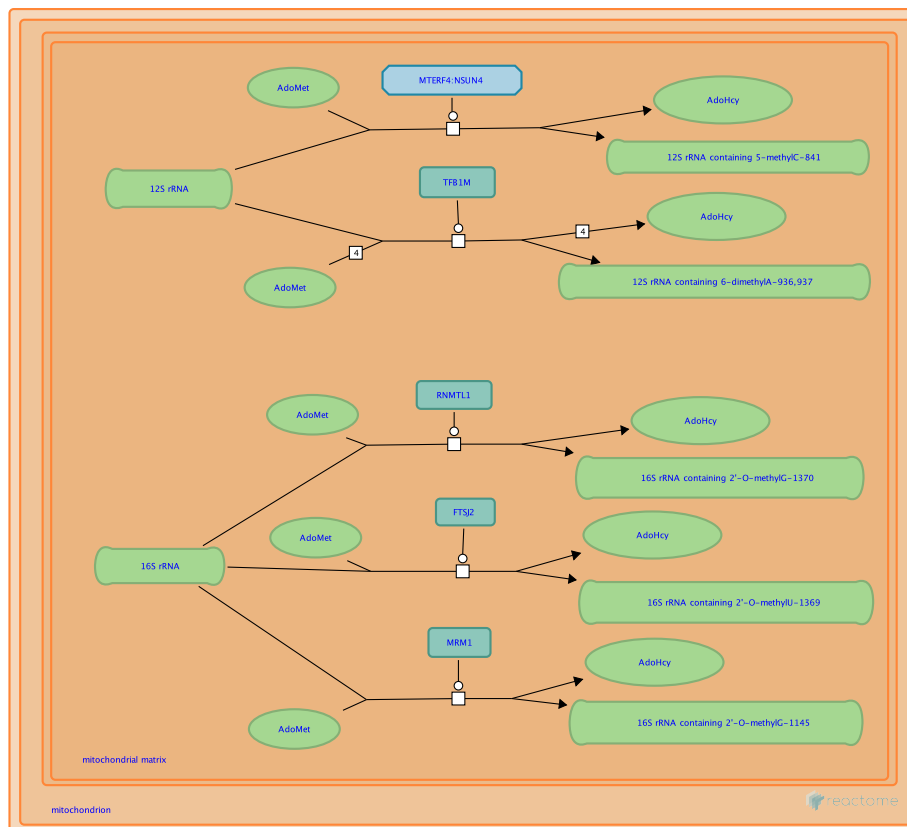


rRNA modification in the mitochondrion



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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.

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

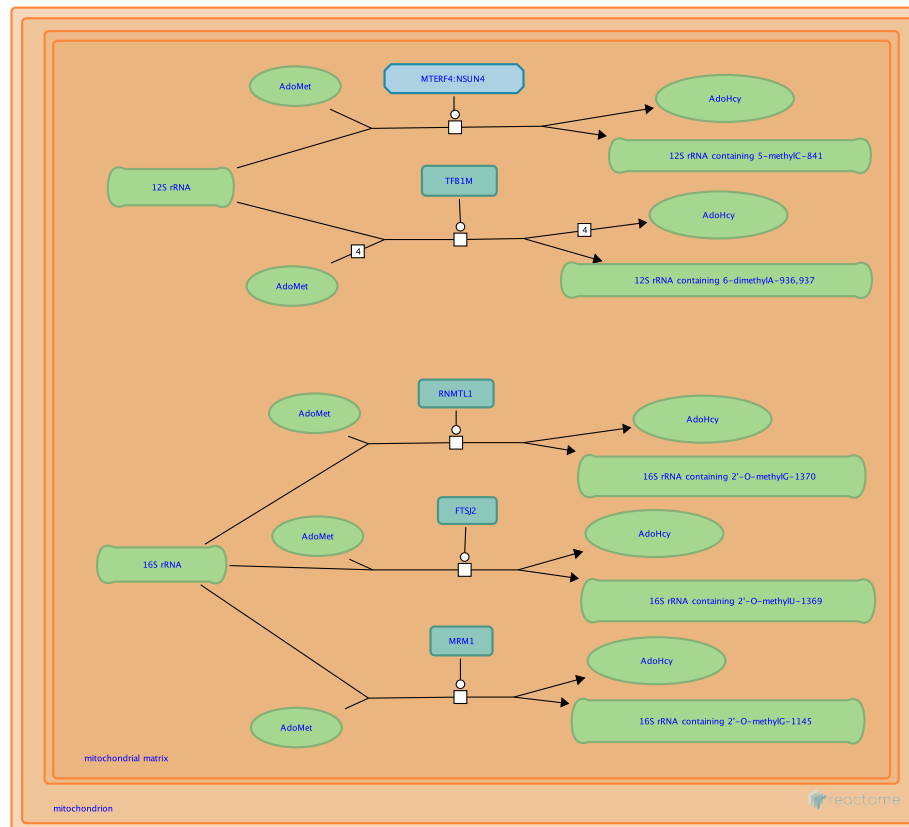
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Reactome database release: 77

This document contains 1 pathway and 5 reactions ([see Table of Contents](#))

rRNA modification in the mitochondrion ↗

Stable identifier: R-HSA-6793080



Five modified nucleotides have been detected in the 12S rRNA: 5-methylcytosine-841 catalyzed by NSUN4, 6-dimethyladenosine-936 catalyzed by TFB1M, 6-dimethyladenosine-937 catalyzed by TFB1M, 5-methyluridine-429, and 4-methylcytosine-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-methylguanosine-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

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

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

Editions

2015-08-28

Authored, Edited

May, B.

2016-04-25

Reviewed

Bogenhagen, DF.

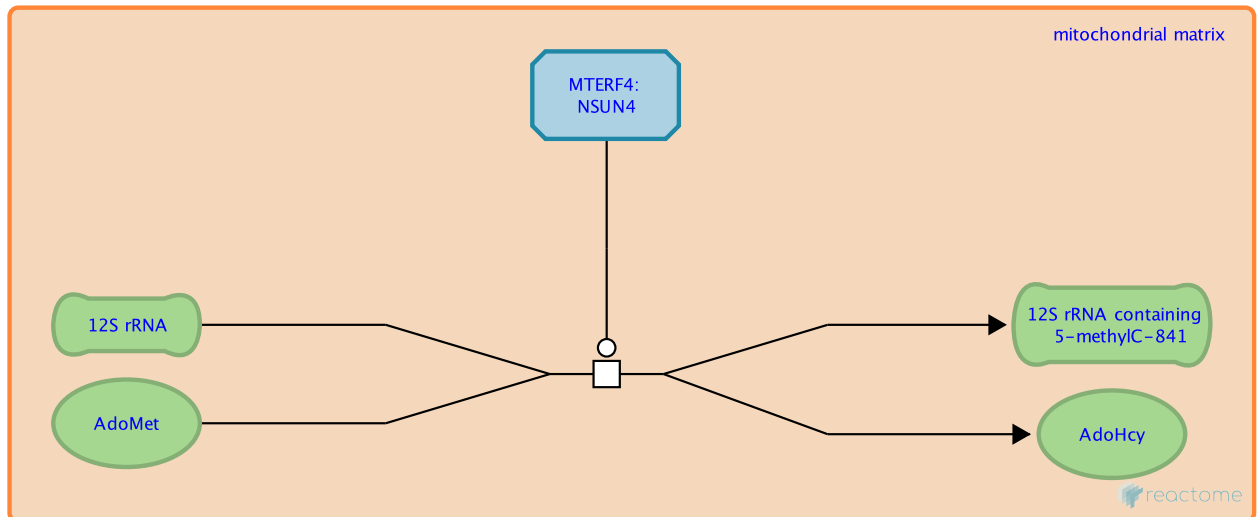
NSUN4 methylates cytidine-841 of 12S rRNA yielding 5-methylcytidine-841 [↗](#)

Location: [rRNA modification in the mitochondrion](#)

Stable identifier: R-HSA-6793057

Type: transition

Compartments: mitochondrial matrix



MTERF4 forms a complex with NSUN4 (Camara et al. 2011, Spahr et al. 2012, Yakubovskaya et al. 2012) and recruits NSUN4 to the ribosome where NSUN4 transfers a methyl group from S-adenosylmethionine to the 5 position of cytidine-841 in 12S rRNA (Camara et al. 2011). Knockout of MTERF4 in mice is lethal and cardiomyocyte-specific knockout is accompanied by mitochondrial cardiomyopathy (Camara et al. 2011).

Literature references

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Editions

2015-08-28	Authored, Edited	May, B.
2016-04-25	Reviewed	Bogenhagen, DF.

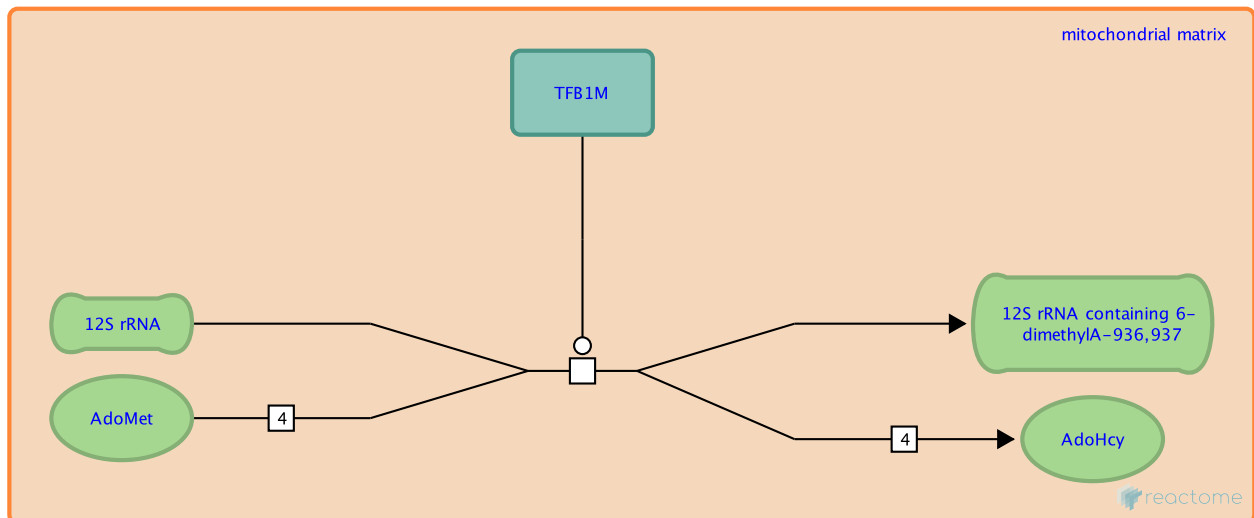
TFB1M dimethylates adenosine-936 and adenosine-937 of 12S rRNA yielding 6-dimethyladenosine-936 and 6-dimethyladenosine-937 ↗

Location: rRNA modification in the mitochondrion

Stable identifier: R-HSA-6793066

Type: transition

Compartments: mitochondrial matrix



TFB1M transfers methyl groups from S-adenosylmethionine to the 6 position of adenosine residues at nucleotides 936 and 937 in 12S mitochondrial rRNA (McCulloch et al. 2002, Seidel-Rogol et al. 2003, Cotney et al. 2009, Guja et al. 2013). The mitochondrial RNA polymerase POLRMT associates directly with TFB1M and increases its methylase activity (Surovtseva and Shadel 2013). Alleles of TFB1M modify the severity of hearing loss associated with the A1555G mutation in 12S rRNA (Bykhovskaya et al. 2004). The A1555G mutation may cause hypermethylation of 12S rRNA which activates AMP kinase, E2F1, and apoptosis (Cotney et al. 2009, Raimundo et al. 2012), however the reported hypermethylation and deafness phenotype have been questioned (Lee et al. 2015). Disruption of *Tfb1m* in mice is lethal and causes loss of adenine methylation of the 12S RNA (Metodieff et al. 2009).

Literature references

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Editions

2015-08-28	Authored, Edited	May, B.
2016-04-25	Reviewed	Bopenhagen, DF.

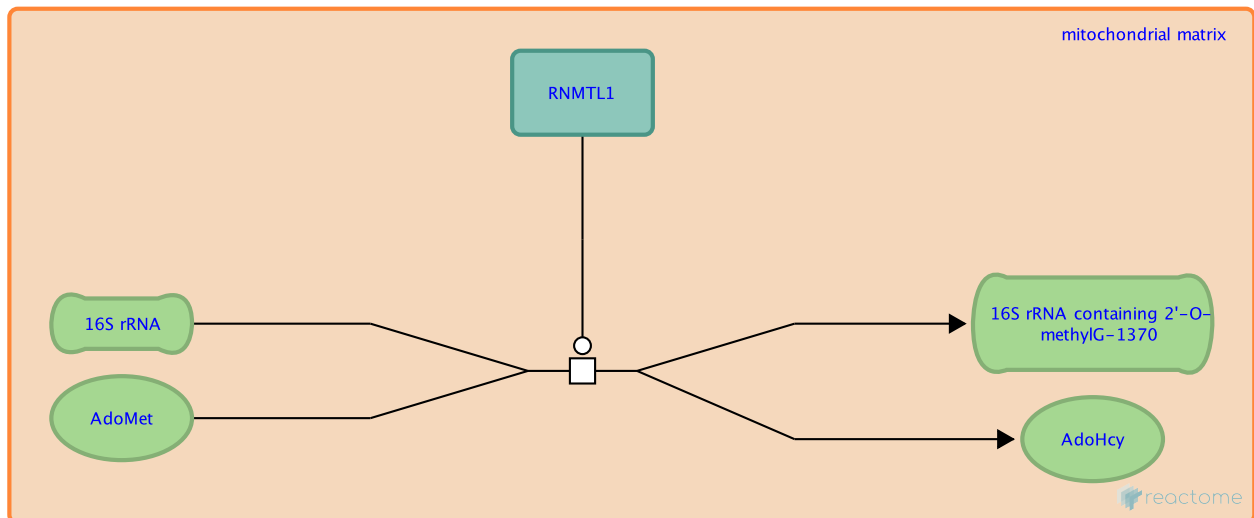
MRM3 (RNMTL1) methylates guanosine-1370 of 16S rRNA yielding 2'-O-methyl-guanosine-1370 ↗

Location: rRNA modification in the mitochondrion

Stable identifier: R-HSA-6793096

Type: transition

Compartments: mitochondrial matrix



MRM3 (RNMTL1) associates with the large mitochondrial ribosomal subunit and transfers a methyl group from S-adenosylmethionine to the 2' hydroxyl group of guanosine-1370 of 16S rRNA (Lee et al. 2013, Lee and Bogenhagen 2014). Inactivation of RNMTL1 causes aberrant assembly of large ribosomal subunits, decreased mitochondrial translation, and respiratory incompetence (Rorbach et al. 2014).

Literature references

Lee, KW., Okot-Kotber, C., LaComb, JF., Bogenhagen, DF. (2013). Mitochondrial ribosomal RNA (rRNA) methyltransferase family members are positioned to modify nascent rRNA in foci near the mitochondrial DNA nucleoid. *J. Biol. Chem.*, 288, 31386-99. ↗

Lee, KW., Bogenhagen, DF. (2014). Assignment of 2'-O-methyltransferases to modification sites on the mammalian mitochondrial large subunit 16 S ribosomal RNA (rRNA). *J. Biol. Chem.*, 289, 24936-42. ↗

Rorbach, J., Boesch, P., Gammage, PA., Nicholls, TJ., Pearce, SF., Patel, D. et al. (2014). MRM2 and MRM3 are involved in biogenesis of the large subunit of the mitochondrial ribosome. *Mol. Biol. Cell*, 25, 2542-55. ↗

Editions

2015-08-29	Authored, Edited	May, B.
2016-04-25	Reviewed	Bogenhagen, DF.

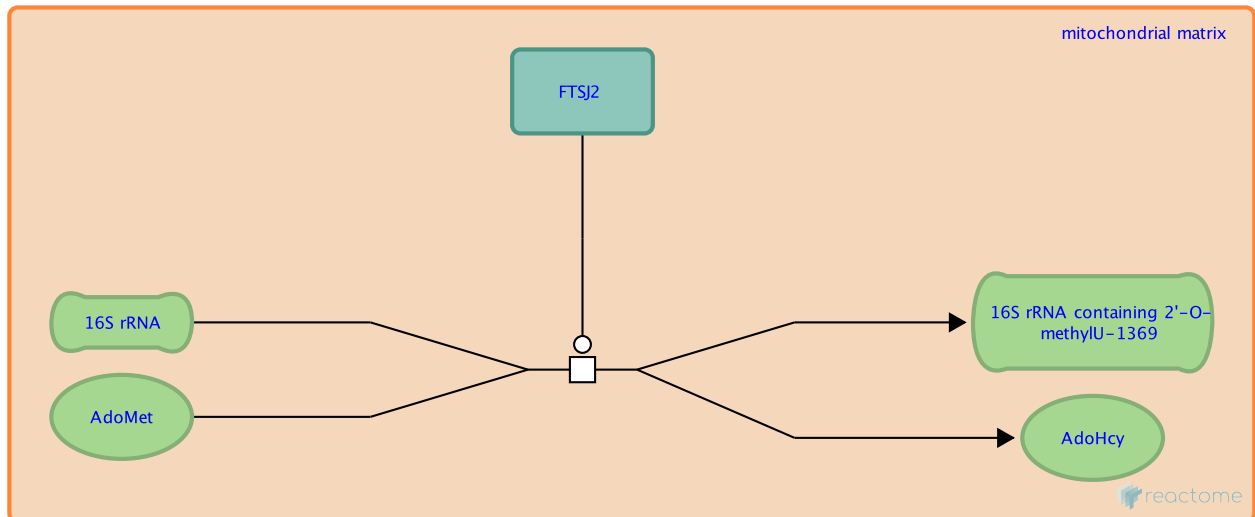
MRM2 (FTSJ2) methylates uridine-1369 of 16S rRNA yielding 2'-O-methyluridine [↗](#)

Location: [rRNA modification in the mitochondrion](#)

Stable identifier: R-HSA-6793127

Type: transition

Compartments: mitochondrial matrix



MRM2 (FTSJ2) located in foci near mitochondrial nucleoids (Lee et al. 2013) transfers a methyl group from S-adenosylmethionine to the 2' hydroxyl of uridine-1369 in 16S rRNA (Lee and Bogenhagen 2014, Rorbach et al. 2014). Inactivation of FTSJ2 causes aberrant assembly of large mitochondrial subunits, reduced mitochondrial translation, and respiratory incompetence (Rorbach et al. 2014).

Literature references

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Editions

2015-08-30	Authored, Edited	May, B.
2016-04-25	Reviewed	Bogenhagen, DF.

MRM1 methylates guanosine-1145 of 16S rRNA yielding 2'-O-methylguanosine-1145

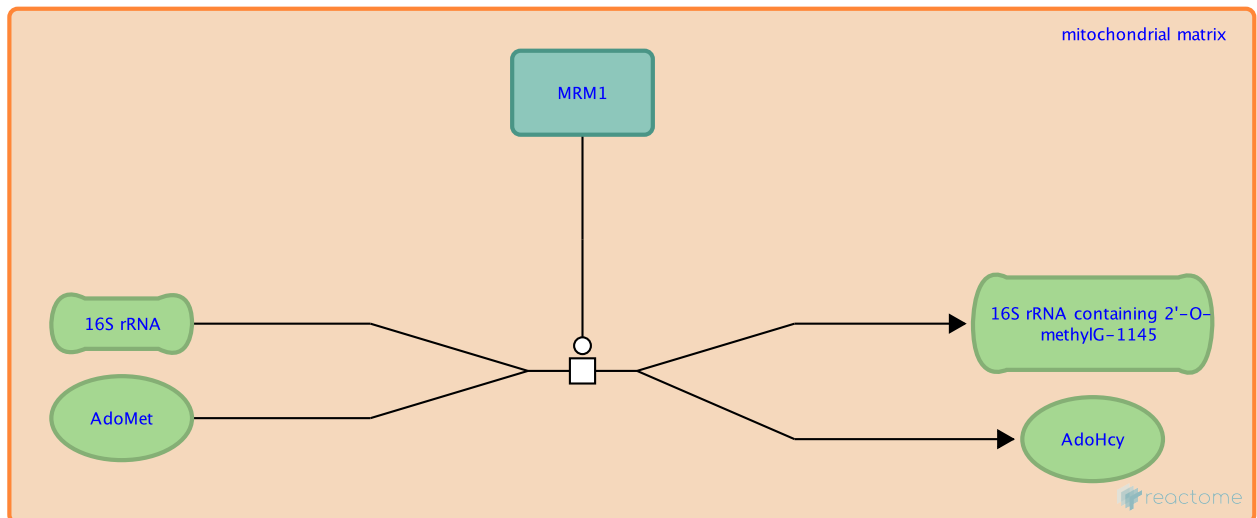


Location: rRNA modification in the mitochondrion

Stable identifier: R-HSA-6793122

Type: transition

Compartments: mitochondrial matrix



MRM1 located in foci near mitochondrial nucleoids (Lee et al. 2013) transfers a methyl group from S-adenosylmethionine to the 2' hydroxyl of guanosine-1145 in 16S rRNA (Lee and Bogenhagen 2014).

Literature references

Lee, KW., Bogenhagen, DF. (2014). Assignment of 2'-O-methyltransferases to modification sites on the mammalian mitochondrial large subunit 16 S ribosomal RNA (rRNA). *J. Biol. Chem.*, 289, 24936-42. [↗](#)

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Editions

2015-08-30

Authored, Edited

May, B.

2016-04-25

Reviewed

Bogenhagen, DF.

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