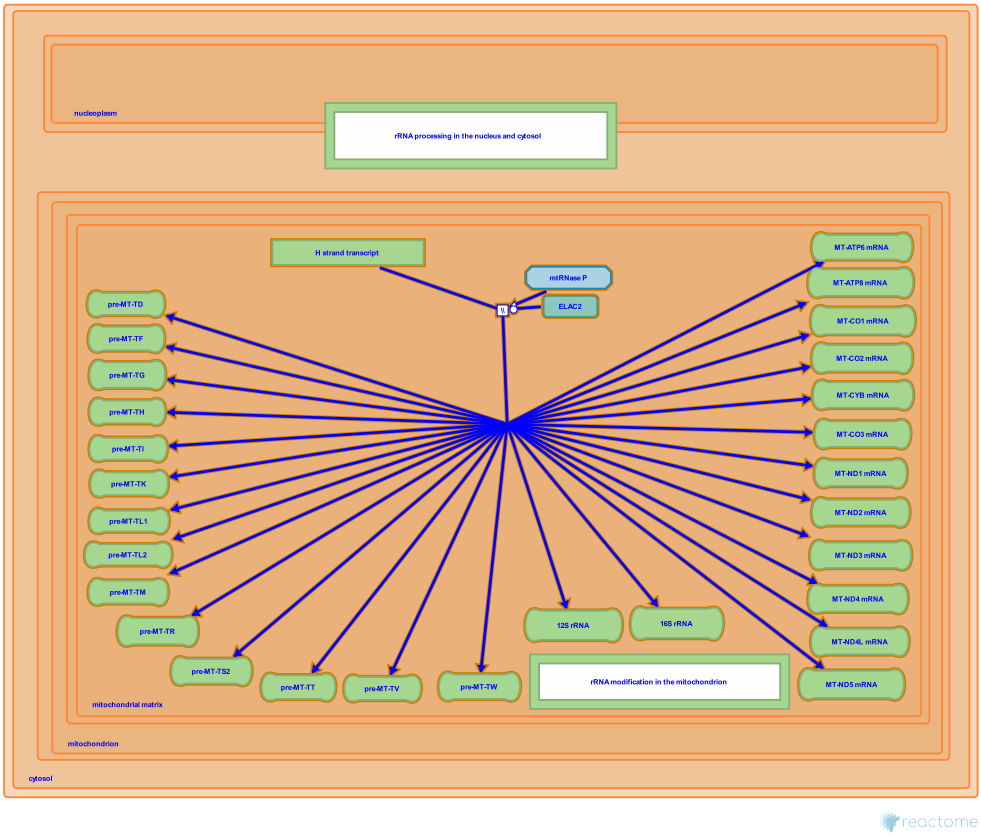
# rRNA processing in the mitochondrion

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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.

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## 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. ↗

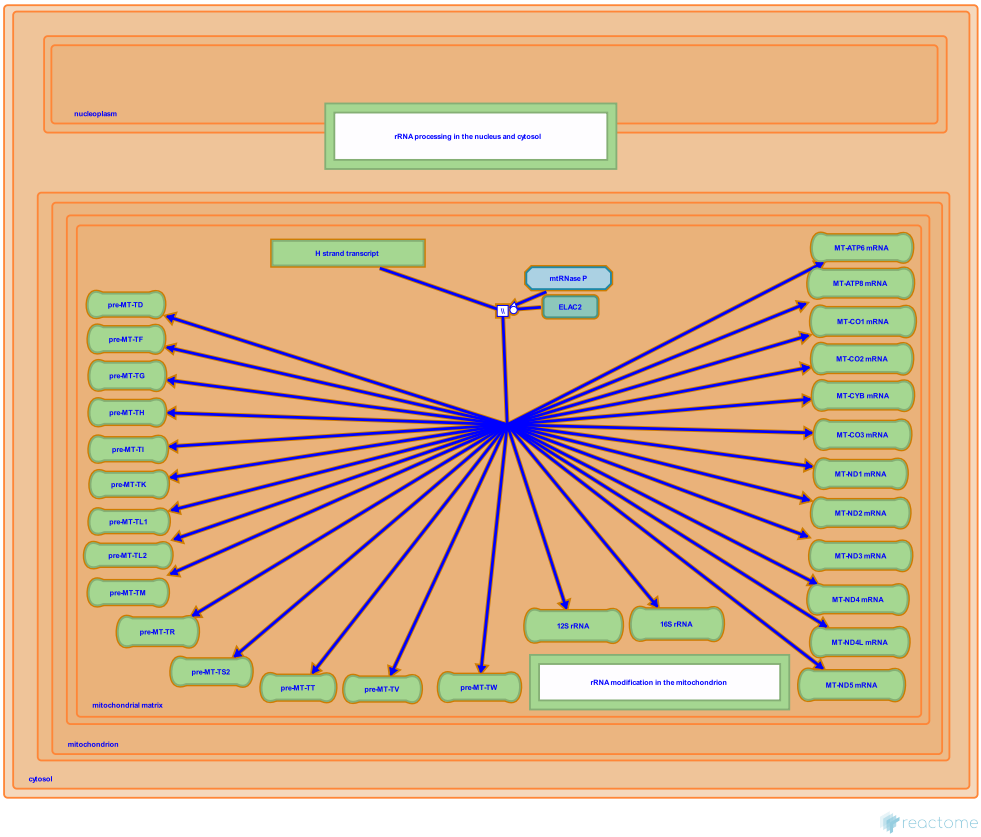
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

## rRNA processing in the mitochondrion ↗

**Stable identifier:** R-HSA-8868766




Mitochondrial ribosomes contain 16S rRNA (large subunit) and 12S rRNA (small subunit) that are encoded in the mitochondrial genome and produced by processing of a long H strand transcript (reviewed in Van Haute et al. 2015). Enzymes encoded in the nucleus and acting in the mitochondrial matrix modify 5 nucleotides in the 12S RNA and 4 nucleotides in the 16S rRNA (reviewed in Van Haute et al. 2015).

## Literature references


Powell, CA., Minczuk, M., Van Haute, L., Nicholls, TJ., Pearce, SF., D'Souza, AR. (2015). Mitochondrial transcript maturation and its disorders. *J. Inherit. Metab. Dis., 38*, 655-80. ↗


## Editions

| | | |
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| 2016-04-25 | Reviewed | Bogenhagen, DF. |
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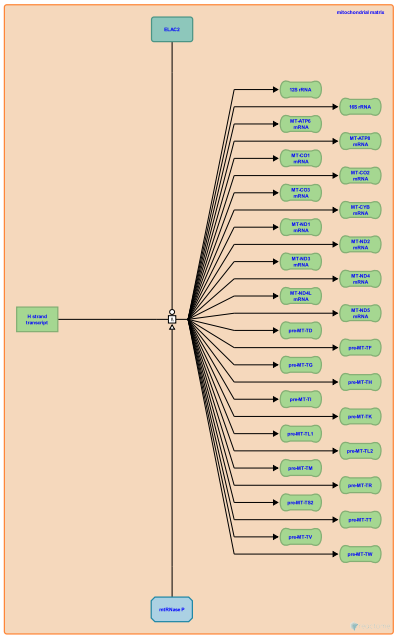
## Mitochondrial RNase P (mtRNase P) cleaves the 5' ends of pre-tRNAs and ELAC2 (RNase Z) cleaves the 3' ends of pre-tRNAs in the H strand transcript ↗

**Location:** rRNA processing in the mitochondrion

**Stable identifier:** R-HSA-6785722

**Type:** omitted

**Compartments:** mitochondrial matrix



RNase P, ELAC2, and additional unknown nucleases cleave H strand transcripts to release the various tRNAs, rRNAs, and mRNAs contained in the long polycistronic transcripts.
Mitochondrial RNase P, comprising 3 protein subunits and no RNA moiety (Holzmann et al. 2008), endonucleolytically cleaves polycistronic mitochondrial transcripts at the 5' ends of the tRNA sequences (Sanchez et al. 2011, Howard et al. 2012, Vilardo et al. 2012, Li et al. 2015, Reinhard et al. 2015, Vilardo and Rossmanith 2015). A subcomplex of RNase P also functions as a tRNA methyltransferase and the SDR5C1 subunit is an amino acid and fatty acid dehydrogenase. Mutations in the SDR5C1 subunit of RNase P cause HSD10 disease, which is characterized by progressive neurodegeneration and cardiomyopathy (Vilardo and Rossmanith 2015)
ELAC2 cleaves polycistronic mitochondrial transcripts at the 3' ends of the tRNA sequences (Brzezniak et al. 2011, Sanchez et al. 2011). Different isoforms of ELAC2 are present in the nucleus and mitochondria (Rossmanith 2011). Mutations in ELAC2 cause cardiac hypertrophy (Haack et al. 2013) and disorders of oxidative phosphorylation (reviewed in Van Haute et al. 2015).
Unknown nucleases also cleave the H strand transcript at sites 5' to MT-CO3, 5' to MT-CO1, and 5' to MT-CYB (reviewed in Van Haute et al. 2015).

## Literature references


Reinhard, L., Sridhara, S., Hallberg, BM. (2015). Structure of the nuclease subunit of human mitochondrial RNase P. *Nucleic Acids Res., 43*, 5664-72. ↗

Zhou, W., Li, F., Liu, X., Yang, X., Shen, Y. (2015). Auto-inhibitory Mechanism of the Human Mitochondrial RNase P Protein Complex. *Sci Rep, 5*, 9878. ↗

Koutmos, M., Lim, WH., Fierke, CA., Howard, MJ. (2012). Mitochondrial ribonuclease P structure provides insight into the evolution of catalytic strategies for precursor-tRNA 5' processing. *Proc. Natl. Acad. Sci. U.S.A., 109*, 16149-54. ↗

Bennett, KL., Löffler, E., Rossmanith, W., Gerner, C., Holzmann, J., Frank, P. (2008). RNase P without RNA: identification and functional reconstitution of the human mitochondrial tRNA processing enzyme. *Cell, 135*, 462-74. ↗

Serjanov, D., Levinger, L. (2012). Pathogenesis-related mutations in the T-loops of human mitochondrial tRNAs affect 3' end processing and tRNA structure. *RNA Biol, 9*, 283-91. ↗

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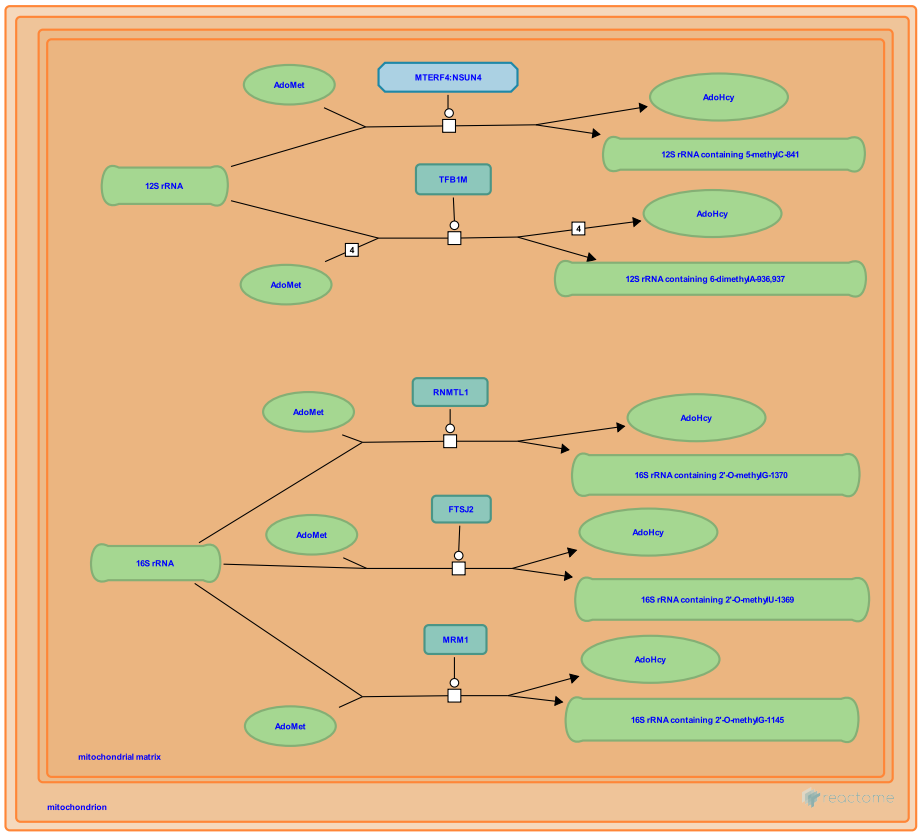
## rRNA modification in the mitochondrion ↗

**Location:** rRNA processing in the mitochondrion

**Stable identifier:** R-HSA-6793080




Five modified nucleotides have been detected in the 12S rRNA: 5-methylcytidine-841 catalyzed by NSUN4, 6-dimethyladenosine-936 catalyzed by TFB1M, 6-dimethyladenosine-937 catalyzed by TFB1M, 5-methyluridine-429, and 4-methylcytidine-839 (reviewed in Van Haute et al. 2015). Four modified nucleotides have been detected in 16S rRNA: 2'-O-methylguanosine-1145 catalyzed by MRM1, 2'-O-methylguanosine-1370 catalyzed by RNMTL1 (MRM3), 2'-O-methyluridine-1369 catalyzed by FTSJ2 (MRM2), and pseudouridine-1397. 2'-O-methyluridine-1369 and 2'-O-methylguanosone-1370 occur in the A-loop of rRNA which is located at the peptidyl transferase center of the large subunit. Here the modified residues play a role in interaction with the aminoacyl site of tRNA. Knockouts of TFB1M and NSUN4 are lethal in mice and mutations in TFB1M may be related to aminoglycoside-induced deafness (reviewed in Van Haute et al. 2015).

## Literature references


Minczuk, M., Rorbach, J. (2012). The post-transcriptional life of mammalian mitochondrial RNA. *Biochem. J., 444*, 357-73. ↗

Powell, CA., Minczuk, M., Van Haute, L., Nicholls, TJ., Pearce, SF., D'Souza, AR. (2015). Mitochondrial transcript maturation and its disorders. *J. Inherit. Metab. Dis., 38*, 655-80. ↗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