tRNA processing in the mitochondrion


European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of Creative Commons Attribution 4.0 International (CC BY 4.0) License. For more information see our license.
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: 67

This document contains 1 pathway and 3 reactions (see Table of Contents)
tRNA processing in the mitochondrion

Stable identifier: R-HSA-6785470

Each strand of the circular mitochondrial genome is transcribed to yield long polycistronic transcripts, the heavy strand transcript and the light strand transcript, which are then cleaved to yield tRNAs, rRNAs, and mRNAs (Mercer et al. 2011, reviewed in Suzuki et al. 2011, Rossmanith 2012, Powell et al. 2015). Mitochondrial RNase P, which is completely distinct from nuclear RNase P in having different protein subunits and no RNA component, cleaves at the 5' ends of tRNAs. RNase Z, an isoform of ELAC2 in mitochondria, cleaves at the 3' ends of tRNAs. (A different isoform of ELAC2 serves as RNase Z in the nucleus.) Unknown nucleases make additional cleavages near the 5' end of MT-CO3, the 5' end of CO1, the 5' end of CYB, and the 3' end of ND6. TRNT1 (CCA-adding enzyme) then post-transcriptionally polymerizes the universal acceptor sequence CCA onto the 3' ends of the cleaved tRNAs. In yeast, plants, and protozoa additional tRNAs encoded in the nucleus are imported into mitochondria from the cytosol (reviewed in Schneider 2011), however human mitochondria encode a complete complement of 22 tRNAs required for translation and tRNA import has not been observed in mammals. Mutations that affect mitochondrial tRNA processing cause human diseases that are generally characterized by abnormalities in energy-requiring tissues such as brain and muscle (reviewed in Suzuki et al. 2011, Sarin and Leidel 2014).

Literature references


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015-06-28</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2015-08-11</td>
<td>Reviewed</td>
<td>Levinger, L.</td>
</tr>
<tr>
<td>2015-08-25</td>
<td>Reviewed</td>
<td>Motorin, Y.</td>
</tr>
<tr>
<td>2015-10-24</td>
<td>Reviewed</td>
<td>Jarrous, N.</td>
</tr>
<tr>
<td>2015-11-07</td>
<td>Reviewed</td>
<td>Powell, CA.</td>
</tr>
<tr>
<td>2015-11-18</td>
<td>Reviewed</td>
<td>Suzuki, T.</td>
</tr>
</tbody>
</table>
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:** tRNA 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**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015-06-29</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2015-08-11</td>
<td>Reviewed</td>
<td>Levinger, L.</td>
</tr>
<tr>
<td>2015-08-25</td>
<td>Reviewed</td>
<td>Motorin, Y.</td>
</tr>
<tr>
<td>2015-10-24</td>
<td>Reviewed</td>
<td>Jarrous, N.</td>
</tr>
<tr>
<td>2015-11-07</td>
<td>Reviewed</td>
<td>Powell, CA.</td>
</tr>
<tr>
<td>2015-11-18</td>
<td>Reviewed</td>
<td>Suzuki, T.</td>
</tr>
</tbody>
</table>
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 L strand transcript.

**Location:** tRNA processing in the mitochondrion

**Stable identifier:** R-HSA-6786854

**Type:** omitted

**Compartments:** mitochondrial matrix

RNase P, ELAC2, and additional unknown nucleases cleave L strand transcripts to release the tRNAs and an mRNA 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).

Unknown nucleases also cleave the L strand transcript at a site 3' to MT-ND6 (reviewed in Van Haute et al. 2015).

**Followed by:** TRNT1 polymerizes CCA at the 3' end of pre-tRNA

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Author/Editor</th>
<th>Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015-07-09</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2015-08-11</td>
<td>Reviewed</td>
<td>Levinger, L.</td>
</tr>
<tr>
<td>2015-08-25</td>
<td>Reviewed</td>
<td>Motorin, Y.</td>
</tr>
<tr>
<td>2015-10-24</td>
<td>Reviewed</td>
<td>Jarrous, N.</td>
</tr>
<tr>
<td>2015-11-07</td>
<td>Reviewed</td>
<td>Powell, CA.</td>
</tr>
<tr>
<td>2015-11-18</td>
<td>Reviewed</td>
<td>Suzuki, T.</td>
</tr>
</tbody>
</table>
TRNT1 polymerizes CCA at the 3' end of pre-tRNA

**Location:** tRNA processing in the mitochondrion

**Stable identifier:** R-HSA-6786881

**Type:** transition

**Compartments:** mitochondrial matrix

TRNT1 (CCA-adding enzyme) polymerizes a nontemplated CCA sequence on the 3' end of mitochondrial tRNA (Nagaike et al. 2001). Mutations in TRNT1 or tRNAs that affect the rate of CCA addition cause pathological consequences in humans (Tomari et al. 2003, Chakraborty et al. 2014, Sasarman et al. 2015).

**Preceded by:** 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 L strand transcript

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015-07-09</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2015-08-11</td>
<td>Reviewed</td>
<td>Levinger, L.</td>
</tr>
<tr>
<td>2015-08-25</td>
<td>Reviewed</td>
<td>Motorin, Y.</td>
</tr>
<tr>
<td>2015-10-24</td>
<td>Reviewed</td>
<td>Jarrous, N.</td>
</tr>
<tr>
<td>2015-11-07</td>
<td>Reviewed</td>
<td>Powell, CA.</td>
</tr>
<tr>
<td>2015-11-18</td>
<td>Reviewed</td>
<td>Suzuki, T.</td>
</tr>
</tbody>
</table>

https://www.reactome.org
Table of Contents

- Introduction
- tRNA processing in the mitochondrion
  - 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
  - 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 L strand transcript
  - TRNT1 polymerizes CCA at the 3' end of pre-tRNA

Table of Contents