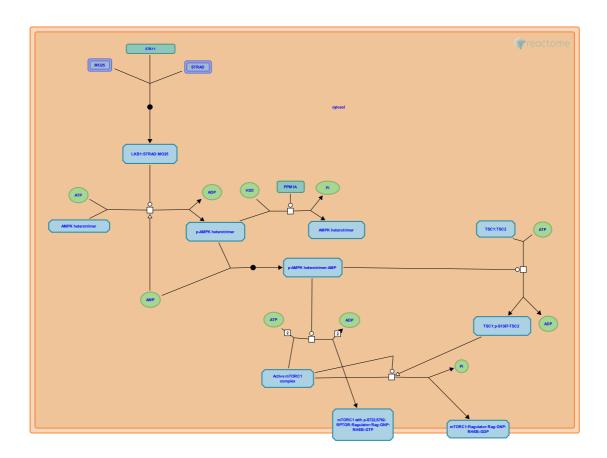


# Energy dependent regulation of mTOR by

## LKB1-AMPK



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

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of <a href="Maintenantoring">Creative Commons Attribution 4.0 International (CC BY 4.0)</a>
<a href="License">License</a>. For more information see our <a href="License">License</a>.

This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the <a href="Reactome-Textbook">Reactome-Textbook</a>.

18/05/2024

#### 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 data-base: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968.

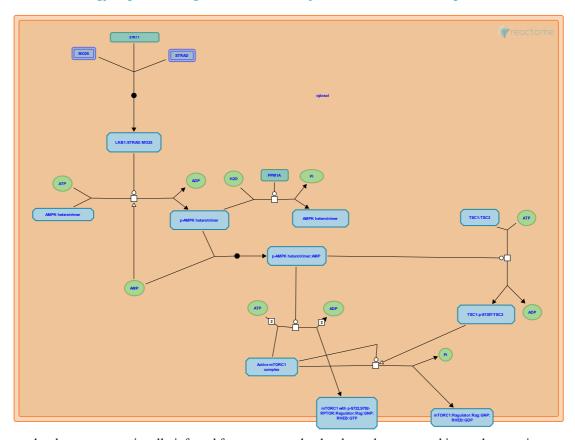
Reactome database release: 88

This document contains 1 pathway and 7 reactions (see Table of Contents)

#### Energy dependent regulation of mTOR by LKB1-AMPK

**Stable identifier:** R-CFA-380972

**Inferred from:** Energy dependent regulation of mTOR by LKB1-AMPK (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. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

### LKB1 forms a trimeric complex with STRAD and MO25 7

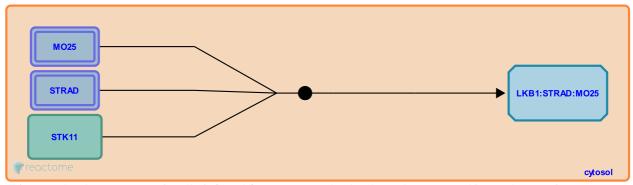
Location: Energy dependent regulation of mTOR by LKB1-AMPK

Stable identifier: R-CFA-380942

Type: binding

**Compartments:** cytosol

Inferred from: LKB1 forms a trimeric complex with STRAD and MO25 (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. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

Followed by: Activation of cytosolic AMPK by phosphorylation

#### Activation of cytosolic AMPK by phosphorylation 7

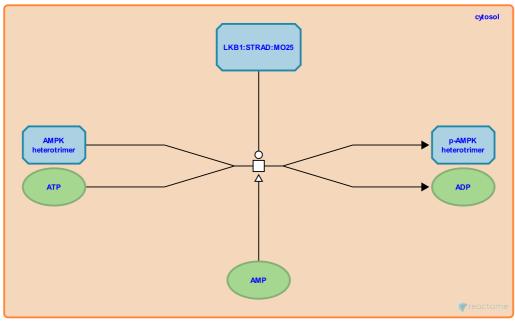
Location: Energy dependent regulation of mTOR by LKB1-AMPK

Stable identifier: R-CFA-200421

**Type:** transition

**Compartments:** cytosol

**Inferred from:** Activation of cytosolic AMPK by 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. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

Preceded by: LKB1 forms a trimeric complex with STRAD and MO25

Followed by: AMPK is dephosphorylated, Phosphorylated AMPK binds AMP

#### **AMPK** is dephosphorylated **↗**

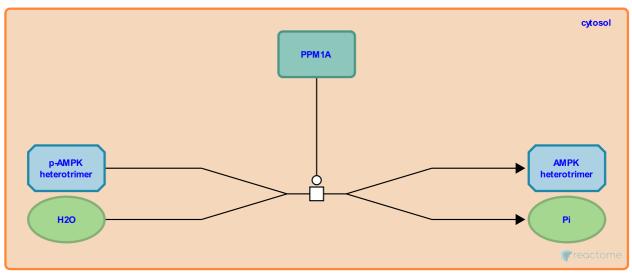
Location: Energy dependent regulation of mTOR by LKB1-AMPK

Stable identifier: R-CFA-380949

Type: transition

**Compartments:** cytosol

Inferred from: AMPK is dephosphorylated (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. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

Preceded by: Activation of cytosolic AMPK by phosphorylation

#### Phosphorylated AMPK binds AMP

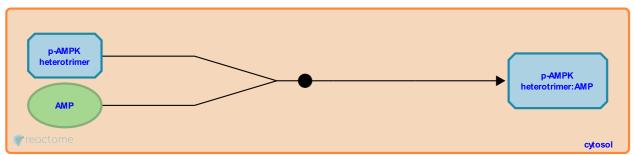
Location: Energy dependent regulation of mTOR by LKB1-AMPK

Stable identifier: R-CFA-380930

**Type:** binding

**Compartments:** cytosol

Inferred from: Phosphorylated AMPK binds AMP (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. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

Preceded by: Activation of cytosolic AMPK by phosphorylation

Followed by: AMPK phosphorylates Raptor in the mTORC1 complex, p-AMPK phosphorylates TSC1:TSC2

#### **AMPK phosphorylates Raptor in the mTORC1 complex ₹**

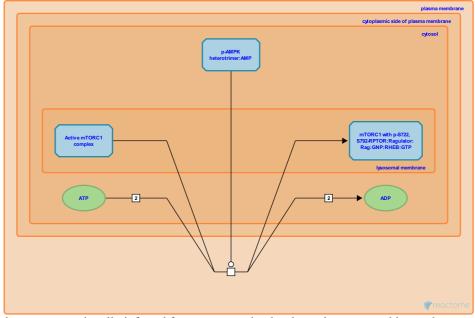
Location: Energy dependent regulation of mTOR by LKB1-AMPK

**Stable identifier:** R-CFA-447074

**Type:** transition

Compartments: plasma membrane, cytosol

**Inferred from:** AMPK phosphorylates Raptor in the mTORC1 complex (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. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

Preceded by: Phosphorylated AMPK binds AMP

#### p-AMPK phosphorylates TSC1:TSC2 >

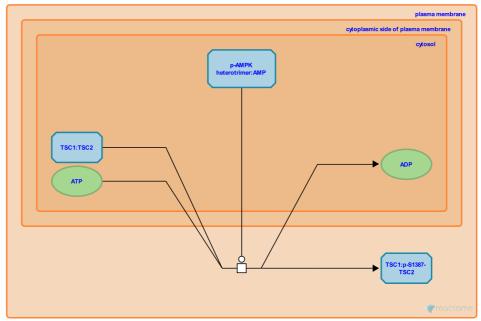
Location: Energy dependent regulation of mTOR by LKB1-AMPK

Stable identifier: R-CFA-380927

**Type:** transition

Compartments: plasma membrane, cytosol

Inferred from: p-AMPK phosphorylates TSC1:TSC2 (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. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

Preceded by: Phosphorylated AMPK binds AMP

### RHEB in mTORC1:RHEB:GTP hydrolyses GTP →

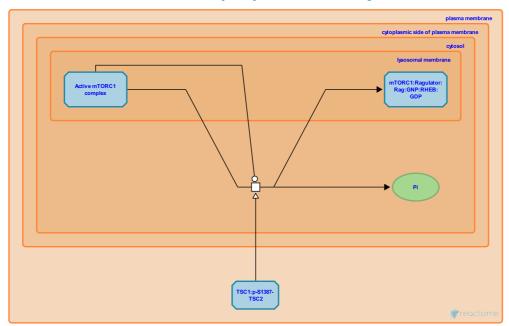
Location: Energy dependent regulation of mTOR by LKB1-AMPK

Stable identifier: R-CFA-380979

**Type:** transition

Compartments: cytosol, lysosomal membrane

Inferred from: RHEB in mTORC1:RHEB:GTP hydrolyses GTP (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. For details on PANTHER see also: <a href="http://www.pantherdb.org/about.jsp">http://www.pantherdb.org/about.jsp</a>

# **Table of Contents**

Introduction	1
Energy dependent regulation of mTOR by LKB1-AMPK	2
> LKB1 forms a trimeric complex with STRAD and MO25	3
→ Activation of cytosolic AMPK by phosphorylation	4
→ AMPK is dephosphorylated	5
→ Phosphorylated AMPK binds AMP	6
→ AMPK phosphorylates Raptor in the mTORC1 complex	7
→ p-AMPK phosphorylates TSC1:TSC2	8
→ RHEB in mTORC1:RHEB:GTP hydrolyses GTP	9
Table of Contents	10