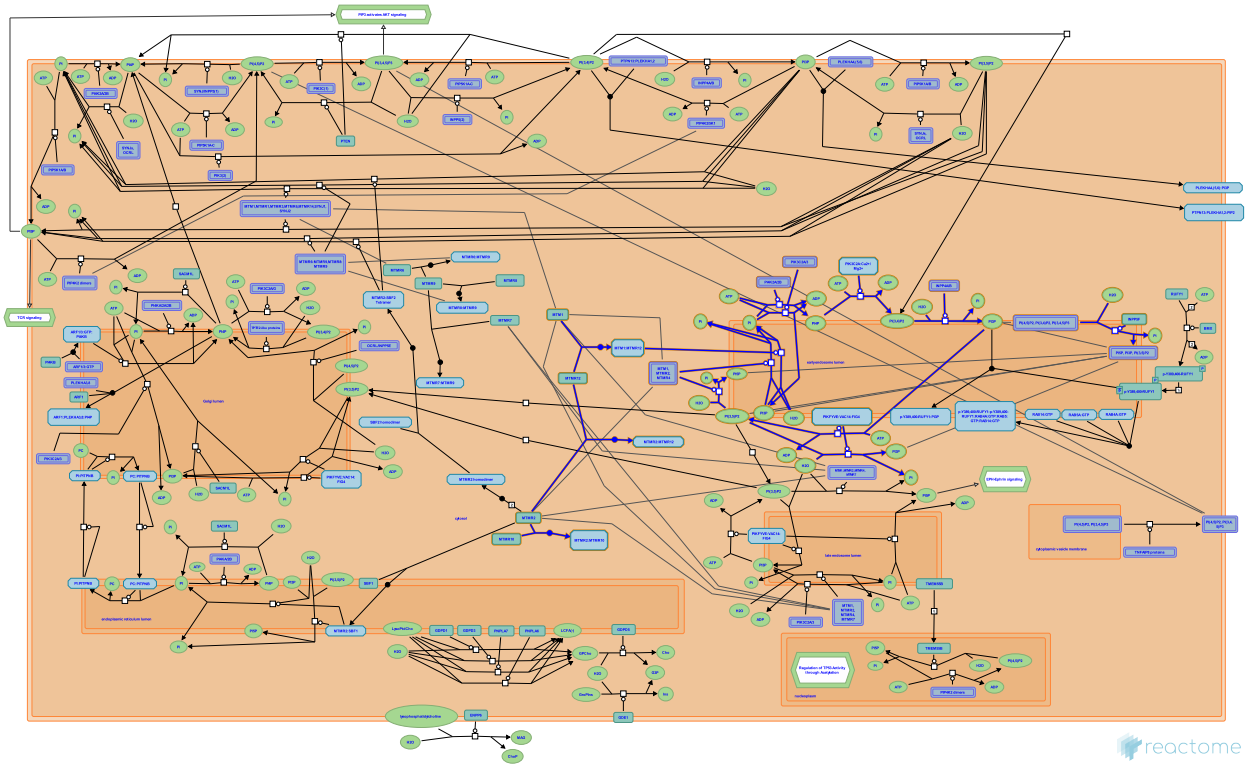
Synthesis of PIPs at the early endosome membrane



D'Eustachio, P., Jupe, S., Orlic-Milacic, M., Rush, MG., Wakelam, M., Williams, MG.

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

03/05/2024

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. ↗

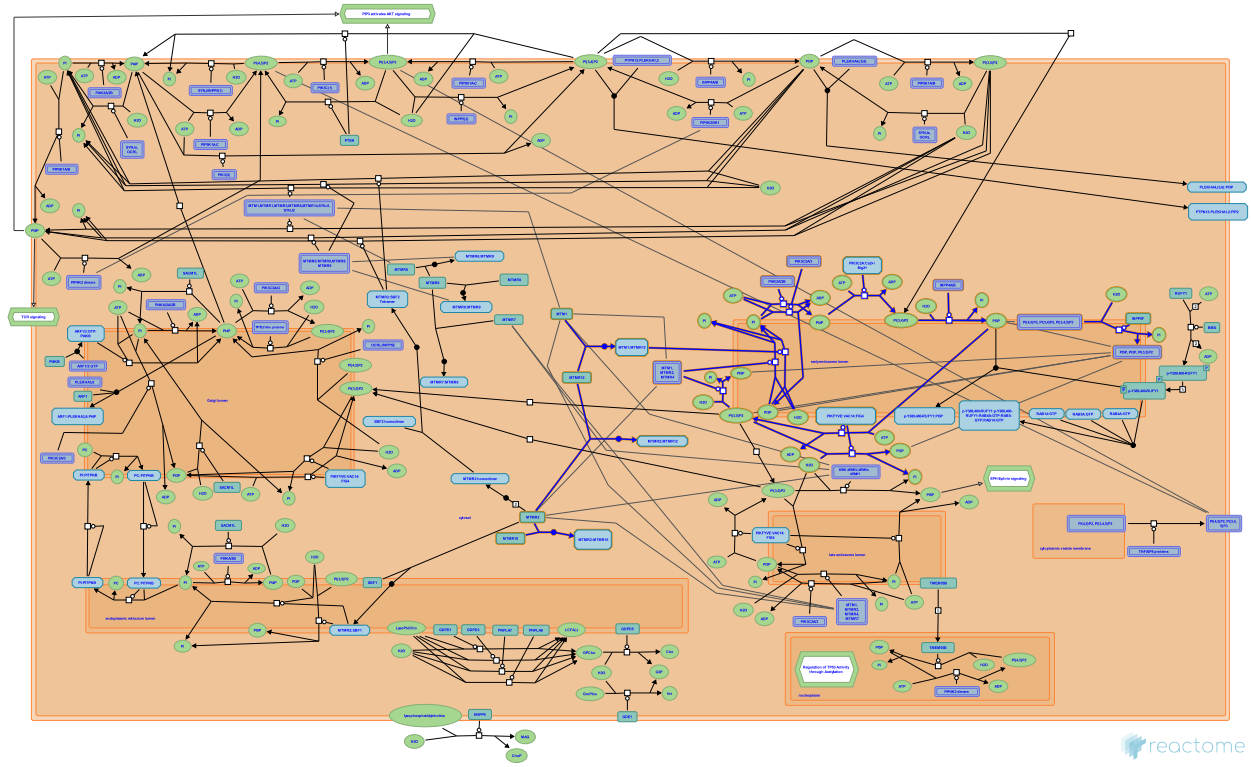
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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 PIPs at the early endosome membrane ↗

Stable identifier: R-HSA-1660516



At the early endosome membrane, phosphatidylinositol 3,5-bisphosphate (PI(3,5)P2) is generated in two steps from phosphatidylinositol 3,4-bisphosphate PI(3,4)P2 by the action of various kinases and phosphatases (Sbrissa et al. 2007, Sbrissa et al. 2008, Cao et al. 2007, Cao et al. 2008, Arcaro et al. 2000, Kim et al. 2002).

Literature references

Waterfield, MD., Arcaro, A., Wallasch, C., Ullrich, A., Zvelebil, MJ., Domin, J. (2000). Class II phosphoinositide 3-kinases are downstream targets of activated polypeptide growth factor receptors. *Mol Cell Biol, 20*, 3817-30. ↗

Bedrick, EJ., Wandinger-Ness, A., Cao, C., Laporte, J., Backer, JM. (2008). Sequential actions of myotubularin lipid phosphatases regulate endosomal PI(3)P and growth factor receptor trafficking. *Mol Biol Cell, 19*, 3334-46. ↗

Sbrissa, D., Ijuin, T., Gruenberg, J., Fu, Z., Shisheva, A., Takenawa, T. et al. (2007). Core protein machinery for mammalian phosphatidylinositol 3,5-bisphosphate synthesis and turnover that regulates the progression of endosomal transport. Novel Sac phosphatase joins the ArPIKfyve-PIKfyve complex. *J Biol Chem, 282*, 23878-91. ↗

Wandinger-Ness, A., Cao, C., Laporte, J., Stein, MP., Backer, JM. (2007). Myotubularin lipid phosphatase binds the hVPS15/hVPS34 lipid kinase complex on endosomes. *Traffic, 8*, 1052-67. ↗

Taylor, GS., Torgersen, KM., Kim, SA., Dixon, JE. (2002). Myotubularin and MTMR2, phosphatidylinositol 3-phosphatases mutated in myotubular myopathy and type 4B Charcot-Marie-Tooth disease. *J Biol Chem, 277*, 4526-31. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-10-18	Authored	Williams, MG.
2012-05-14	Reviewed	Wakelam, M.
2017-02-24	Revised	Orlic-Milacic, M.

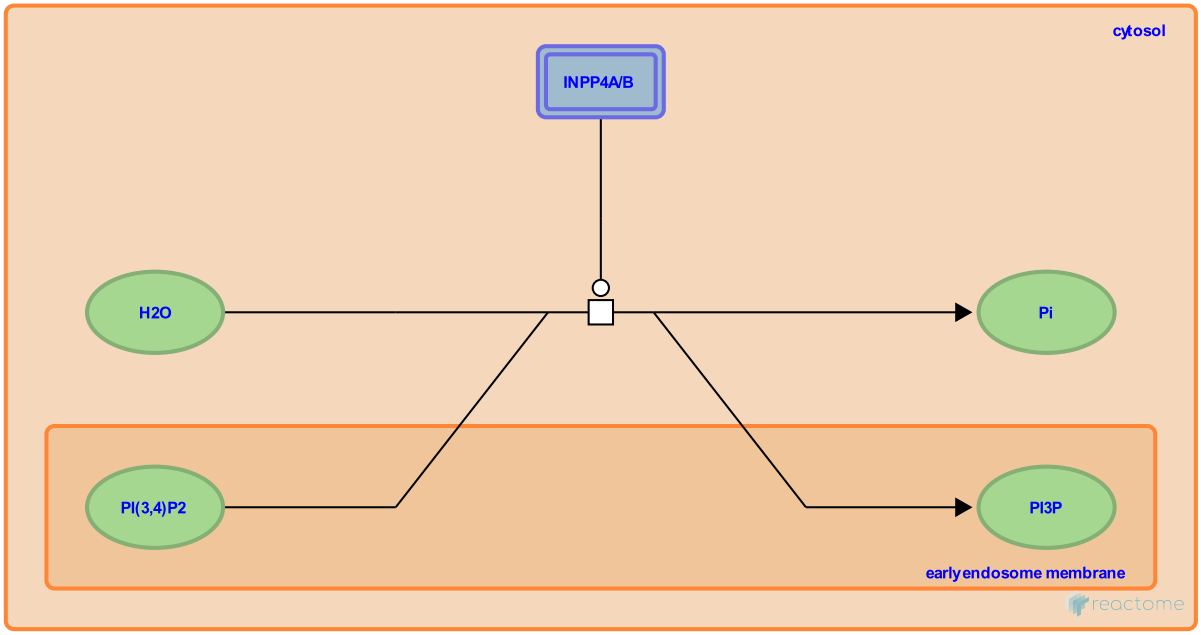
PI(3,4)P2 is dephosphorylated to PI3P by INPP4A/B at the early endosome membrane ↗

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-1676162

Type: transition

Compartments: cytosol, early endosome membrane



At the early endosome membrane, type I (INPP4A) (Norris et al. 1995, Ivetac et al. 2005) and type II inositol-3,4-bisphosphate 4-phosphatase (INPP4B) (Norris et al. 1997) colocalise with early and recycling endosomes through their C2 domains which bind to the phosphatidylinositol 3,4-bisphosphate (PI(3,4)P2) present in these membranes. It is here that phosphatidylinositol 3,4-bisphosphate (PI(3,4)P2) is dephosphorylated by INPP4A/B to phosphatidylinositol 3-phosphate (PI3P).

Preceded by: PI4P is phosphorylated to PI(3,4)P2 by PIK3C2A at the early endosome membrane

Followed by: PI3P is dephosphorylated to PI by MTM1:MTMR12, PI3P is phosphorylated to PI(3,5)P2 by PIKFYVE at the early endosome membrane, PI3P is dephosphorylated to PI by MTM proteins at the early endosome membrane

Literature references

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

Luff, S., Majerus, PW., Kisseleva, MV., Rowe, T., Zhang, XM., Tiganis, T. et al. (2005). The type Ialpha inositol polyphosphate 4-phosphatase generates and terminates phosphoinositide 3-kinase signals on endosomes and the plasma membrane. *Mol Biol Cell, 16*, 2218-33. ↗

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. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-10-18	Authored	Williams, MG.
2012-05-14	Reviewed	Wakelam, M.

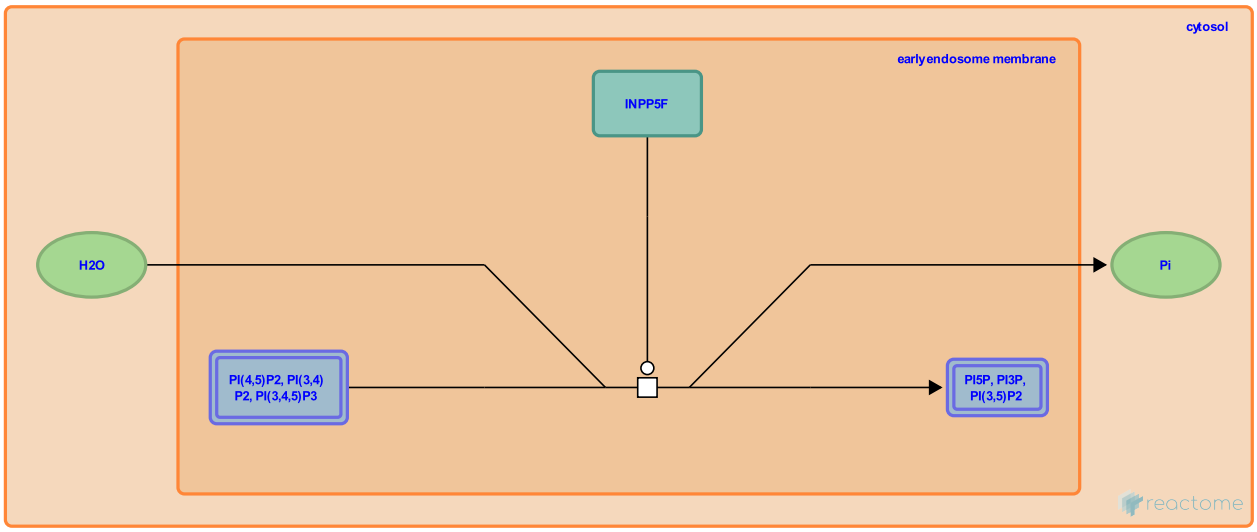
PI(4,5)P2, PI(3,4)P2 and PI(3,4,5)P3 are dephosphorylated to PI5P, PI3P and PI(3,4)P by INPP5F at the endosome membrane ↗

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-8849969

Type: transition

Compartments: early endosome membrane, cytosol



Characterization of human INPP5F (SAC2) identified that it is a 4-phosphatase with highest activity against PI(4,5)P2, PI(3,4)P2, and PI(3,4,5)P3, generating PI(5)P, PI(3)P and PI(3,5)P2 respectively (Nakatsu et al. 2015, Hsu et al. 2015). Inpp5f -/- mice have elevated level of PIP3 and exhibit accentuated cardiac hypertrophy as measured by heart size, myocyte size and gene expression (Zhu et al. 2009).

Literature references

Messa, M., Zou, Y., Strittmatter, SM., Nández, R., De Camilli, P., Nakatsu, F. et al. (2015). Sac2/INPP5F is an inositol 4-phosphatase that functions in the endocytic pathway. *J. Cell Biol., 209*, 85-95. ↗

Editions

2015-12-18	Authored	Jupe, S.
2016-01-04	Edited	Jupe, S.
2016-01-05	Reviewed	D'Eustachio, P.

PI3P is phosphorylated to PI(3,5)P2 by PIKFYVE at the early endosome membrane ↗

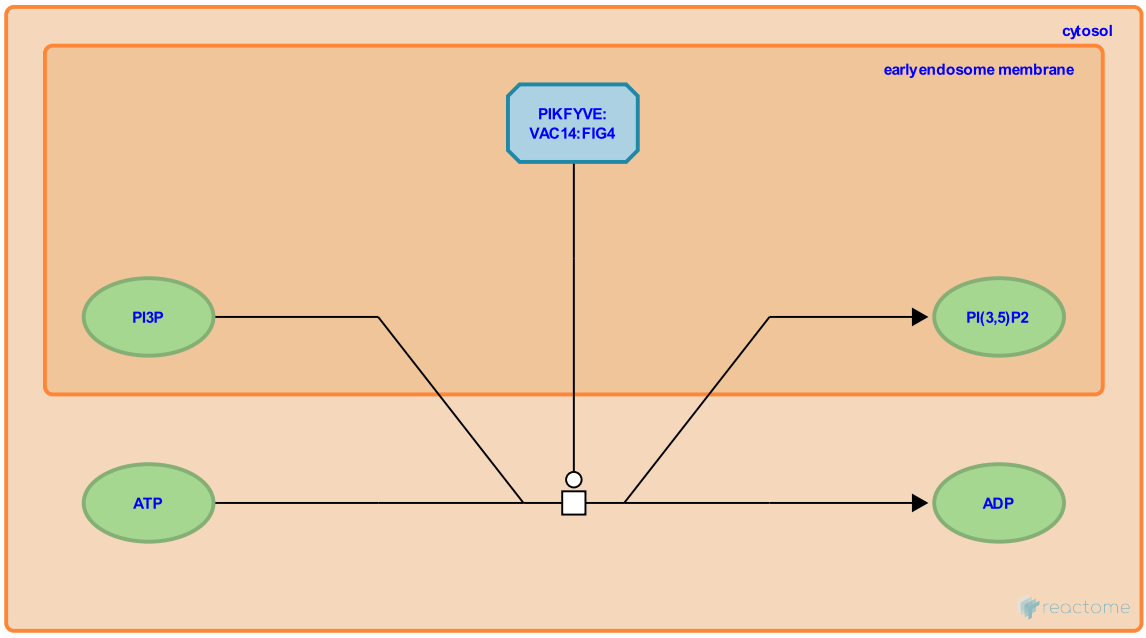
Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-1676168

Type: transition

Compartments: cytosol, early endosome membrane

Inferred from: PI3P is phosphorylated to PI(3,5)P2 by Pikfyve at the early endosome membrane (Mus musculus)



At the early endosome membrane, the PAS complex, consisting of FYVE finger-containing phosphoinositide kinase (PIKFYVE), yeast VAC14 homologue (VAC14), and polyphosphoinositide phosphatase aka SAC3 (FIG4), binds to the membrane via PIKFYVE's FYVE finger (Sbrissa et al. 2002, Cao et al. 2007). The PIKFYVE kinase component phosphorylates phosphatidylinositol 3-phosphate (PI3P) to phosphatidylinositol 3,5-bisphosphate PI(3,5)P2 (Sbrissa et al. 1999). The PAS complex is present in the cytosol and is recruited to the membrane (Sbrissa et al. 2007).

Preceded by: PI(3,4)P2 is dephosphorylated to PI3P by INPP4A/B at the early endosome membrane, PI is phosphorylated to PI3P by PIK3C2A/3 at the early endosome membrane, PI(3,5)P2 is dephosphorylated to PI3P by FIG4 at the early endosome membrane

Followed by: PI(3,5)P2 is dephosphorylated to PI5P by MTM proteins at the early endosome membrane, PI(3,5)P2 is dephosphorylated to PI3P by FIG4 at the early endosome membrane

Literature references

Sbrissa, D., Shisheva, A., Ikonomov, OC. (2002). Phosphatidylinositol 3-phosphate-interacting domains in PIKfyve. Binding specificity and role in PIKfyve. Endomenbrane localization. *J Biol Chem, 277*, 6073-9. ↗

Sbrissa, D., Shisheva, A., Ikonomov, OC. (1999). PIKfyve, a mammalian ortholog of yeast Fab1p lipid kinase, synthesizes 5-phosphoinositides. Effect of insulin. *J Biol Chem, 274*, 21589-97. ↗

Sbrissa, D., Ijuin, T., Gruenberg, J., Fu, Z., Shisheva, A., Takenawa, T. et al. (2007). Core protein machinery for mammalian phosphatidylinositol 3,5-bisphosphate synthesis and turnover that regulates the progression of endosomal transport. Novel Sac phosphatase joins the ArPIKfyve-PIKfyve complex. *J Biol Chem, 282*, 23878-91. ↗

Wandinger-Ness, A., Cao, C., Laporte, J., Stein, MP., Backer, JM. (2007). Myotubularin lipid phosphatase binds the hVPS15/hVPS34 lipid kinase complex on endosomes. *Traffic, 8*, 1052-67. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-10-18	Authored	Williams, MG.
2012-05-14	Reviewed	Wakelam, M.

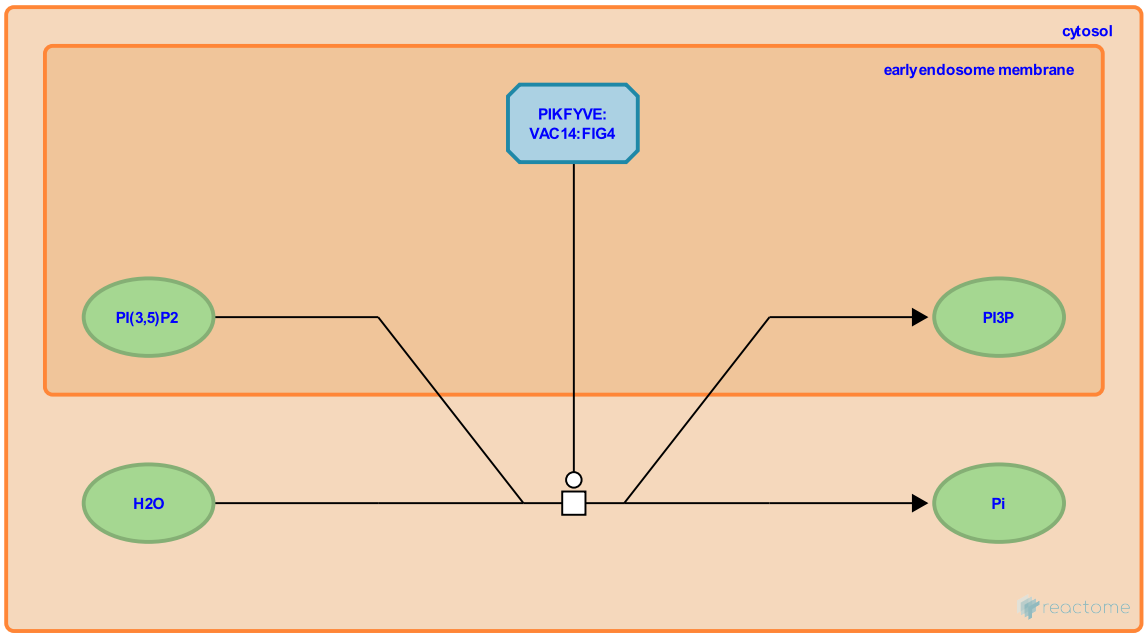
PI(3,5)P2 is dephosphorylated to PI3P by FIG4 at the early endosome membrane ↗

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-1676174

Type: transition

Compartments: cytosol, early endosome membrane



At the early endosome membrane, the PAS complex, consisting of FYVE finger-containing phosphoinositide kinase (PIKFYVE), yeast VAC14 homologue (VAC14), and polyphosphoinositide phosphatase aka SAC3 (FIG4), binds to the membrane via PIKFYVE's FYVE finger. The FIG4 phosphatase component dephosphorylates phosphatidylinositol 3,5-bisphosphate (PI(3,5)P2) to phosphatidylinositol 3-phosphate (PI3P) (Sbrissa et al. 2007, Sbrissa et al. 2008).

Preceded by: PI3P is phosphorylated to PI(3,5)P2 by PIKFYVE at the early endosome membrane

Followed by: PI3P is dephosphorylated to PI by MTM1:MTMR12, PI3P is dephosphorylated to PI by MTM proteins at the early endosome membrane, PI3P is phosphorylated to PI(3,5)P2 by PIKFYVE at the early endosome membrane

Literature references

Sbrissa, D., Ijuin, T., Gruenberg, J., Fu, Z., Shisheva, A., Takenawa, T. et al. (2007). Core protein machinery for mammalian phosphatidylinositol 3,5-bisphosphate synthesis and turnover that regulates the progression of endosomal transport. Novel Sac phosphatase joins the ArPIKfyve-PIKfyve complex. *J Biol Chem, 282*, 23878-91. ↗

Sbrissa, D., Shisheva, A., Ikonomov, OC., Fenner, H. (2008). ArPIKfyve homomeric and heteromeric interactions scaffold PIKfyve and Sac3 in a complex to promote PIKfyve activity and functionality. *J Mol Biol, 384*, 766-79. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-10-18	Authored	Williams, MG.
2012-05-14	Reviewed	Wakelam, M.

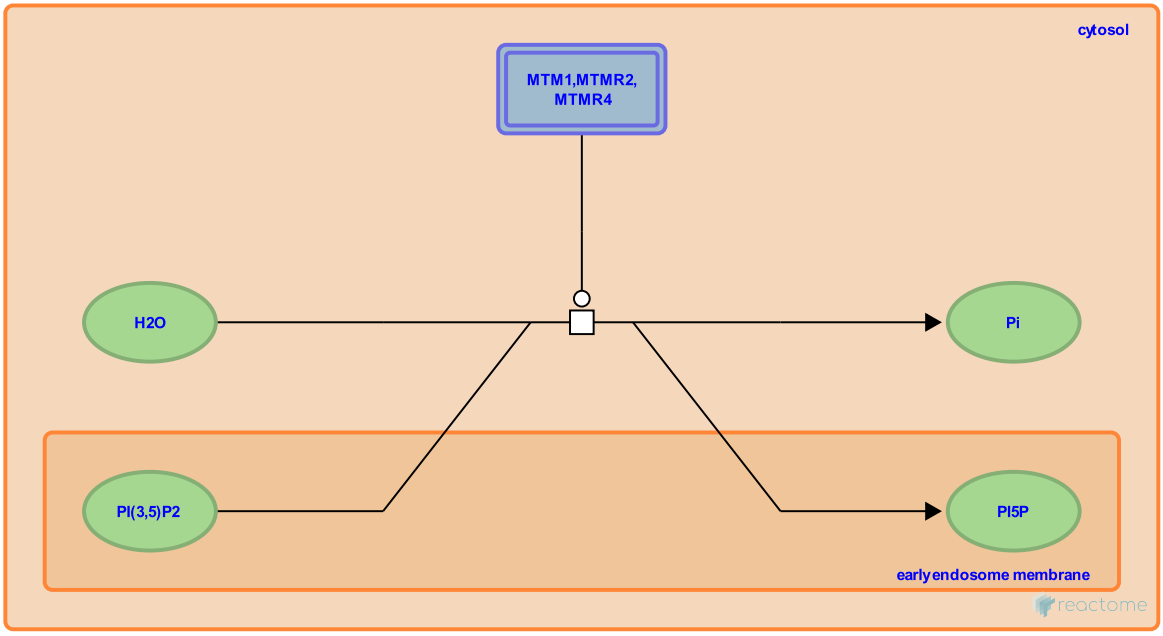
PI(3,5)P2 is dephosphorylated to PI5P by MTM proteins at the early endosome membrane ↗

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-1676105

Type: transition

Compartments: cytosol, early endosome membrane



At the early endosome membrane, myotubularin (MTM1), myotubularin-related protein 2 (MTMR2) and myotubularin-related protein 4 (MTMR4) dephosphorylate phosphatidylinositol 3,5-bisphosphate (PI(3,5)P2) to phosphatidylinositol 5-phosphate (PI5P).

The following lists the above proteins with their corresponding literature references: MTM1 (Cao et al. 2007, Cao et al. 2008), MTMR2 (Cao et al. 2008), and MTMR4 (Lorenzo et al. 2006).

Preceded by: PI3P is phosphorylated to PI(3,5)P2 by PIKFYVE at the early endosome membrane

Literature references

Lorenzo, O., Clague, MJ., Urbé, S. (2006). Systematic analysis of myotubularins: heteromeric interactions, subcellular localisation and endosome related functions. *J Cell Sci, 119*, 2953-9. ↗

Bedrick, EJ., Wandinger-Ness, A., Cao, C., Laporte, J., Backer, JM. (2008). Sequential actions of myotubularin lipid phosphatases regulate endosomal PI(3)P and growth factor receptor trafficking. *Mol Biol Cell, 19*, 3334-46. ↗

Wandinger-Ness, A., Cao, C., Laporte, J., Stein, MP., Backer, JM. (2007). Myotubularin lipid phosphatase binds the hVPS15/hVPS34 lipid kinase complex on endosomes. *Traffic, 8*, 1052-67. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-10-18	Authored	Williams, MG.
2012-05-14	Reviewed	Wakelam, M.
2017-01-10	Reviewed	Rush, MG.
2017-01-25	Edited	Orlic-Milacic, M.

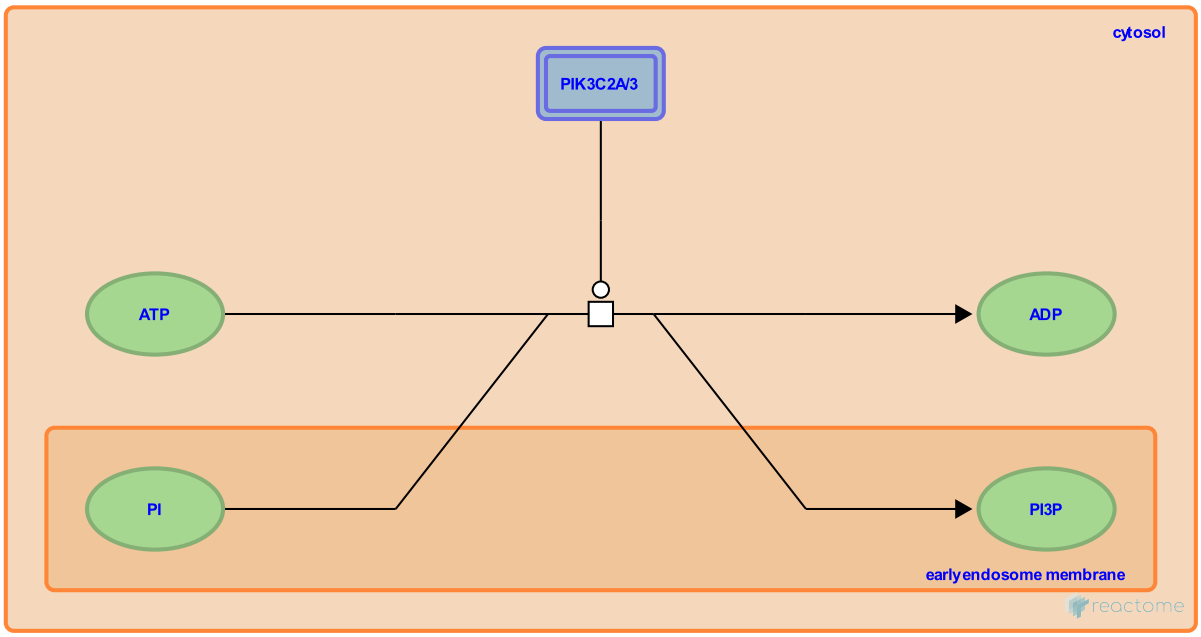
PI is phosphorylated to PI3P by PIK3C2A/3 at the early endosome membrane ↗

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-1675939

Type: transition

Compartments: cytosol, early endosome membrane



At the early endosome membrane, phosphatidylinositol 3-kinase catalytic subunit type 3 (PIK3C3) aka VPS34 binds to phosphoinositide 3-kinase regulatory subunit 4 (PIK3R4). The PIK3C3:PIK3R4 complex and phosphatidylinositol-4-phosphate 3-kinase C2 domain-containing subunit alpha (PIK3C2A) phosphorylate phosphatidylinositol (PI) to phosphatidylinositol 3-phosphate (PI3P).

The following lists the above proteins with their corresponding literature references: PIK3C3:PIK3R4 complex (Panaretou et al. 1997, Volinia et al. 1995, Cao et al. 2007) and PIK3C2A (Arcaro et al. 2000, Domin et al. 2000).

Preceded by: PI3P is dephosphorylated to PI by MTM proteins at the early endosome membrane

Followed by: PI3P is dephosphorylated to PI by MTM1:MTMR12, PI3P is phosphorylated to PI(3,5)P2 by PIKFYVE at the early endosome membrane, PI3P is dephosphorylated to PI by MTM proteins at the early endosome membrane

Literature references

Waterfield, MD., Dhand, R., Stein, R., MacDougall, LK., Vanhaesebroeck, B., Volinia, S. et al. (1995). A human phosphatidylinositol 3-kinase complex related to the yeast Vps34p-Vps15p protein sorting system. *EMBO J, 14*, 3339-48 . ↗

Waterfield, MD., Domin, J., Panaretou, C., Cockcroft, S. (1997). Characterization of p150, an adaptor protein for the human phosphatidylinositol (PtdIns) 3-kinase. Substrate presentation by phosphatidylinositol transfer protein to the p150.Ptdins 3-kinase complex. *J Biol Chem, 272*, 2477-85. ↗

Waterfield, MD., Arcaro, A., Wallasch, C., Ullrich, A., Zvelebil, MJ., Domin, J. (2000). Class II phosphoinositide 3-kinases are downstream targets of activated polypeptide growth factor receptors. *Mol Cell Biol, 20*, 3817-30. ↗

Waterfield, MD., Gaidarov, I., Domin, J., Smith, ME., Keen, JH. (2000). The class II phosphoinositide 3-kinase PI3K-C2alpha is concentrated in the trans-Golgi network and present in clathrin-coated vesicles. *J Biol Chem, 275*, 11943-50. ↗

Wandinger-Ness, A., Cao, C., Laporte, J., Stein, MP., Backer, JM. (2007). Myotubularin lipid phosphatase binds the hVPS15/hVPS34 lipid kinase complex on endosomes. *Traffic, 8*, 1052-67. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-10-18	Authored	Williams, MG.
2012-05-14	Reviewed	Wakelam, M.

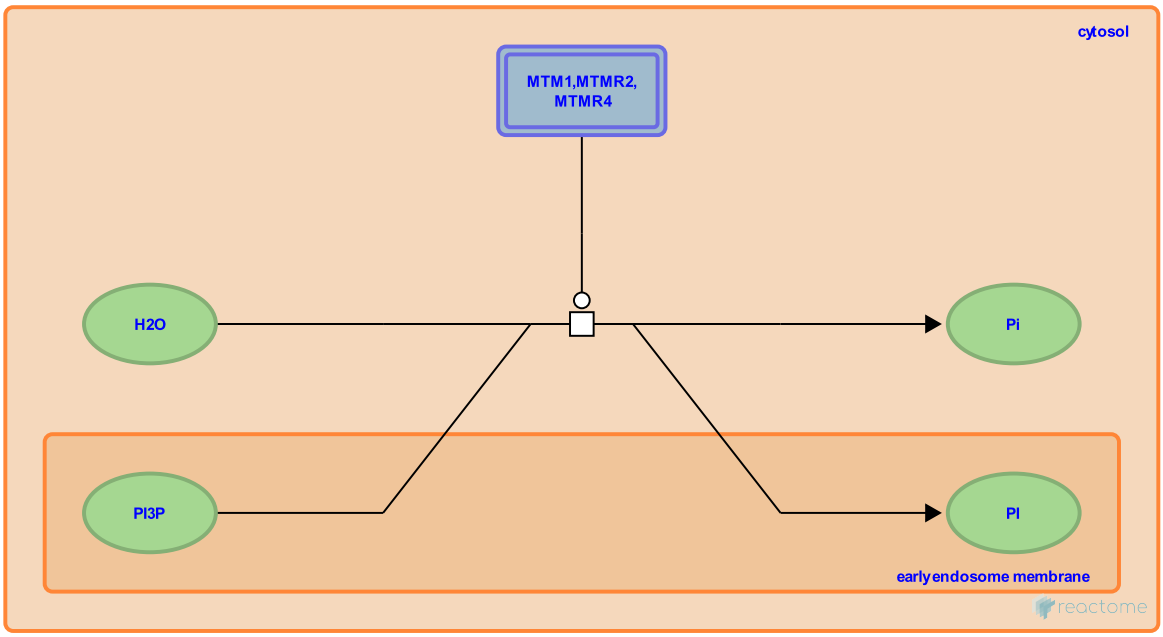
PI3P is dephosphorylated to PI by MTM proteins at the early endosome membrane ↗

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-1676141

Type: transition

Compartments: cytosol, early endosome membrane



At the early endosome membrane, myotubularin (MTM1), myotubularin-related protein 2 (MTMR2), and myotubularin-related protein 4 (MTMR4) dephosphorylate phosphatidylinositol 3-phosphate (PI3P) to phosphatidylinositol (PI).

The following lists the above proteins with their corresponding literature references: MTM1 (Cao et al. 2007, Cao et al. 2008, Kim et al. 2002), MTMR2 (Cao et al. 2008, Kim et al. 2002), and MTMR4 (Lorenzo et al. 2006, Zhao et al. 2001).

Preceded by: PI(3,4)P2 is dephosphorylated to PI3P by INPP4A/B at the early endosome membrane, PI is phosphorylated to PI3P by PIK3C2A/3 at the early endosome membrane, PI(3,5)P2 is dephosphorylated to PI3P by FIG4 at the early endosome membrane

Followed by: PI is phosphorylated to PI3P by PIK3C2A/3 at the early endosome membrane, PI is phosphorylated to PI4P by PI4K2A/B at the early endosome membrane

Literature references

Lorenzo, O., Clague, MJ., Urbé, S. (2006). Systematic analysis of myotubularins: heteromeric interactions, subcellular localisation and endosome related functions. *J Cell Sci, 119*, 2953-9. ↗

Zhao, R., Zhao, ZJ., Chen, J., Qi, Y. (2001). FYVE-DSP2, a FYVE domain-containing dual specificity protein phosphatase that dephosphorylates phosphotidylinositol 3-phosphate. *Exp Cell Res, 265*, 329-38. ↗

Bedrick, EJ., Wandinger-Ness, A., Cao, C., Laporte, J., Backer, JM. (2008). Sequential actions of myotubularin lipid phosphatases regulate endosomal PI(3)P and growth factor receptor trafficking. *Mol Biol Cell, 19*, 3334-46. ↗

Wandinger-Ness, A., Cao, C., Laporte, J., Stein, MP., Backer, JM. (2007). Myotubularin lipid phosphatase binds the hVPS15/hVPS34 lipid kinase complex on endosomes. *Traffic, 8*, 1052-67. ↗

Taylor, GS., Torgersen, KM., Kim, SA., Dixon, JE. (2002). Myotubularin and MTMR2, phosphatidylinositol 3-phosphatases mutated in myotubular myopathy and type 4B Charcot-Marie-Tooth disease. *J Biol Chem, 277*, 4526-31. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-10-18	Authored	Williams, MG.
2012-05-14	Reviewed	Wakelam, M.
2017-01-10	Reviewed	Rush, MG.
2017-01-25	Edited	Orlic-Milacic, M.

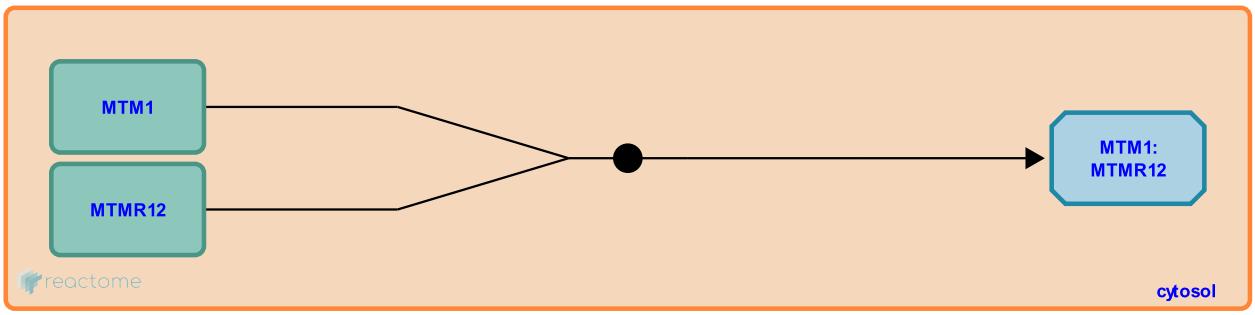
MTMR12 binds MTM1 ↗

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-6809680

Type: binding

Compartments: cytosol



MTM1 forms a complex with MTMR12 (3 PAP), an enzymatically inactive myotubularin family member. MTMR12 promotes MTM1 recruitment to cytosolic vesicular structures, presumably early or late endosomes. Complex formation stabilizes both MTM1 and MTMR12 proteins (Caldwell et al. 1991, Nandurkar et al. 2003, Gupta et al. 2013).

Followed by: PI3P is dephosphorylated to PI by MTM1:MTMR12

Literature references

Gundry, SR., Gupta, VA., Smith, LL., Shimazu, J., McIntire, JE., Talbot, EA. et al. (2013). Loss of catalytically inactive lipid phosphatase myotubularin-related protein 12 impairs myotubularin stability and promotes centronuclear myopathy in zebrafish. *PLoS Genet., 9*, e1003583. ↗

Majerus, PW., Lips, DL., Caldwell, KK., Bansal, VS. (1991). Isolation and characterization of two 3-phosphatases that hydrolyze both phosphatidylinositol 3-phosphate and inositol 1,3-bisphosphate. *J. Biol. Chem., 266*, 18378-86. ↗

Corcoran, L., Majerus, PW., Mitchell, CA., Selan, C., Layton, M., Mochizuki, Y. et al. (2003). Identification of myotubularin as the lipid phosphatase catalytic subunit associated with the 3-phosphatase adapter protein, 3-PAP. *Proc. Natl. Acad. Sci. U.S.A., 100*, 8660-5. ↗

Editions

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

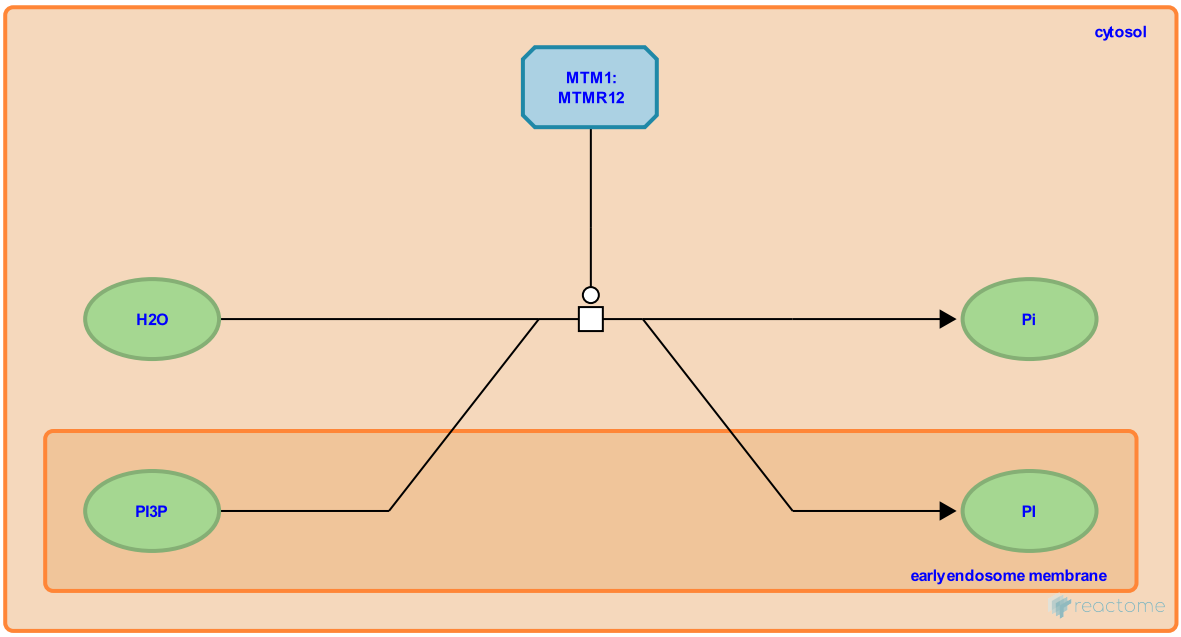
PI3P is dephosphorylated to PI by MTM1:MTMR12

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-6809720

Type: transition

Compartments: cytosol, early endosome membrane



Binding of MTMR12 to MTM1 enhances phosphatidylinositol-3-phosphatase activity of MTM1 at cytosolic vesicular structures, presumably early or late endosomes (Caldwell et al. 1991, Nandurkar et al. 2003, Gupta et al. 2013).

Preceded by: PI(3,4)P2 is dephosphorylated to PI3P by INPP4A/B at the early endosome membrane, PI is phosphorylated to PI3P by PIK3C2A/3 at the early endosome membrane, MTMR12 binds MTM1, PI(3,5)P2 is dephosphorylated to PI3P by FIG4 at the early endosome membrane

Literature references

Gundry, SR., Gupta, VA., Smith, LL., Shimazu, J., McIntire, JE., Talbot, EA. et al. (2013). Loss of catalytically inactive lipid phosphatase myotubularin-related protein 12 impairs myotubularin stability and promotes centronuclear myopathy in zebrafish. *PLoS Genet., 9*, e1003583.

Majerus, PW., Lips, DL., Caldwell, KK., Bansal, VS. (1991). Isolation and characterization of two 3-phosphatases that hydrolyze both phosphatidylinositol 3-phosphate and inositol 1,3-bisphosphate. *J. Biol. Chem., 266*, 18378-86.

Corcoran, L., Majerus, PW., Mitchell, CA., Selan, C., Layton, M., Mochizuki, Y. et al. (2003). Identification of myotubularin as the lipid phosphatase catalytic subunit associated with the 3-phosphatase adapter protein, 3-PAP. *Proc. Natl. Acad. Sci. U.S.A., 100*, 8660-5.

Editions

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

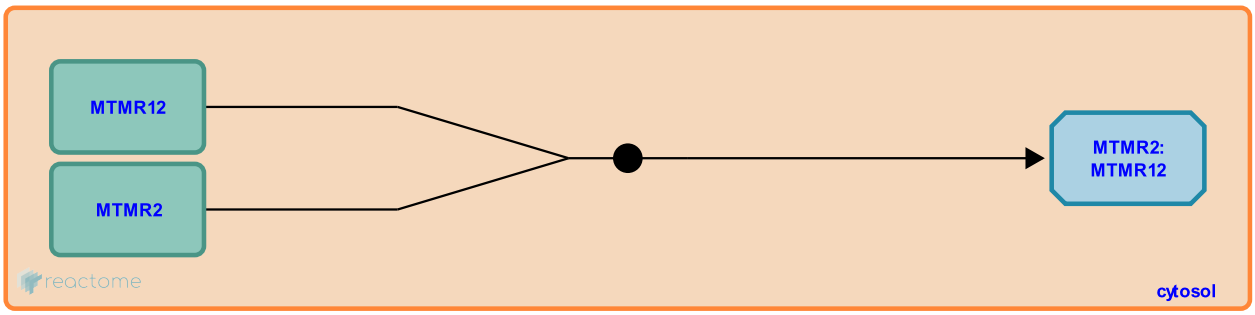
MTMR12 binds MTMR2 ↗

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-6809707

Type: binding

Compartments: cytosol



MTMR2 forms a complex with MTMR12, an enzymatically inactive myotubularin family member. The consequences of this interaction on enzymatic activity and localization of MTMR2 have not been examined (Nandurkar et al. 2003).

Literature references

Corcoran, L., Majerus, PW., Mitchell, CA., Selan, C., Layton, M., Mochizuki, Y. et al. (2003). Identification of myotubularin as the lipid phosphatase catalytic subunit associated with the 3-phosphatase adapter protein, 3-PAP. *Proc. Natl. Acad. Sci. U.S.A., 100*, 8660-5. ↗

Editions

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

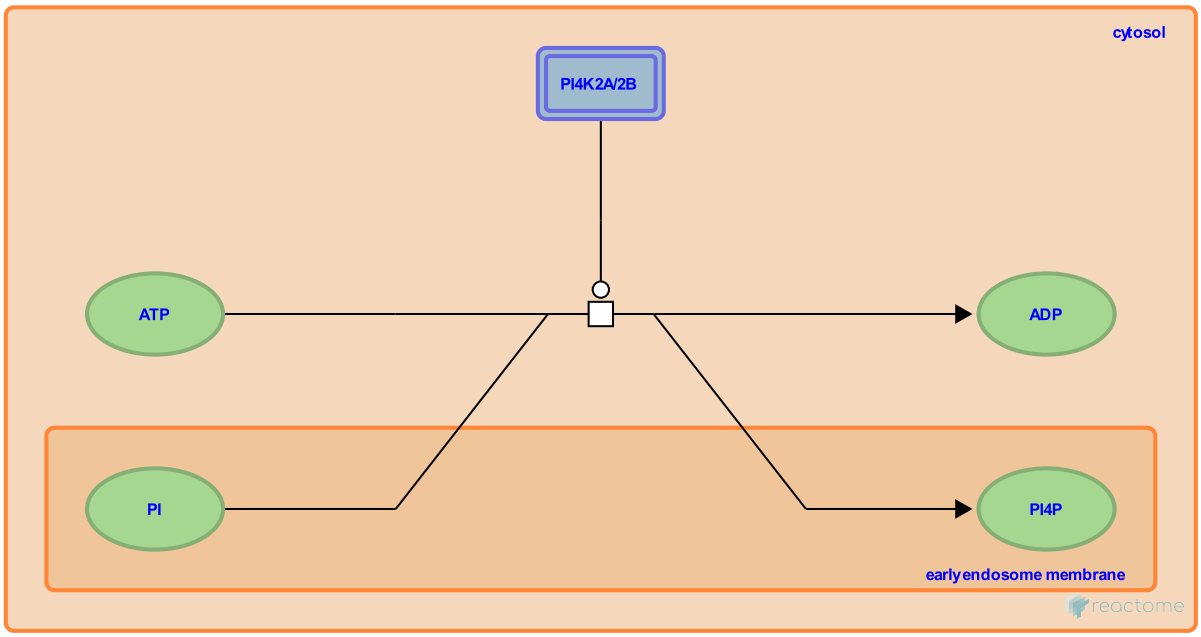
PI is phosphorylated to PI4P by PI4K2A/B at the early endosome membrane ↗

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-1675974

Type: transition

Compartments: cytosol, early endosome membrane



At the early endosome membrane, phosphatidylinositol 4-kinase type 2-alpha/beta (PI4K2A/B) (Balla et al. 2002) phosphorylates phosphatidylinositol (PI) to produce phosphatidylinositol 4-phosphate (PI4P).

Preceded by: PI3P is dephosphorylated to PI by MTM proteins at the early endosome membrane

Followed by: PI4P is phosphorylated to PI(3,4)P2 by PIK3C2A at the early endosome membrane

Literature references

Balla, T., Tuymetova, G., Balla, A., Barshishat, M., Geiszt, M. (2002). Characterization of type II phosphatidylinositol 4-kinase isoforms reveals association of the enzymes with endosomal vesicular compartments. *J Biol Chem, 277*, 20041-50. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-10-18	Authored	Williams, MG.
2012-05-14	Reviewed	Wakelam, M.

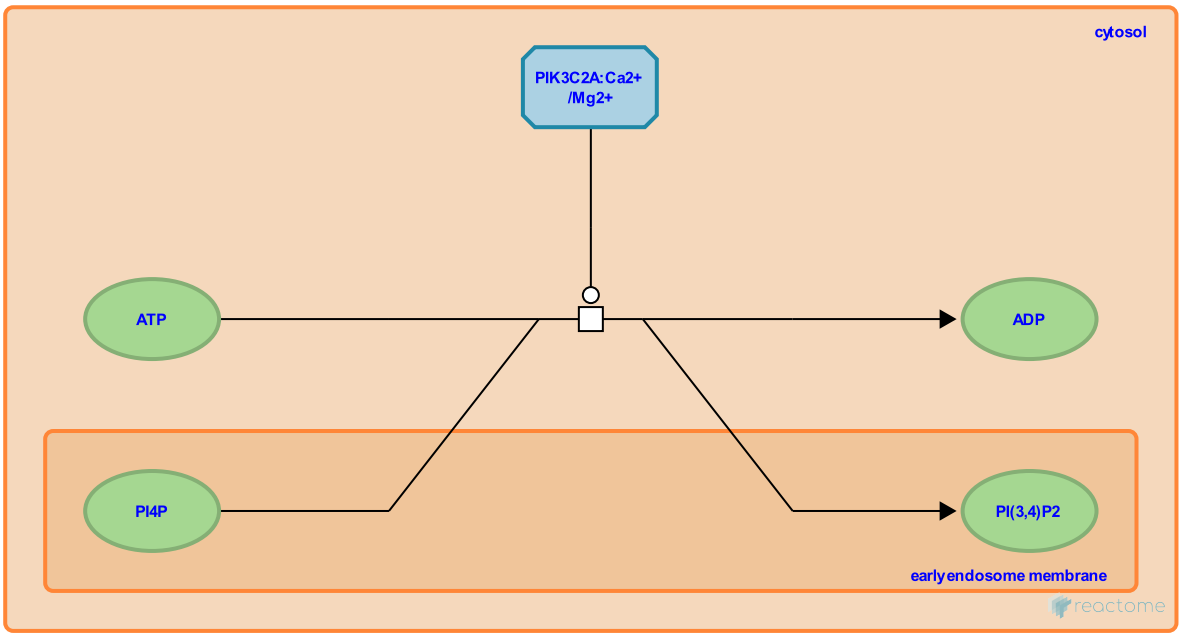
PI4P is phosphorylated to PI(3,4)P2 by PIK3C2A at the early endosome membrane ↗

Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-1676206

Type: transition

Compartments: cytosol, early endosome membrane



At the early endosome membrane, phosphatidylinositol-4-phosphate 3-kinase C2 domain-containing subunit alpha (PIK3C2A) (Kraq et al. 2010, Arcaro et al. 2000) phosphorylates phosphatidylinositol 4-phosphate (PI4P) to phosphatidylinositol 3,4-bisphosphate (PI(3,4)P2).

Preceded by: PI is phosphorylated to PI4P by PI4K2A/B at the early endosome membrane

Followed by: PI(3,4)P2 is dephosphorylated to PI3P by INPP4A/B at the early endosome membrane

Literature references

Waterfield, MD., Arcaro, A., Wallasch, C., Ullrich, A., Zvelebil, MJ., Domin, J. (2000). Class II phosphoinositide 3-kinases are downstream targets of activated polypeptide growth factor receptors. *Mol Cell Biol, 20*, 3817-30. ↗

Krag, C., Salcini, AE., Malmberg, EK. (2010). PI3KC2?, a class II PI3K, is required for dynamin-independent internalization pathways. *J Cell Sci, 123*, 4240-50. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-10-18	Authored	Williams, MG.
2012-05-14	Reviewed	Wakelam, M.

MTMR2 binds MTMR10 ↗

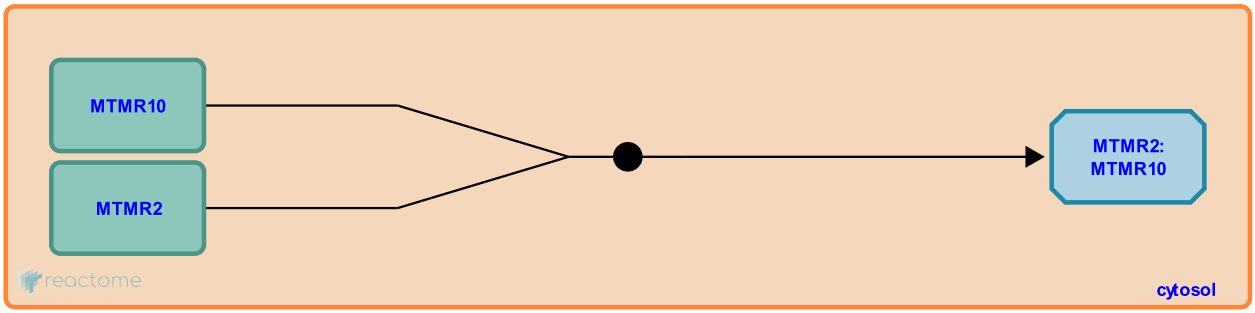
Location: Synthesis of PIPs at the early endosome membrane

Stable identifier: R-HSA-6810030

Type: binding

Compartments: cytosol

Inferred from: Mtmr2 binds MTMR10 (Homo sapiens)



Based on a high throughput study of human interactome in HeLa cells, MTMR2 forms a complex with MTMR10, an enzymatically inactive myotubularin family member. The function of this complex has not been examined (Hein et al. 2015).

Literature references

Hyman, AA., Toyoda, Y., Poser, I., Hubner, NC., Weisswange, I., Cox, J. et al. (2015). A Human Interactome in Three Quantitative Dimensions Organized by Stoichiometries and Abundances. *Cell, 163,* 712-23. ↗

Editions

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

Table of Contents