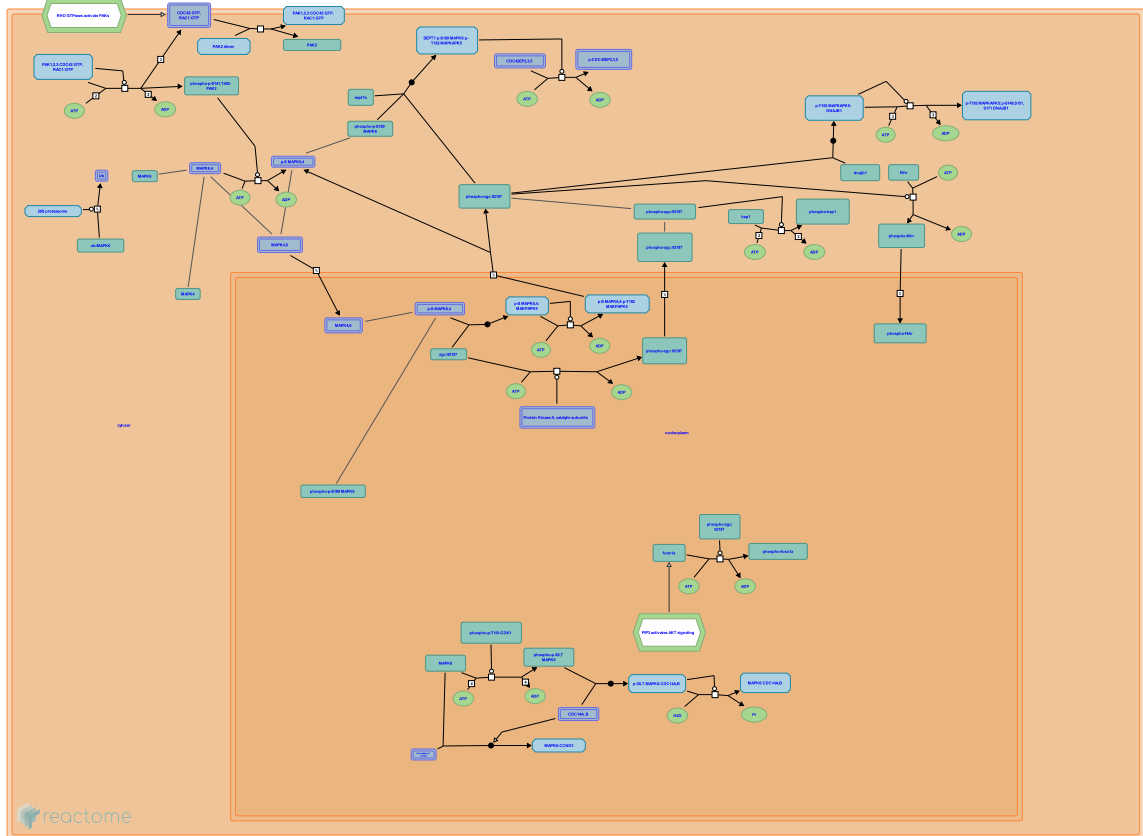


# MAPK6/MAPK4 signaling



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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/).

06/05/2024

## 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

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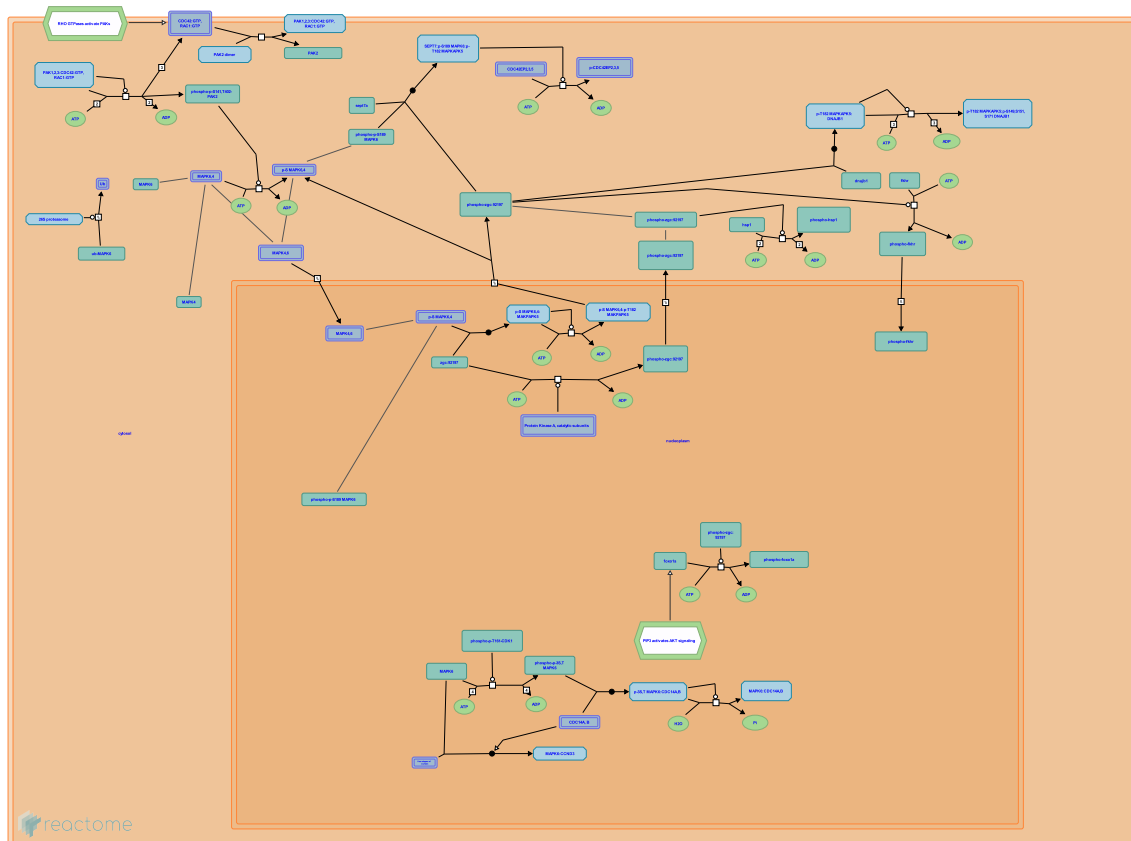
Reactome database release: 88

This document contains 1 pathway and 22 reactions ([see Table of Contents](#))

## MAPK6/MAPK4 signaling ↗

**Stable identifier:** R-DRE-5687128

**Inferred from:** MAPK6/MAPK4 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.](http://www.pantherdb.org/about.jsp) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

## Activation of PAKs by RAC1 and CDC42 ↗

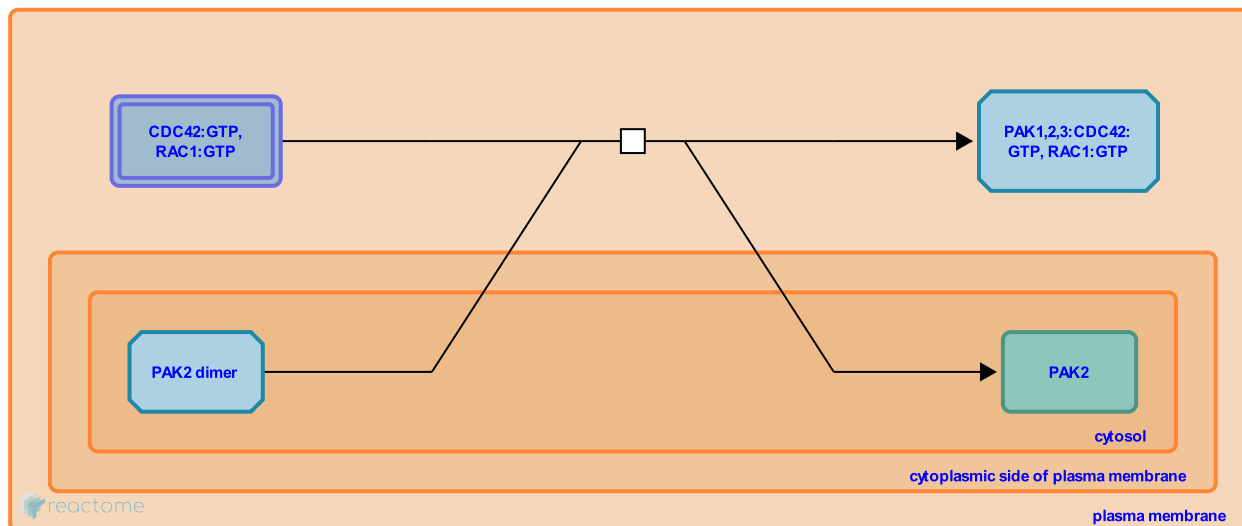
**Location:** MAPK6/MAPK4 signaling

**Stable identifier:** R-DRE-389788

**Type:** transition

**Compartments:** plasma membrane, cytosol

**Inferred from:** Activation of PAKs by RAC1 and CDC42 (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.](http://www.pantherdb.org/about.jsp) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

## Autophosphorylation of PAK1,2,3 ↗

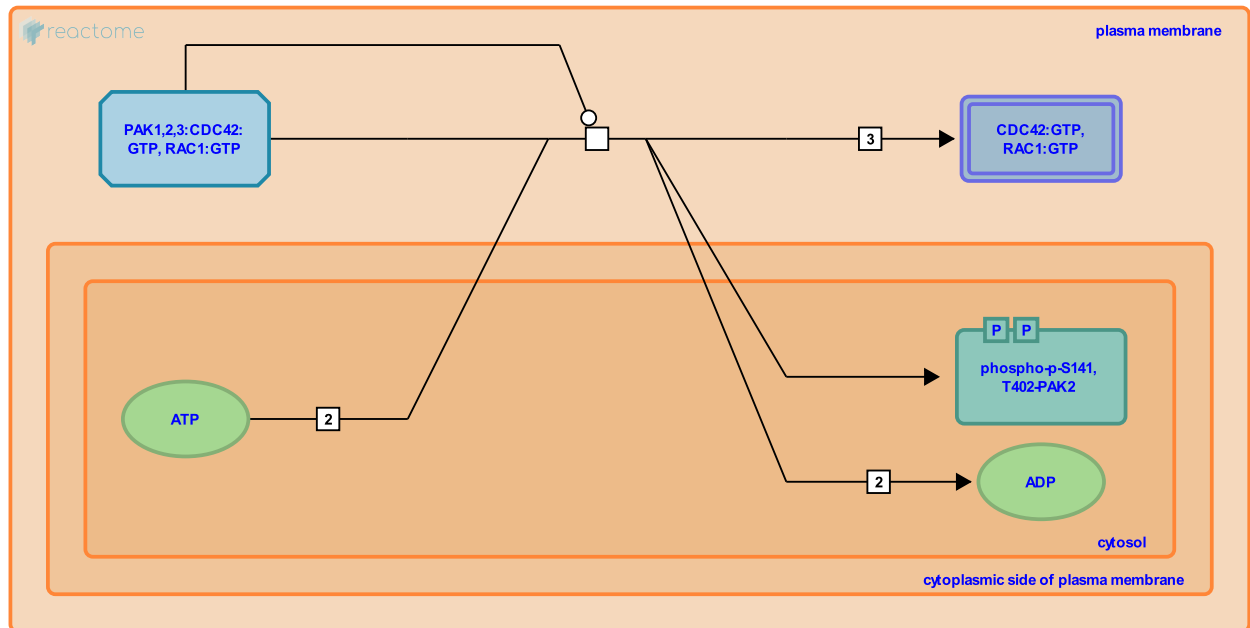
**Location:** MAPK6/MAPK4 signaling

**Stable identifier:** R-DRE-5627775

**Type:** transition

**Compartments:** plasma membrane, cytosol

**Inferred from:** Autophosphorylation of PAK1,2,3 (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.](http://www.pantherdb.org/about.jsp) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Followed by:** PAK1,2,3 phosphorylates MAPK6,4

## PAK1,2,3 phosphorylates MAPK6,4 ↗

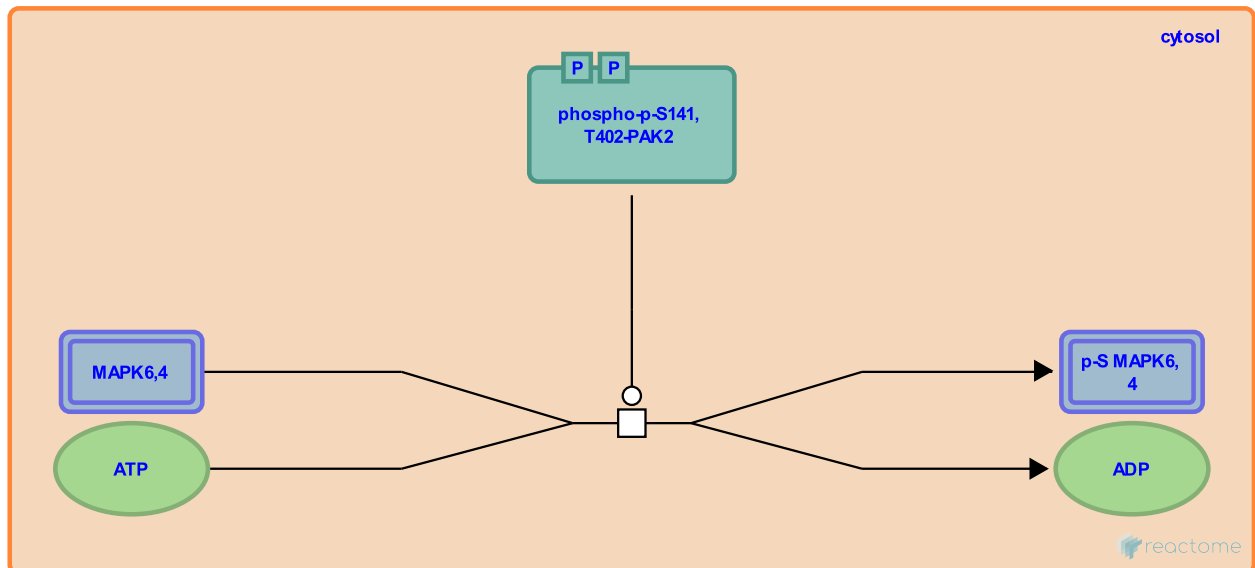
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5687086

**Type:** transition

**Compartments:** cytosol

**Inferred from:** [PAK1,2,3 phosphorylates MAPK6,4 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [Autophosphorylation of PAK1,2,3](#)

## MAPK4,6 translocate to nucleus ↗

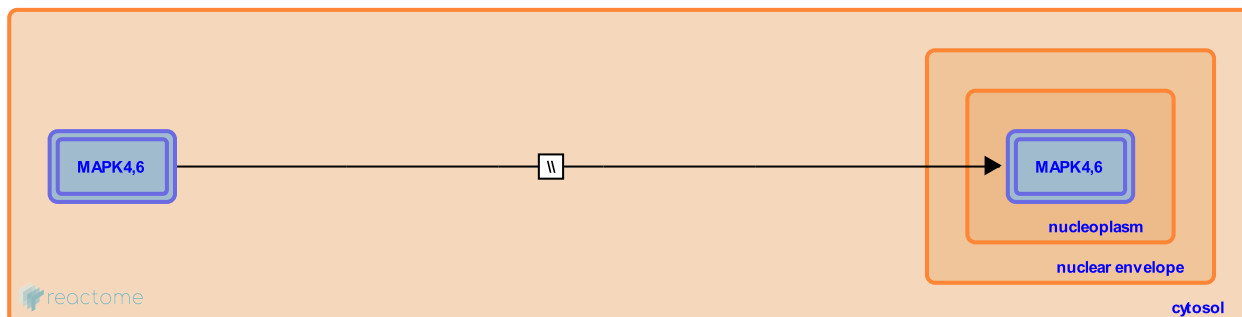
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5687107

**Type:** omitted

**Compartments:** cytosol

**Inferred from:** [MAPK4,6 translocate to nucleus \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

**Followed by:** [p-S MAPK6,4 binds MAPKAPK5](#)

## MAPK6 is degraded by the 26S proteasome ↗

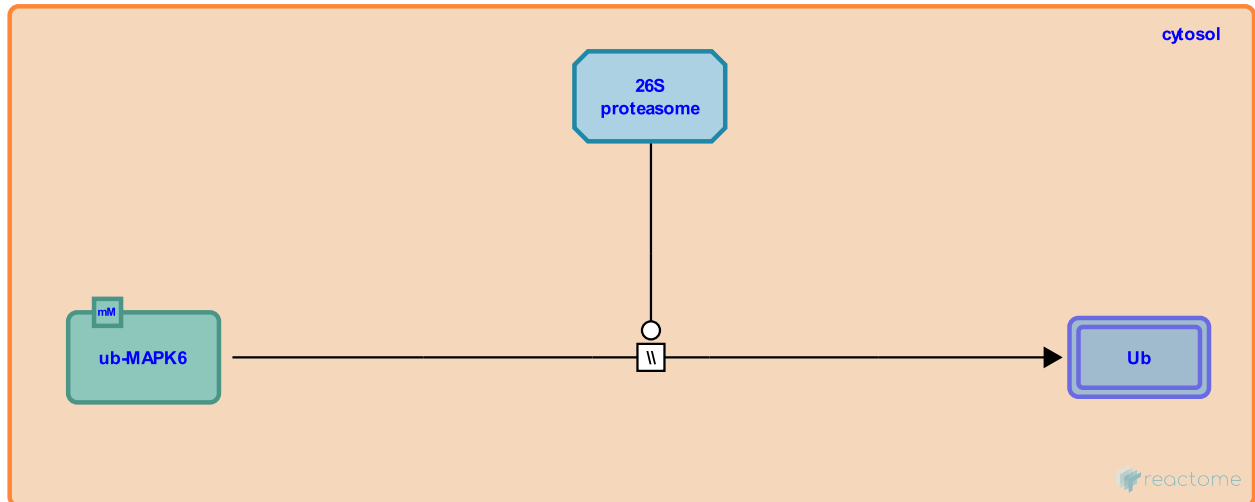
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5687112

**Type:** omitted

**Compartments:** cytosol

**Inferred from:** [MAPK6 is degraded by the 26S proteasome \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>



## CDK1 phosphorylates MAPK6 ↗

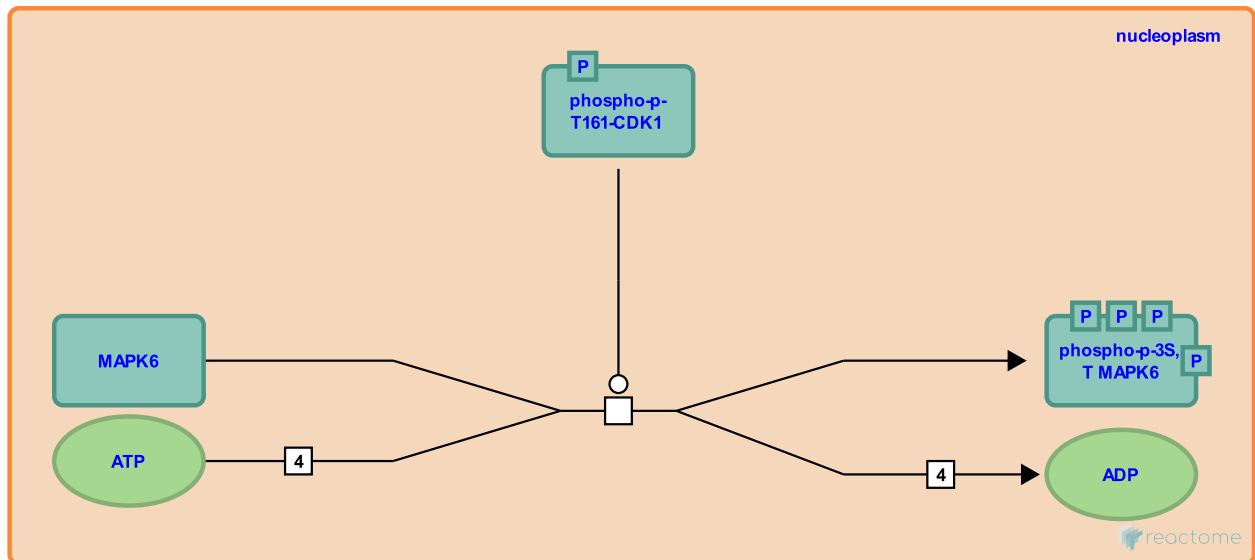
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5692755

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** [CDK1 phosphorylates MAPK6 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

## CDC14A,B bind MAPK6 ↗

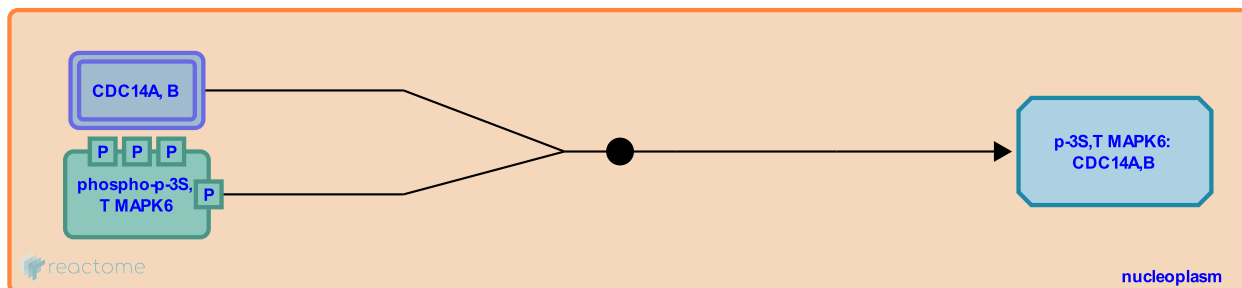
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5692749

**Type:** binding

**Compartments:** nucleoplasm

**Inferred from:** [CDC14A,B bind MAPK6 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

## CDC14A,B dephosphorylate p-3S,T MAPK6 ↗

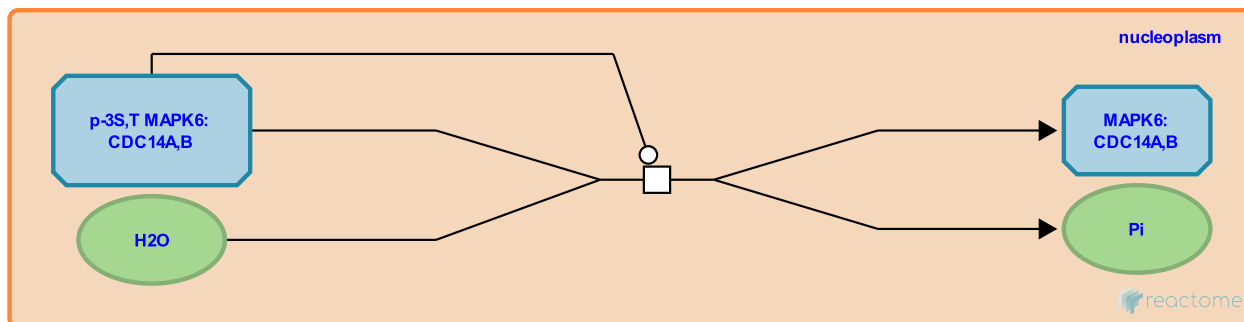
**Location:** MAPK6/MAPK4 signaling

**Stable identifier:** R-DRE-5692754

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** CDC14A,B dephosphorylate p-3S,T MAPK6 (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: <http://www.pantherdb.org/about.jsp>

## MAPK6 binds CCND3 ↗

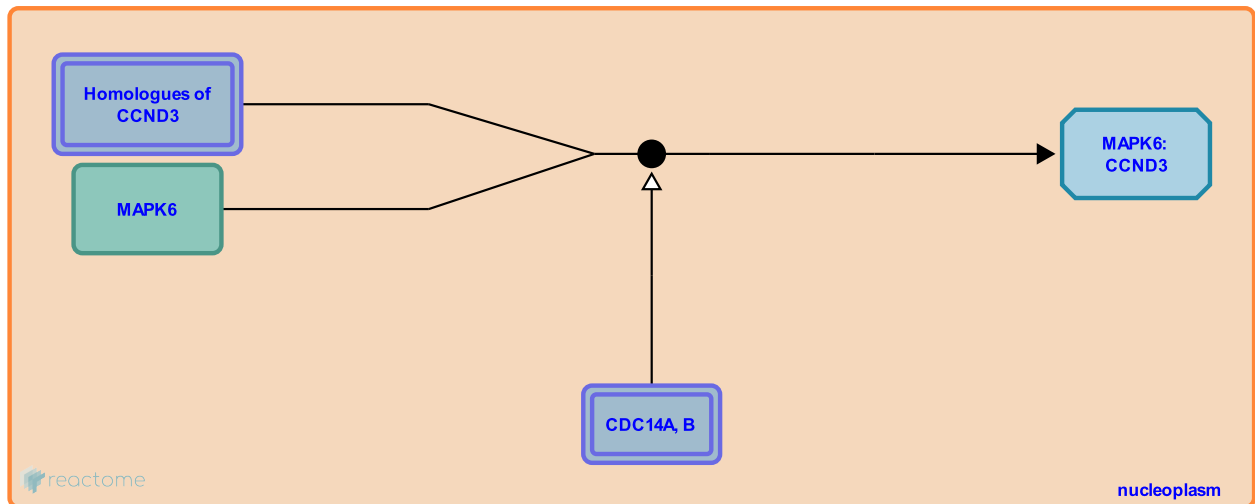
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5692764

**Type:** binding

**Compartments:** nucleoplasm

**Inferred from:** [MAPK6 binds CCND3 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

## p-S MAPK6,4 binds MAPKAPK5 ↗

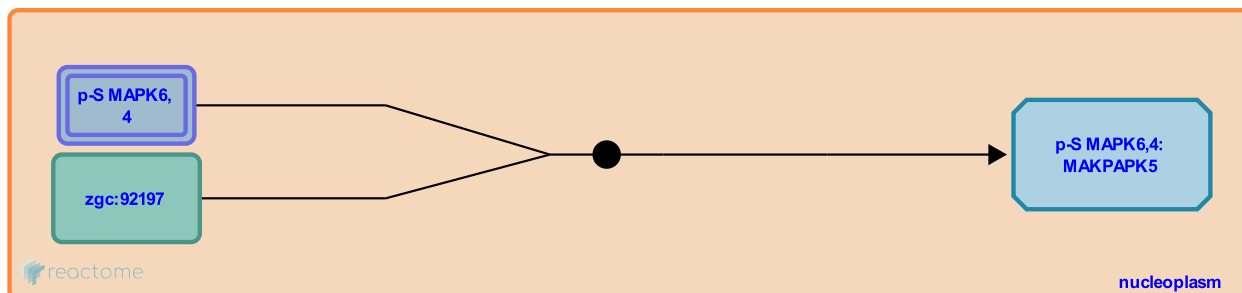
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5687091

**Type:** binding

**Compartments:** nucleoplasm

**Inferred from:** [p-S MAPK6,4 binds MAPKAPK5 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [MAPK4,6 translocate to nucleus](#)

**Followed by:** [p-S MAPK6,4 phosphorylate MAPKAPK5](#)

## p-S MAPK6,4 phosphorylate MAPKAPK5 ↗

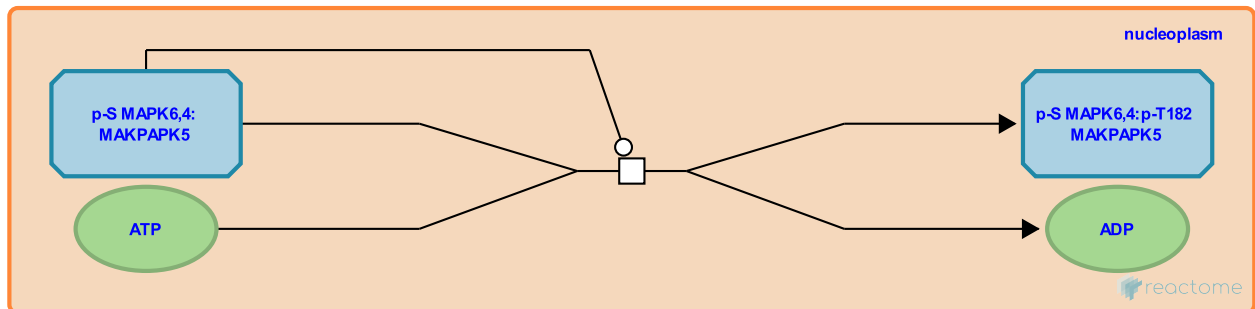
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5687094

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** [p-S MAPK6,4 phosphorylate MAPKAPK5 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [p-S MAPK6,4 binds MAPKAPK5](#)

**Followed by:** [p-S MAPK6,4:p-T182 MAPKAPK5 translocate to the cytosol](#)

## p-S MAPK6,4:p-T182 MAPKAPK5 translocate to the cytosol ↗

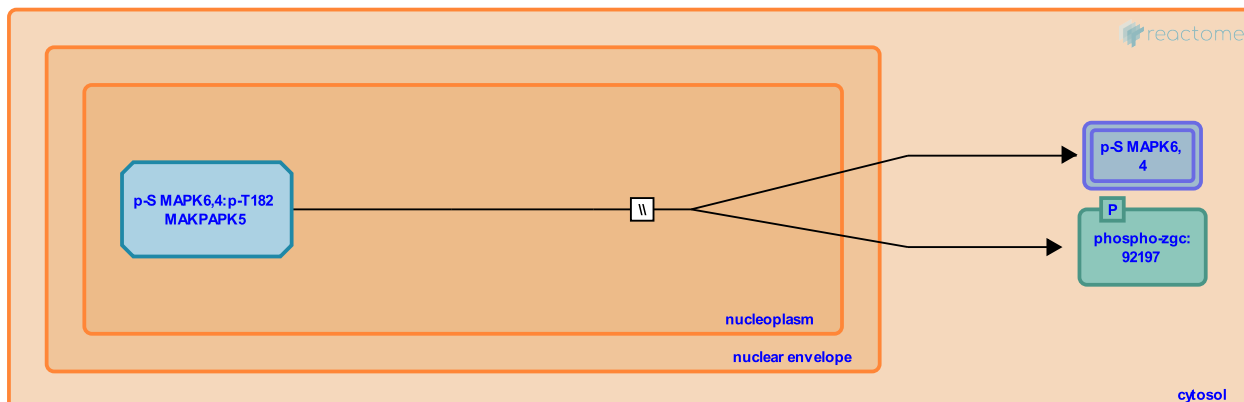
**Location:** MAPK6/MAPK4 signaling

**Stable identifier:** R-DRE-5687120

**Type:** omitted

**Compartments:** nucleoplasm

**Inferred from:** p-S MAPK6,4:p-T182 MAPKAPK5 translocate to the cytosol (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.](http://www.pantherdb.org/about.jsp) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** p-S MAPK6,4 phosphorylate MAPKAPK5

**Followed by:** p-T182 MAPKAPK5 phosphorylates FOXO3, p-T182 MAPKAPK5 binds DNAJB1, p-S MAPKAPK5 phosphorylates HSPB1

## p-T182 MAPKAPK5 phosphorylates FOXO1 ↗

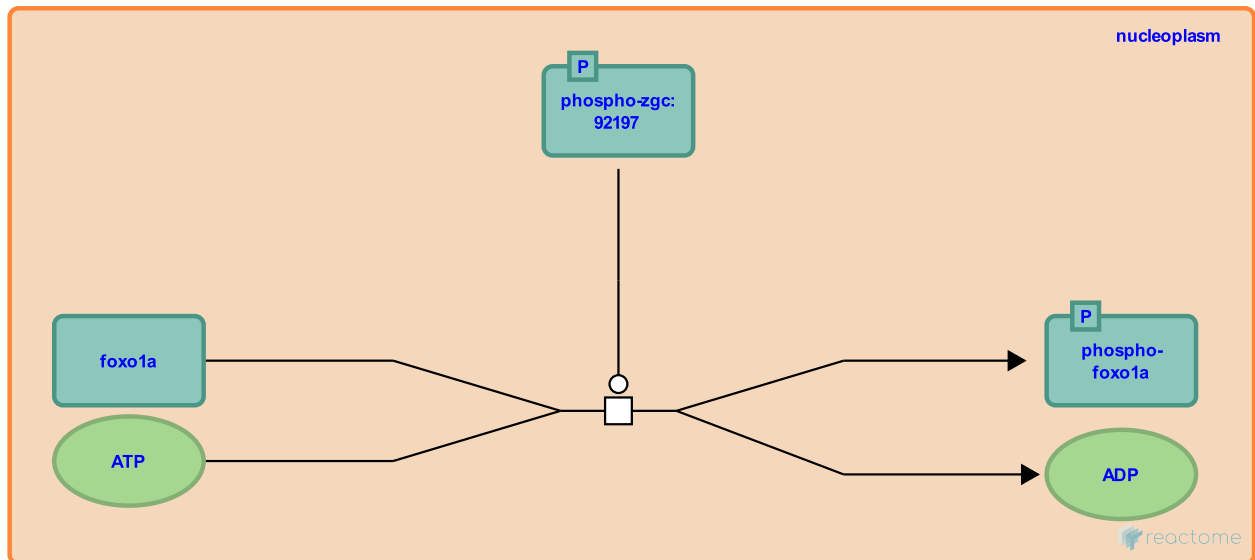
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5692779

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** [p-T182 MAPKAPK5 phosphorylates FOXO1 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>



## PKA phosphorylates MAPKAPK5 ↗

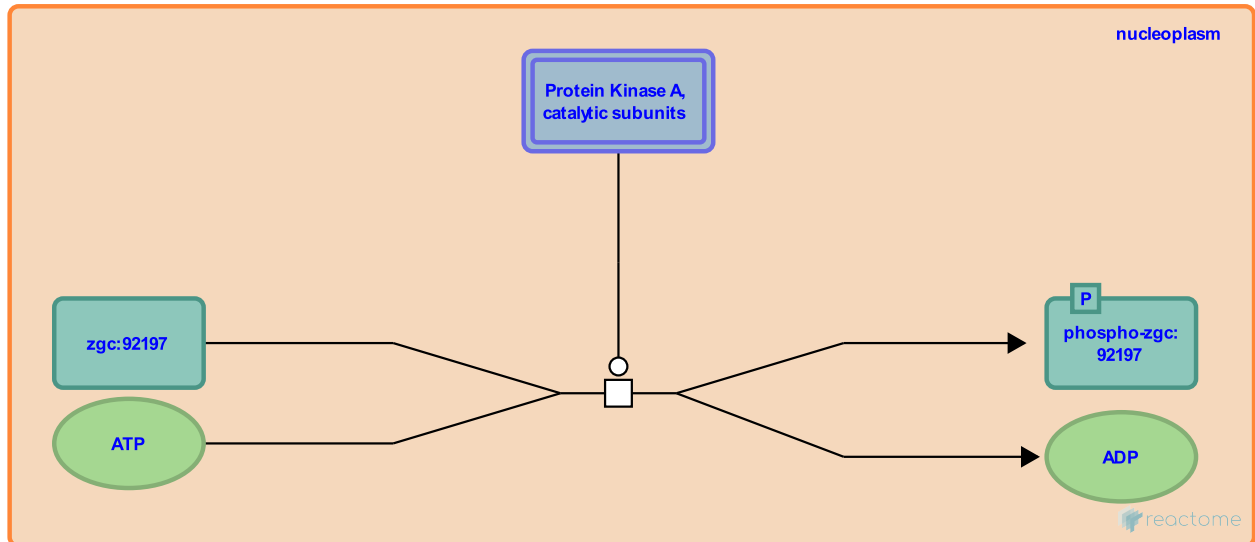
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5687088

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** [PKA phosphorylates MAPKAPK5 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

**Followed by:** [p-S115 MAPKAPK5 translocates to the cytosol](#)

## p-S115 MAPKAPK5 translocates to the cytosol ↗

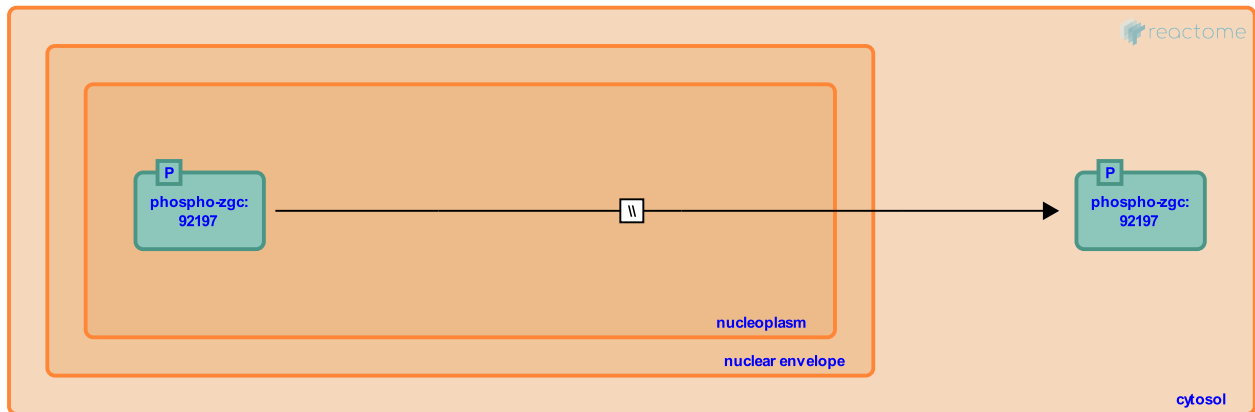
**Location:** MAPK6/MAPK4 signaling

**Stable identifier:** R-DRE-5687123

**Type:** omitted

**Compartments:** nucleoplasm

**Inferred from:** p-S115 MAPKAPK5 translocates to the cytosol (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.](http://www.pantherdb.org/about.jsp) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** PKA phosphorylates MAPKAPK5

**Followed by:** p-S MAPKAPK5 phosphorylates HSPB1

## p-S MAPKAPK5 phosphorylates HSPB1 ↗

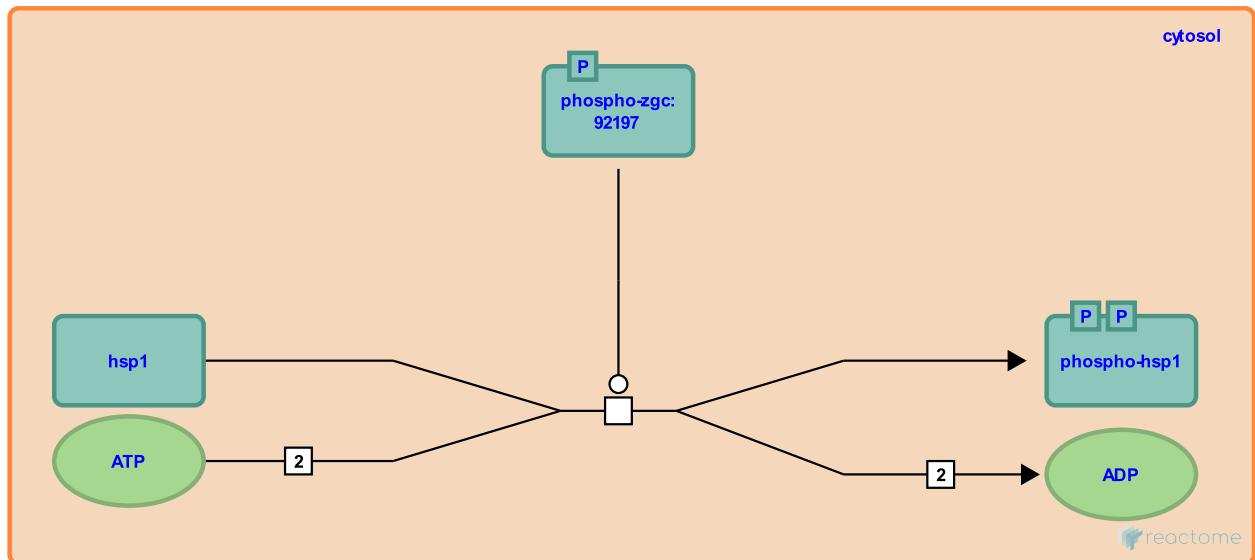
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5687121

**Type:** transition

**Compartments:** cytosol

**Inferred from:** [p-S MAPKAPK5 phosphorylates HSPB1 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [p-S MAPK6,4;p-T182 MAPKAPK5 translocate to the cytosol](#), [p-S115 MAPKAPK5 translocates to the cytosol](#)

## p-T182 MAPKAPK5 binds DNAJB1 ↗

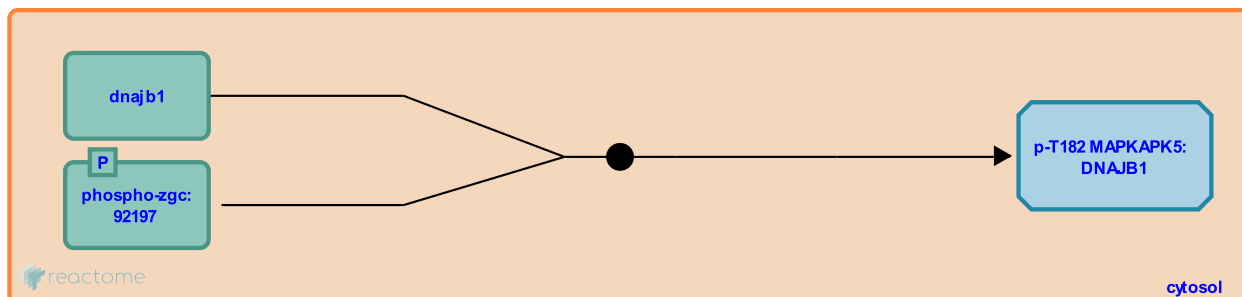
**Location:** MAPK6/MAPK4 signaling

**Stable identifier:** R-DRE-5690245

**Type:** binding

**Compartments:** cytosol

**Inferred from:** p-T182 MAPKAPK5 binds DNAJB1 (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.](http://www.pantherdb.org/about.jsp) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** p-S MAPK6,4;p-T182 MAPKAPK5 translocate to the cytosol

**Followed by:** p-T182-MAPKAPK5 phosphorylates DNAJB1

## p-T182-MAPKAPK5 phosphorylates DNAJB1 ↗

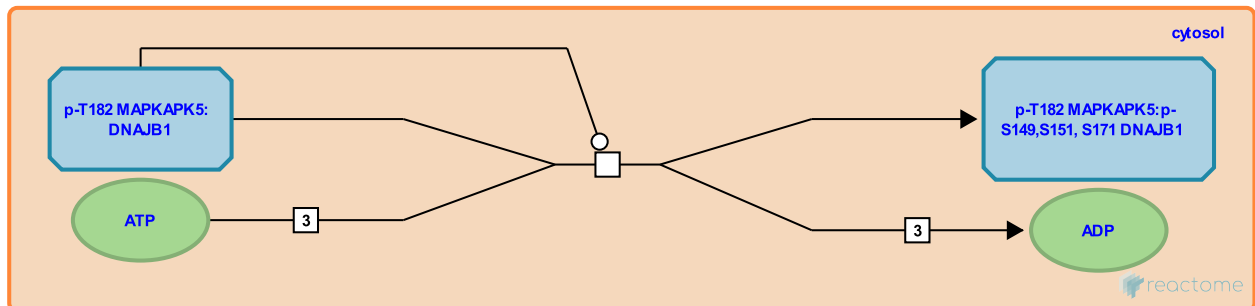
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5690250

**Type:** transition

**Compartments:** cytosol

**Inferred from:** [p-T182-MAPKAPK5 phosphorylates DNAJB1 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [p-T182 MAPKAPK5 binds DNAJB1](#)

## p-T182 MAPKAPK5 phosphorylates FOXO3 ↗

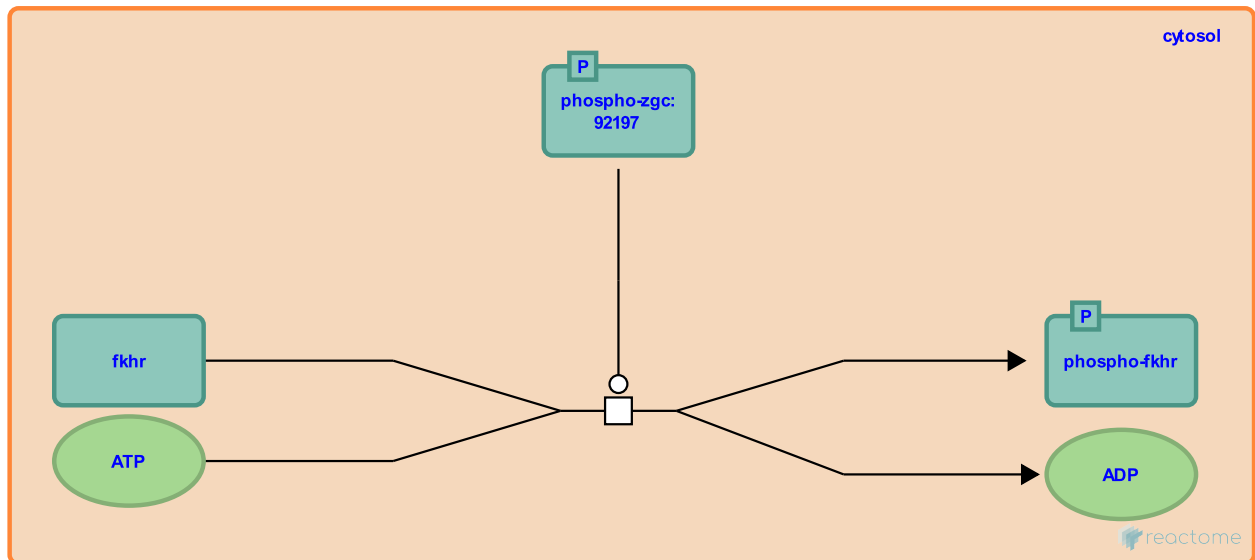
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5687101

**Type:** transition

**Compartments:** cytosol

**Inferred from:** [p-T182 MAPKAPK5 phosphorylates FOXO3 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [p-S MAPK6,4;p-T182 MAPKAPK5 translocate to the cytosol](#)

## p-S215 FOXO3 translocates to the nucleus ↗

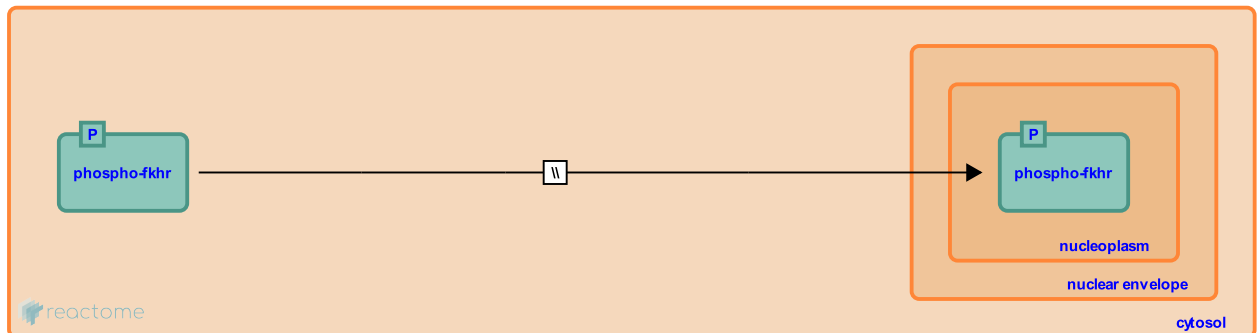
**Location:** MAPK6/MAPK4 signaling

**Stable identifier:** R-DRE-5687126

**Type:** omitted

**Compartments:** cytosol

**Inferred from:** p-S215 FOXO3 translocates to the nucleus (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.](http://www.pantherdb.org/about.jsp) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

## SEPT7 binds p-S189 MAPK6 and p-T182 MAPKAPK5 ↗

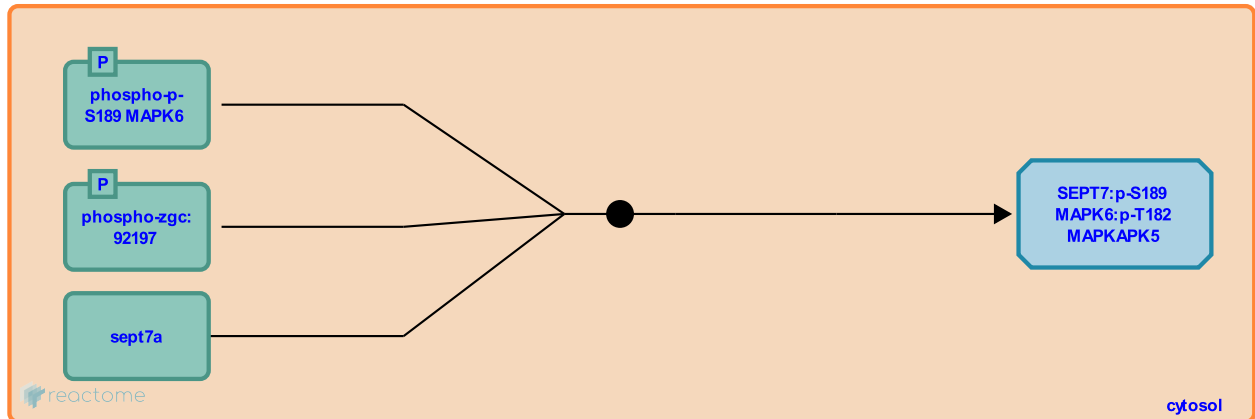
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5692770

**Type:** binding

**Compartments:** cytosol

**Inferred from:** [SEPT7 binds p-S189 MAPK6 and p-T182 MAPKAPK5 \(Homo sapiens\)](#)



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: <http://www.pantherdb.org/about.jsp>



## SEPT7:p-S189 MAPK6:p-T182 MAPKAPK5 phosphorylates CDC42EPs ↗

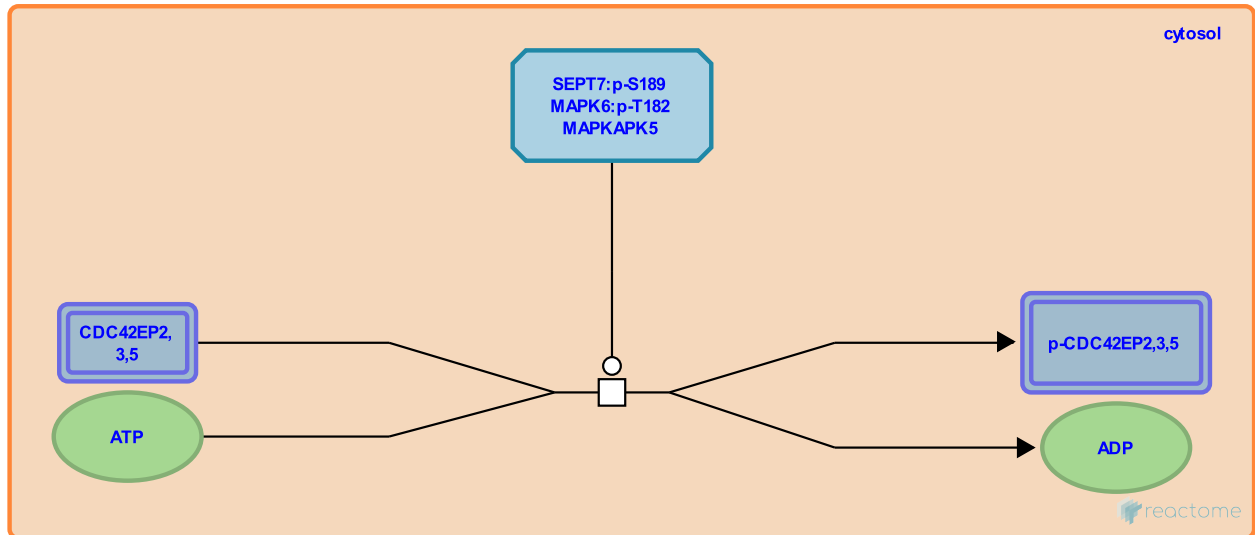
**Location:** [MAPK6/MAPK4 signaling](#)

**Stable identifier:** R-DRE-5692775

**Type:** transition

**Compartments:** cytosol

**Inferred from:** [SEPT7:p-S189 MAPK6:p-T182 MAPKAPK5 phosphorylates CDC42EPs \(Homo sapiens\)](#)



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.

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# Table of Contents

Introduction	1
MAPK6/MAPK4 signaling	2
↳ Activation of PAKs by RAC1 and CDC42	3
↳ Autophosphorylation of PAK1,2,3	4
↳ PAK1,2,3 phosphorylates MAPK6,4	5
↳ MAPK4,6 translocate to nucleus	6
↳ MAPK6 is degraded by the 26S proteasome	7
↳ CDK1 phosphorylates MAPK6	8
↳ CDC14A,B bind MAPK6	9
↳ CDC14A,B dephosphorylate p-3S,T MAPK6	10
↳ MAPK6 binds CCND3	11
↳ p-S MAPK6,4 binds MAPKAPK5	12
↳ p-S MAPK6,4 phosphorylate MAPKAPK5	13
↳ p-S MAPK6,4:p-T182 MAPKAPK5 translocate to the cytosol	14
↳ p-T182 MAPKAPK5 phosphorylates FOXO1	15
↳ PKA phosphorylates MAPKAPK5	16
↳ p-S115 MAPKAPK5 translocates to the cytosol	17
↳ p-S MAPKAPK5 phosphorylates HSPB1	18
↳ p-T182 MAPKAPK5 binds DNAJB1	19
↳ p-T182-MAPKAPK5 phosphorylates DNAJB1	20
↳ p-T182 MAPKAPK5 phosphorylates FOXO3	21
↳ p-S215 FOXO3 translocates to the nucleus	22
↳ SEPT7 binds p-S189 MAPK6 and p-T182 MAPKAPK5	23
↳ SEPT7:p-S189 MAPK6:p-T182 MAPKAPK5 phosphorylates CDC42EPs	24
Table of Contents	25