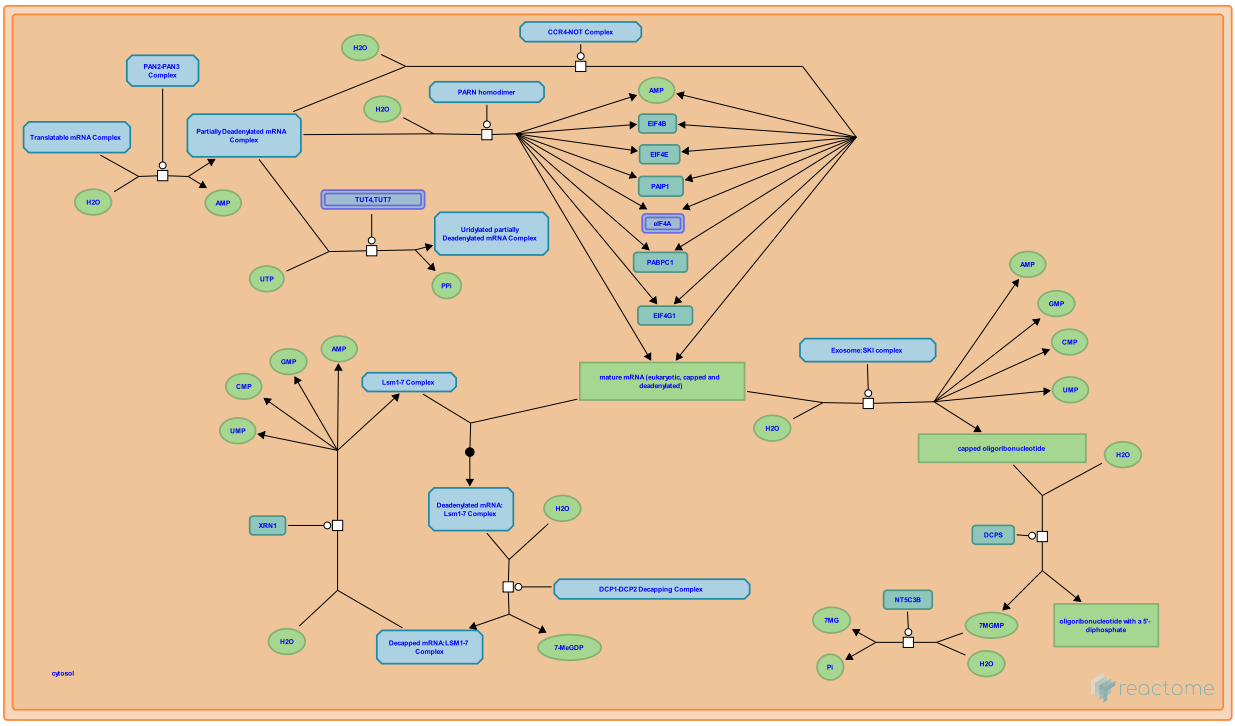
Deadenylation-dependent mRNA decay



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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).

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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. ↗

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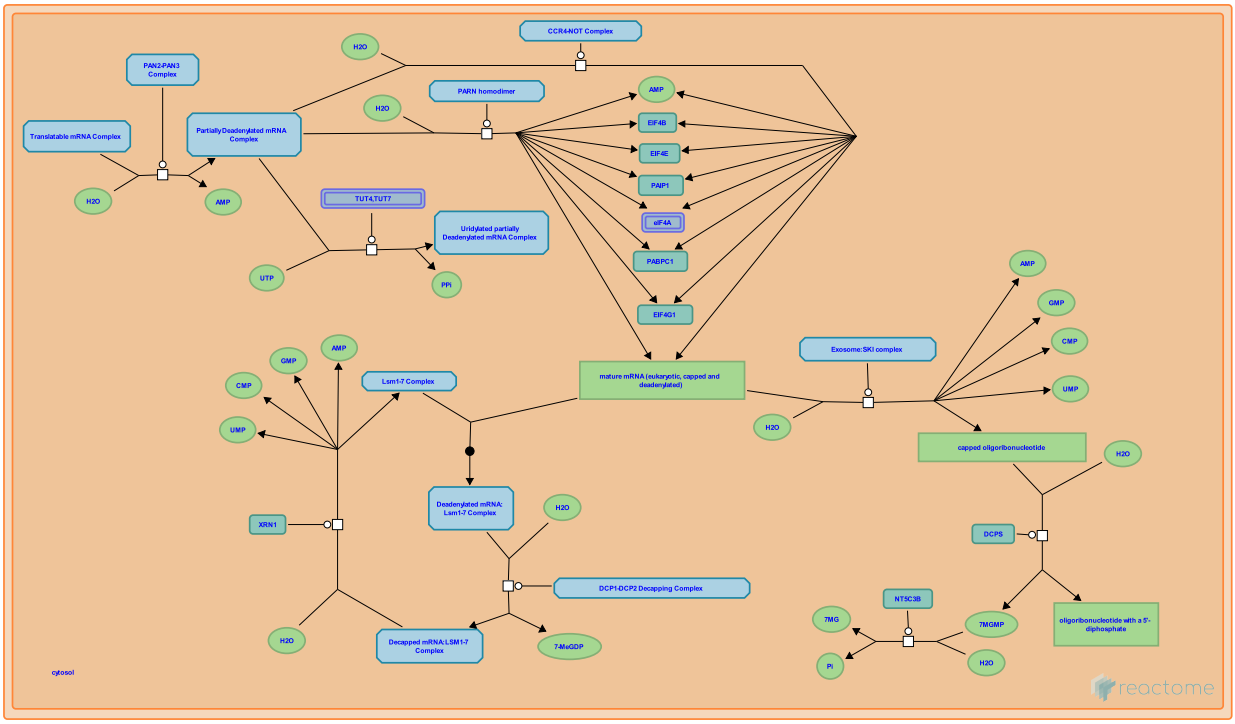
Deadenylation-dependent mRNA decay ↗

Stable identifier: R-HSA-429914

Compartments: cytosol



After undergoing rounds of translation, mRNA is normally destroyed by the deadenylation-dependent pathway. Though the trigger is unclear, deadenylation likely proceeds in two steps: one catalyzed by the PAN2-PAN3 complex that shortens the poly(A) tail from about 200 adenosine residues to about 80 residues and one catalyzed by the CCR4-NOT complex or by the PARN enzyme that shortens the tail to about 10-15 residues.
After deadenylation the mRNA is then hydrolyzed by either the 5' to 3' pathway or the 3' to 5' pathway. It is unknown what determinants target a mRNA to one pathway or the other.
The 5' to 3' pathway is initiated by binding of the Lsm1-7 complex to the 3' oligoadenylate tail followed by decapping by the DCP1-DCP2 complex. The 5' to 3' exoribonuclease XRN1 then hydrolyzes the remaining RNA.
The 3' to 5' pathway is initiated by the exosome complex at the 3' end of the mRNA. The exosome processively hydrolyzes the mRNA from 3' to 5', leaving only a capped oligoribonucleotide. The cap is then removed by the scavenging decapping enzyme DCPS.

Literature references

Song, H., Parker, R. (2004). The enzymes and control of eukaryotic mRNA turnover. *Nat Struct Mol Biol, 11*, 121-7. ↗

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Fritz, DT., Wilusz, J., Bergman, N., Wilusz, CJ., Kilpatrick, WJ. (2004). Messenger RNA decay in mammalian cells: the exonuclease perspective. *Cell Biochem Biophys, 41*, 265-78. ↗

Houseley, J., Tollervey, D. (2009). The many pathways of RNA degradation. *Cell, 136*, 763-76. ↗

Garneau, NL., Wilusz, J., Wilusz, CJ. (2007). The highways and byways of mRNA decay. *Nat Rev Mol Cell Biol, 8*, 113-26. ↗

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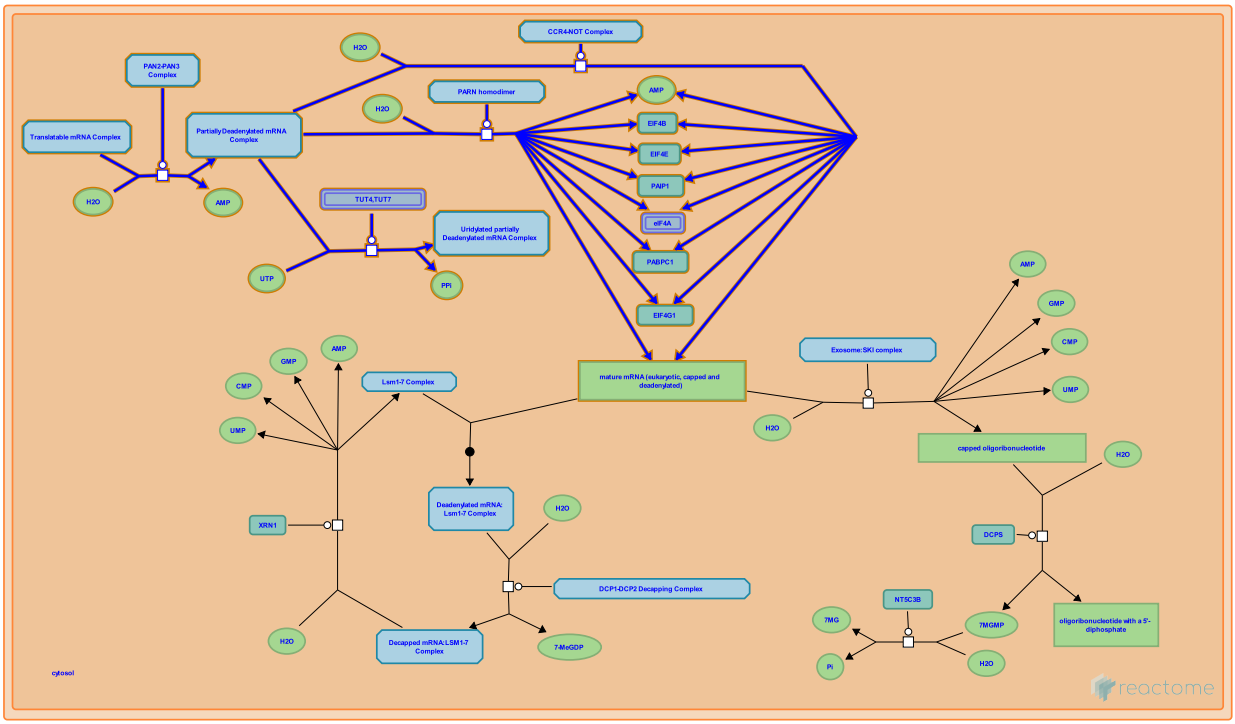
Deadenylation of mRNA ↗

Location: Deadenylation-dependent mRNA decay

Stable identifier: R-HSA-429947

Compartments: cytosol



Deadenylation of mRNA proceeds in two steps. According to current models, in the first step the poly(A) tail is shortened from about 200 adenosine residues to about 80 residues by the PAN2-PAN3 complex. In the second step the poly(A) tail is further shortened to 10-15 residues by either the CCR4-NOT complex or by the PARN exoribonuclease. How a particular mRNA is targeted to CCR4-NOT or PARN is unknown.
A number of other deadenylase enzymes can be identified in genomic searches. One particularly interesting one is nocturin, a protein that is related to the CCR-1 deadenylase and plays a role in circadian rhythms.
There is also evidence for networking between deadenylation and other aspects of gene expression. CCR4-NOT, for example, is known to be a transcription factor. PARN is part of a complex that regulates poly(A) tail length and hence translation in developing oocytes.

Literature references

Green, CB., Douris, N. (2008). NOC out the fat: a short review of the circadian deadenylase Nocturnin. *Ann Med, 40*, 622-6. ↗

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Richter, JD., Kim, JH. (2006). Opposing polymerase-deadenylase activities regulate cytoplasmic polyadenylation. *Mol Cell, 24*, 173-83. ↗

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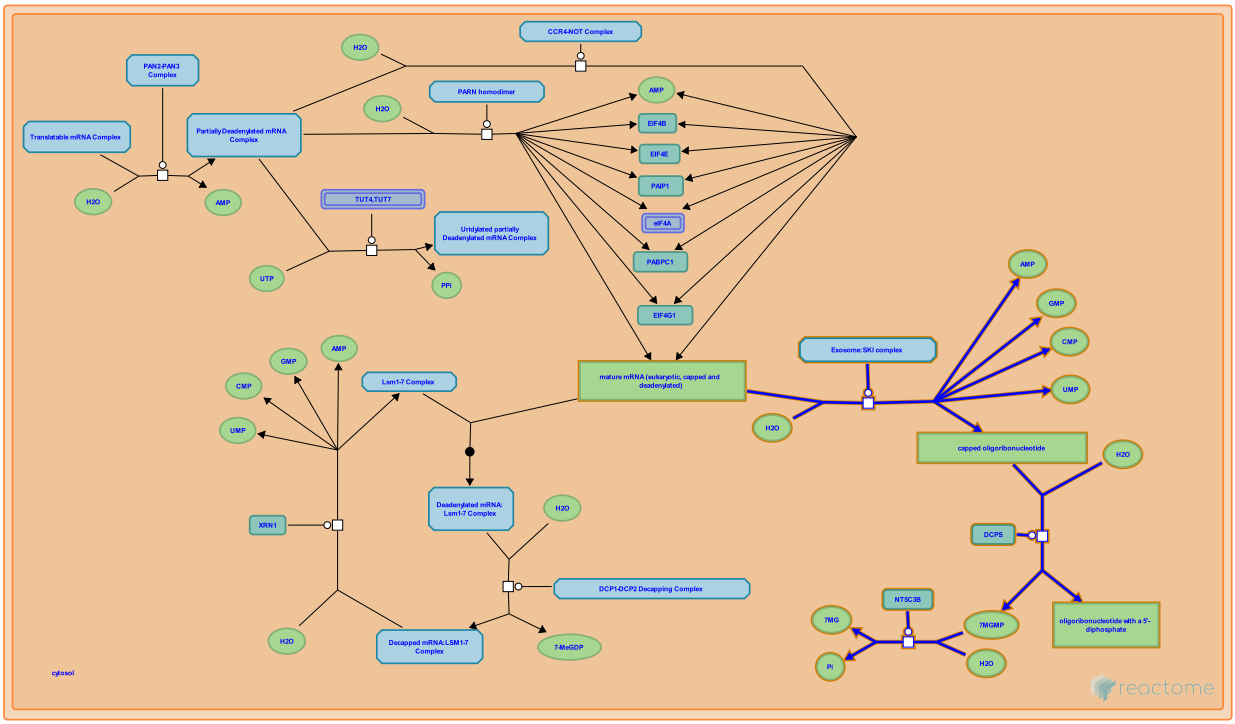
mRNA decay by 3' to 5' exoribonuclease ↗

Location: Deadenylation-dependent mRNA decay

Stable identifier: R-HSA-429958

Compartments: cytosol



The degradation of mRNA from 3' to 5' occurs in two steps. First, the exosome exoribonuclease complex binds the 3' end of the oligoadenylated mRNA and hydrolyzes it from 3' to 5', yielding ribonucleotides having 5'-monophosphates, until a capped oligoribonucleotide remains. Second, the scavenging decapping enzyme DCPS hydrolyzes the 7-methylguanosine cap.

Literature references

Song, H., Parker, R. (2004). The enzymes and control of eukaryotic mRNA turnover. *Nat Struct Mol Biol, 11*, 121-7. ↗

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Fritz, DT., Wilusz, J., Bergman, N., Wilusz, CJ., Kilpatrick, WJ. (2004). Messenger RNA decay in mammalian cells: the exonuclease perspective. *Cell Biochem Biophys, 41*, 265-78. ↗

Houseley, J., Tollervey, D. (2009). The many pathways of RNA degradation. *Cell, 136*, 763-76. ↗

Garneau, NL., Wilusz, J., Wilusz, CJ. (2007). The highways and byways of mRNA decay. *Nat Rev Mol Cell Biol, 8*, 113-26. ↗

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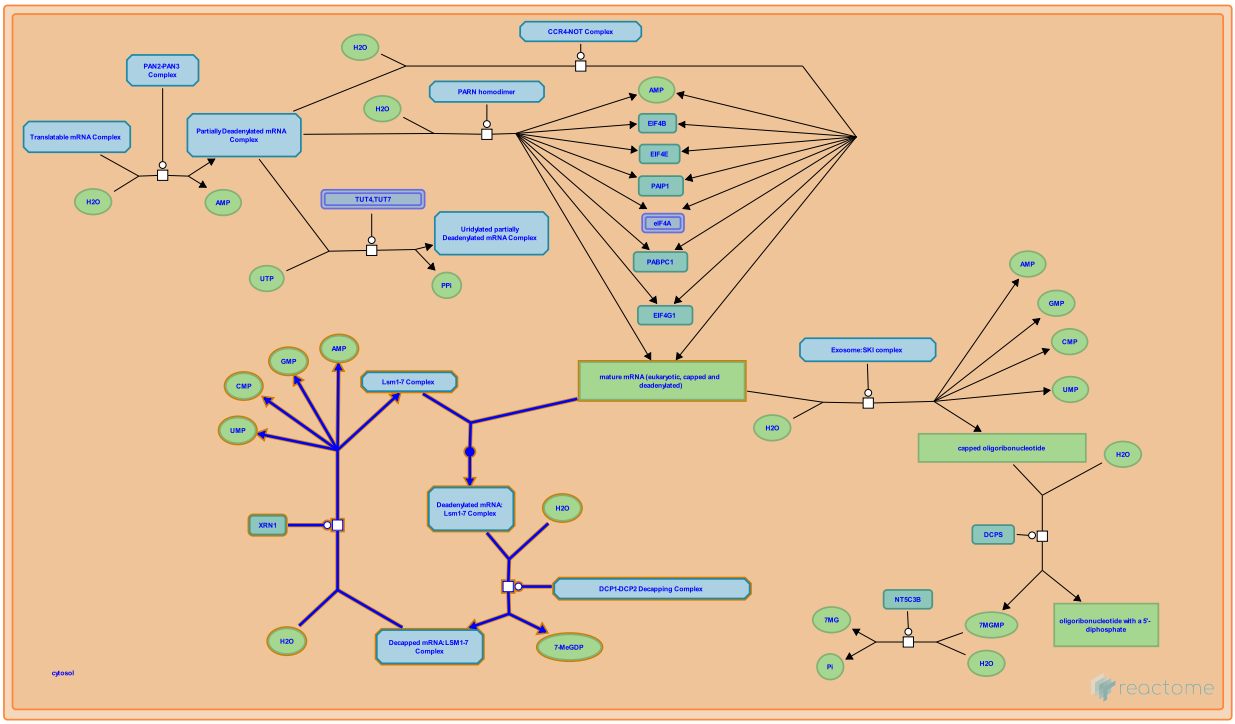
mRNA decay by 5' to 3' exoribonuclease ↗

Location: Deadenylation-dependent mRNA decay

Stable identifier: R-HSA-430039

Compartments: cytosol



Degradation of mRNA from 5' to 3' occurs in three steps. First, the mRNA is bound at its 3' end by the Lsm1-7 complex. The bound Lsm1-7 may prevent nucleases from accessing the 3' end. Second, the 7-methylguanosine cap of the mRNA is hydrolyzed by the DCP1-DCP2 complex. Third, the 5' end of the decapped mRNA is attacked by the XRN1 exoribonuclease which digests the remainder of the mRNA from 5' to 3'. These processes may be physically connected by PATL1, the homolog of yeast Pat1, which stably binds the Lsm1-7 complex and interacts with the DCP1-DCP2 decapping complex and the Ccr4-NOT deadenylation complex (Ozgur et al. 2010).

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Song, H., Parker, R. (2004). The enzymes and control of eukaryotic mRNA turnover. *Nat Struct Mol Biol, 11*, 121-7. ↗

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