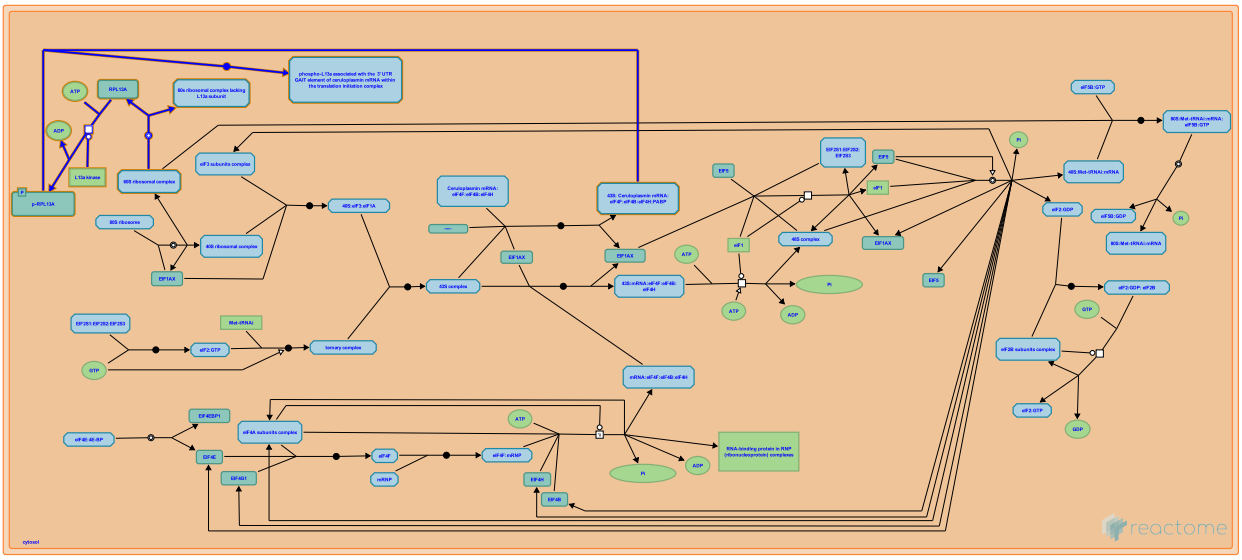
L13a-mediated translational silencing of Ceruloplasmin expression



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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).

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. ↗

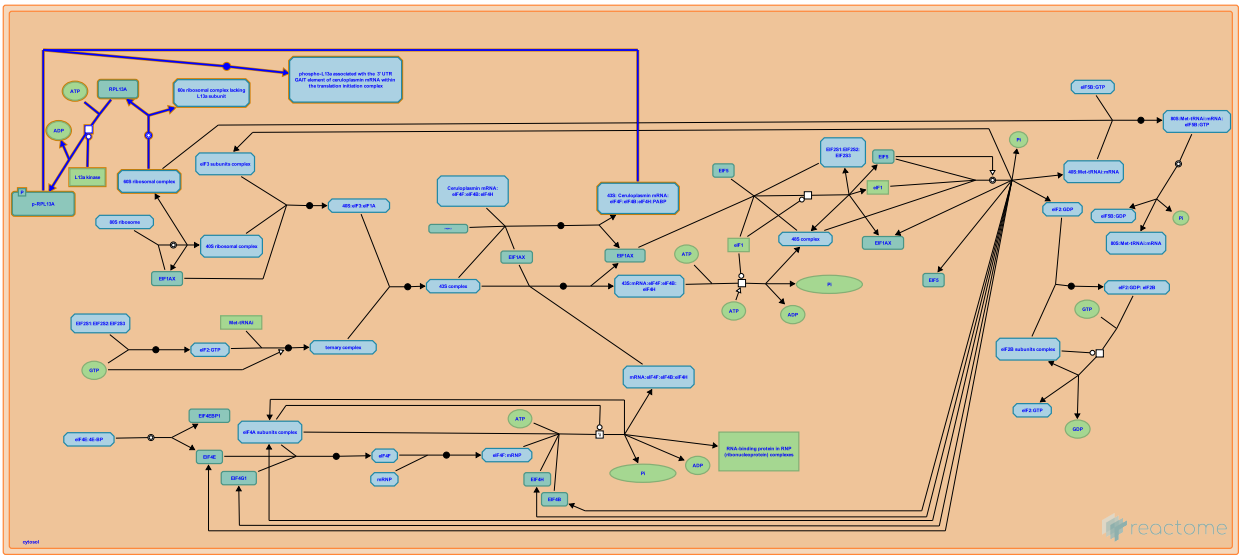
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

L13a-mediated translational silencing of Ceruloplasmin expression ↗

Stable identifier: R-HSA-156827

Compartments: cytosol



While circularization of mRNA during translation initiation is thought to contribute to an increase in the efficiency of translation, it also appears to provide a mechanism for translational silencing. This might be achieved by bringing inhibitory 3' UTR-binding proteins into a position in which they interfere either with the function of the translation initiation complex or with the assembly of the ribosome (Mazumder et al 2001). Translational silencing of Ceruloplasmin (Cp) occurs 16 hrs after its induction by INF-gamma (Mazumder et al., 1997). Although the mechanism by which silencing occurs has not yet been determined, this process is mediated by the L13a subunit of the 60s ribosome and thought to require circularization of the Cp mRNA (Sampath et al., 2003; Mazumder et al., 2001; Mazumder et al., 2003). Between 14 and 16 hrs after INF gamma induction, the L13a subunit of the 60s ribosome is phosphorylated and released from the 60s subunit. Phosphorylated L13a then associates with the GAIT element in the 3' UTR of the Cp mRNA inhibiting its translation.

Literature references

Mazumder, B., Sampath, P., Seshadri, V., Maitra, RK., DiCorleto, PE., Fox, PL. (2003). Regulated release of L13a from the 60S ribosomal subunit as a mechanism of transcript-specific translational control. *Cell, 115*, 187-98. ↗

Editions

2004-12-13	Authored	Matthews, L.
2013-11-25	Edited	Matthews, L.

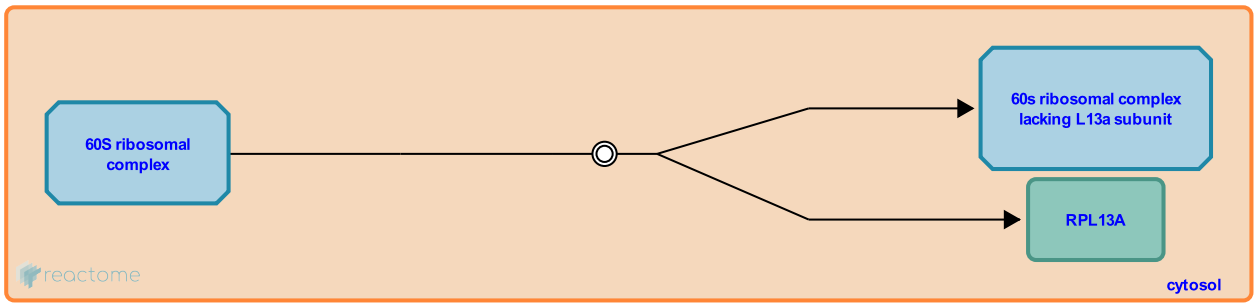
Dissociation of L13a from the 60s ribosomal subunit ↗

Location: L13a-mediated translational silencing of Ceruloplasmin expression

Stable identifier: R-HSA-156826

Type: dissociation

Compartments: cytosol



The L13a subunit of the 60s ribosome is phosphorylated about 16 hours after INF gamma induction by an unknown kinase. At this time, L13a is also released from the 60s subunit (Mazumder et al.,2003). It is unclear, however, whether phosphorylation occurs before or after the release of L13a. Here, phosphorylation is shown as occurring after release.

Followed by: INF-gamma induced phosphorylation of L13a

Literature references

Mazumder, B., Sampath, P., Seshadri, V., Maitra, RK., DiCorleto, PE., Fox, PL. (2003). Regulated release of L13a from the 60S ribosomal subunit as a mechanism of transcript-specific translational control. *Cell, 115*, 187-98. ↗

Editions

2004-12-13	Authored	Matthews, L.

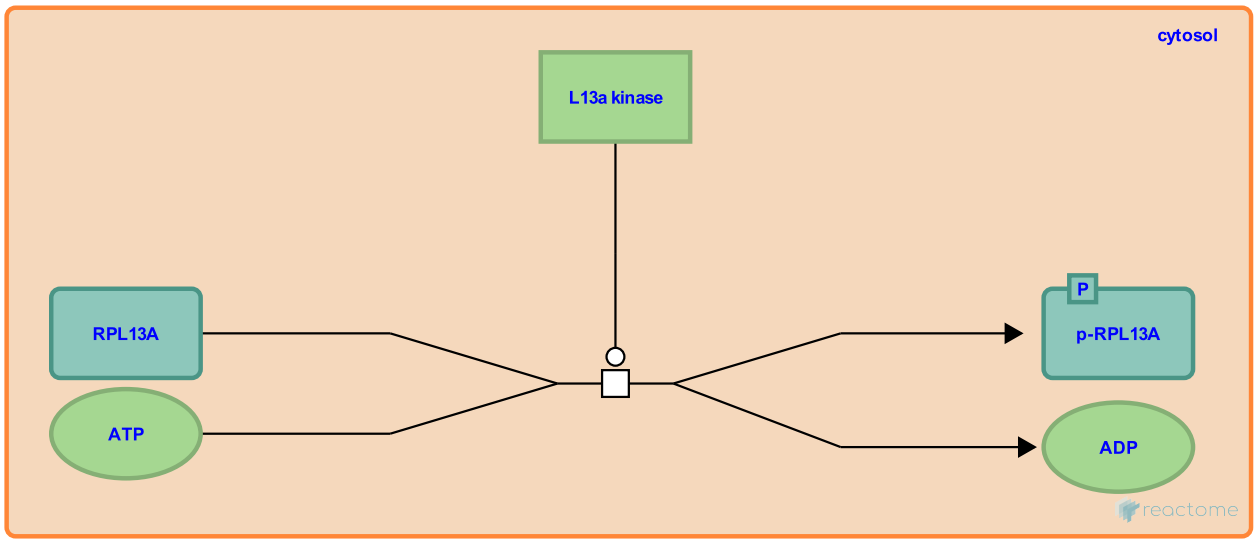
INF-gamma induced phosphorylation of L13a ↗

Location: L13a-mediated translational silencing of Ceruloplasmin expression

Stable identifier: R-HSA-156832

Type: transition

Compartments: cytosol



The L13a subunit of the 60s ribosome is phosphorylated about 16 hours after INF gamma induction by an unknown kinase. At this time, L13a is also released from the 60s subunit (Mazumder et al.,2003). It is unclear, however, whether phosphorylation occurs before or after the release of L13a. Here, phosphorylation is shown as occurring after release.

Preceded by: Dissociation of L13a from the 60s ribosomal subunit

Followed by: Association of phospho-L13a with GAIT element of Ceruloplasmin mRNA

Literature references

Mazumder, B., Sampath, P., Seshadri, V., Maitra, RK., DiCorleto, PE., Fox, PL. (2003). Regulated release of L13a from the 60S ribosomal subunit as a mechanism of transcript-specific translational control. *Cell, 115*, 187-98. ↗

Editions

2004-12-13	Authored	Matthews, L.

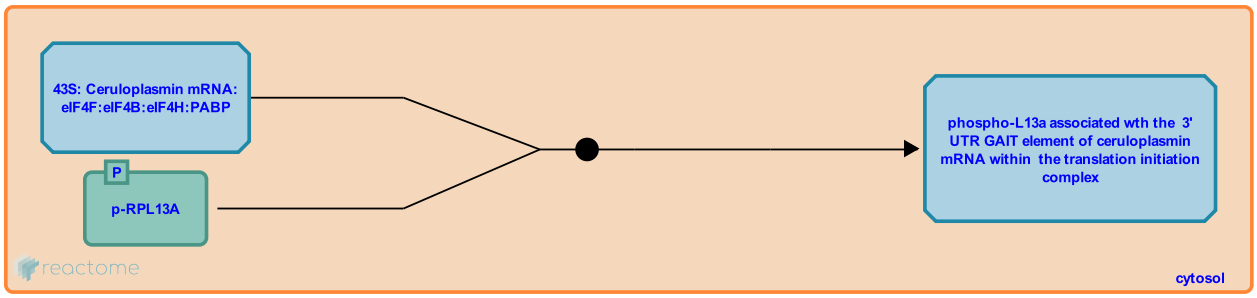
Association of phospho-L13a with GAIT element of Ceruloplasmin mRNA ↗

Location: L13a-mediated translational silencing of Ceruloplasmin expression

Stable identifier: R-HSA-156823

Type: binding

Compartments: cytosol



Although the mechanism through which L13a prevents translation initiation has not been determined, Mazumder et al. (2003) have described four alternatives. L13a could (1) inhibit the function of eIF4F, (2) block the recruitment of the 43S preinitiation complex, (3) prevent scanning of the 43S complex to the initiation codon, or 4) interfere with joining of the 60S ribosomal subunit.

Preceded by: INF-gamma induced phosphorylation of L13a

Literature references

Sampath, P., Mazumder, B., Seshadri, V., Fox, PL. (2003). Transcript-selective translational silencing by gamma interferon is directed by a novel structural element in the ceruloplasmin mRNA 3' untranslated region. *Mol Cell Biol , 23*, 1509-19. ↗

Editions

2004-12-13	Authored	Matthews, L.
2013-11-25	Edited	Matthews, L.

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