PDPK1 phosphorylates AKT at T308

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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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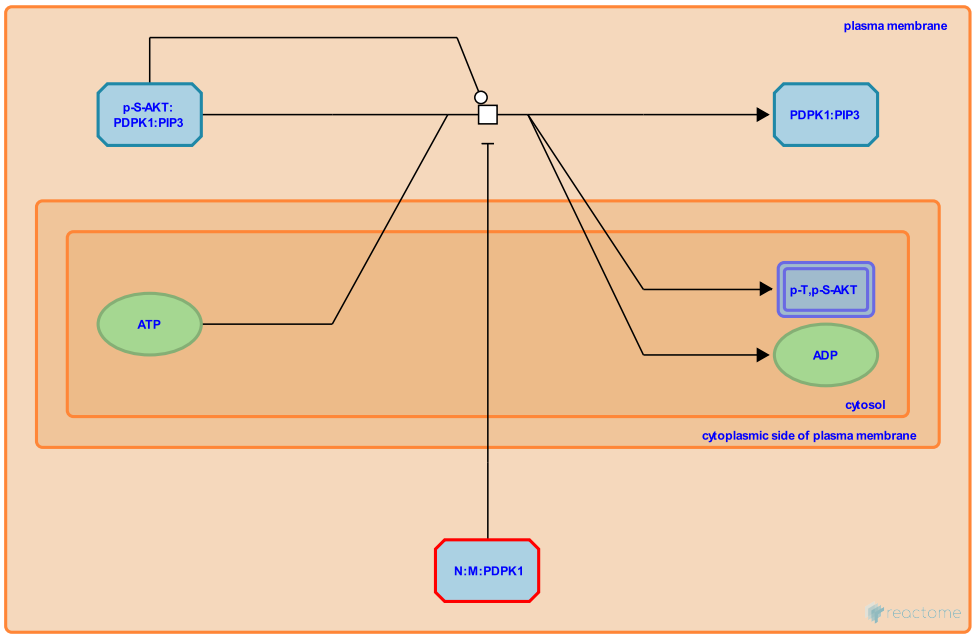
Stable identifier: R-HSA-198270

Type: transition

Compartments: cytosol, plasma membrane



Once AKT is localized at the plasma membrane, it is phosphorylated at two critical residues for its full activation. These residues are a threonine (T308 in AKT1) in the activation loop within the catalytic domain, and a serine (S473 in AKT1), in a hydrophobic motif (HM) within the carboxy terminal, non-catalytic region. PDPK1 (PDK1) is the activation loop kinase; this kinase can also directly phosphorylate p70S6K. The HM kinase, previously termed PDK2, has been identified as the mammalian TOR (Target Of Rapamycin; Sarbassov et al., 2005) but several other kinases are also able to phosphorylate AKT at S473. Phosphorylation of AKT at S473 by TORC2 complex is a prerequisite for PDPK1-mediated phosphorylation of AKT threonine T308 (Scheid et al. 2002, Sarabassov et al. 2005).

Literature references

Rue, L., Woodgett, J., Dedhar, S., Gray, V., Delcommenne, M., Tan, C. (1998). Phosphoinositide-3-OH kinase-dependent regulation of glycogen synthase kinase 3 and protein kinase B/AKT by the integrin-linked kinase. *Proc Natl Acad Sci U S A, 95*, 11211-6. ↗

Coffer, PJ., Burgering, BM. (1995). Protein kinase B (c-Akt) in phosphatidylinositol-3-OH kinase signal transduction. *Nature, 376*, 599-602. ↗

Editions

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2007-11-08	Reviewed	Greene, LA.
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