

# TORC2 (mTOR) phosphorylates AKT at S473

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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. 7
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. A
- 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. *オ*

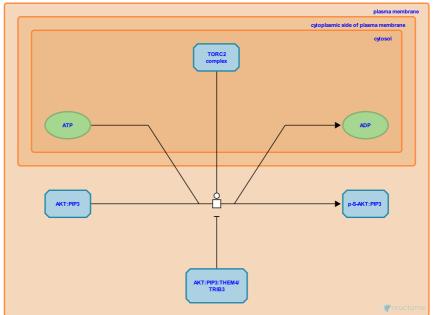
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# TORC2 (mTOR) phosphorylates AKT at S473 7

Stable identifier: R-HSA-198640

#### Type: transition

Compartments: cytosol, plasma membrane



Under conditions of growth and mitogen stimulation S473 phosphorylation of AKT is carried out by mTOR (mammalian Target of Rapamycin). This kinase is found in two structurally and functionally distinct protein complexes, named TOR complex 1 (TORC1) and TOR complex 2 (TORC2). It is TORC2 complex, which is composed of mTOR, RICTOR, SIN1 (also named MAPKAP1) and LST8, that phosphorylates AKT at S473 (Sarbassov et al., 2005). This complex also regulates actin cytoskeletal reorganization (Jacinto et al., 2004; Sarbassov et al., 2004). TORC1, on the other hand, is a major regulator of ribosomal biogenesis and protein synthesis (Hay and Sonenberg, 2004). TORC1 regulates these processes largely by the phosphorylation/inactivation of the repressors of mRNA translation 4E binding proteins (4E BPs) and by the phosphorylation/activation of ribosomal S6 kinase (S6K1). TORC1 is also the principal regulator of autophagy. In other physiological conditions, other kinases may be responsible for AKT S473 phosphorylation.

Phosphorylation of AKT on S473 by TORC2 complex is a prerequisite for AKT phosphorylation on T308 by PDPK1 (Scheid et al. 2002, Sarabassov et al. 2005).

### Literature references

- Ali, SM., Sabatini, DM., Sarbassov, DD., Guertin, DA. (2005). Phosphorylation and regulation of Akt/PKB by the rictor-mTOR complex. *Science*, 307, 1098-101. 7
- Woodgett, JR., Scheid, MP., Marignani, PA. (2002). Multiple phosphoinositide 3-kinase-dependent steps in activation of protein kinase B. *Mol Cell Biol, 22*, 6247-60. ↗

### **Editions**

2006-10-10	Authored	Annibali, D., Nasi, S.
2007-11-08	Reviewed	Greene, LA.
2012-07-18	Revised	Orlic-Milacic, M.
2012-08-03	Edited	Matthews, L.
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