# Decay of mRNA in

# SMG6:SMG5:SMG7:mRNA complex

May, B., Neu-Yilik, G.

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



16/01/2021

# 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. ↗

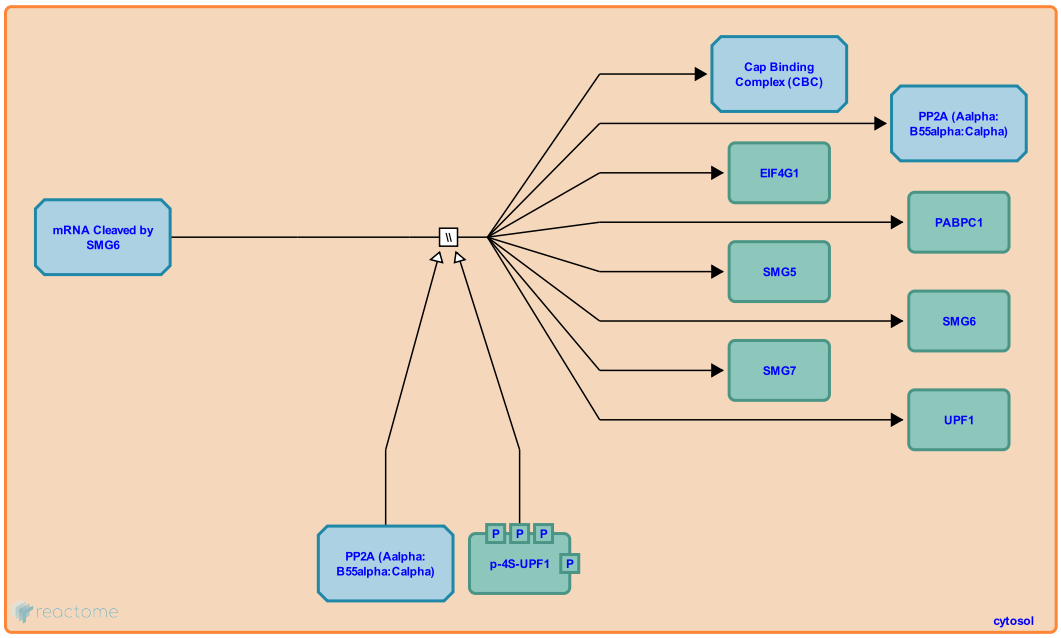
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

## Decay of mRNA in SMG6:SMG5:SMG7:mRNA complex ↗

**Stable identifier:** R-HSA-927830

**Type:** omitted

**Compartments:** cytosol




SMG6 endonucleolytically cleaves an mRNA it is believed that the resulting fragments are degraded by exonucleases, possibly XRN1, a 5'-to-3' nuclease, and the exosome complex, a 3'-to-5' nuclease (Huntzinger et al. 2008, Eberle et al. 2009). Inhibition of XRN1 is observed to cause accumulation of SMG6-cleaved intermediates therefore XRN1 is postulated to act downstream of SMG6 (Huntzinger et al. 2008).

In general, during Nonsense-Mediated Decay mRNAs are observed to be deadenlyated (implicating the PAN2 complex, PARN complex, and CCR4 complex), decapped (implicating the DCP1:DCP2 complex), and exoribonucleolytically digested (implicating the XRN1 5'-to-3' exonuclease and exosome 3'-to-5' exonuclease) (Lykke-Andersen 2002, Chen et al. 2003, Lejeune et al. 2003, Couttet and Grange 2004, Unterholzner and Izaurralde 2004, Yamashita et al. 2005). UPF1 is observed to associate with the decapping enzymes DCP1a and DCP2, however the specific decay reactions that occur after SMG6, SMG5 and SMG7 have associated with an mRNA are unknown (Lykke-Andersen et al. 2002). Likewise, SMG6 may be present in complexes separate from SMG5 and SMG7 and these complexes may have different routes of decay (reviewed in Nicholson et al. 2010, Muhlemann and Lykke-Andersen 2010).

ATPase activity of UPF1 is necessary for NMD and may reflect ATP-dependent helicase activity that disassembles the mRNA-protein complex (Franks et al. 2010). UPF1 must be dephosphorylated by PP2A for NMD to continue (Ohnishi et al. 2003, Chiu et al. 2003). Presumably the dephosphoryation recycles UPF1 for interaction with other mRNA complexes.

## Literature references


Chen, CY., Shyu, AB. (2003). Rapid deadenylation triggered by a nonsense codon precedes decay of the RNA body in a mammalian cytoplasmic nonsense-mediated decay pathway. *Mol Cell Biol, 23,* 4805-13. ↗

Eberle, AB., Lykke-Andersen, S., Muhlemann, O., Jensen, TH. (2009). SMG6 promotes endonucleolytic cleavage of nonsense mRNA in human cells. *Nat Struct Mol Biol, 16,* 49-55. ↗

Chiu, SY., Serin, G., Ohara, O., Maquat, LE. (2003). Characterization of human Smg5/7a: a protein with similarities to Caenorhabditis elegans SMG5 and SMG7 that functions in the dephosphorylation of Upf1. *RNA, 9*, 77-87. ↗

Lejeune, F., Li, X., Maquat, LE. (2003). Nonsense-mediated mRNA decay in mammalian cells involves decapping, deadenylating, and exonucleolytic activities. *Mol Cell, 12*, 675-87. ↗

Lykke-Andersen, J. (2002). Identification of a human decapping complex associated with hUpf proteins in nonsense-mediated decay. *Mol Cell Biol, 22*, 8114-21. ↗

## Editions

| | | |
|---|---|---|
| 2010-08-06 | Authored, Edited | May, B. |
| 2011-05-19 | Reviewed | Neu-Yilik, G. |