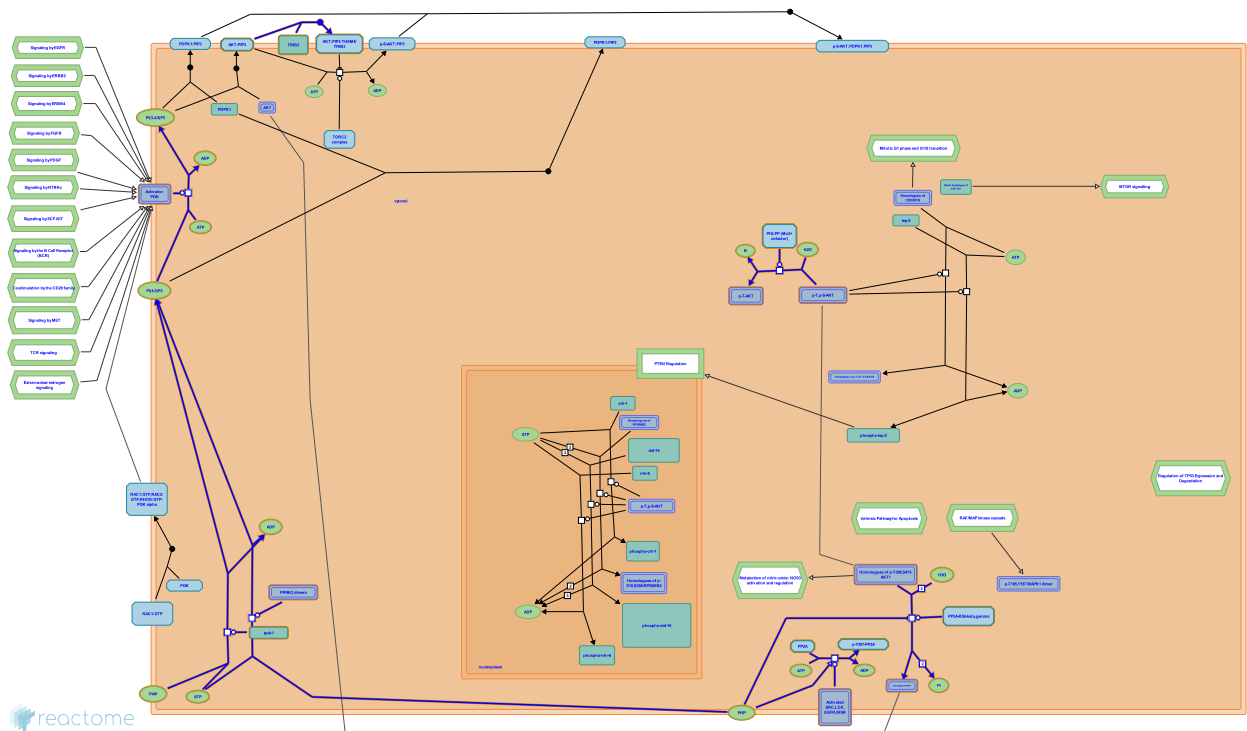


Negative regulation of the PI3K/AKT network



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

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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](https://reactome.org/textbook).

04/02/2023

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. [↗](#)

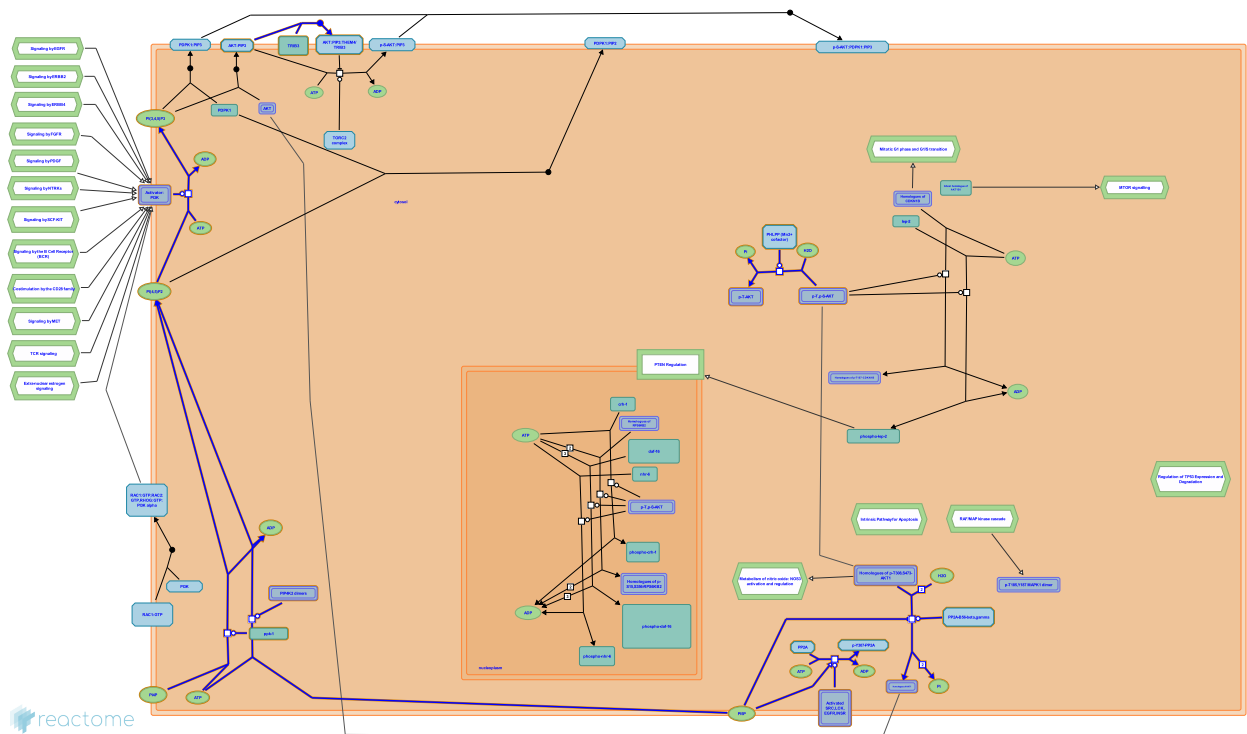
Reactome database release: 83

This document contains 2 pathways and 2 reactions ([see Table of Contents](#))

Negative regulation of the PI3K/AKT network ↗

Stable identifier: R-CEL-199418

Inferred from: Negative regulation of the PI3K/AKT network (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

THEM4 (CTMP) and/or TRIB3 inhibit AKT phosphorylation ↗

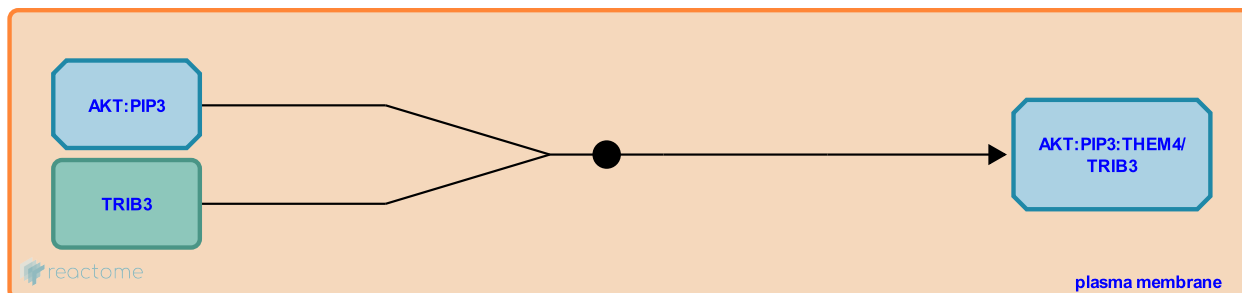
Location: [Negative regulation of the PI3K/AKT network](#)

Stable identifier: R-CEL-199443

Type: binding

Compartments: plasma membrane

Inferred from: [THEM4 \(CTMP\) and/or TRIB3 inhibit AKT phosphorylation \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

PHLPP dephosphorylates S473 in AKT ↗

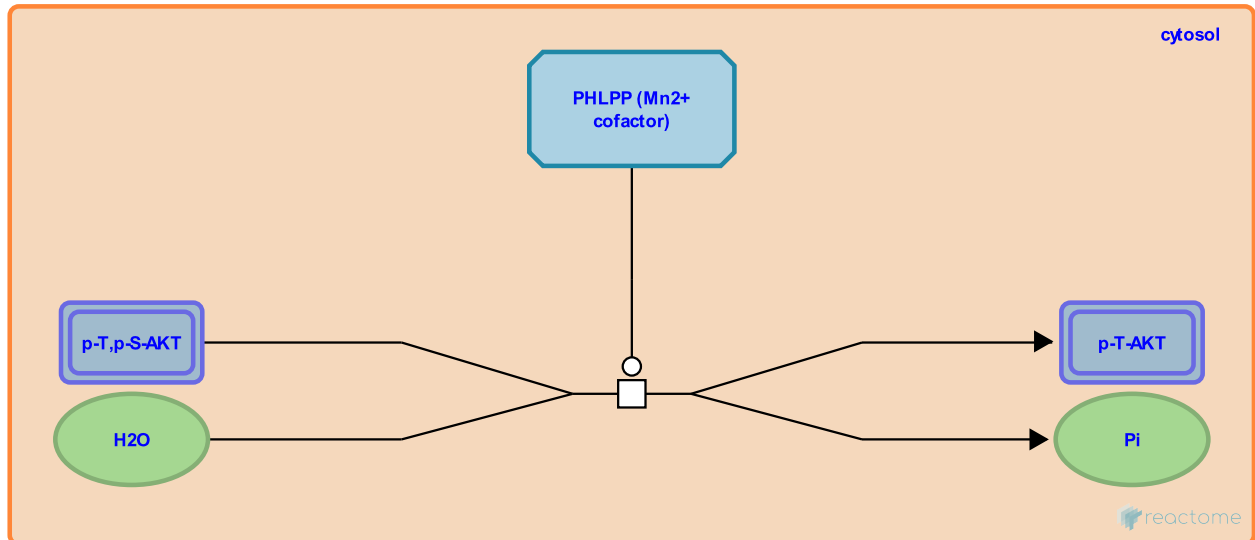
Location: [Negative regulation of the PI3K/AKT network](#)

Stable identifier: R-CEL-199425

Type: transition

Compartments: cytosol

Inferred from: [PHLPP dephosphorylates S473 in AKT \(Homo sapiens\)](#)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

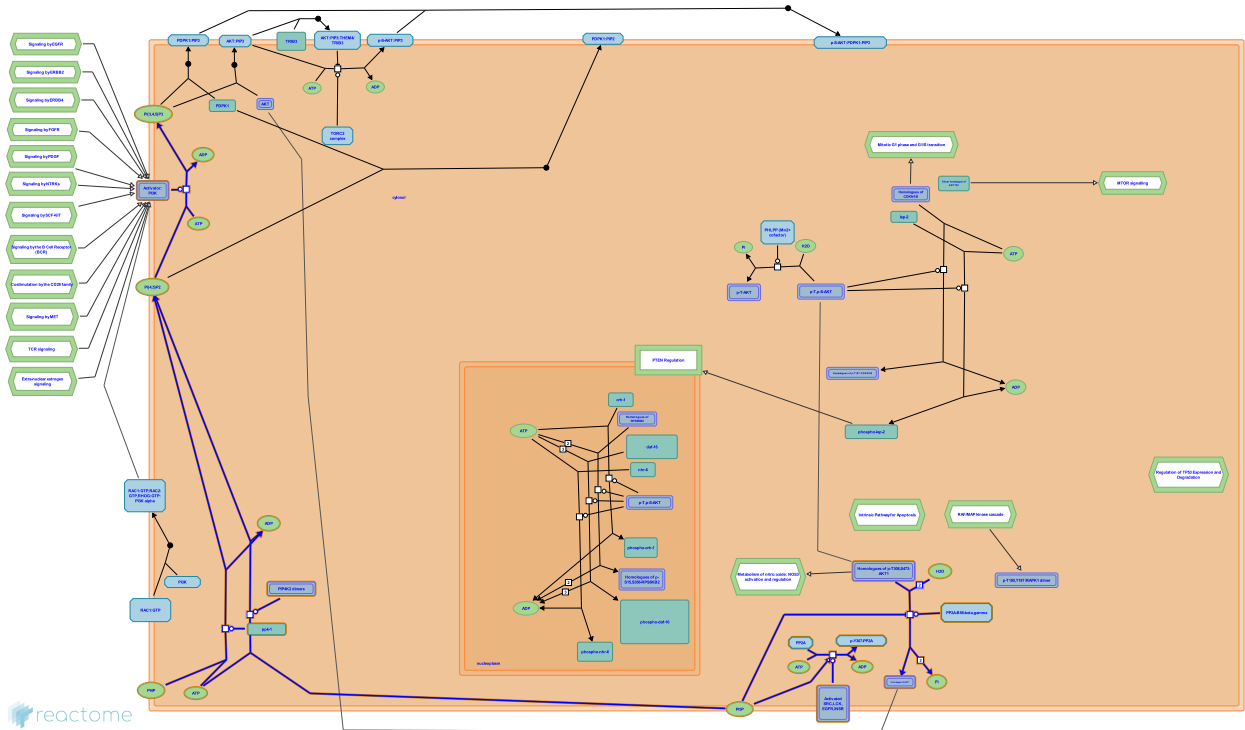
[More details and caveats of the event inference in Reactome.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

PI5P, PP2A and IER3 Regulate PI3K/AKT Signaling ↗

Location: Negative regulation of the PI3K/AKT network

Stable identifier: R-CEL-6811558

Inferred from: PI5P, PP2A and IER3 Regulate PI3K/AKT Signaling (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

[More details and caveats of the event inference in Reactome.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

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