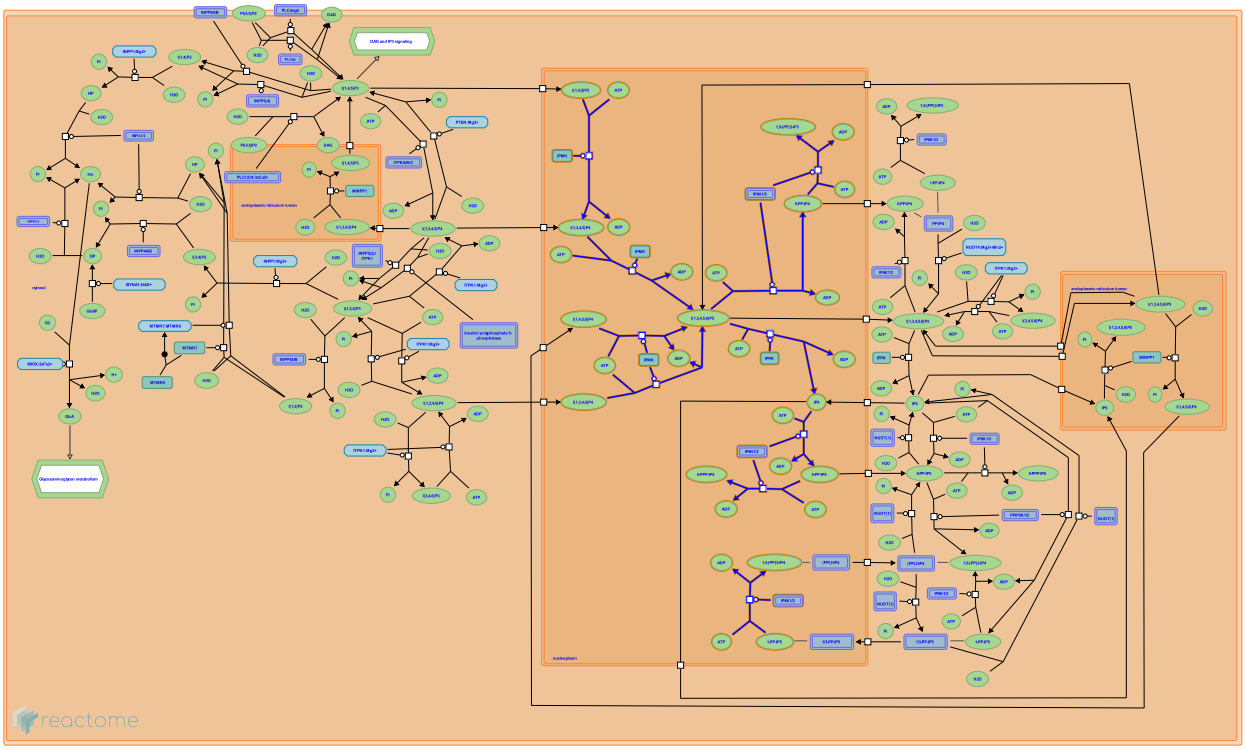
Synthesis of IPs in the nucleus



Williams, MG., Wundenberg, T.

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.

01/05/2024

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. ↗

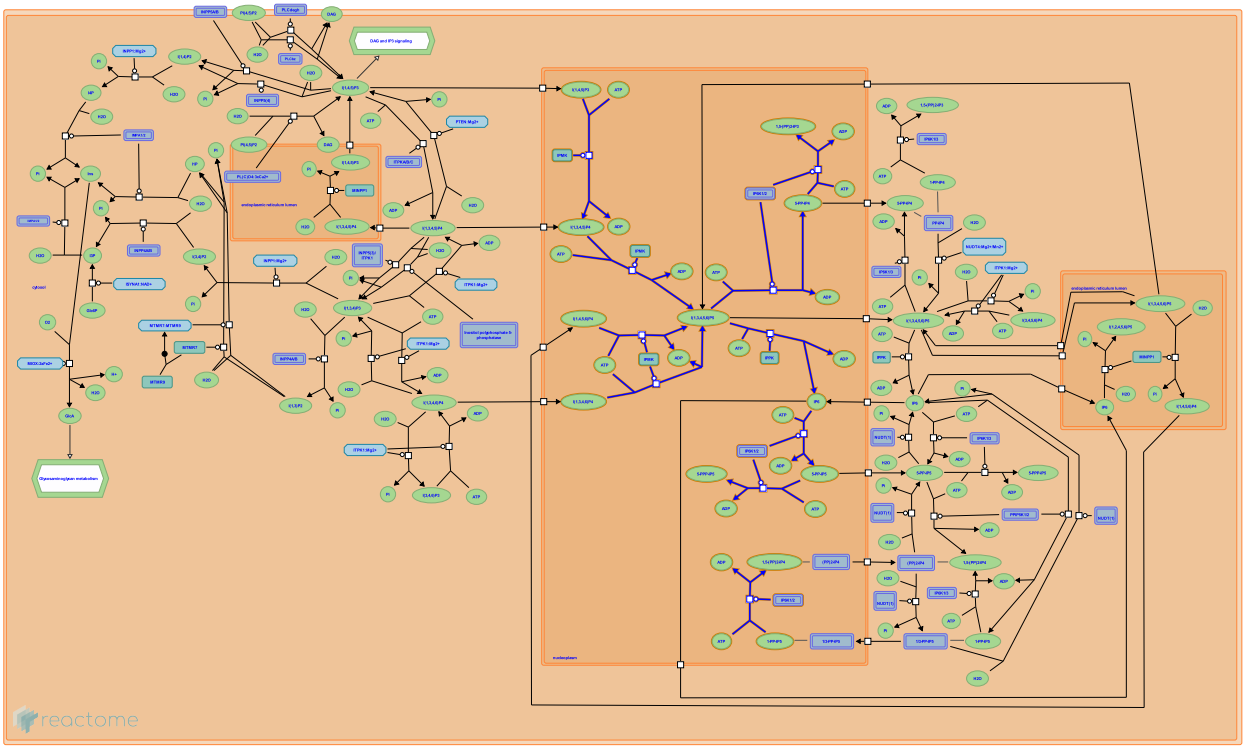
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Synthesis of IPs in the nucleus ↗

Stable identifier: R-HSA-1855191



Within the nucleus, inositol polyphosphate multikinase (IPMK), inositol-pentakisphosphate 2-kinase (IPPK), inositol hexakisphosphate kinase 1 (IP6K1) and 2 (IP6K2) produce IP5, IP6, IP7, and IP8 inositol phosphate molecules (Irvine & Schell 2001, Alcazar-Romain & Wente 2008, York 2006, Monserrate and York 2010, Nalaskowski et al. 2002, Chang et al. 2002, Chang & Majerus 2006, Saiardi et al. 2001, Saiardi et al. 2000, Draskovic et al. 2008, Mulugu et al. 2007).

Literature references

Monserrate, JP., York, JD. (2010). Inositol phosphate synthesis and the nuclear processes they affect. *Curr Opin Cell Biol, 22*, 365-73. ↗

Saiardi, A., Snyder, SH., Caffrey, JJ., Shears, SB. (2000). The inositol hexakisphosphate kinase family. Catalytic flexibility and function in yeast vacuole biogenesis. *J Biol Chem, 275*, 24686-92. ↗

Wente, SR., Alcázar-Román, AR. (2008). Inositol polyphosphates: a new frontier for regulating gene expression. *Chromosoma, 117*, 1-13. ↗

Majerus, PW., Chang, SC. (2006). Inositol polyphosphate multikinase regulates inositol 1,4,5,6-tetrakisphosphate. *Biochem Biophys Res Commun, 339*, 209-16. ↗

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

Editions

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

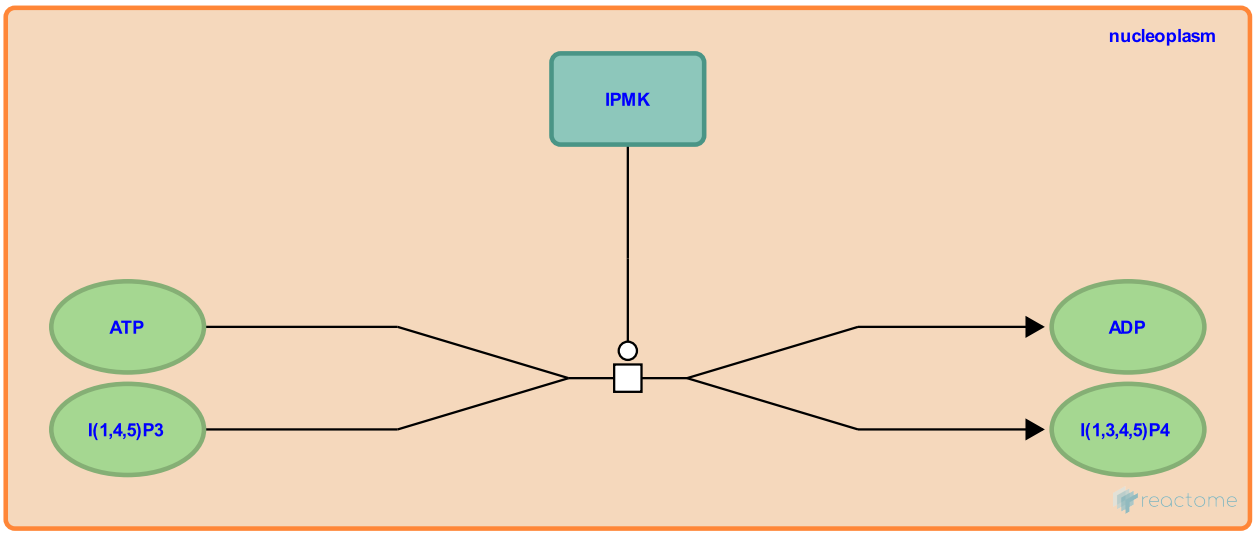
I(1,4,5)P3 is phosphorylated to I(1,3,4,5)P4 by IPMK in the nucleus ↗

Location: Synthesis of IPs in the nucleus

Stable identifier: R-HSA-1855233

Type: transition

Compartments: nucleoplasm



In the nucleus, inositol polyphosphate multikinase (IPMK) phosphorylates inositol 1,4,5-trisphosphate (I(1,4,5)P3) to inositol 1,3,4,5-tetrakisphosphate (I(1,3,4,5)P4) (Nalaskowski et al. 2002, Chang et al. 2002, Chang & Majerus 2006).

Followed by: I(1,3,4,5)P4 is phosphorylated to I(1,3,4,5,6)P5 by IPMK in the nucleus

Literature references

Majerus, PW., Chang, SC. (2006). Inositol polyphosphate multikinase regulates inositol 1,4,5,6-tetrakisphosphate. *Biochem Biophys Res Commun, 339*, 209-16. ↗

Wente, SR., Majerus, PW., Feng, Y., Miller, AL., Chang, SC. (2002). The human homolog of the rat inositol phosphate multikinase is an inositol 1,3,4,6-tetrakisphosphate 5-kinase. *J Biol Chem, 277*, 43836-43. ↗

Nalaskowski, MM., Deschermeier, C., Mayr, GW., Fanick, W. (2002). The human homologue of yeast ArgRIII protein is an inositol phosphate multikinase with predominantly nuclear localization. *Biochem J, 366*, 549-56. ↗

Editions

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

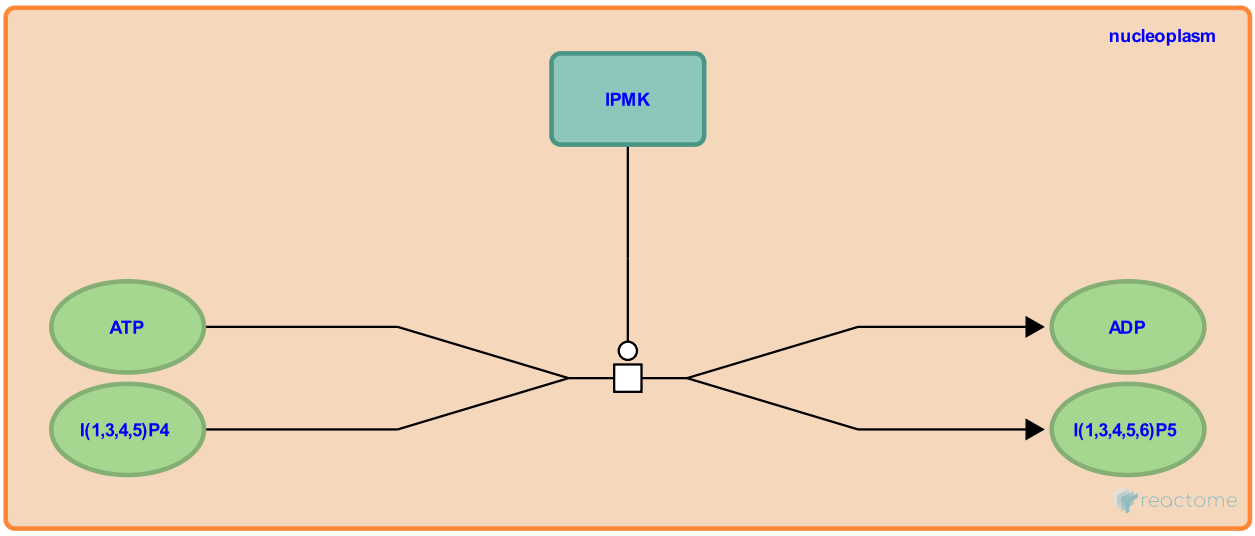
I(1,3,4,5)P4 is phosphorylated to I(1,3,4,5,6)P5 by IPMK in the nucleus ↗

Location: Synthesis of IPs in the nucleus

Stable identifier: R-HSA-1855206

Type: transition

Compartments: nucleoplasm



In the nucleus, inositol polyphosphate multikinase (IPMK) phosphorylates inositol 1,3,4,5-tetrakisphosphate (I(1,3,4,5)P4) to inositol 1,3,4,5,6-pentakisphosphate (I(1,3,4,5,6)P5) (Nalaskowski et al. 2002, Chang & Majerus 2006).

Preceded by: I(1,4,5)P3 is phosphorylated to I(1,3,4,5)P4 by IPMK in the nucleus

Followed by: I(1,3,4,5,6)P5 is phosphorylated to 5-PP-IP4 by IP6K1/2 in the nucleus, I(1,3,4,5,6)P5 is phosphorylated to IP6 by IPPK (IP5-2K) in the nucleus

Literature references

Majerus, PW., Chang, SC. (2006). Inositol polyphosphate multikinase regulates inositol 1,4,5,6-tetrakisphosphate. *Biochem Biophys Res Commun, 339*, 209-16. ↗

Nalaskowski, MM., Deschermeier, C., Mayr, GW., Fanick, W. (2002). The human homologue of yeast ArgRIII protein is an inositol phosphate multikinase with predominantly nuclear localization. *Biochem J, 366*, 549-56. ↗

Editions

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

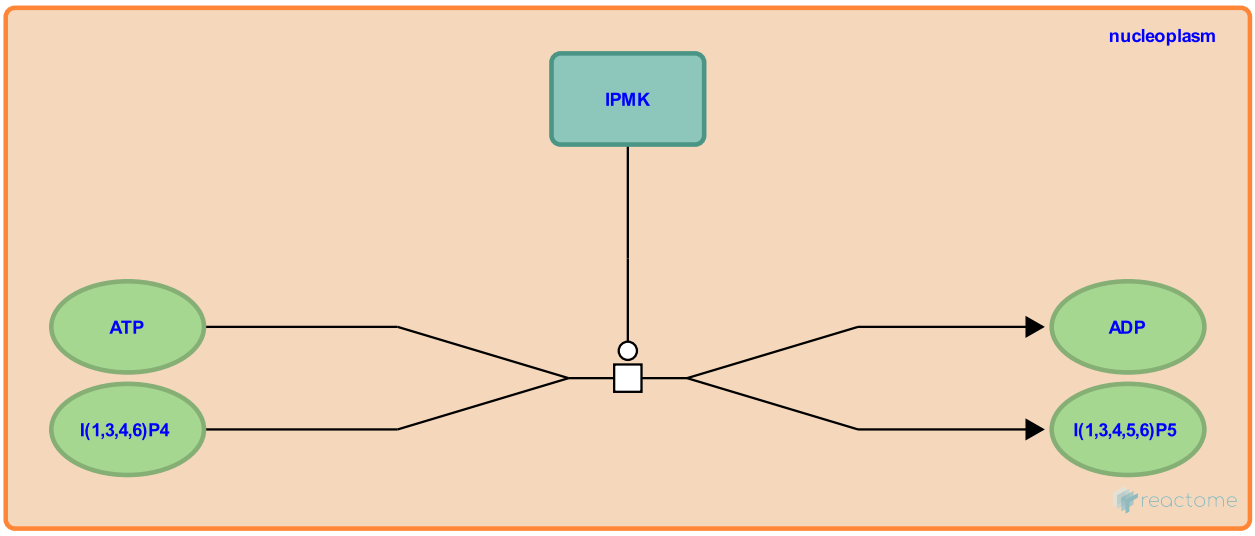
I(1,3,4,6)P4 is phosphorylated to I(1,3,4,5,6)P5 by IPMK in the nucleus ↗

Location: Synthesis of IPs in the nucleus

Stable identifier: R-HSA-1855228

Type: transition

Compartments: nucleoplasm



In the nucleus, inositol polyphosphate multikinase (IPMK) phosphorylates inositol 1,3,4,6-tetrakisphosphate (I(1,3,4,6)P4) to inositol 1,3,4,5,6-pentakisphosphate (I(1,3,4,5,6)P5) (Chang et al. 2002, Chang & Majerus 2006).

Followed by: I(1,3,4,5,6)P5 is phosphorylated to IP6 by IPPK (IP5-2K) in the nucleus, I(1,3,4,5,6)P5 is phosphorylated to 5-PP-IP4 by IP6K1/2 in the nucleus

Literature references

Majerus, PW., Chang, SC. (2006). Inositol polyphosphate multikinase regulates inositol 1,4,5,6-tetrakisphosphate. *Biochem Biophys Res Commun, 339*, 209-16. ↗

Wente, SR., Majerus, PW., Feng, Y., Miller, AL., Chang, SC. (2002). The human homolog of the rat inositol phosphate multikinase is an inositol 1,3,4,6-tetrakisphosphate 5-kinase. *J Biol Chem, 277*, 43836-43. ↗

Editions

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

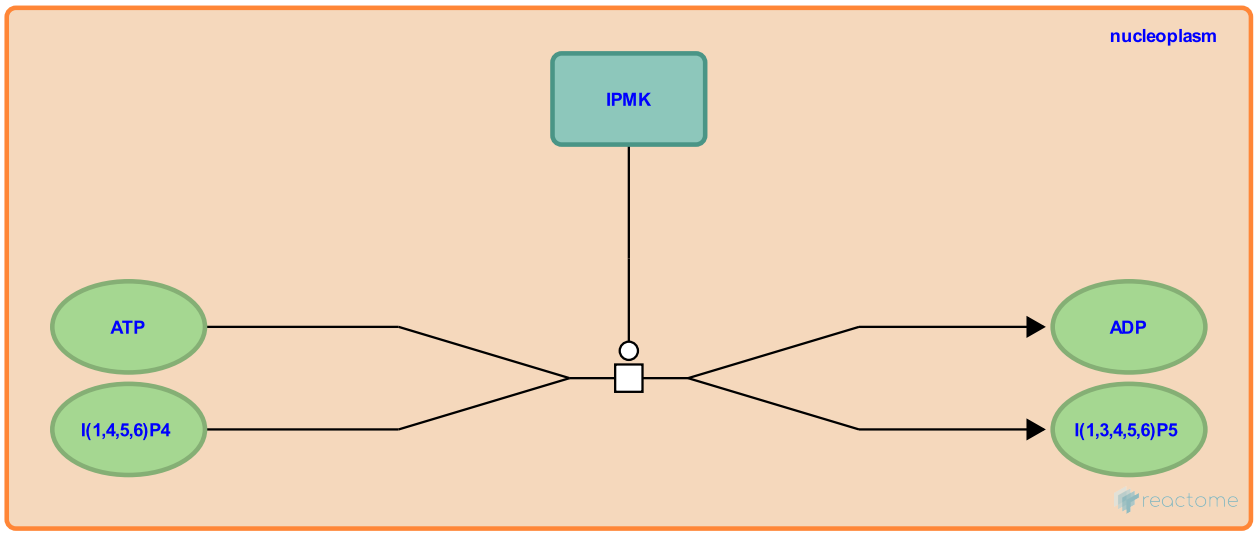
I(1,4,5,6)P4 is phosphorylated to I(1,3,4,5,6)P5 by IPMK in the nucleus ↗

Location: Synthesis of IPs in the nucleus

Stable identifier: R-HSA-1855185

Type: transition

Compartments: nucleoplasm



In the nucleus, inositol polyphosphate multikinase (IPMK) phosphorylates inositol 1,4,5,6-tetrakisphosphate (I(1,4,5,6)P4) to inositol 1,3,4,5,6-pentakisphosphate (I(1,3,4,5,6)P5) (Nalaskowski et al. 2002, Chang & Majerus 2006).

Followed by: I(1,3,4,5,6)P5 is phosphorylated to 5-PP-IP4 by IP6K1/2 in the nucleus, I(1,3,4,5,6)P5 is phosphorylated to IP6 by IPPK (IP5-2K) in the nucleus

Literature references

Majerus, PW., Chang, SC. (2006). Inositol polyphosphate multikinase regulates inositol 1,4,5,6-tetrakisphosphate. *Biochem Biophys Res Commun, 339*, 209-16. ↗

Nalaskowski, MM., Deschermeier, C., Mayr, GW., Fanick, W. (2002). The human homologue of yeast ArgRIII protein is an inositol phosphate multikinase with predominantly nuclear localization. *Biochem J, 366*, 549-56. ↗

Editions

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

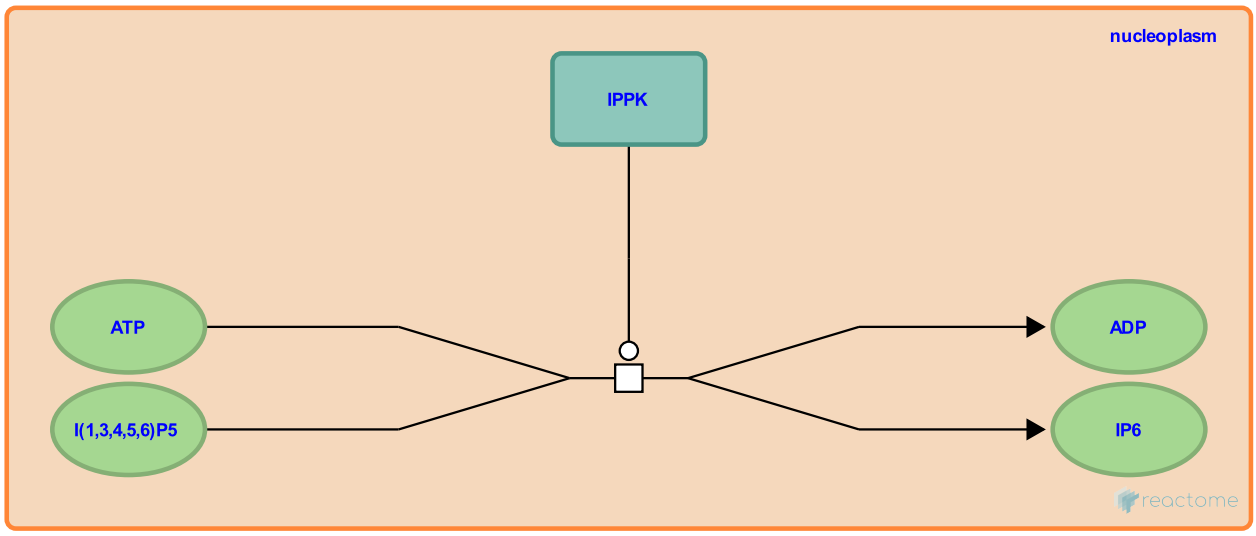
I(1,3,4,5,6)P5 is phosphorylated to IP6 by IPPK (IP5-2K) in the nucleus ↗

Location: Synthesis of IPs in the nucleus

Stable identifier: R-HSA-1855176

Type: transition

Compartments: nucleoplasm



In the nucleus, inositol-pentakisphosphate 2-kinase (IPPK - also known as IP5-2K) phosphorylates inositol 1,3,4,5,6-pentakisphosphate (I(1,3,4,5,6)P5) to inositol 1,2,3,4,5,6-hexakisphosphate (IP6) (Verbsky et al. 2002, Brehm et al. 2007, Choi et al. 2007).

Preceded by: I(1,4,5,6)P4 is phosphorylated to I(1,3,4,5,6)P5 by IPMK in the nucleus, I(1,3,4,5)P4 is phosphorylated to I(1,3,4,5,6)P5 by IPMK in the nucleus, I(1,3,4,6)P4 is phosphorylated to I(1,3,4,5,6)P5 by IPMK in the nucleus

Followed by: IP6 is phosphorylated to 5-PP-IP5 by IP6K1/2 in the nucleus

Literature references

Nalaskowski, MM., Windhorst, S., Schenk, TM., Kobras, M., Brehm, MA., Mayr, GW. et al. (2007). Intracellular localization of human Ins(1,3,4,5,6)P5 2-kinase. *Biochem J, 408*, 335-45. ↗

Cho, J., Williams, J., Falck, JR., Choi, JH., Shears, SB. (2007). Purification, sequencing, and molecular identification of a mammalian PP-InsP5 kinase that is activated when cells are exposed to hyperosmotic stress. *J Biol Chem, 282* , 30763-75. ↗

Wente, SR., Majerus, PW., Kisseleva, MV., Wilson, MP., Verbsky, JW. (2002). The synthesis of inositol hexakisphosphate. Characterization of human inositol 1,3,4,5,6-pentakisphosphate 2-kinase. *J Biol Chem, 277*, 31857-62. ↗

Editions

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

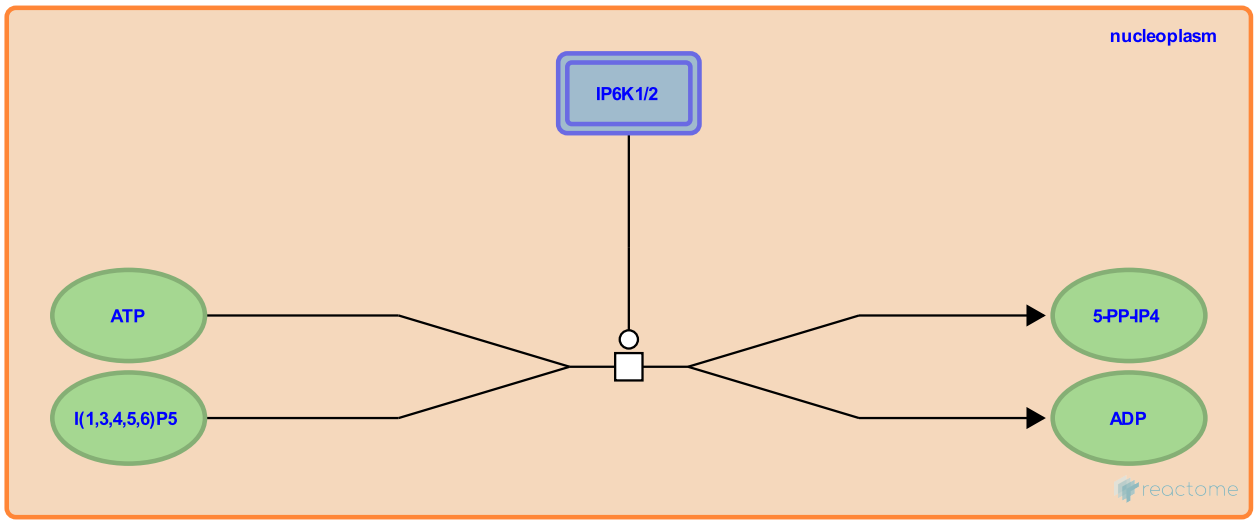
I(1,3,4,5,6)P5 is phosphorylated to 5-PP-IP4 by IP6K1/2 in the nucleus ↗

Location: Synthesis of IPs in the nucleus

Stable identifier: R-HSA-1855181

Type: transition

Compartments: nucleoplasm



In the nucleus, inositol hexakisphosphate kinase 1 (IP6K1) and 2 (IP6K2) phosphorylate inositol 1,3,4,5,6-pentakisphosphate (I(1,3,4,5,6)P5) to inositol 5-diphospho-(1,3,4,6)-tetrakisphosphate (5-PP-IP4) (Saiardi et al. 2001, Saiardi et al. 2000, Draskovic et al. 2008).

Preceded by: I(1,4,5,6)P4 is phosphorylated to I(1,3,4,5,6)P5 by IPMK in the nucleus, I(1,3,4,5)P4 is phosphorylated to I(1,3,4,5,6)P5 by IPMK in the nucleus, I(1,3,4,6)P4 is phosphorylated to I(1,3,4,5,6)P5 by IPMK in the nucleus

Followed by: 5-PP-IP4 is phosphorylated to 1,5-(PP)2-IP3 by IP6K1/2 in the nucleus

Literature references

Saiardi, A., Snyder, SH., Caffrey, JJ., Shears, SB. (2000). The inositol hexakisphosphate kinase family. Catalytic flexibility and function in yeast vacuole biogenesis. *J Biol Chem, 275*, 24686-92. ↗

Ilc, G., Bhandari, R., Burton, A., Kovacevic, M., Saiardi, A., Podobnik, M. et al. (2008). Inositol hexakisphosphate kinase products contain diphosphate and triphosphate groups. *Chem Biol, 15*, 274-86. ↗

Nagata, E., Saiardi, A., Snyder, SH., Snowman, AM., Luo, HR. (2001). Identification and characterization of a novel inositol hexakisphosphate kinase. *J Biol Chem, 276*, 39179-85. ↗

Editions

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

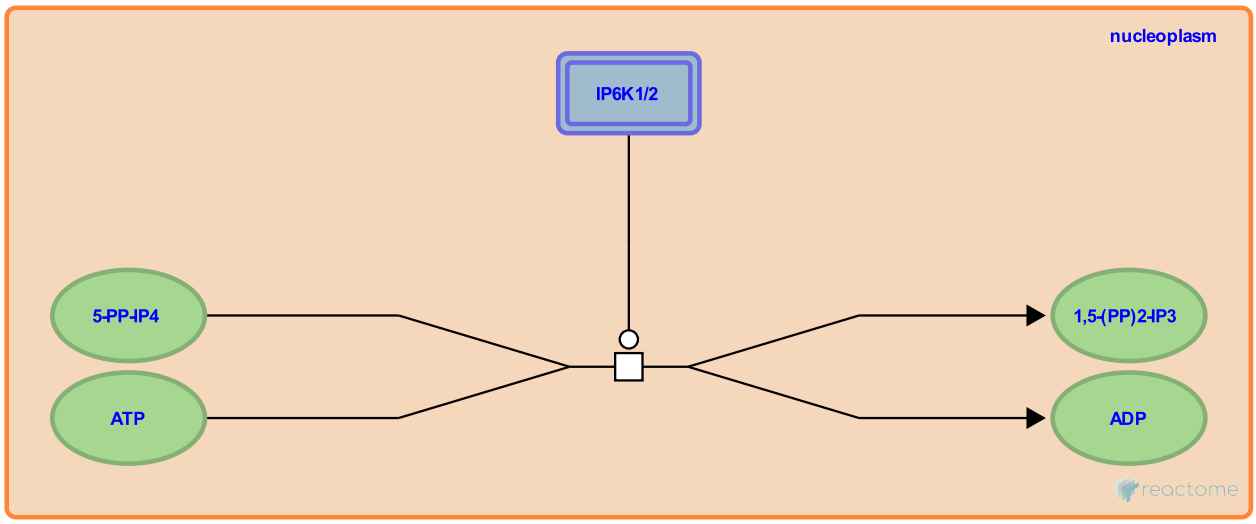
5-PP-IP4 is phosphorylated to 1,5-(PP)2-IP3 by IP6K1/2 in the nucleus ↗

Location: Synthesis of IPs in the nucleus

Stable identifier: R-HSA-1855230

Type: transition

Compartments: nucleoplasm



In the nucleus, inositol hexakisphosphate kinase 1 (IP6K1) and 2 (IP6K2) phosphorylate5-diphospho-1,3,4,6-tetrakisphosphate (5-PP-IP4) to inositol 1,5-bisdiphospho-3,4,6-trisphosphate (1,5-(PP)2-IP3) (Saiardi et al. 2001, Saiardi et al. 2000, Draskovic et al. 2008).

Preceded by: I(1,3,4,5,6)P5 is phosphorylated to 5-PP-IP4 by IP6K1/2 in the nucleus

Literature references

Saiardi, A., Snyder, SH., Caffrey, JJ., Shears, SB. (2000). The inositol hexakisphosphate kinase family. Catalytic flexibility and function in yeast vacuole biogenesis. *J Biol Chem, 275*, 24686-92. ↗

Ilc, G., Bhandari, R., Burton, A., Kovacevic, M., Saiardi, A., Podobnik, M. et al. (2008). Inositol hexakisphosphate kinase products contain diphosphate and triphosphate groups. *Chem Biol, 15*, 274-86. ↗

Nagata, E., Saiardi, A., Snyder, SH., Snowman, AM., Luo, HR. (2001). Identification and characterization of a novel inositol hexakisphosphate kinase. *J Biol Chem, 276*, 39179-85. ↗

Editions

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

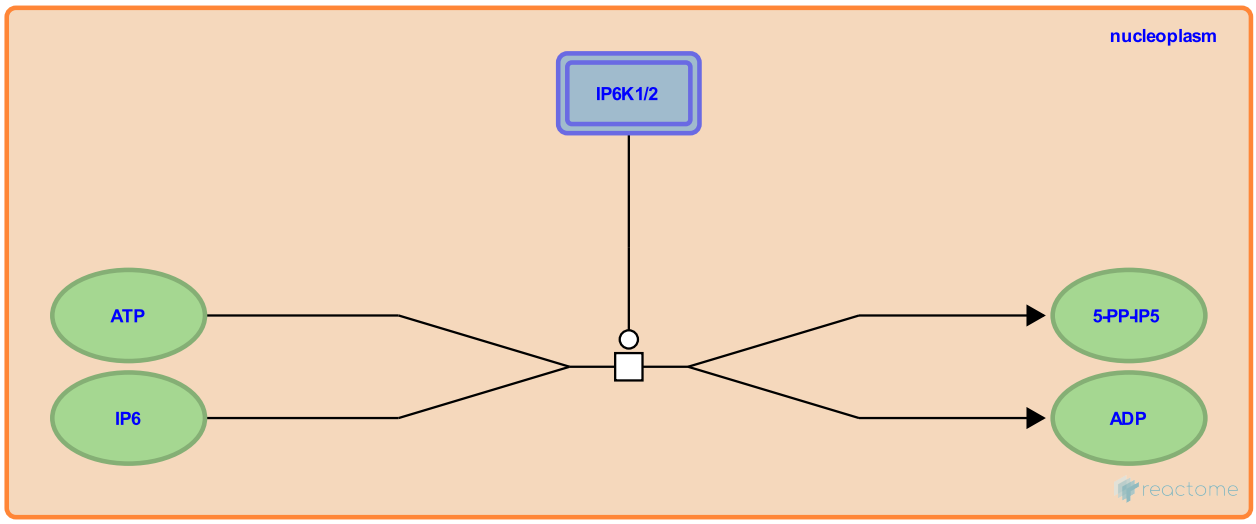
IP6 is phosphorylated to 5-PP-IP5 by IP6K1/2 in the nucleus ↗

Location: Synthesis of IPs in the nucleus

Stable identifier: R-HSA-1855207

Type: transition

Compartments: nucleoplasm



In the nucleus, inositol hexakisphosphate kinase 1 (IP6K1) and 2 (IP6K2) phosphorylate inositol 1,2,3,4,5,6-hexakisphosphate (IP6) to inositol 5-diphospho-1,2,3,4,6-pentakisphosphate (5-PP-IP5).

The following lists the above proteins with their corresponding literature references: IP6K1 (Saiardi et al. 2001, Mulugu et al. 2007, Draskovic et al. 2008) and IP6K2 (Saiardi et al. 2001, Mulugu et al. 2007, Draskovic et al. 2008).

Preceded by: I(1,3,4,5,6)P5 is phosphorylated to IP6 by IPPK (IP5-2K) in the nucleus

Followed by: 5-PP-IP5 is phosphorylated to 5-PPP-IP5 by IP6K1/2 in the nucleus

Literature references

Ilc, G., Bhandari, R., Burton, A., Kovacevic, M., Saiardi, A., Podobnik, M. et al. (2008). Inositol hexakisphosphate kinase products contain diphosphate and triphosphate groups. *Chem Biol, 15*, 274-86. ↗

Nagata, E., Saiardi, A., Snyder, SH., Snowman, AM., Luo, HR. (2001). Identification and characterization of a novel inositol hexakisphosphate kinase. *J Biol Chem, 276*, 39179-85. ↗

Haystead, TA., Dollins, DE., Ribeiro, AA., Otto, JC., Bai, W., York, JD. et al. (2007). A conserved family of enzymes that phosphorylate inositol hexakisphosphate. *Science, 316*, 106-9. ↗

Editions

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

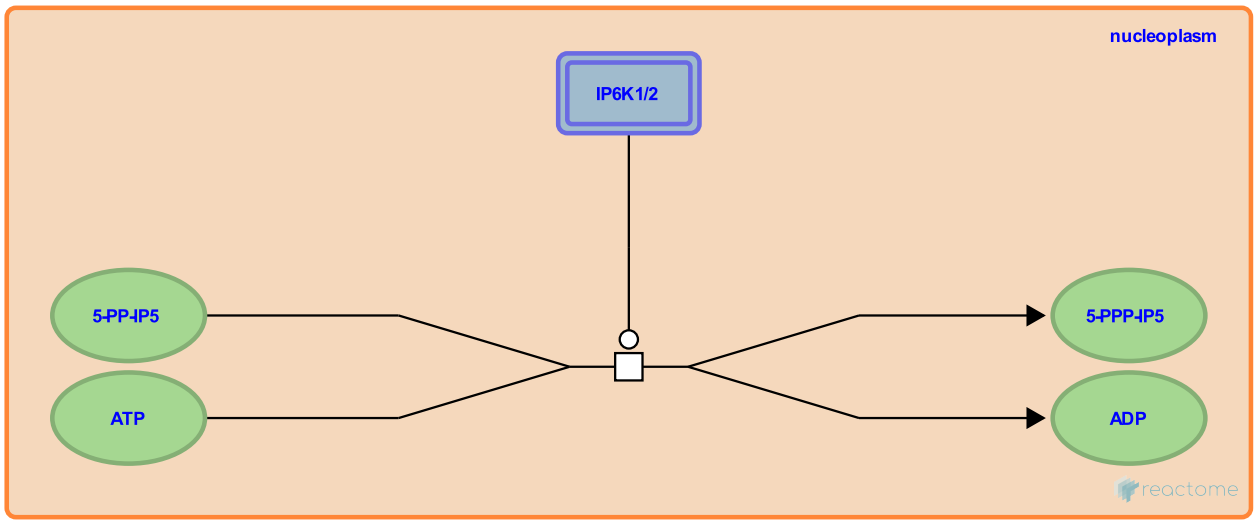
5-PP-IP5 is phosphorylated to 5-PPP-IP5 by IP6K1/2 in the nucleus ↗

Location: Synthesis of IPs in the nucleus

Stable identifier: R-HSA-1855224

Type: transition

Compartments: nucleoplasm



In the nucleus, inositol hexakisphosphate kinase 1 (IP6K1) and 2 (IP6K2) phosphorylate inositol 5-diphospho-1,2,3,4,6-pentakisphosphate (5-PP-IP5) to inositol 5-triphospho- 1,2,3,4,6-pentakisphosphate (5-PPP-IP5) (Saiardi et al. 2001, Draskovic et al. 2008) and IP6K2 (Saiardi et al. 2001, Draskovic et al. 2008). While this reaction has been demonstrated to occur in vitro, the extent to which it occurs in vivo is less clear.

Preceded by: IP6 is phosphorylated to 5-PP-IP5 by IP6K1/2 in the nucleus

Literature references

Ilc, G., Bhandari, R., Burton, A., Kovacevic, M., Saiardi, A., Podobnik, M. et al. (2008). Inositol hexakisphosphate kinase products contain diphosphate and triphosphate groups. *Chem Biol, 15*, 274-86. ↗

Nagata, E., Saiardi, A., Snyder, SH., Snowman, AM., Luo, HR. (2001). Identification and characterization of a novel inositol hexakisphosphate kinase. *J Biol Chem, 276*, 39179-85. ↗

Editions

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

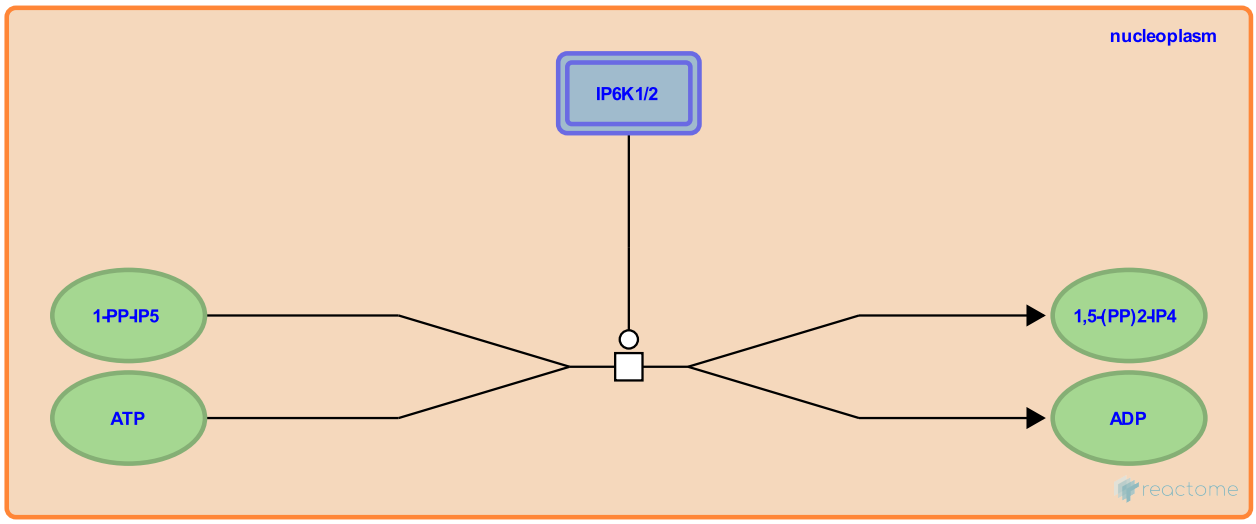
1-PP-IP5 is phosphorylated to 1,5-(PP)2-IP4 by IP6K1/2 in the nucleus ↗

Location: Synthesis of IPs in the nucleus

Stable identifier: R-HSA-1855157

Type: transition

Compartments: nucleoplasm



In the nucleus, inositol hexakisphosphate kinase 1 (IP6K1) and 2 (IP6K2) phosphorylate 1-diphospho-2,3,4,5,6-pentakisphosphate (1-PP-IP5) to make inositol 1,5-bisdiphospho-2,3,4,6-tetrakisphosphate (1,5-(PP)2-IP4) (Saiardi et al. 2001, Mulugu et al. 2007).

Literature references

Nagata, E., Saiardi, A., Snyder, SH., Snowman, AM., Luo, HR. (2001). Identification and characterization of a novel inositol hexakisphosphate kinase. *J Biol Chem, 276*, 39179-85. ↗

Haystead, TA., Dollins, DE., Ribeiro, AA., Otto, JC., Bai, W., York, JD. et al. (2007). A conserved family of enzymes that phosphorylate inositol hexakisphosphate. *Science, 316*, 106-9. ↗

Editions

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

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