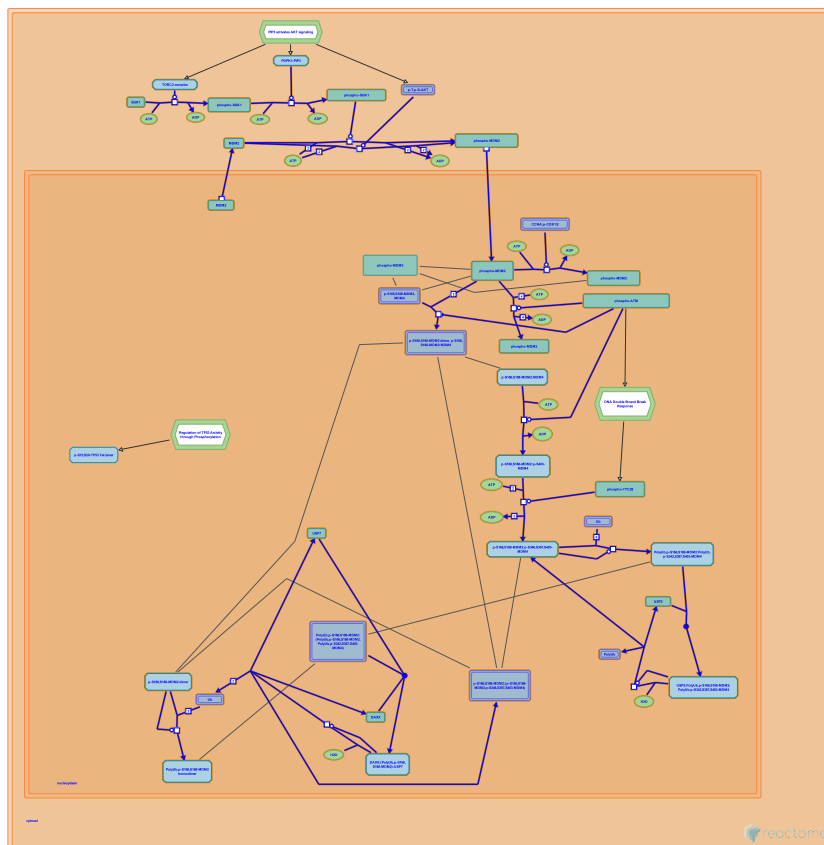


Regulation of TP53 Degradation



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

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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.

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. [↗](#)

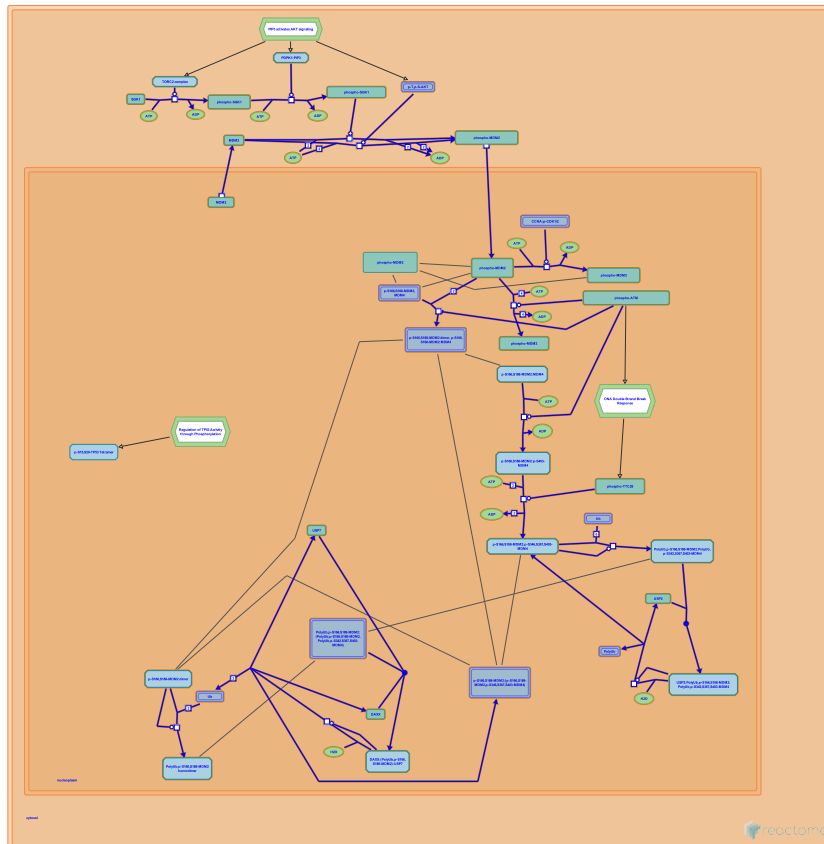
Reactome database release: 74

This document contains 1 pathway and 17 reactions ([see Table of Contents](#))

Regulation of TP53 Degradation ↗

Stable identifier: R-CFA-6804757

Inferred from: Regulation of TP53 Degradation (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>

MDM2 translocates to the cytosol ↗

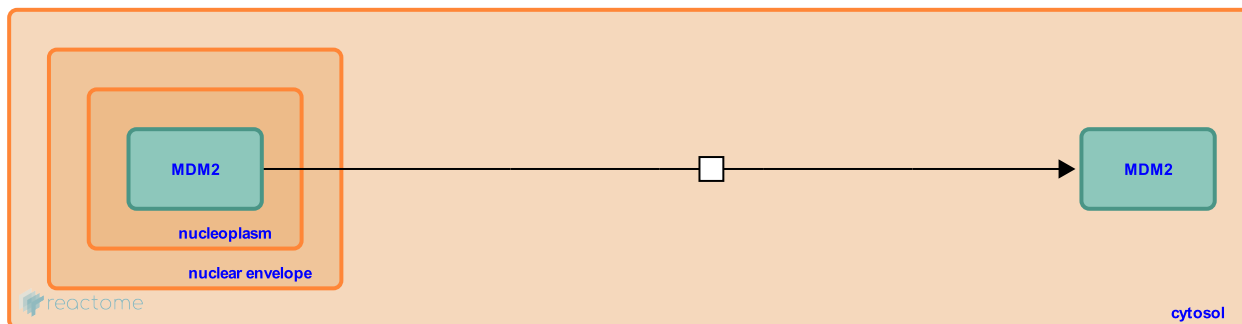
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6795667

Type: transition

Compartments: cytosol, nucleoplasm

Inferred from: [MDM2 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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Followed by: [AKT phosphorylates MDM2](#)

AKT phosphorylates MDM2 ↗

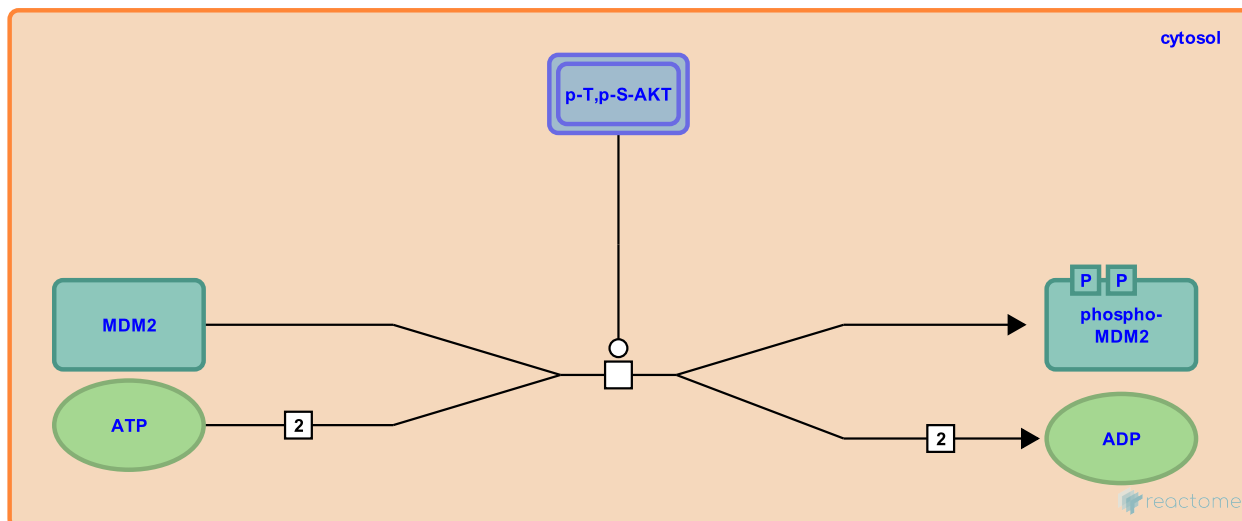
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-198599

Type: transition

Compartments: cytosol

Inferred from: [AKT phosphorylates MDM2 \(Homo sapiens\)](#)



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>

Preceded by: [MDM2 translocates to the cytosol](#)

Followed by: [MDM2 translocates to the nucleus](#)

TORC2 complex phosphorylates SGK1 ↗

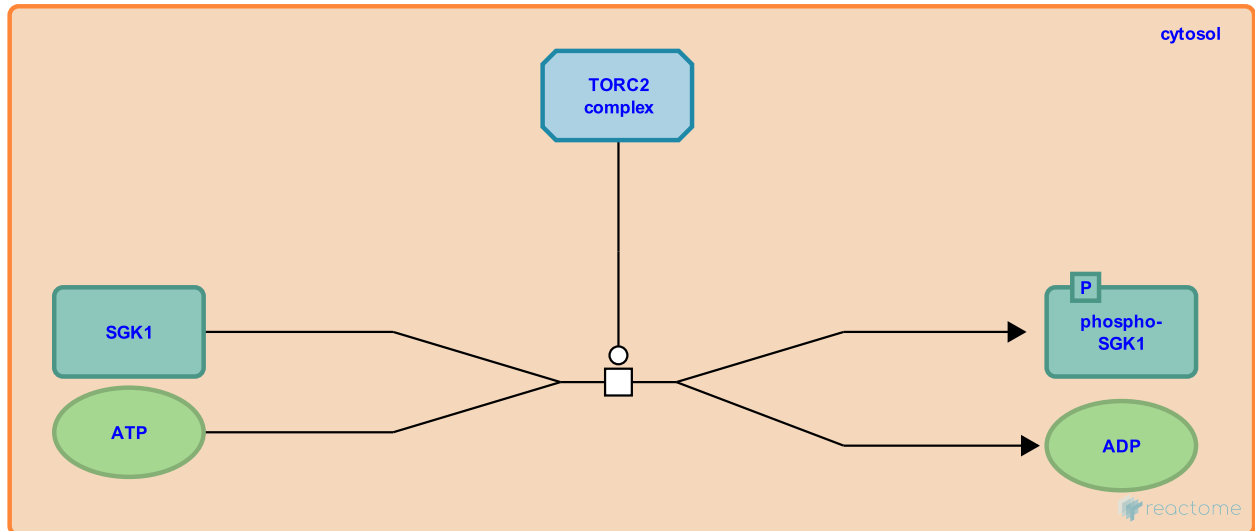
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6795290

Type: transition

Compartments: cytosol

Inferred from: [TORC2 complex phosphorylates SGK1 \(Homo sapiens\)](#)



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>

Followed by: [PDPK1 phosphorylates SGK1](#)

PDPK1 phosphorylates SGK1 ↗

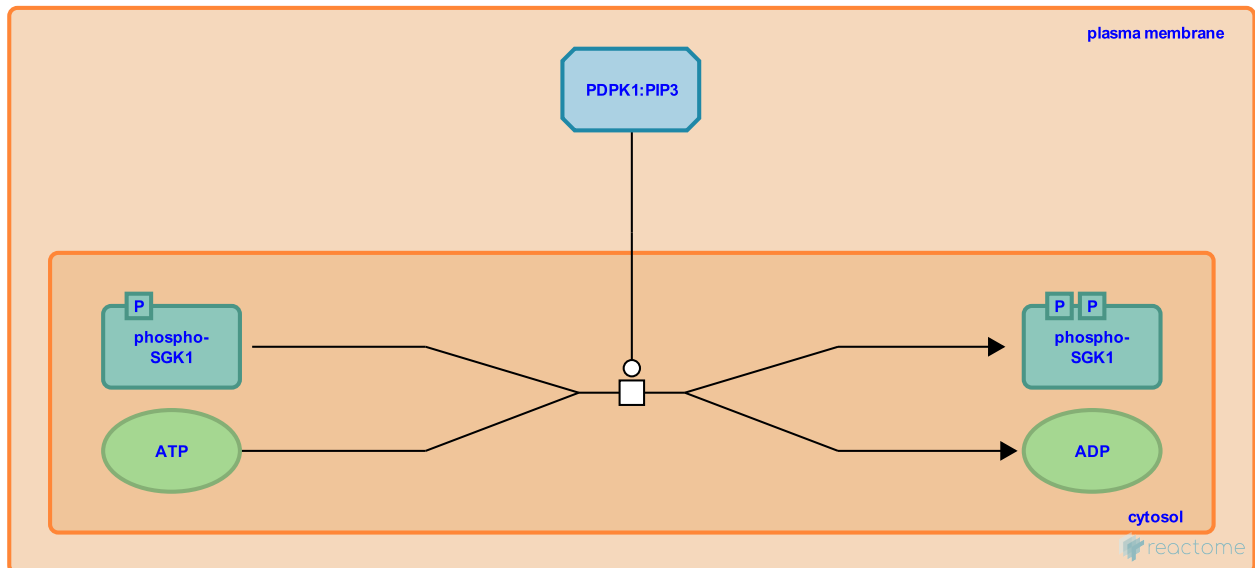
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6795473

Type: transition

Compartments: cytosol, plasma membrane

Inferred from: [PDPK1 phosphorylates SGK1 \(Homo sapiens\)](#)



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>

Preceded by: [TORC2 complex phosphorylates SGK1](#)

Followed by: [SGK1 phosphorylates MDM2](#)

SGK1 phosphorylates MDM2 ↗

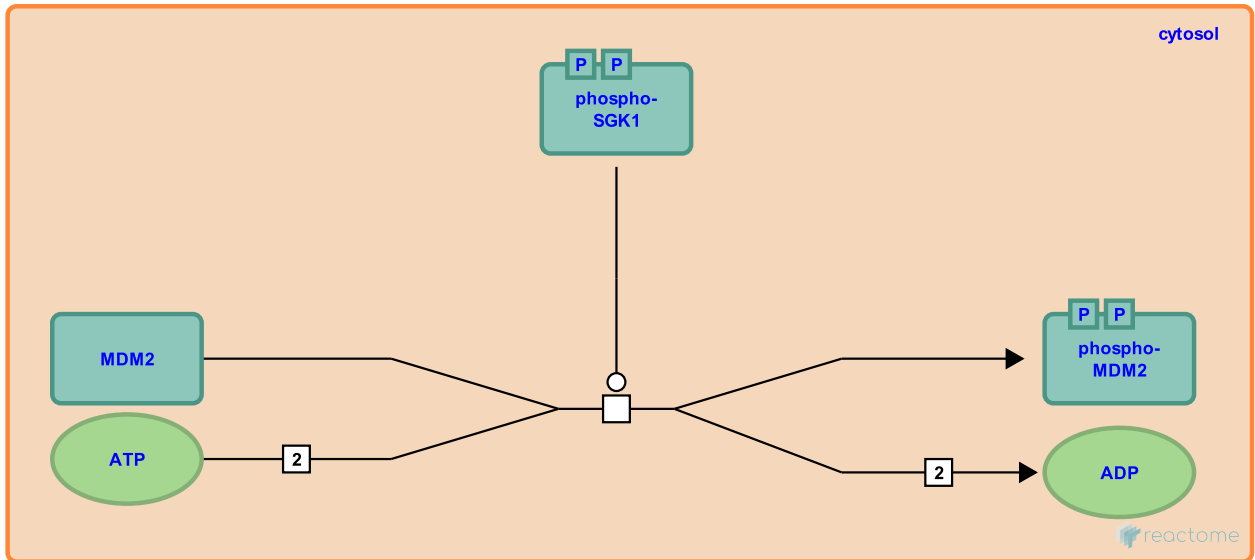
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6795460

Type: transition

Compartments: cytosol

Inferred from: [SGK1 phosphorylates MDM2 \(Homo sapiens\)](#)



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>

Preceded by: [PDPK1 phosphorylates SGK1](#)

Followed by: [MDM2 translocates to the nucleus](#)

MDM2 translocates to the nucleus ↗

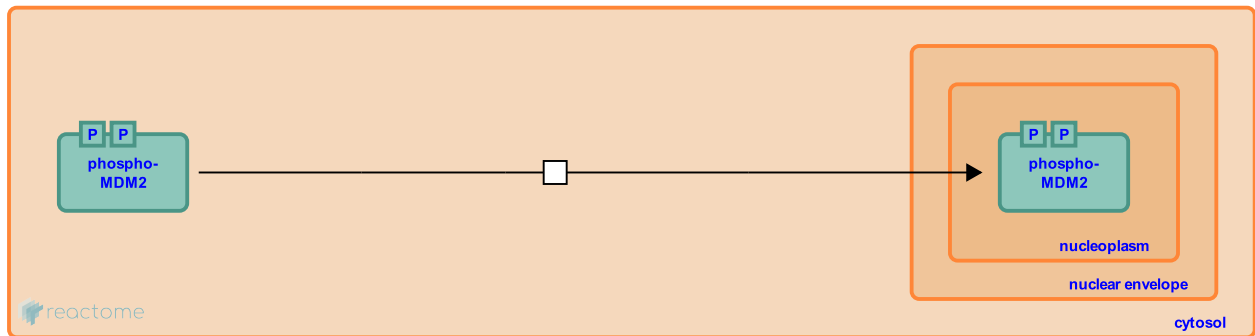
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6793666

Type: transition

Compartments: cytosol, nucleoplasm

Inferred from: [MDM2 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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

Preceded by: [AKT phosphorylates MDM2](#), [SGK1 phosphorylates MDM2](#)

Followed by: [\(CDK1,CDK2\):CCNA phosphorylates MDM2 at T218](#), [ATM phosphorylates MDM2](#), [MDM2 forms homo- or heterodimers](#)

MDM2 forms homo- or heterodimers ↗

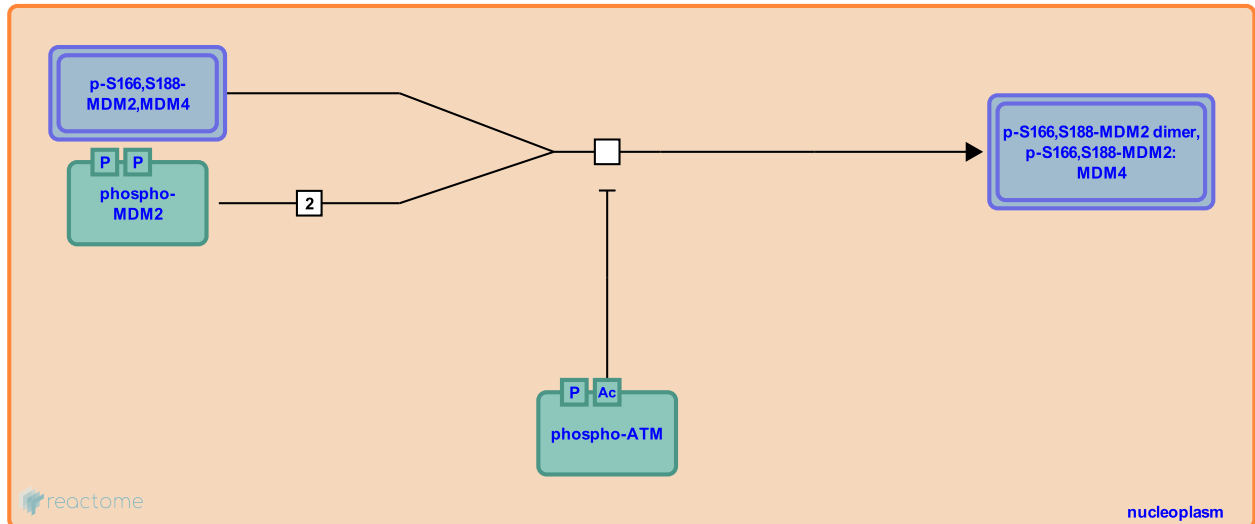
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6804741

Type: transition

Compartments: nucleoplasm

Inferred from: [MDM2 forms homo- or heterodimers \(Homo sapiens\)](#)



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>

Preceded by: [MDM2 translocates to the nucleus](#)

Followed by: [MDM2 homodimers auto-ubiquitinate](#), [Phosphorylation of MDM4 by ATM](#)

MDM2 homodimers auto-ubiquitinate ↗

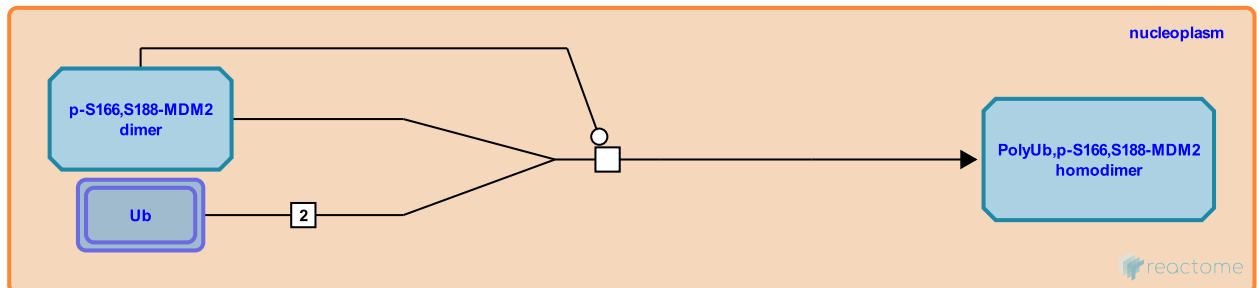
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6804942

Type: transition

Compartments: nucleoplasm

Inferred from: [MDM2 homodimers auto-ubiquitinate \(Homo sapiens\)](#)



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>

Preceded by: [MDM2 forms homo- or heterodimers](#)

Followed by: [DAXX binds Ub-MDM2 and USP7](#)

ATM phosphorylates MDM2 ↗

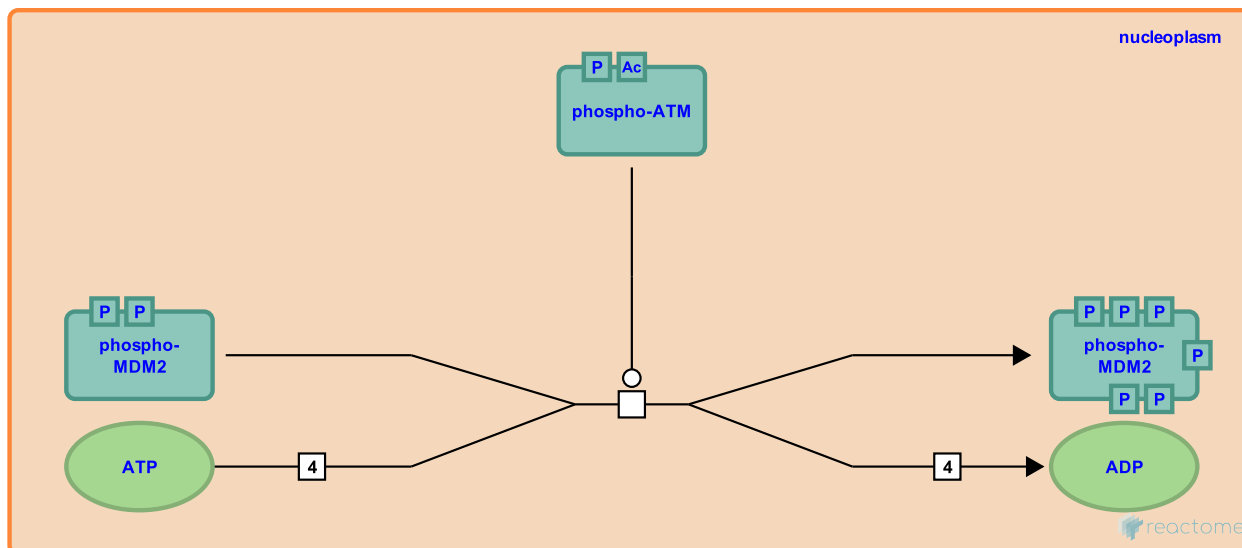
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6804955

Type: transition

Compartments: nucleoplasm

Inferred from: [ATM phosphorylates MDM2 \(Homo sapiens\)](#)



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>

Preceded by: [MDM2 translocates to the nucleus](#)

Phosphorylation of MDM4 by ATM ↗

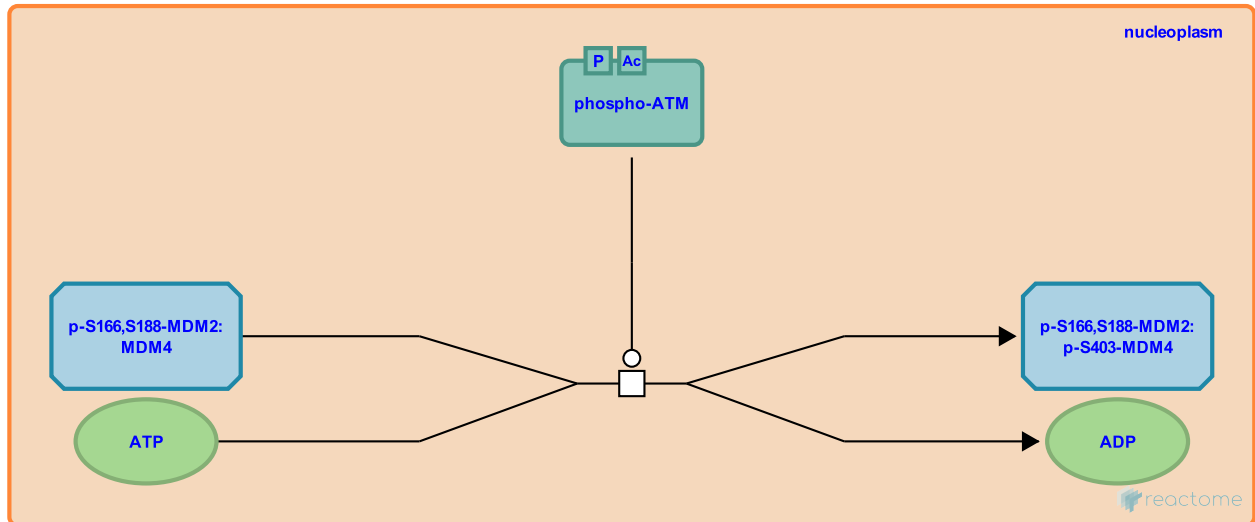
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-349455

Type: transition

Compartments: nucleoplasm

Inferred from: [Phosphorylation of MDM4 by ATM \(Homo sapiens\)](#)



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>

Preceded by: [MDM2 forms homo- or heterodimers](#)

Followed by: [Phosphorylation of MDM4 by CHEK2](#)

Phosphorylation of MDM4 by CHEK2 ↗

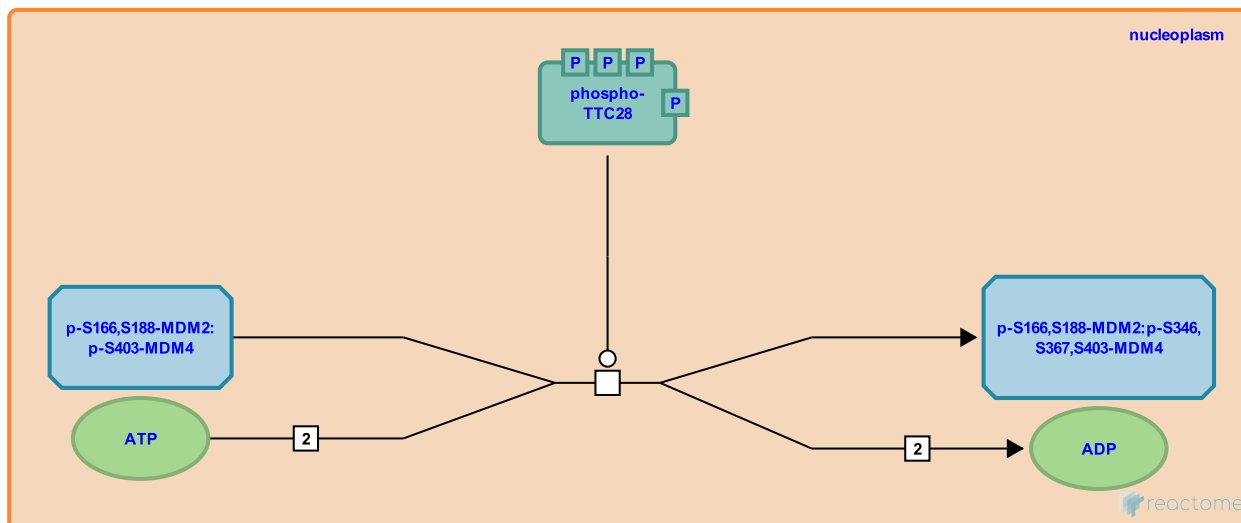
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-349426

Type: transition

Compartments: nucleoplasm

Inferred from: [Phosphorylation of MDM4 by CHEK2 \(Homo sapiens\)](#)



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>

Preceded by: [Phosphorylation of MDM4 by ATM](#)

Followed by: [MDM2 ubiquitinates phosphorylated MDM4](#)

MDM2 ubiquitinates phosphorylated MDM4 ↗

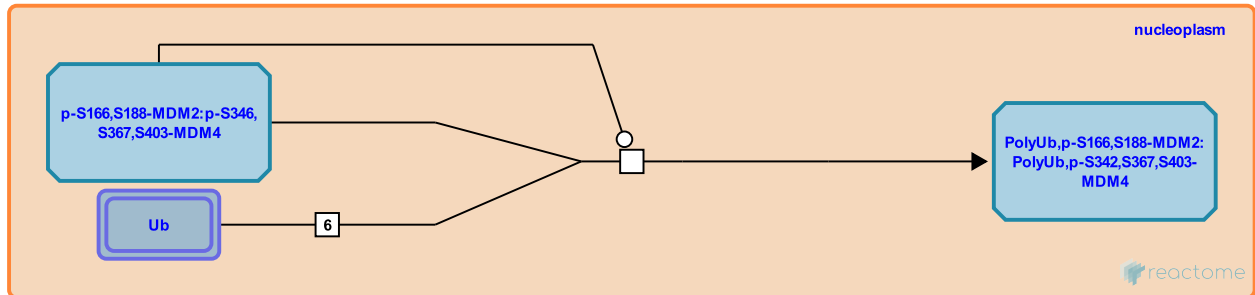
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6804724

Type: transition

Compartments: nucleoplasm

Inferred from: [MDM2 ubiquitinates phosphorylated MDM4 \(Homo sapiens\)](#)



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>

Preceded by: [Phosphorylation of MDM4 by CHEK2](#)

Followed by: [USP2 binds the heterodimer of MDM2 and MDM4](#), [DAXX binds Ub-MDM2](#) and [USP7](#)

DAXX binds Ub-MDM2 and USP7 ↗

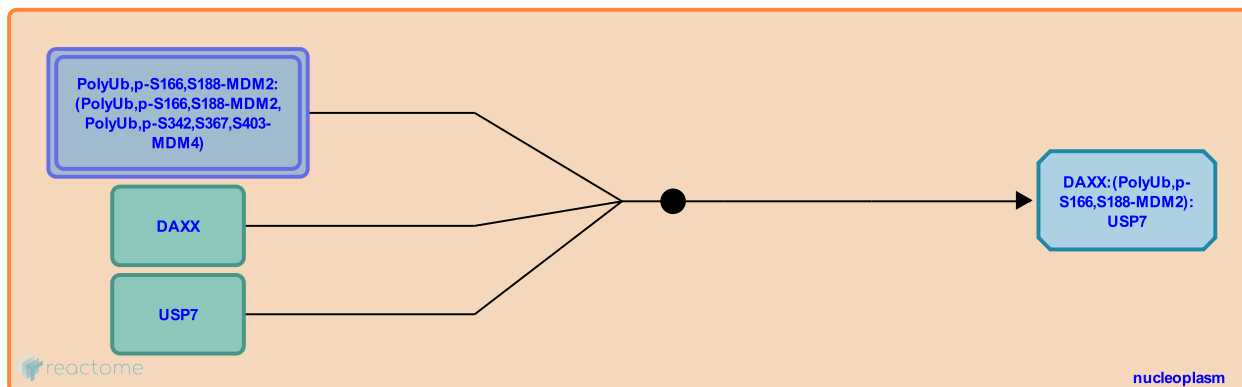
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-3222072

Type: binding

Compartments: nucleoplasm

Inferred from: [DAXX binds Ub-MDM2 and USP7 \(Homo sapiens\)](#)



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>

Preceded by: [MDM2 homodimers auto-ubiquitinate](#), [MDM2 ubiquitinates phosphorylated MDM4](#)

Followed by: [USP7 deubiquitinates MDM2](#)

USP7 deubiquitinates MDM2 ↗

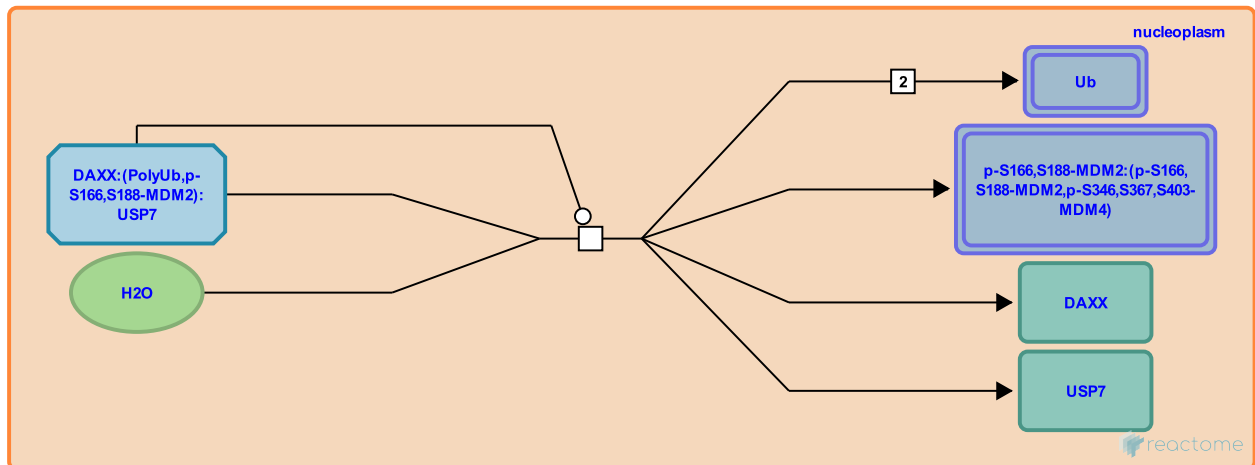
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-3215295

Type: transition

Compartments: nucleoplasm

Inferred from: [USP7 deubiquitinates MDM2 \(Homo sapiens\)](#)



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>

Preceded by: [DAXX binds Ub-MDM2 and USP7](#)

USP2 binds the heterodimer of MDM2 and MDM4 ↗

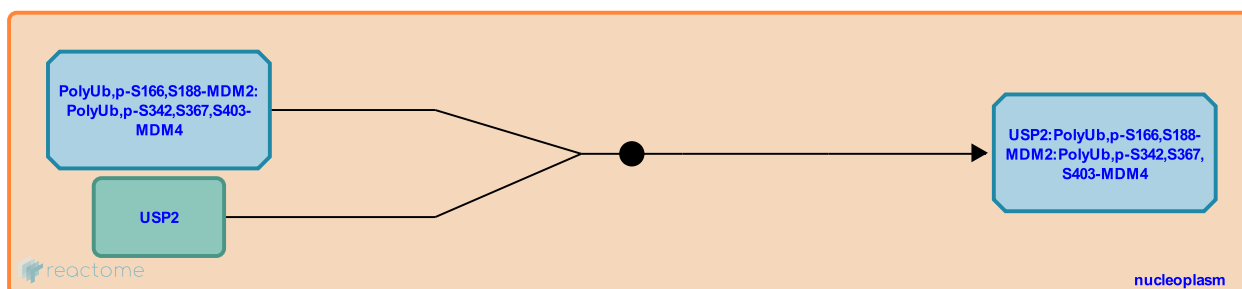
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6805022

Type: binding

Compartments: nucleoplasm

Inferred from: [USP2 binds the heterodimer of MDM2 and MDM4 \(Homo sapiens\)](#)



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>

Preceded by: [MDM2 ubiquitinates phosphorylated MDM4](#)

Followed by: [USP2 deubiquitinates MDM2,MDM4](#)

USP2 deubiquitinates MDM2,MDM4 ↗

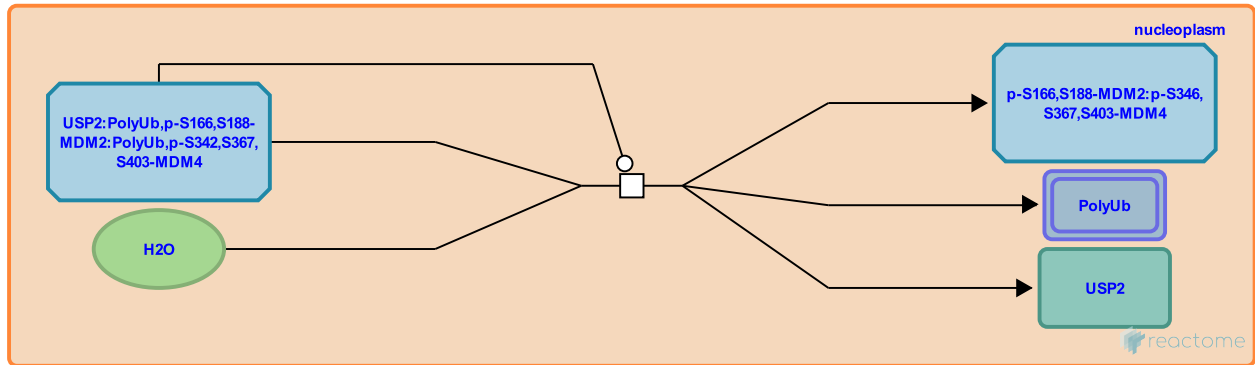
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-5689972

Type: transition

Compartments: nucleoplasm

Inferred from: [USP2 deubiquitinates MDM2,MDM4 \(Homo sapiens\)](#)



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>

Preceded by: [USP2 binds the heterodimer of MDM2 and MDM4](#)

(CDK1,CDK2):CCNA phosphorylates MDM2 at T218 ↗

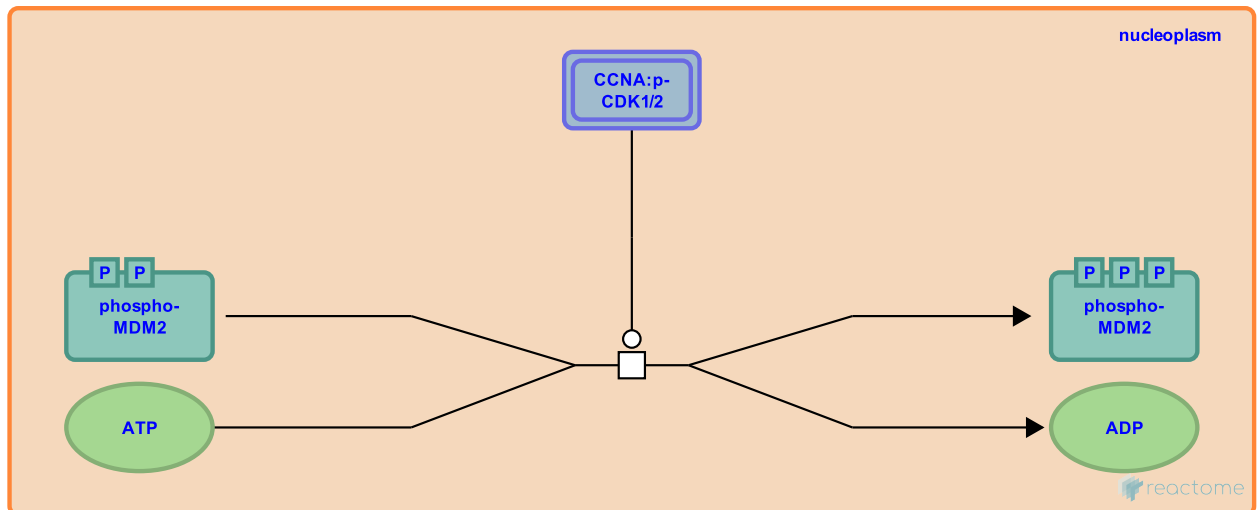
Location: [Regulation of TP53 Degradation](#)

Stable identifier: R-CFA-6793661

Type: transition

Compartments: nucleoplasm

Inferred from: (CDK1,CDK2):CCNA phosphorylates MDM2 at T218 (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>

Preceded by: [MDM2 translocates to the nucleus](#)

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