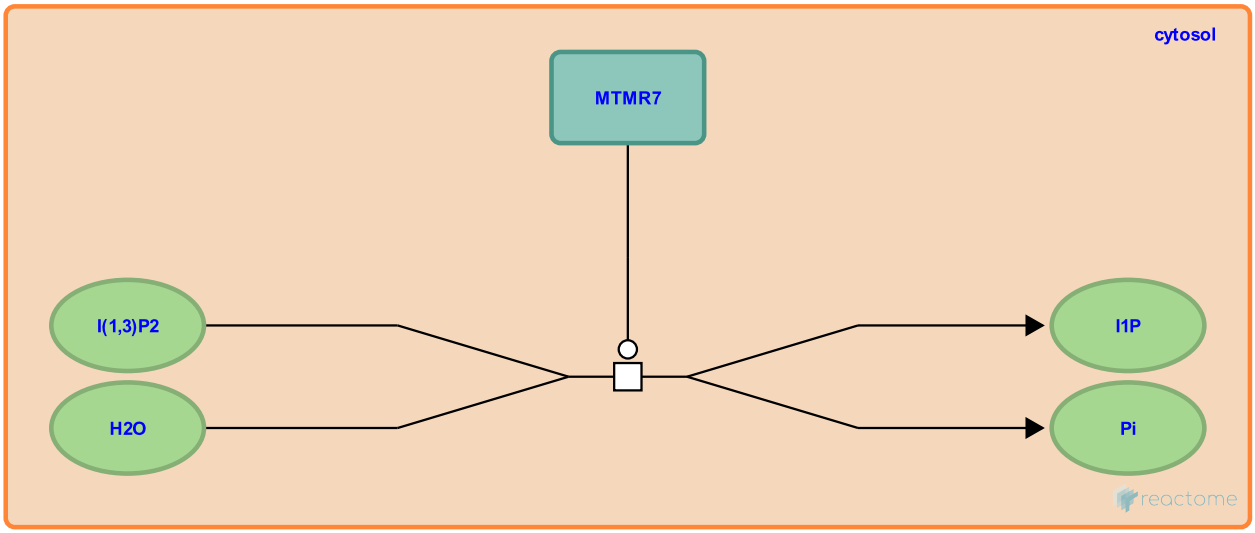
Location: Synthesis of IP2, IP, and Ins in the cytosol

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

Mochizuki, Y., Majerus, PW. (2003). Characterization of myotubularin-related protein 7 and its binding partner, myotubularin-related protein 9. *Proc Natl Acad Sci U S A, 100*, 9768-73. ↗

Editions

2015-11-13	Authored	Orlic-Milacic, M.
2017-01-10	Reviewed	Rush, MG.
2017-01-25	Edited	Orlic-Milacic, M.

MTMR7 binds MTMR9 ↗

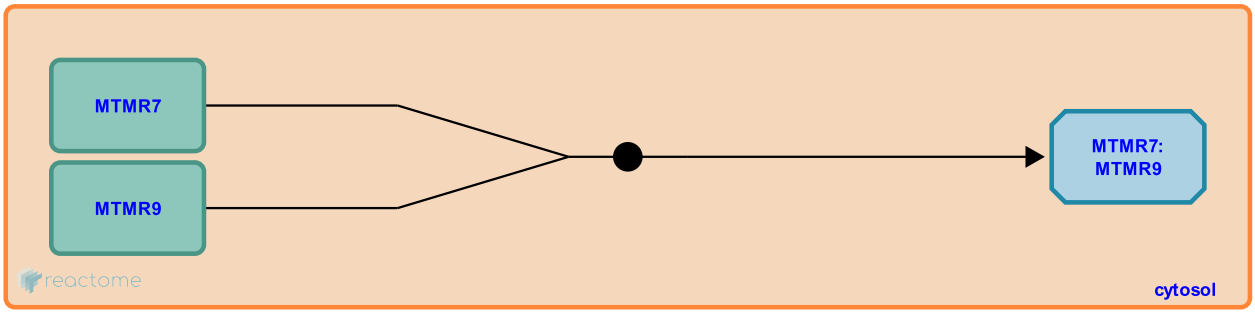
Location: Synthesis of IP2, IP, and Ins in the cytosol

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

Literature references

Mochizuki, Y., Majerus, PW. (2003). Characterization of myotubularin-related protein 7 and its binding partner, myotubularin-related protein 9. *Proc Natl Acad Sci U S A, 100*, 9768-73. ↗

Editions

2015-11-13	Authored	Orlic-Milacic, M.
2017-01-10	Reviewed	Rush, MG.
2017-01-25	Edited	Orlic-Milacic, M.

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

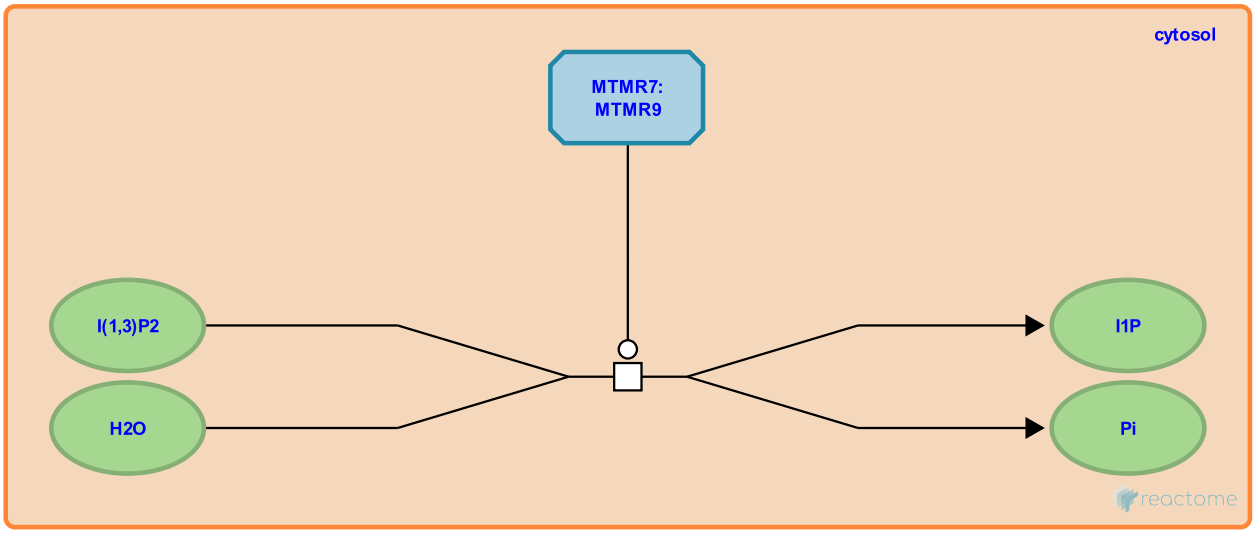
Location: Synthesis of IP2, IP, and Ins in the cytosol

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

Literature references

Mochizuki, Y., Majerus, PW. (2003). Characterization of myotubularin-related protein 7 and its binding partner, myotubularin-related protein 9. *Proc Natl Acad Sci U S A, 100*, 9768-73. ↗

Editions

2015-11-13	Authored	Orlic-Milacic, M.
2017-01-10	Reviewed	Rush, MG.
2017-01-25	Edited	Orlic-Milacic, M.

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