AUF1 (hnRNP D0) binds and destabilizes mRNA

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28/08/2019
**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**


Reactome database release: 69

This document contains 1 pathway and 4 reactions (see Table of Contents)
AUF1 (hnRNP D0) binds and destabilizes mRNA

Stable identifier: R-HSA-450408

Compartments: cytosol

AUF1 (hnRNP D0) dimers bind U-rich regions of AU-rich elements (AREs) in the 3' untranslated regions of mRNAs. The binding causes AUF1 dimers to assemble into higher order tetrameric complexes. Di-phosphorylated AUF1 bound to RNA recruits additional proteins, including eIF4G, polyA-binding protein, Hsp, Hsc70, Hsp27, NSEP-1, NSAP-1, and IMP-2 which target the mRNA and AUF1 for degradation. Unphosphorylated AUF1 is thought to be less able to recruit additional proteins. AUF1 also interacts directly or indirectly with HuR and the RNA-induced silencing complex (RISC).

AUF1 complexed with RNA and other proteins is ubiquitinated and targeted for destruction by the proteasome while the bound mRNA is degraded. Inhibition of ubiquitin addition to AUF1 blocks mRNA degradation. The mechanism by which ubiquitin-dependent proteolysis is coupled to mRNA degradation is unknown.

At least 4 isoforms of AUF1 exist: p45 (45 kDa) contains all exons, p42 lacks exon 2, p40 lacks exon 7, and p37 lacks exons 2 and 7. The presence of exon 7 in p42 and p45 seems to block ubiquitination while the absence of exon 7 (p37 and p40) targets AUF1 for ubiquitination and destabilizes bound RNAs. Lack of exon 2 (p37 and p42) is associated with higher affinity for RNA and 14-3-3sigma (SFN).

AUF1 binds and destabilizes mRNAs encoding Interleukin-1 beta (IL1B), Tumor Necrosis Factor alpha (TNFA), Cyclin-dependent kinase inhibitor 1 (CDNK1A, p21), Cyclin-D1 (CCND1), Granulocyte-macrophage colony stimulating factor (GM-CSF, CSF2), inducible Nitric oxide synthase (iNOS, NOS2), Proto-oncogene cFos (FOS), Myc proto-oncogene (MYC), Apoptosis regulator Bcl-2 (BCL2).

Literature references


**Editions**

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AUF1 (hnRNP D0) dimers bind AU-rich element in 3' UTR of mRNA

Location: AUF1 (hnRNP D0) binds and destabilizes mRNA

Stable identifier: R-HSA-450434

Type: binding

Compartments: cytosol

AUF1 monomers form dimers which bind the U-rich sequences in AU-rich elements of mRNAs. Binding of the mRNA causes the dimers of AUF1 to form tetramers. Nonphosphorylated AUF1 isoform p40 causes the mRNA to form a rigid structure whereas p40 that is phosphorylated at serines 83 and 87 does not. This difference may cause nonphosphorylated p40 to fail to destabilize the bound mRNA.

Followed by: AUF1 binds translation and heat shock proteins

Literature references


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AUF1 binds translation and heat shock proteins

Location: AUF1 (hnRNP D0) binds and destabilizes mRNA

Stable identifier: R-HSA-450551

Type: binding

Compartments: cytosol

Tetrameric AUF1 bound to RNA forms a complex with other proteins, including elongation factor eIF4G, polyA-binding protein PABP, Hsp, Hsc70, and Hsp27. AUF1 also directly interacts with polyadenylate.

Preceded by: AUF1(hnRNP D0) dimers bind AU-rich element in 3' UTR of mRNA

Followed by: AUF1 (hnRNP D0) is ubiquitinylated

Literature references


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https://www.reactome.org
AUF1 (hnRNP D0) is ubiquitylated

Location: AUF1 (hnRNP D0) binds and destabilizes mRNA

Stable identifier: R-HSA-450580

Type: omitted

Compartments: cytosol

AUF1 is ubiquitinated at unknown sites. The number of ubiquitin molecules conjugated to AUF1 and their linkage is unknown. Ubiquitination is required for subsequent degradation of both AUF1 and the mRNA bound by AUF1. It is uncertain if AUF1 is in a larger complex when it is ubiquitinated.

Preceded by: AUF1 binds translation and heat shock proteins

Followed by: AUF1:mRNA complex is destroyed

Literature references


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AUF1:mRNA complex is destroyed

**Location:** AUF1 (hnRNP D0) binds and destabilizes mRNA

**Stable identifier:** R-HSA-450466

**Type:** omitted

**Compartments:** cytosol

Ubiquitin-dependent proteolysis of AUF1 and nuclease-dependent destruction of AUF1-bound mRNA are coupled in an unknown way. It is possible that ubiquitinated AUF1 targets other members of the AUF1 and signal transduction regulated complex (ASTRC), such as polyA-binding protein, for degradation and this renders the mRNA susceptible to nucleases.

**Preceded by:** AUF1 (hnRNP D0) is ubiquitinylated

**Literature references**


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