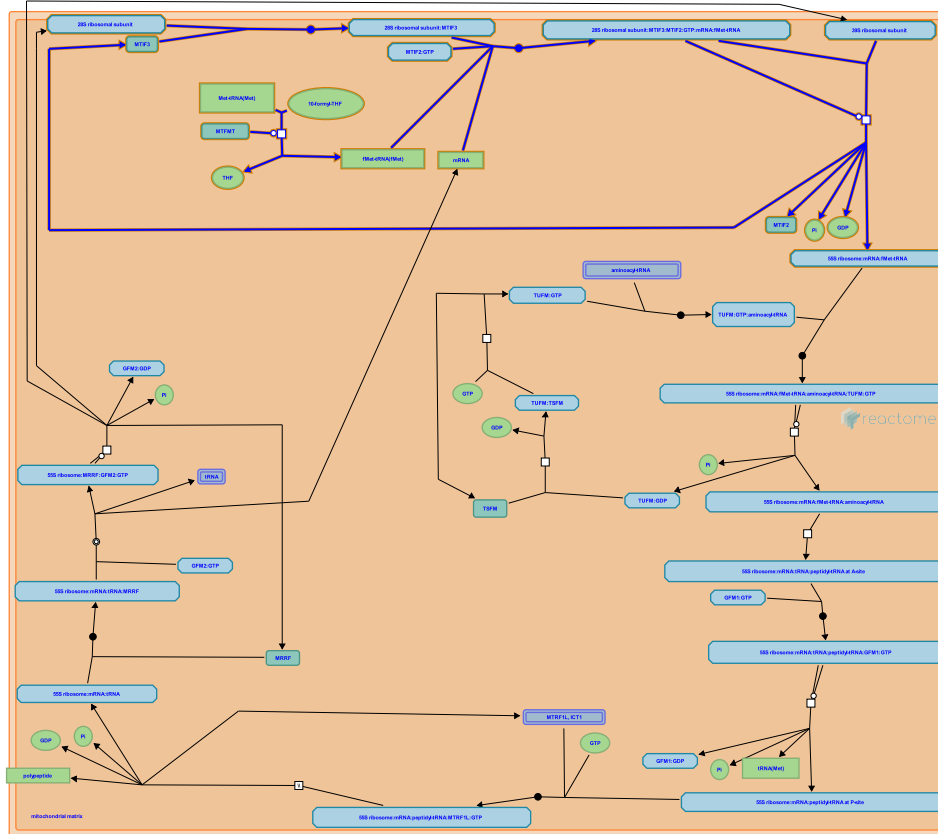


Mitochondrial translation initiation



Chrzanowska-Lightowlers, ZM., May, B., Spremulli, LL.

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

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](https://reactome.org/textbook).

05/05/2024

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

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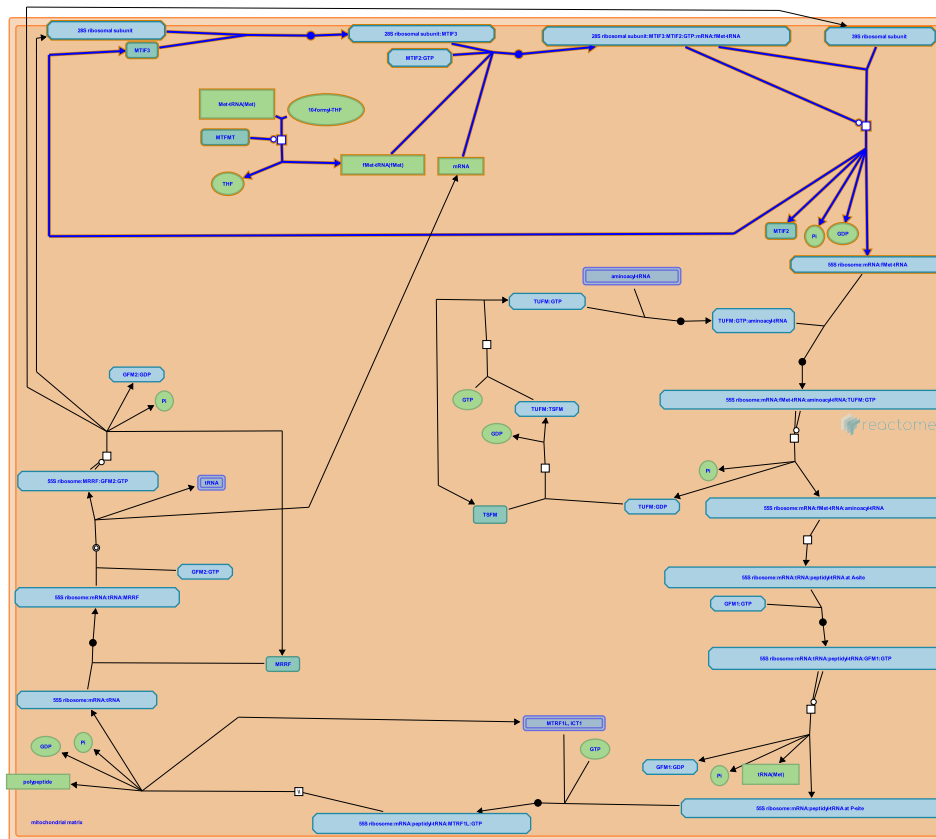
Reactome database release: 88

This document contains 1 pathway and 4 reactions ([see Table of Contents](#))

Mitochondrial translation initiation ↗

Stable identifier: R-HSA-5368286

Compartments: mitochondrial matrix, mitochondrial inner membrane



Translation initiates with the mitochondrial mRNA binding the 28S subunit:MTIF3 (28S subunit:IF-3Mt, 28S subunit:IF3mt) complex together with MTIF2:GTP (IF-2Mt:GTP, IF2mt:GTP) (reviewed in Christian and Spremulli 2012, Kuzmenko et al. 2014). As inferred from bovine homologs, the 28S subunit, 39S subunit, and 55S holo-ribosome associate with the matrix-side face of the inner membrane and the translation products are inserted into the inner membrane as translation occurs (Liu and Spremulli 2000). Mitochondrial mRNAs have either no untranslated leader or short leaders of 1-3 nucleotides, with the exception of the 2 bicistronic transcripts, RNA7 and RNA14, which have overlapping orfs that encode ND4L/ND4 and ATP8/ATP6 respectively.. Binding of N-formylmethionine-tRNA to the start codon results in a stable complex between the mRNA and the 28S subunit while absence of a start codon at the 5' end of the mRNA causes the mRNA to slide through the 28S subunit and eventually dissociate. The 39S subunit then binds the 28S subunit:mRNA complex, GTP is hydrolyzed, and the initiation factors MTIF3 and MTIF2:GDP dissociate.

Literature references

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- Liu, M., Spremulli, L. (2000). Interaction of mammalian mitochondrial ribosomes with the inner membrane. *J. Biol. Chem.*, 275, 29400-6. ↗
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Editions

2014-04-26	Authored, Edited	May, B.
2014-08-29	Reviewed	Chrzanowska-Lightowlers, ZM.
2014-09-20	Reviewed	Spremulli, LL.

MTFMT formylates methionyl-tRNA ↗

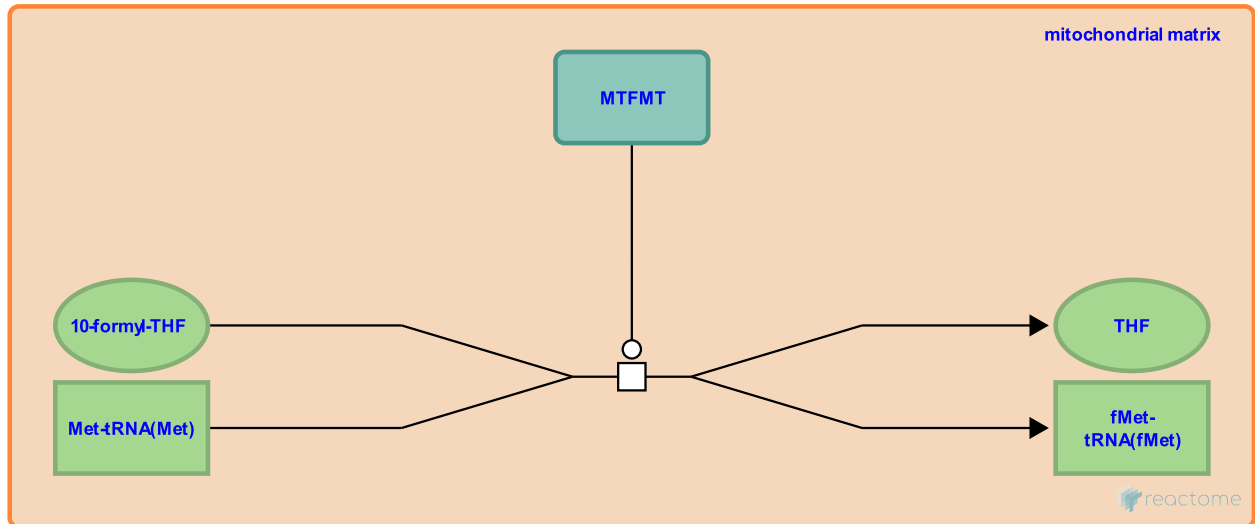
Location: [Mitochondrial translation initiation](#)

Stable identifier: R-HSA-5389841

Type: transition

Compartments: mitochondrial matrix

Inferred from: [MTFMT formylates methionyl-tRNA \(Bos taurus\)](#)



Like bacteria, mitochondria initiate translation with N-formylmethionine. Unlike bacteria, mammalian mitochondria do not have a tRNA dedicated to N-formylmethionine. Instead, the mitochondrial enzyme MTFMT (methionyl-tRNA formyltransferase, FMT, FMT1) transfers a formyl group from 10-formyltetrahydrofolate (10-formyl-THF) to the amino group of methionyl-tRNA in a portion of the methionyl-tRNAs in the matrix.

Followed by: [28S subunit:MTIF3 binds MTIF2:GTP, mRNA, and formylMet-tRNA](#)

Literature references

Calvo, SE., Belcher-Timme, CA., Köhrer, C., Patel, J., Thorburn, DR., RajBhandary, UL. et al. (2011). Mutations in MTFMT underlie a human disorder of formylation causing impaired mitochondrial translation. *Cell Metab.*, 14, 428-34. ↗

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MTIF3 binds 28S ribosomal subunit ↗

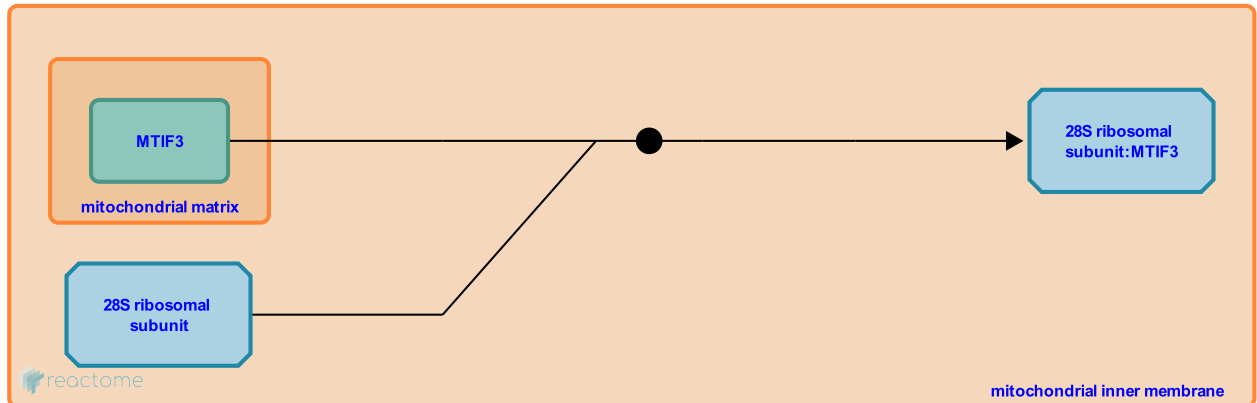
Location: [Mitochondrial translation initiation](#)

Stable identifier: R-HSA-5368279

Type: binding

Compartments: mitochondrial inner membrane, mitochondrial matrix

Inferred from: [MTIF3 binds 28S ribosomal subunit \(Bos taurus\)](#)



As inferred from bovine mitochondrial homologs, MTIF3 (IF-3Mt, IF3mt) binds the 28S ribosomal subunit in preparation for binding mRNA and initiating translation. MTIF3 also dissociates 55S particles that have not already been dissociated by GFM2 plus MRRF and displaces N-formylmethionyl-tRNA from the 28S subunit in the absence of mRNA but cannot displace mRNA from the 28S subunit. The activity of MTIF3 is necessary for translation initiation.. The 28S subunit associates with the matrix-side face of the inner mitochondrial membrane and translation products are inserted directly into the membrane.

Followed by: [28S subunit:MTIF3 binds MTIF2:GTP, mRNA, and formylMet-tRNA](#)

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28S subunit:MTIF3 binds MTIF2:GTP, mRNA, and formylMet-tRNA ↗

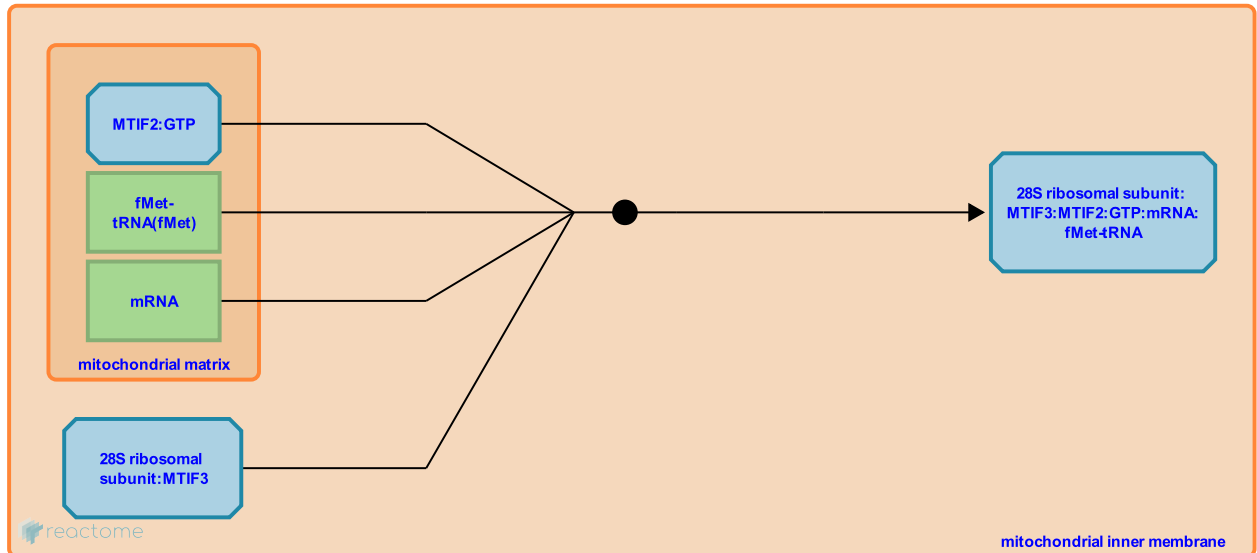
Location: [Mitochondrial translation initiation](#)

Stable identifier: R-HSA-5389849

Type: binding

Compartments: mitochondrial inner membrane, mitochondrial matrix

Inferred from: [28S subunit binds MITF2:GTP, mRNA, and formylMet-tRNA \(Bos taurus\)](#)



As inferred from bovine homologs, the 28S ribosomal subunit in a complex with MTIF3 (IF-3Mt, IF3mt) binds mRNA and, at some point, MTIF2:GTP (IF-2Mt:GTP, IF2mt:GTP). If an initiation codon is present at the 5' end of the mRNA then MTIF2:GTP assists the binding of N-formylmethionyl-tRNA and a stable, productive initiation complex results. If no initiation codon is present, the mRNA slides through the 28S subunit and then dissociates.

Preceded by: [MTIF3 binds 28S ribosomal subunit](#), [MTFMT formylates methionyl-tRNA](#)

Followed by: [39S subunit binds 28S subunit:mRNA:fMet-tRNA](#)

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39S subunit binds 28S subunit:mRNA:fMet-tRNA [↗](#)

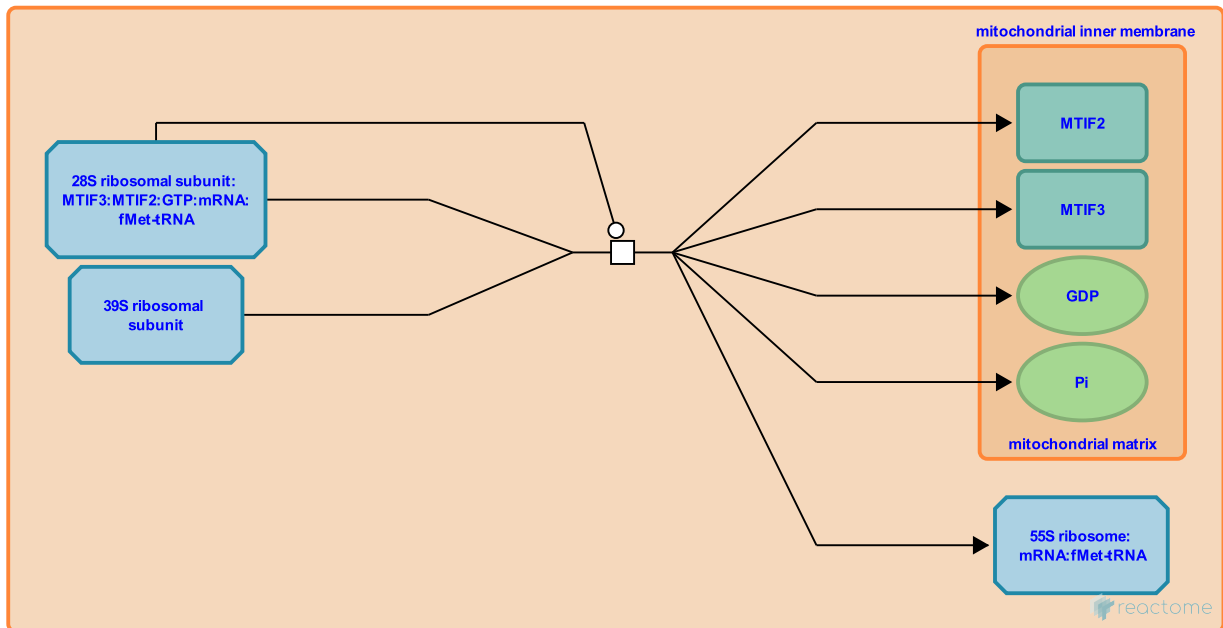
Location: [Mitochondrial translation initiation](#)

Stable identifier: R-HSA-5389839

Type: transition

Compartments: mitochondrial inner membrane, mitochondrial matrix

Inferred from: [39S subunit binds 28S subunit:mRNA:fMet-tRNA \(Bos taurus\)](#)



As inferred from bovine homologs, the 39S ribosomal subunit binds the 28S subunit:mRNA:N-formylmethionyl-tRNA complex, MTIF2 hydrolyzes GTP, then MTIF2, GDP, and MTIF3 dissociate. (MTIF2 has a very low affinity for GDP so it is unclear whether MTIF2 and GDP remain associated after hydrolysis of GTP.) The 28S subunit, 39S subunit, and 55S holoribosome associate with the inner mitochondrial membrane during translation and in the absence of translation.

Preceded by: [28S subunit:MTIF3 binds MTIF2:GTP, mRNA, and formylMet-tRNA](#)

Editions

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Table of Contents

Introduction	1
☰ Mitochondrial translation initiation	2
↳ MTFMT formylates methionyl-tRNA	3
↳ MTIF3 binds 28S ribosomal subunit	4
↳ 28S subunit:MTIF3 binds MTIF2:GTP, mRNA, and formylMet-tRNA	5
↳ 39S subunit binds 28S subunit:mRNA:fMet-tRNA	6
Table of Contents	7