

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

Wakelam, M., Williams, MG.

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

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of Creative Commons Attribution 4.0 International (CC BY 4.0) License. For more information see our license.

# 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.

Reactome database release: 74

This document contains 1 reaction (see Table of Contents)

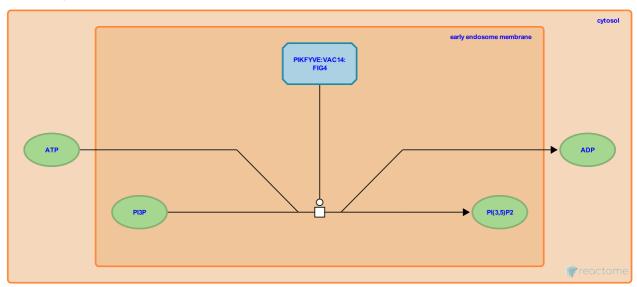
# PI3P is phosphorylated to PI(3,5)P2 by PIKFYVE at the early endosome membrane

Stable identifier: R-HSA-1676168

**Type:** transition

**Compartments:** early endosome membrane, cytosol

**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).

### Literature references

Sbrissa, D., Ikonomov, OC., Fu, Z., Ijuin, T., Gruenberg, J., 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.

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

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

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

### **Editions**

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