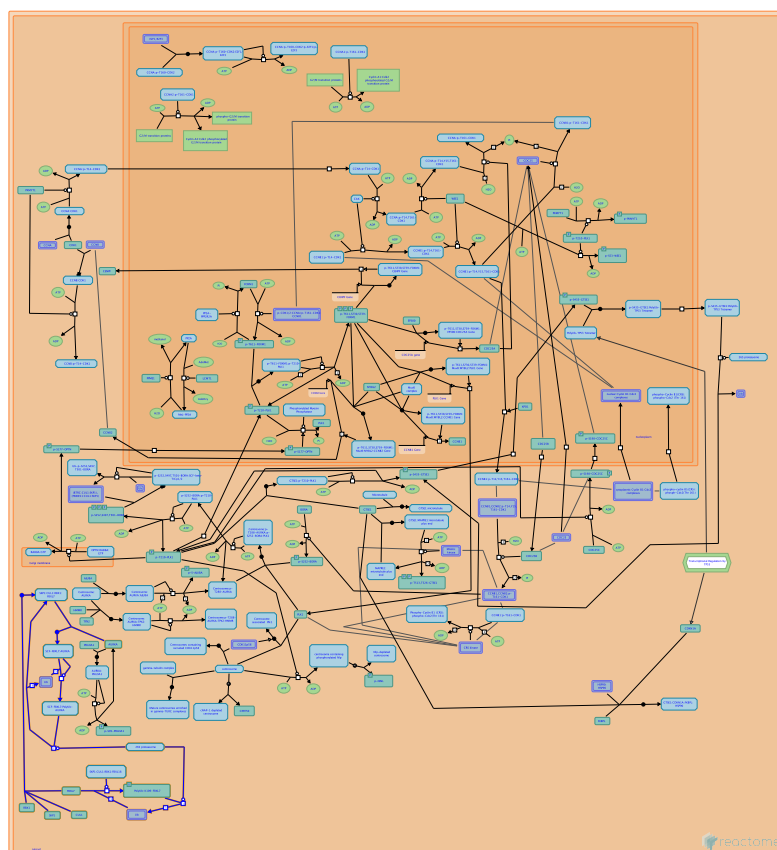


FBXL7 down-regulates AURKA during mitotic entry and in early mitosis



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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. [↗](#)

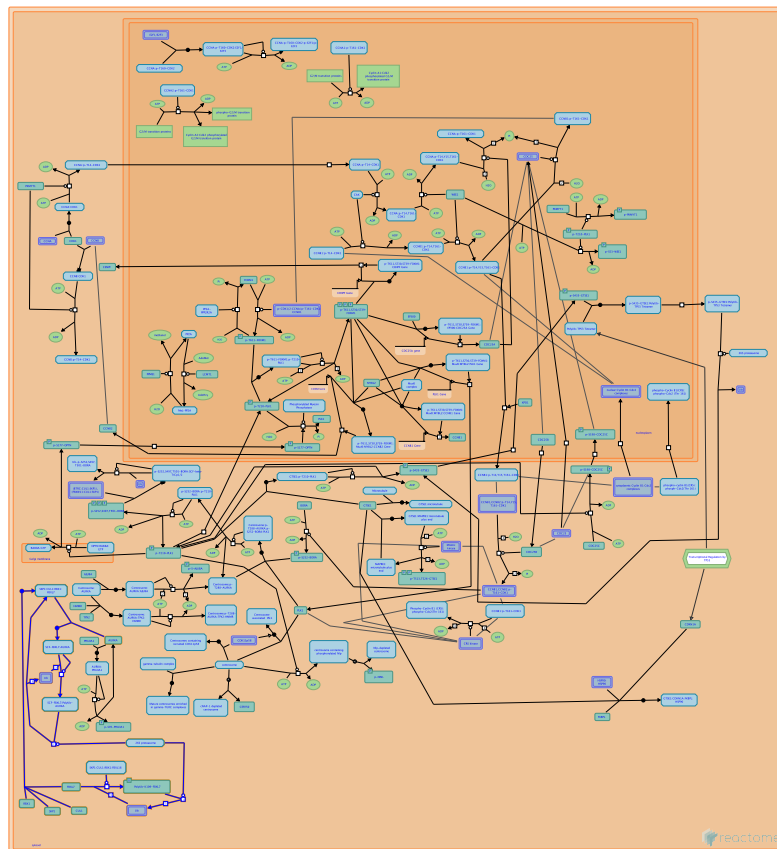
Reactome database release: 77

This document contains 1 pathway and 6 reactions ([see Table of Contents](#))

FBXL7 down-regulates AURKA during mitotic entry and in early mitosis [↗](#)

Stable identifier: R-HSA-8854050

Compartments: cytosol



The protein levels of aurora kinase A (AURKA) during mitotic entry and in early mitosis can be reduced by the action of the SCF-FBXL7 E3 ubiquitin ligase complex consisting of SKP1, CUL1, RBX1 and FBXL7 subunits. FBXL7 is the substrate recognition subunit of the SCF-FBXL7 complex that associates with the centrosome-bound AURKA, promoting its ubiquitination and proteasome-mediated degradation. Overexpression of FBXL7 results in G2/M cell cycle arrest and apoptosis (Coon et al. 2011).

FBXL7 protein levels are down-regulated by the action of the SCF-FBXL18 E3 ubiquitin ligase complex, consisting of SKP1, CUL1, RBX1 and the substrate recognition subunit FBXL18. FBXL18 binds to the FQ motif of FBXL7, targeting it for ubiquitination and proteasome-mediated degradation, counteracting its pro-apoptotic activity (Liu et al. 2015). Cell cycle stage-dependency of down-regulation of FBXL7 by FBXL18 is unknown.

Literature references

- Liu, Y., Lear, T., Zhao, Y., Zhao, J., Zou, C., Chen, BB. et al. (2015). F-box protein Fbx18 mediates polyubiquitylation and proteasomal degradation of the pro-apoptotic SCF subunit Fbx17. *Cell Death Dis*, 6, e1630. [↗](#)
- Coon, TA., Glasser, JR., Mallampalli, RK., Chen, BB. (2012). Novel E3 ligase component FBXL7 ubiquitinates and degrades Aurora A, causing mitotic arrest. *Cell Cycle*, 11, 721-9. [↗](#)

Editions

2016-01-27	Authored, Edited	Orlic-Milacic, M.
2016-05-13	Reviewed	Lindon, C., Grant, R.

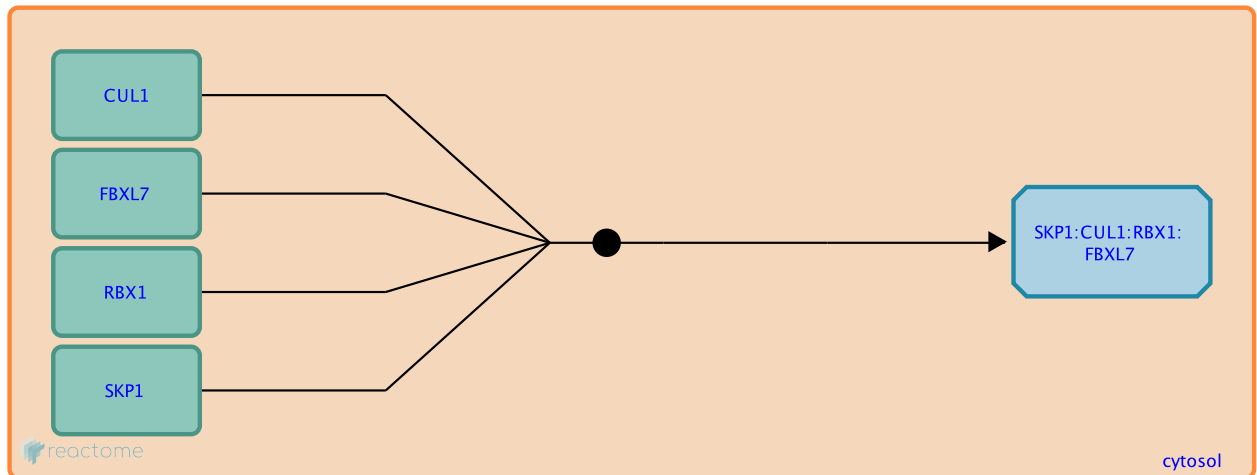
Formation of the SCF-FBXL7 complex ↗

Location: [FBXL7 down-regulates AURKA during mitotic entry and in early mitosis](#)

Stable identifier: R-HSA-8854052

Type: binding

Compartments: cytosol



FBXL7 associates with SKP1, CUL1 and RBX1 to form the SCF E3 ubiquitin ligase complex (Coon et al. 2011).

Followed by: [SCF:FBXL7 binds AURKA](#)

Literature references

Coon, TA., Glasser, JR., Mallampalli, RK., Chen, BB. (2012). Novel E3 ligase component FBXL7 ubiquitinates and degrades Aurora A, causing mitotic arrest. *Cell Cycle*, 11, 721-9. ↗

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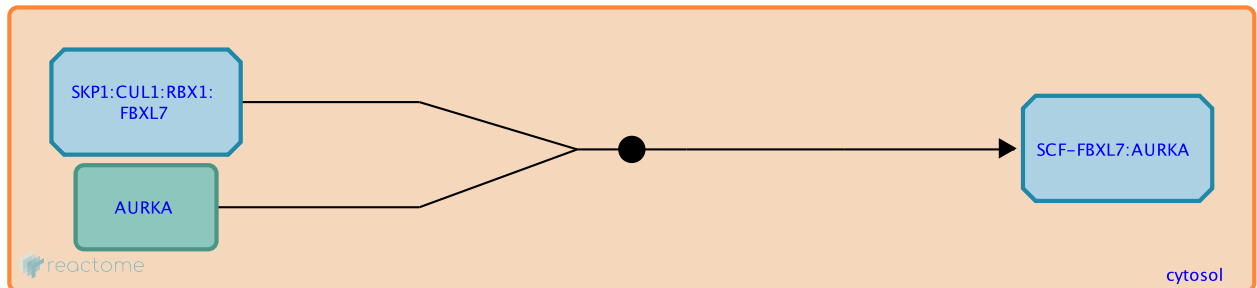
SCF:FBXL7 binds AURKA ↗

Location: [FBXL7 down-regulates AURKA during mitotic entry and in early mitosis](#)

Stable identifier: R-HSA-8853496

Type: binding

Compartments: cytosol



FBXL7, a component of the SCF E3 ubiquitin ligase complex, associates with aurora kinase A (AURKA) during mitosis (Coon et al. 2012).

Preceded by: [Formation of the SCF-FBXL7 complex](#)

Followed by: [SCF-FBXL7 ubiquitinates AURKA](#)

Literature references

Coon, TA., Glasser, JR., Mallampalli, RK., Chen, BB. (2012). Novel E3 ligase component FBXL7 ubiquitinates and degrades Aurora A, causing mitotic arrest. *Cell Cycle*, 11, 721-9. ↗

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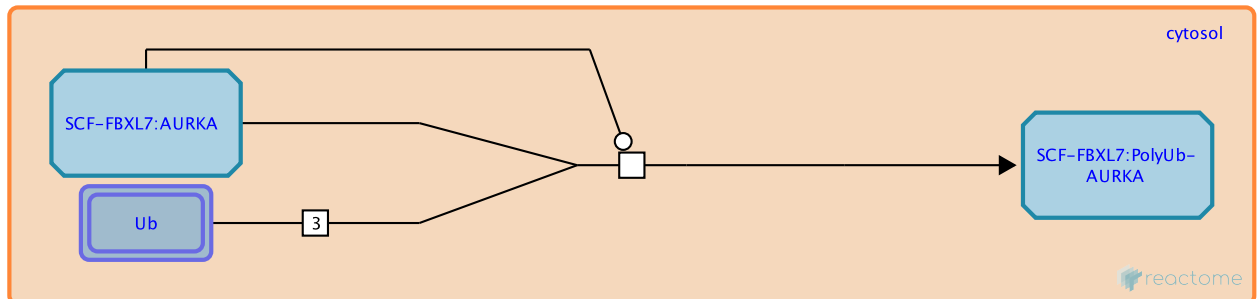
SCF-FBXL7 ubiquitinates AURKA ↗

Location: FBXL7 down-regulates AURKA during mitotic entry and in early mitosis

Stable identifier: R-HSA-8854041

Type: transition

Compartments: cytosol



The SCF-FBXL7 E3 ubiquitin ligase complex, composed of SKP1, CUL1, RBX1 and FBXL7, ubiquitinates aurora kinase A (AURKA), targeting it for degradation (Coon et al. 2012).

Preceded by: SCF:FBXL7 binds AURKA

Followed by: Proteasome degrades AURKA ubiquitinated by SCF-FBXL7

Literature references

Coon, TA., Glasser, JR., Mallampalli, RK., Chen, BB. (2012). Novel E3 ligase component FBXL7 ubiquitinates and degrades Aurora A, causing mitotic arrest. *Cell Cycle*, 11, 721-9. ↗

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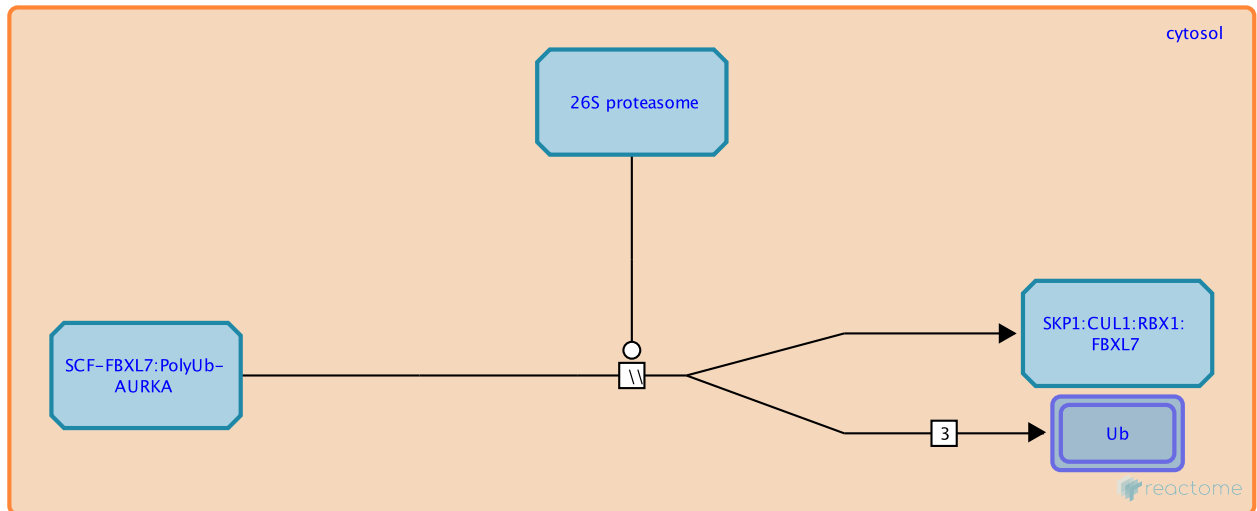
Proteasome degrades AURKA ubiquitinated by SCF-FBXL7 ↗

Location: FBXL7 down-regulates AURKA during mitotic entry and in early mitosis

Stable identifier: R-HSA-8854044

Type: omitted

Compartments: cytosol



Upon ubiquitination by the SCF-FBXL7 E3 ubiquitin ligase complex, aurora kinase A (AURKA) is degraded by the proteasome (Coon et al. 2012).

Preceded by: [SCF-FBXL7 ubiquitinates AURKA](#)

Literature references

Coon, TA., Glasser, JR., Mallampalli, RK., Chen, BB. (2012). Novel E3 ligase component FBXL7 ubiquitinates and degrades Aurora A, causing mitotic arrest. *Cell Cycle*, 11, 721-9. ↗

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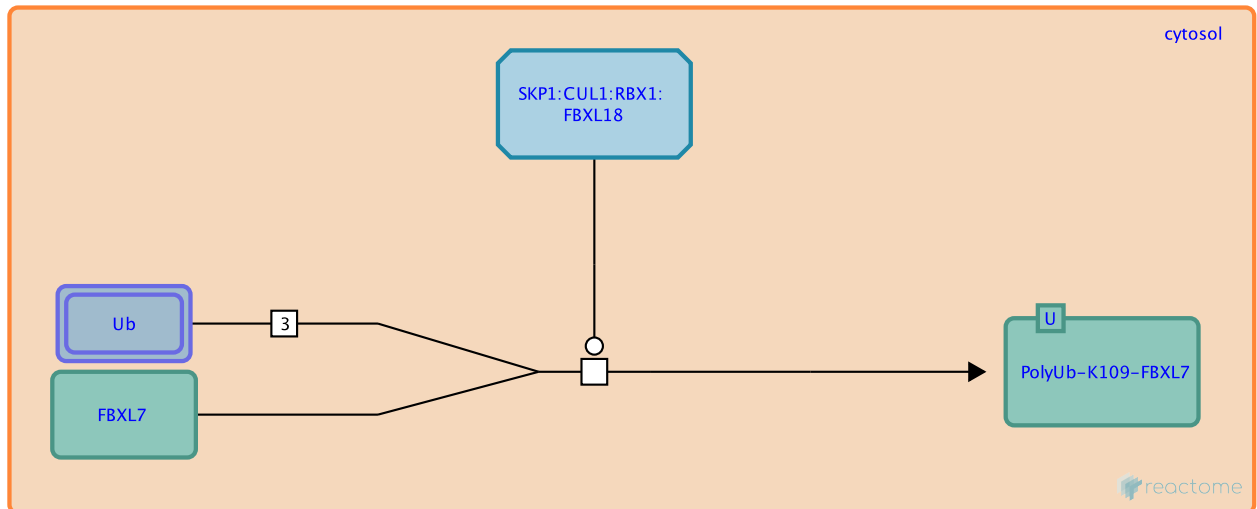
SCF-FBXL18 ubiquitinates FBXL7 ↗

Location: [FBXL7 down-regulates AURKA during mitotic entry and in early mitosis](#)

Stable identifier: R-HSA-8854051

Type: transition

Compartments: cytosol



FBXL18, a substrate recognition subunit of the SCF E3 ubiquitin ligase complex can bind to the FQ motif of FBXL7. The E3 ubiquitin ligase complex SCF-FBXL18 (SKP1:CUL1:RBX1:FBXL18) polyubiquitinates FBXL7 on lysine residue K109, targeting it for proteasome-mediated degradation (Liu et al. 2015).

Followed by: [Proteasome-mediated degradation of PolyUb-FBXL7](#)

Literature references

Liu, Y., Lear, T., Zhao, Y., Zhao, J., Zou, C., Chen, BB. et al. (2015). F-box protein Fbx18 mediates polyubiquitylation and proteasomal degradation of the pro-apoptotic SCF subunit Fbx17. *Cell Death Dis*, 6, e1630. ↗

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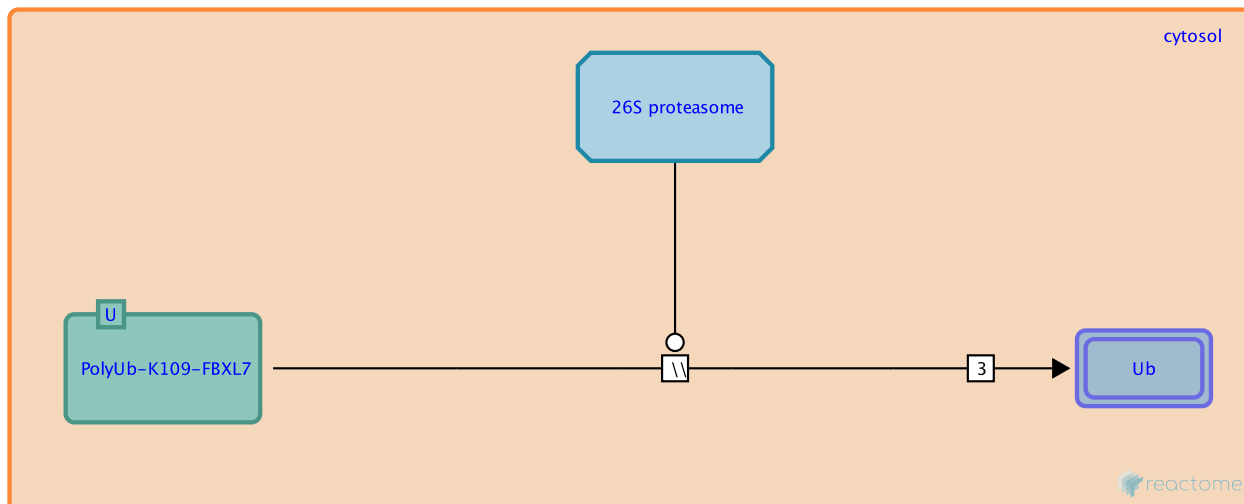
Proteasome-mediated degradation of PolyUb-FBXL7 [↗](#)

Location: [FBXL7 down-regulates AURKA during mitotic entry and in early mitosis](#)

Stable identifier: R-HSA-8854071

Type: omitted

Compartments: cytosol



FBXL7, polyubiquitinated by the FBXL18-containing SCF complex, is degraded by the proteasome (Liu et al. 2015).

Preceded by: [SCF-FBXL18 ubiquitinates FBXL7](#)

Literature references

Liu, Y., Lear, T., Zhao, Y., Zhao, J., Zou, C., Chen, BB. et al. (2015). F-box protein Fbx18 mediates polyubiquitylation and proteasomal degradation of the pro-apoptotic SCF subunit Fbx17. *Cell Death Dis*, 6, e1630. [↗](#)

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