PTEN dephosphorylates PIP3

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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.

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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. ↗

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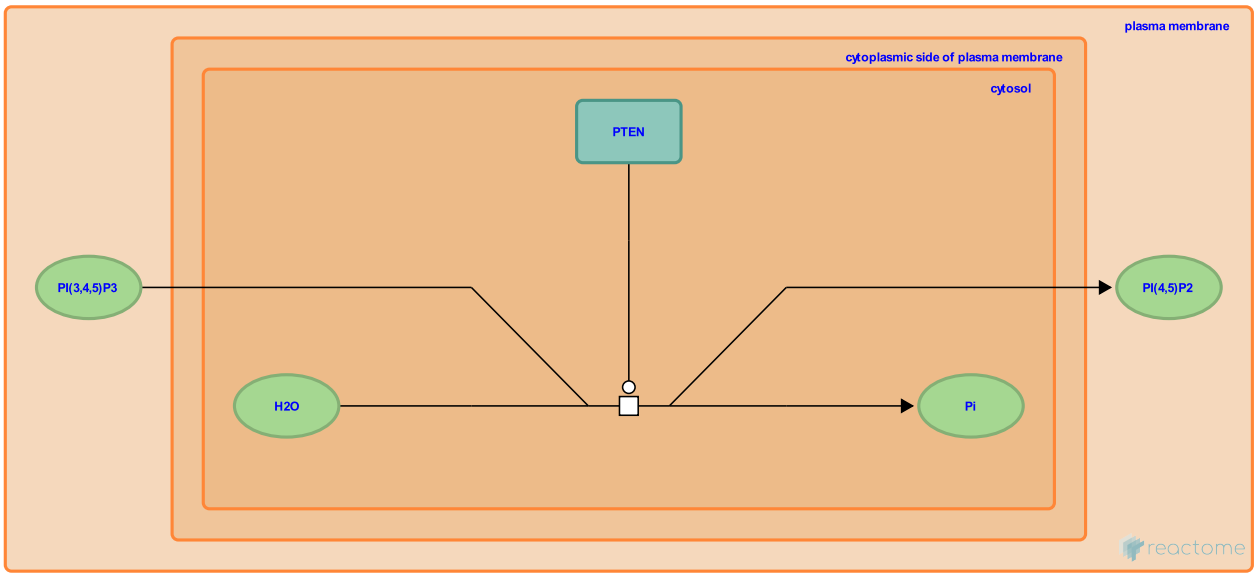
Stable identifier: R-HSA-199456

Type: transition

Compartments: cytosol, plasma membrane



At the plasma membrane, phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase and dual-specificity protein phosphatase aka phosphatase and tensin homolog (PTEN) dephosphorylates phosphatidylinositol 3,4,5-trisphosphate (PI(3,4,5)P3) to phosphatidylinositol 4,5-bisphosphate (PI(4,5)P2) (Maehama & Dixon 1998, Myers et al. 1998, Das et al. 2003). The PI3K network is negatively regulated by phospholipid phosphatases that dephosphorylate PIP3, thus hampering AKT activation (Myers et al. 1998). The tumour suppressor PTEN is the primary phospholipid phosphatase.
Early studies indicated that magnesium ion, Mg2+, was needed for the catalytic activity of PTEN isolated from bovine thymus (Kabuyama et al. 1996). Subsequent studies have shown that PTEN was catalytically active in buffers free of magnesium and magnesium was not detected as part of the PTEN crystal (Lee et al. 1999).

Literature references

Georgescu, MM., Pavletich, NP., Shi, Y., Maehama, T., Pandolfi, P., Yang, H. et al. (1999). Crystal structure of the PTEN tumor suppressor: implications for its phosphoinositide phosphatase activity and membrane association. *Cell, 99*, 323-34. ↗

Das, S., Cho, W., Dixon, JE. (2003). Membrane-binding and activation mechanism of PTEN. *Proc Natl Acad Sci U S A, 100*, 7491-6. ↗

Dixon, JE., Maehama, T. (1998). The tumor suppressor, PTEN/MMAC1, dephosphorylates the lipid second messenger, phosphatidylinositol 3,4,5-trisphosphate. *J Biol Chem, 273*, 13375-8. ↗

Stolarov, JP., van der Kaay, J., Myers, MP., Pass, I., Downes, CP., Batty, IH. et al. (1998). The lipid phosphatase activity of PTEN is critical for its tumor supressor function. *Proc Natl Acad Sci U S A, 95*, 13513-8. ↗

Fukui, Y., Kabuyama, Y., Homma, Y., Nakatsu, N. (1996). Purification and characterization of the phosphatidylinositol-3,4,5-trisphosphate phosphatase in bovine thymus. *Eur. J. Biochem., 238*, 350-6. ↗

Editions

2006-10-10	Authored	Annibali, D., Nasi, S.
2007-11-08	Reviewed	Greene, LA.
2012-05-14	Reviewed	Wakelam, M.
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