p-AMPK phosphorylates TSC1:TSC2

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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

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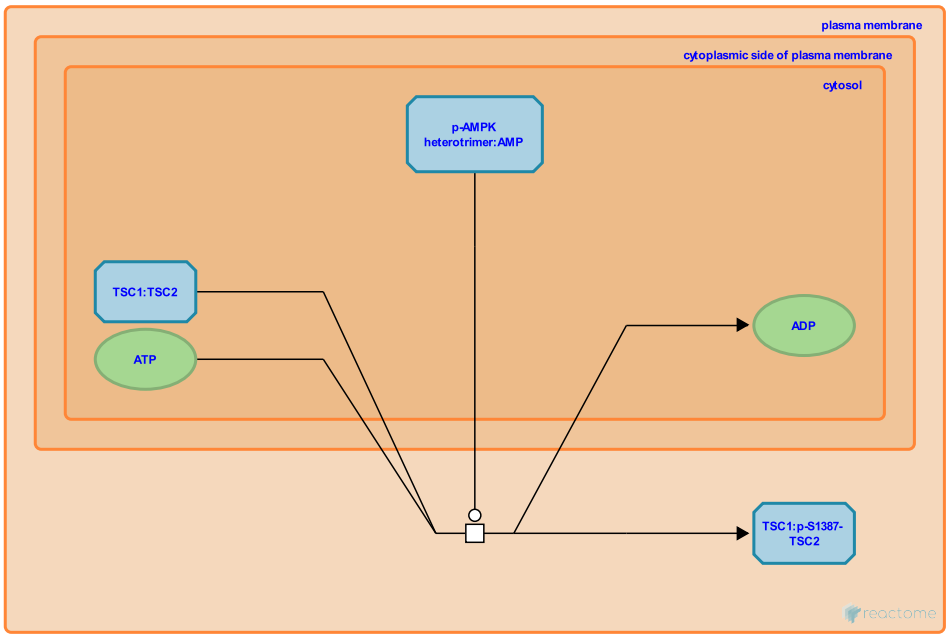
Stable identifier: R-HSA-380927

Type: transition

Compartments: cytosol, plasma membrane



Activated AMPK (phosphorylated on the alpha subunit and with AMP bound) phosphorylates TSC2 (also known as tuberin) on Ser-1387, thereby activating the GTPase activating protein (GAP) activity of the Tuberous Sclerosis Complex (TSC). The TSC tumor suppressor is a critical upstream inhibitor of the mTORC1 complex. TSC is a GTPase-activating protein that stimulates the intrinsic GTPase activity of the small G-protein Rheb. This inactivates Rheb by stimulating its GTPase activity. The GDP-bound form of Rheb looses the ability to activate the kinase activity of the mTORC1 complex (Sancak et al. 2007). Loss of TSC1 or TSC2 leads to hyperactivation of mTORC1.

Phosphorylation of TSC1 and TSC2 serves as an integration point for a wide variety of environmental signals that regulate mTORC1 (Sabatini 2006). Mitogen-activated kinases including Akt, Erk, and Rsk directly phosphorylate TSC2, leading to its inactivation by an unknown mechanism. Another Akt substrate, PRAS40, was recently shown to bind and inhibit the mTORC1 complex. Upon phosphorylation by Akt, PRAS40 no longer inhibits mTORC1 (Sancak et al. 2007; Vander Haar et al. 2007).

Literature references

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Editions

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