**Introduction**

Reactome is an 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**


Reactome database release: 69

This document contains 1 pathway and 4 reactions (see Table of Contents)
Deadenylation of mRNA

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


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<td>2009-09-17</td>
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The PAN2-PAN3 exoribonuclease complex hydrolyzes the poly(A) tail of a mRNA, shortening the tail from about 200 adenosine residues to about 80 adenosine residues and yielding adenosine 5’-monophosphate. PAN2 is the exoribonuclease component of the complex; PAN3 is required for cellular localization. The poly(A)-binding protein (PABP) interacts with PAN3 and recruits the PAN2-PAN3 complex to mRNA.

Following by: PARN deadenylates mRNA, CCR4-NOT complex deadenylates mRNA

Literature references


The PARN exoribonuclease hydrolyzes adenosine residues at the 3' ends of polyadenylated mRNA, shortening the poly(A) tail from about 80 adenosine residues to about 10-15 residues and yielding adenosine 5'-monophosphate. PARN interacts simultaneously with the poly(A) tail and with the 7-methylguanosine cap of the mRNA, therefore it is believed that PARN displaces the eIF4F cap-binding complex. The trigger for deadenylation by PARN is unknown. PARN is also part of a complex that regulates poly(A) tail length and hence translation in developing oocytes.

**Preceded by:** PAN2-PAN3 complex partially deadenylates mRNA

**Literature references**


**Editions**

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CCR4-NOT complex deadenylates mRNA

**Location:** Deadenylation of mRNA

**Stable identifier:** R-HSA-429955

**Type:** transition

**Compartments:** cytosol

The CCR4-NOT complex hydrolyzes adenosine residues at the 3' end of polyadenylated mRNA, shortening the number of adenosine residues to about 10-15 residues and yielding adenosine 5'-monophosphate. CNOT6 and CNOT6L are the exoribonucleases responsible for hydrolysis. Activity of the CCR4-NOT complex is inhibited by PABP bound to the poly(A) tail of the mRNA. The trigger for activation of deadenylation by the CCR4-NOT complex is unknown. Complexes containing CNOT7 rather than CNOT8 appear to be responsible for cytoplasmic mRNA decay.

**Preceded by:** PAN2-PAN3 complex partially deadenylates mRNA

**Literature references**

Chen, J., Chiang, YC., Denis, CL. (2002). CCR4, a 3'-5' poly(A) RNA and ssDNA exonuclease, is the catalytic component of the cytoplasmic deadenylase. *EMBO J*, 21, 1414-26.


**Editions**

2009-07-22 Authored, Edited May, B.

2009-09-17 Reviewed Wilusz, J.
ZCCHC6, ZCCHC11 are mRNA uridytransferases

**Location:** Deadenylation of mRNA

**Stable identifier:** R-HSA-8941312

**Type:** transition

**Compartments:** cytosol

Uridylytransferases mediates the terminal uridylation of mRNAs, RISC-cleaved transcripts and of various non-coding RNAs including miRNAs and their precursors mRNAs (Scott and Norbury 2013, Lee et al. 2014, Munoz-Tello et al. 2015, Scheer et al. 2016).

TUT4 and TUT7 (ZCCHC11, ZCCHC6) are mRNA uridylation enzymes that can act on the majority of mammalian mRNAs (Lim et al. 2014). More than 85% of mRNAs are uridylated at a frequency of higher than 1% in NIH 3T3 and HeLa cells (Chang et al. 2014). Uridylated tails were found mainly on mRNAs with polyA tails of less than 25 nucleotides, suggesting that uridylation may occur after deadenylation. There was a negative correlation between uridylation frequency and mRNA half-life, suggesting a role of uridylation in general mRNA decay (Lim et al. 2014). TUT4 and TUT7 (ZCCHC11, ZCCHC6) also uridylate replication-dependent histone mRNAs, which are not polyadenylated, to facilitate their degradation (Lackey et al 2016, Schmidt et al. 2011, Mullen & Marzluff 2008, Hoefig et al. 2013, Slevin et al. 2014). TUT4 and TUT7 also uridylate miRNAs and their precursors (Thornton et al. 2014, Lee et al. 2014, Ha & Kim 2014). Mono-uridylation of pre-miRNA facilitates miRNA processing, while polyuridylation of pre-miRNA triggers their degradation (Heo et al. 2012).

**Literature references**


**Editions**

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