Synthesis of PIPs at the late endosome membrane

Orlic-Milacic, M., Rush, MG., Wakelam, M., Williams, MG.

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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.

17/11/2022
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 7 reactions (see Table of Contents)
At the late endosome membrane, the primary event is the dephosphorylation of the phosphoinositide phosphatidylinositol 3,5-bisphosphate (PI(3,5)P2) to phosphatidylinositol 3-phosphate (PI3P) and phosphatidylinositol 5-phosphate (PI5P) (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**


**Editions**

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

**Location:** Synthesis of PIPs at the late endosome membrane

**Stable identifier:** R-HSA-1675910

**Type:** transition

**Compartments:** late endosome membrane, cytosol

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

At the late 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(3,5)P2 is dephosphorylated to PI3P by FIG4 at the late endosome membrane, PI is phosphorylated to PI3P by PIK3C2A/3 at the late endosome membrane

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

**Literature references**


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

**Location:** Synthesis of PIPs at the late endosome membrane

**Stable identifier:** R-HSA-1676020

**Type:** transition

**Compartments:** late endosome membrane, cytosol

At the late 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 late endosome membrane

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

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

**Location:** Synthesis of PIPs at the late endosome membrane

**Stable identifier:** R-HSA-1676065

**Type:** transition

**Compartments:** late endosome membrane, cytosol

At the late endosome membrane, myotubularin (MTM1), myotubularin-related protein 2 (MTMR2), myotubularin-related protein 4 (MTMR4), and myotubularin-related protein 7 (MTMR7) 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, Tsujita et al. 2004, Tronchere et al. 2004), MTMR2 (Cao et al. 2008), MTMR4 (Lorenzo et al. 2006), and MTMR7 (Mochizuki & Majerus 2003, Lorenzo et al. 2006).

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

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MTMR7 binds MTMR9

**Location:** Synthesis of PIPs at the late endosome membrane

**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).

**Literature references**


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PI is phosphorylated to PI5P by PIKFYVE at the late endosome membrane

**Location:** Synthesis of PIPs at the late endosome membrane

**Stable identifier:** R-HSA-1675866

**Type:** transition

**Compartments:** late endosome membrane, cytosol

**Inferred from:** PI is phosphorylated to PI5P by Pikfyve at the late endosome membrane (Mus musculus)

At the late 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 PIKFYVE kinase component phosphorylates phosphatidylinositol (PI) to phosphatidylinositol 5-phosphate (PI5P) (Sbrissa et al. 1999, Sbrissa et al. 2002). The PAS complex is present in the cytosol and is recruited to the membrane.

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

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

**Location:** Synthesis of PIPs at the late endosome membrane

**Stable identifier:** R-HSA-1676024

**Type:** transition

**Compartments:** late endosome membrane, cytosol

At the late 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).


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

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

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

**Location:** Synthesis of PIPs at the late endosome membrane

**Stable identifier:** R-HSA-1675795

**Type:** transition

**Compartments:** late endosome membrane, cytosol

At the late endosome membrane, myotubularin (MTM1), myotubularin-related protein 2 (MTMR2), myotubularin-related protein 4 (MTMR4), and myotubularin-related protein 7 (MTMR7) 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, Tsujita et al. 2004, Tronchere et al. 2004, Kim et al. 2002); MTMR2 (Cao et al. 2008, Kim et al. 2002); MTMR4 (Lorenzo et al. 2006); and MTMR7 (Mochizuki & Majerus 2003, Lorenzo et al. 2006).

**Preceded by:** PI(3,5)P2 is dephosphorylated to PI3P by FIG4 at the late endosome membrane, PI is phosphorylated to PI3P by PIK3C2A/3 at the late endosome membrane

**Followed by:** PI is phosphorylated to PI5P by PIKFYVE at the late endosome membrane, PI is phosphorylated to PI3P by PIK3C2A/3 at the late endosome membrane

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  - PI is phosphorylated to PI3P by PIK3C2A/3 at the late endosome membrane
  - PI3P is dephosphorylated to PI by MTM proteins at the late endosome membrane