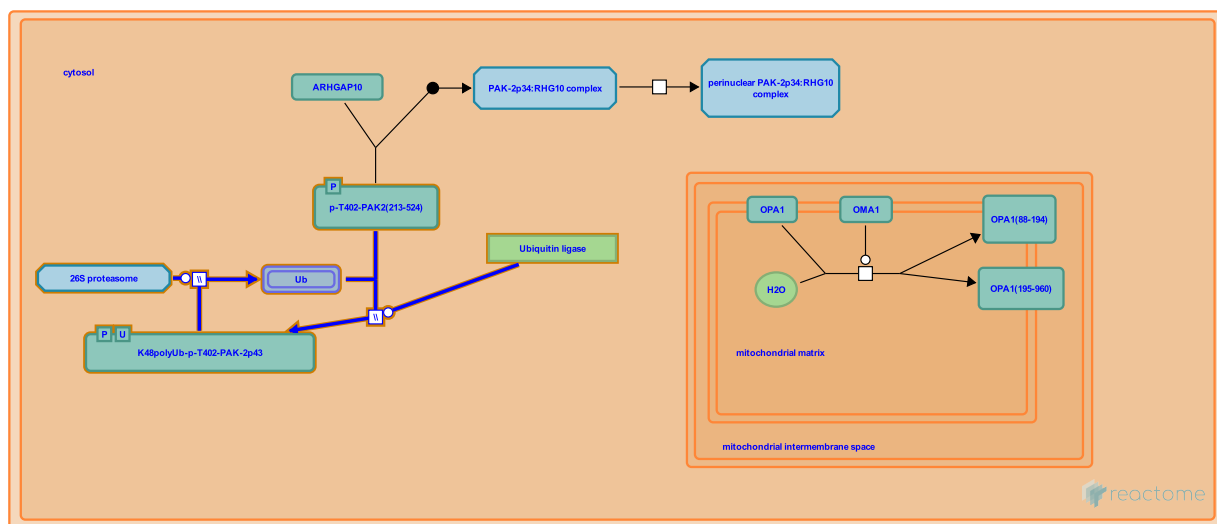


Regulation of activated PAK-2p34 by proteasome mediated degradation



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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

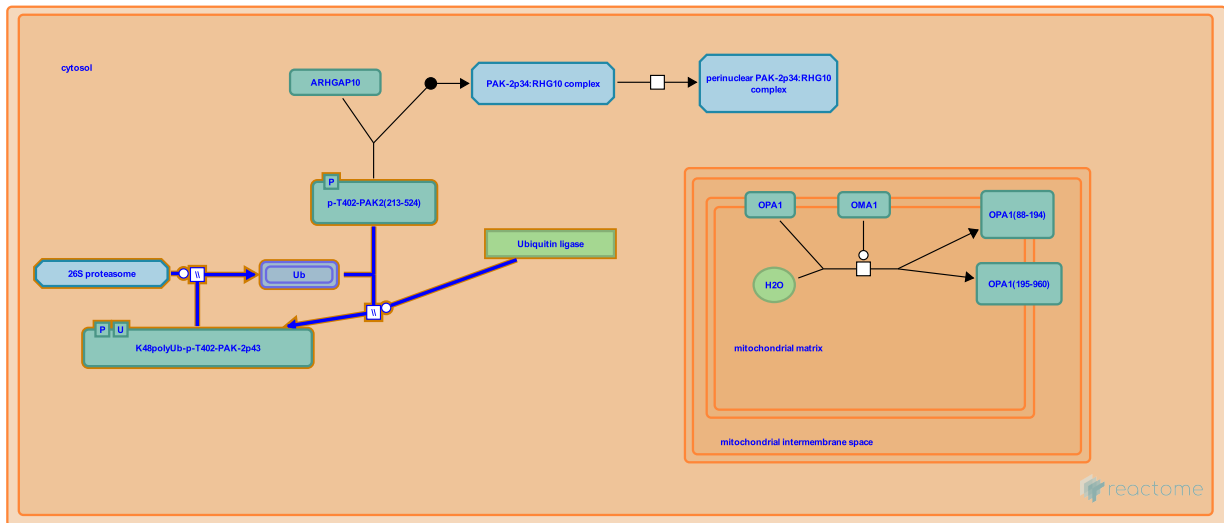
- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). 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: 75

This document contains 1 pathway and 2 reactions ([see Table of Contents](#))

Regulation of activated PAK-2p34 by proteasome mediated degradation ↗

Stable identifier: R-HSA-211733



Stimulation of cell death by PAK-2 requires the generation and stabilization of the caspase-activated form, PAK-2p34 (Walter et al., 1998;Jakobi et al., 2003). Levels of proteolytically activated PAK-2p34 protein are controlled by ubiquitin-mediated proteolysis. PAK-2p34 but not full-length PAK-2 is degraded by the 26 S proteasome (Jakobi et al., 2003). It is not known whether ubiquitination and degradation of PAK-2p34 occurs in the cytoplasm or in the nucleus.

Literature references

- Walter, BN., Huang, Z., Jakobi, R., Tuazon, PT., Alnemri, ES., Litwack, G. et al. (1998). Cleavage and activation of p21-activated protein kinase gamma-PAK by CPP32 (caspase 3). Effects of autophosphorylation on activity. *J Biol Chem*, 273, 28733-9. ↗
- Jakobi, R., McCarthy, CC., Koepfel, MA., Stringer, DK. (2003). Caspase-activated PAK-2 is regulated by subcellular targeting and proteasomal degradation. *J Biol Chem*, 278, 38675-85. ↗

Editions

| | | |
|------------|----------|--------------|
| 2008-02-04 | Edited | Matthews, L. |
| 2008-02-05 | Authored | Jakobi, R. |
| 2008-05-21 | Reviewed | Chang, E. |
| 2008-06-12 | Edited | Matthews, L. |

Ubiquitination of PAK-2p34 ↗

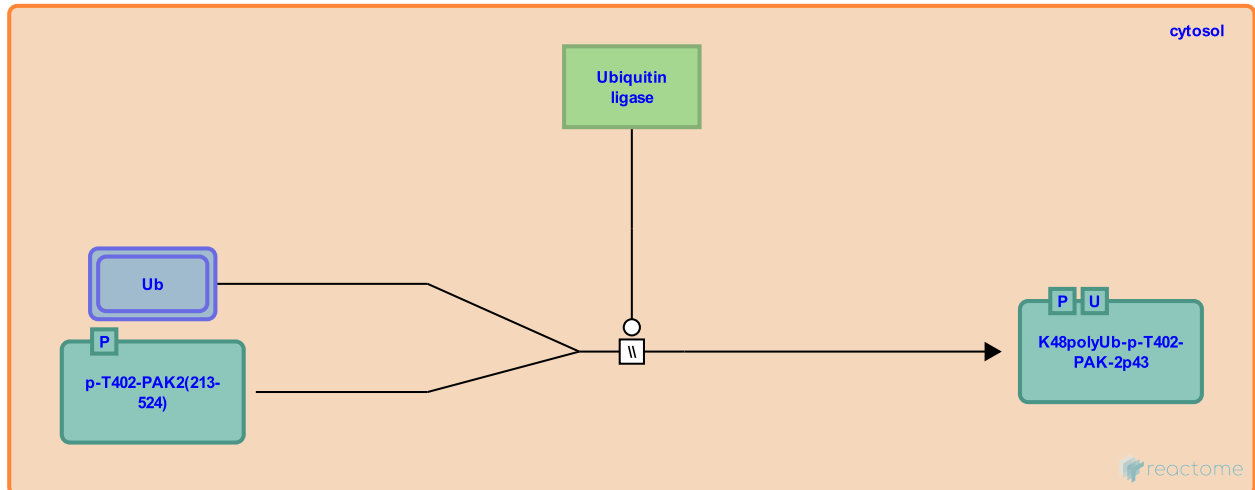
Location: [Regulation of activated PAK-2p34 by proteasome mediated degradation](#)

Stable identifier: R-HSA-211734

Type: omitted

Compartments: cytosol

Inferred from: [Ubiquitination of PAK-2p34 \(Oryctolagus cuniculus\)](#)



PAK-2p34 is ubiquitinated prior to degradation (Jakobi et al., 2003). Here, ubiquitination of PAK-2p34 is described as occurring in the cytosol. However, to date it is not known whether this occurs in the nucleus or in the cytoplasm. Evidence for this reaction comes from experiments using both human and rabbit proteins. The polyubiquitin synthesized in the reaction is inferred to contain lysine-48 (K48) linkages because the modified protein is targeted to the proteasome (Komander 2009).

Followed by: [Proteasome mediated degradation of PAK-2p34](#)

Editions

| | | |
|------------|----------|--------------|
| 2008-02-04 | Edited | Matthews, L. |
| 2008-02-05 | Authored | Jakobi, R. |
| 2008-05-21 | Reviewed | Chang, E. |
| 2008-05-23 | Edited | Matthews, L. |

Proteasome mediated degradation of PAK-2p34 [↗](#)

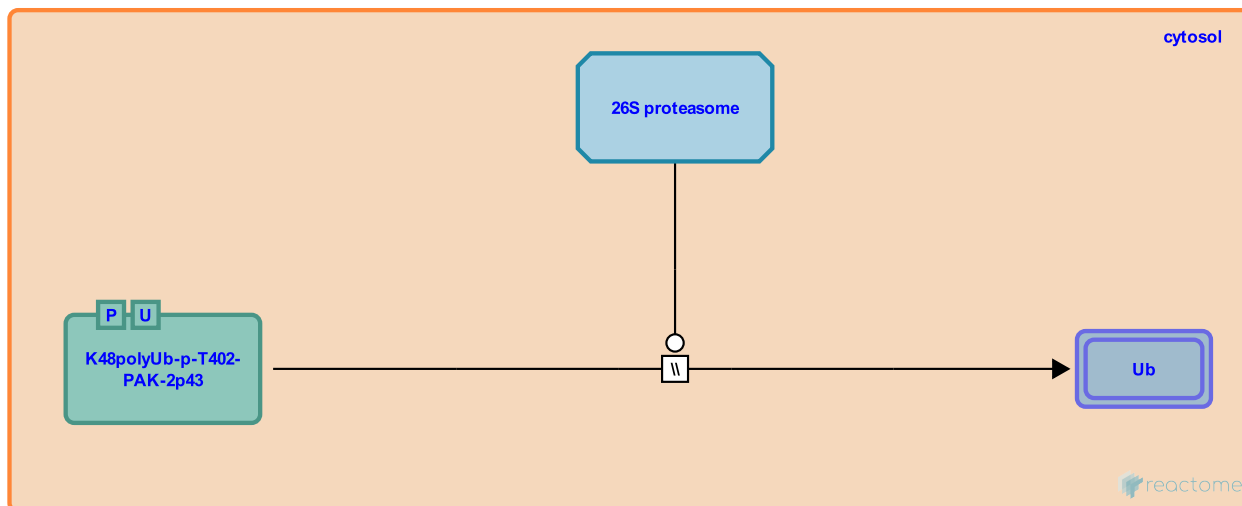
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Stable identifier: R-HSA-211715

Type: omitted

Compartments: cytosol

Inferred from: [Proteasome mediated degradation of PAK-2p34 \(Homo sapiens\)](#)



Proteolytically activated PAK-2p34, but not full-length PAK-2, is degraded rapidly by the proteasome (Jakobi et al., 2003). Here, degradation of PAK-2p34 is described as occurring in the cytosol. However, to date it is not known whether this occurs in the nucleus or in the cytoplasm.

Preceded by: [Ubiquitination of PAK-2p34](#)

Literature references

Jakobi, R., McCarthy, CC., Koepfel, MA., Stringer, DK. (2003). Caspase-activated PAK-2 is regulated by subcellular targeting and proteasomal degradation. *J Biol Chem*, 278, 38675-85. [↗](#)

Editions

| | | |
|------------|----------|--------------|
| 2008-02-04 | Edited | Matthews, L. |
| 2008-02-05 | Authored | Jakobi, R. |
| 2008-05-21 | Reviewed | Chang, E. |

Table of Contents

| | |
|---|---|
| Introduction | 1 |
| ▣ Regulation of activated PAK-2p34 by proteasome mediated degradation | 2 |
| ▣ Ubiquitination of PAK-2p34 | 3 |
| ▣ Proteasome mediated degradation of PAK-2p34 | 4 |
| Table of Contents | 5 |