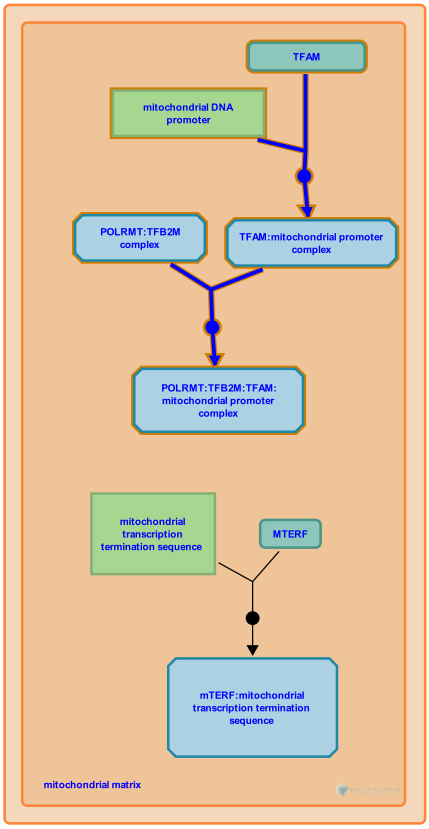
Mitochondrial transcription initiation



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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. ↗

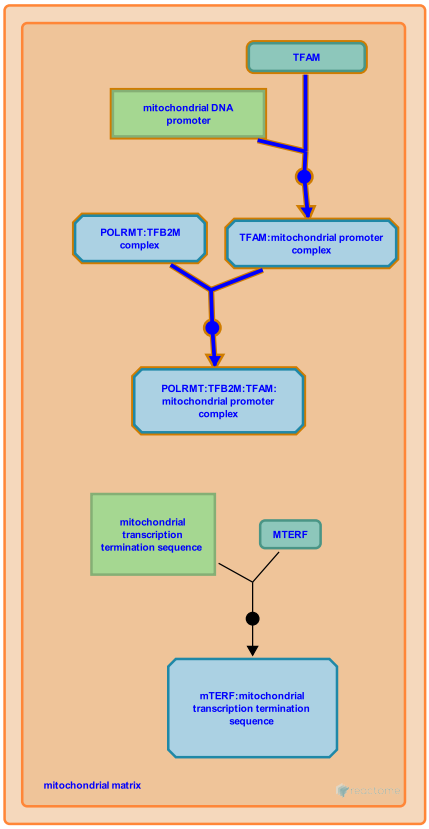
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Mitochondrial transcription initiation ↗

Stable identifier: R-HSA-163282



Human mtDNA is transcribed by a dedicated mitochondrial RNA polymerase (POLRMT), which displays significant sequence similarity to the monomeric RNA polymerases found in bacteriophages. In contrast to the phage T7 RNA polymerase, POLRMT cannot interact with promoter DNA and initiate transcription on its own, but requires the presence of the mitochondrial transcription factor A (TFAM), and either transcription factor B1 (TFB1M) or B2 (TFB2M). The 4 proteins of the basal mitochondrial transcription machinery have been purified in recombinant form and used to reconstitute transcription in vitro with a promoter containing DNA fragment (Falkenberg et al., 2002). Although both TFB1M and TFB2M can support in vitro transcription with POLRMT, TFB2M is at least two orders of magnitude more active than TFB1M and the physiological role of TFB1M in mitochondrial transcription has not yet been completely defined. The TFB1M and TFB2M display primary sequence similarity to a family of rRNA methyltransferases, which dimethylates two adjacent adenosine bases near the 3' end of the small subunit rRNA during ribosome biogenesis (Falkenberg et al., 2002; McCulloch et al., 2002). Human TFB1M is, in fact, a dual function protein, which not only support mitochondrial transcription in vitro, but also acts as a rRNA methyltransferase (Seidel-Rogol et al., 2003). The methyltransferase activity is not required for transcription, since point mutations in conserved methyltransferase motifs of TFB1M revealed that it stimulates transcription in vitro independently of S-adenosylmethionine binding and rRNA methyltransferase activity.

Literature references

Clayton, DA. (2000). Transcription and replication of mitochondrial DNA. *Hum Reprod, 15*, 11-7. ↗

Montoya, J., Fernandez-Silva, P., Enriquez, JA. (2003). Replication and transcription of mammalian mitochondrial DNA. *Exp Physiol, 88*, 41-56. ↗

Editions

2005-04-26	Authored	Gustafsson, CM.
2024-03-06	Reviewed	Cantatore, P.
2024-03-06	Edited	Matthews, L.

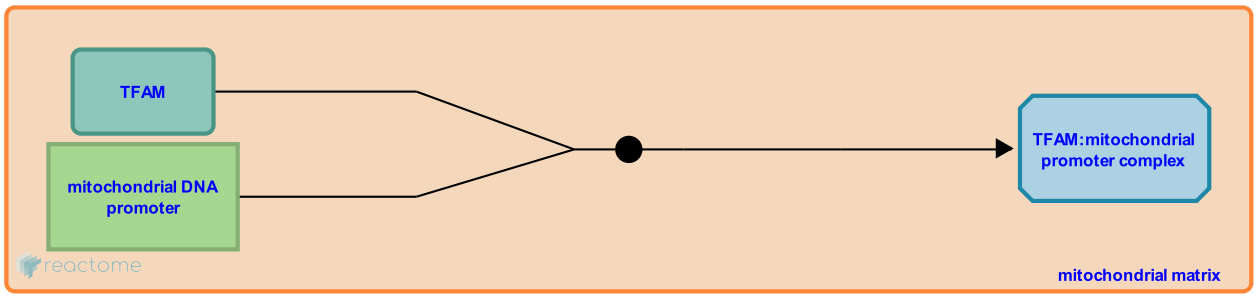
TFAM binds to mitochondrial promoters ↗

Location: Mitochondrial transcription initiation

Stable identifier: R-HSA-163310

Type: binding

Compartments: mitochondrial matrix



Studies of human LSP have revealed that a minimal DNA fragment corresponding to position -28 to +16 relative to the transcription initiation site is able to support transcription initiation in a mitochondrial extract (Chang and Clayton, 1984). TFAM interacts directly with nucleotides between positions -35 and -17 (Fisher et al., 1987), and the exact distance between the TFAM-binding site and the transcription start site is essential for promoter activity (Dairaghi et al., 1995).

Followed by: Association of TFAM:mt promoter complex with POLRMT:TFB2M

Literature references

Topper, JN., Fisher, RP. (1987). Promoter selection in human mitochondria involves binding of a transcription factor to orientation-independent upstream regulatory elements. *Cell, 50*, 247-58. ↗

Editions

2005-04-26	Authored	Gustafsson, CM.
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2024-03-06	Edited	Matthews, L.

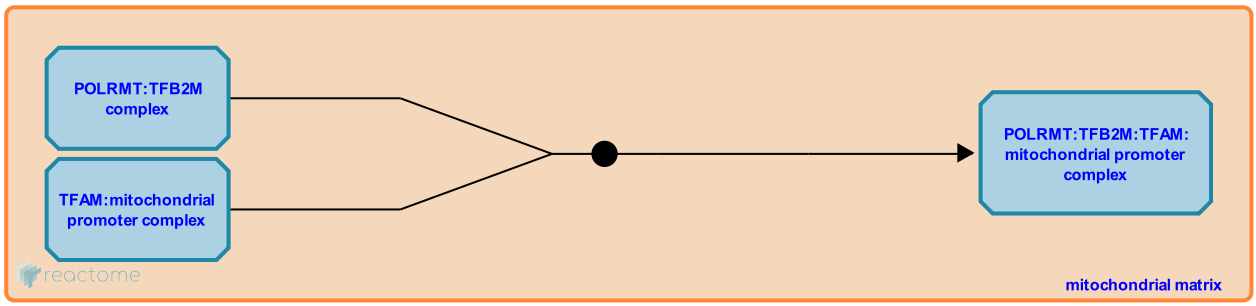
Association of TFAM:mt promoter complex with POLRMT:TFB2M ↗

Location: Mitochondrial transcription initiation

Stable identifier: R-HSA-163296

Type: binding

Compartments: mitochondrial matrix



At the beginning of this reaction, 1 molecule of 'POLRMT:TFB2M complex', and 1 molecule of 'TFAM:mitochondrial promoter complex' are present. At the end of this reaction, 1 molecule of 'POLRMT:TFB2M:TFAM:mitochondrial promoter complex' is present.

This reaction takes place in the 'mitochondrial matrix'.

Preceded by: TFAM binds to mitochondrial promoters

Literature references

Gaspari, M., Trifunovic, A., Larsson, NG., Gustafsson, CM., Rantanen, A., Falkenberg, M. (2002). Mitochondrial transcription factors B1 and B2 activate transcription of human mtDNA. *Nat Genet, 31*, 289-94. ↗

Gaspari, M., Larsson, NG., Gustafsson, CM., Falkenberg, M. (2004). The mitochondrial RNA polymerase contributes critically to promoter specificity in mammalian cells. *EMBO J, 23*, 4606-14. ↗

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