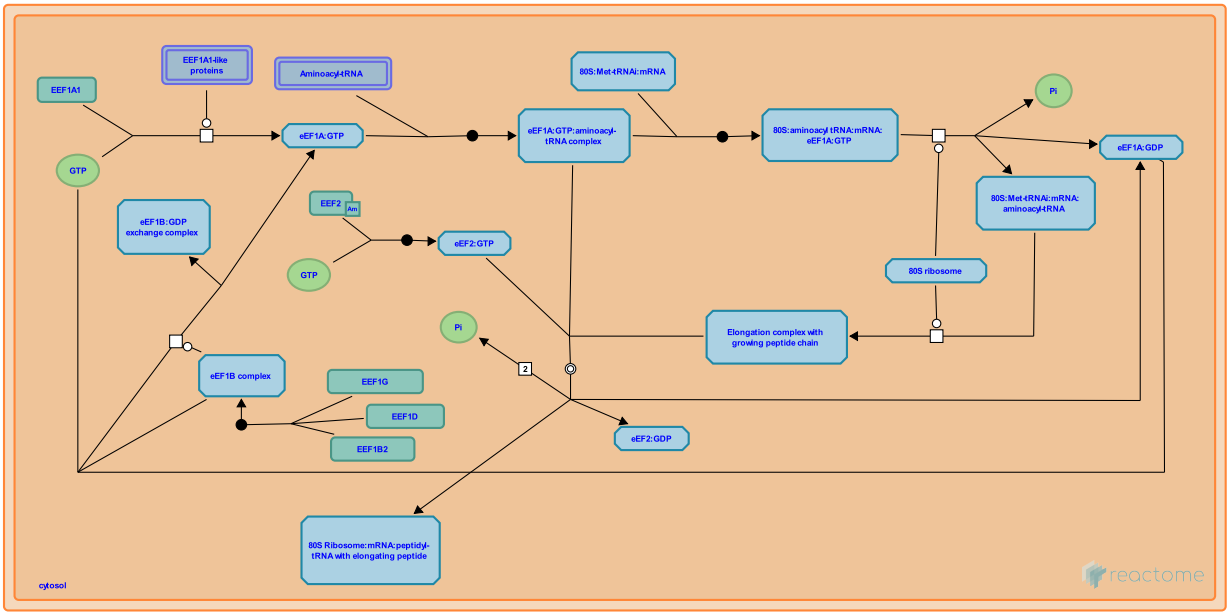
Eukaryotic Translation Elongation



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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. ↗

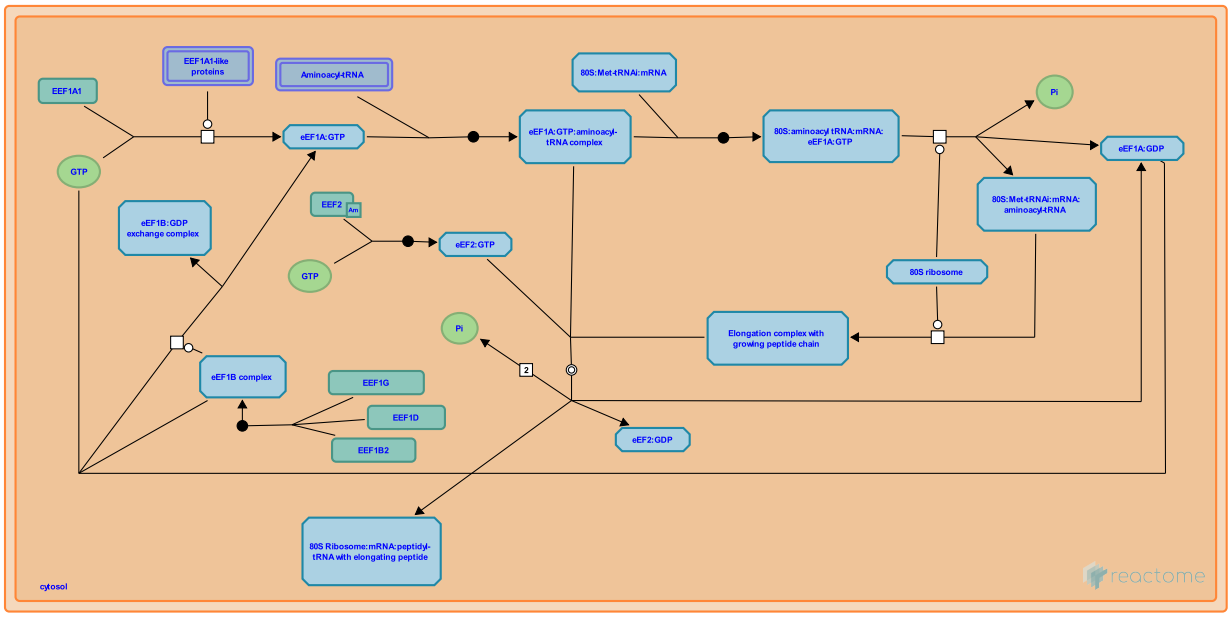
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Eukaryotic Translation Elongation ↗

Stable identifier: R-HSA-156842

Compartments: cytosol



The translation elongation cycle adds one amino acid at a time to a growing polypeptide according to the sequence of codons found in the mRNA. The next available codon on the mRNA is exposed in the aminoacyl-tRNA (aa-tRNA) binding site (A site) on the 30S subunit.
A: Ternary complexes of aa -tRNA:eEF1A:GTP enter the ribosome and enable the anticodon of the tRNA to make a codon/anticodon interaction with the A-site codon of the mRNA. B: Upon cognate recognition, the eEF1A:GTP is brought into the GTPase activating center of the ribosome, GTP is hydrolyzed and eEF1A:GDP leaves the ribosome. C: The peptidyl transferase center of ribosome catalyses the formation of a peptide bond between the incoming amino acid and the peptide found in the peptidyl-tRNA binding site (P site). D: In the pre-translocation state of the ribosome, the eEF2:GTP enters the ribosome, physically translocating the peptidyl-tRNA out of the A site to P site and leaves the ribosome eEF2:GDP. This action of eEF2:GTP accounts for the precise movement of the mRNA by 3 nucleotides.Consequently, deacylated tRNA is shifted to the E site. A ribosome associated ATPase activity is proposed to stimulate the release of deacylated tRNA from the E site subsequent to translocation (Elskaya et al., 1991). In this post-translocation state, the ribosome is now ready to receive a new ternary complex.
This process is illustrated below with: an amino acyl-tRNA with an amino acid, a peptidyl-tRNA with a growing peptide, a deacylated tRNA with an -OH, and a ribosome with A,P and E sites to accommodate these three forms of tRNA.

Literature references

Kapp, LD., Lorsch, JR. (2004). The molecular mechanics of eukaryotic translation. *Annu Rev Biochem, 73,* 657-704. ↗

Editions

2005-03-13	Authored	Gopinathrao, G.

eEF1A complexes with GTP ↗

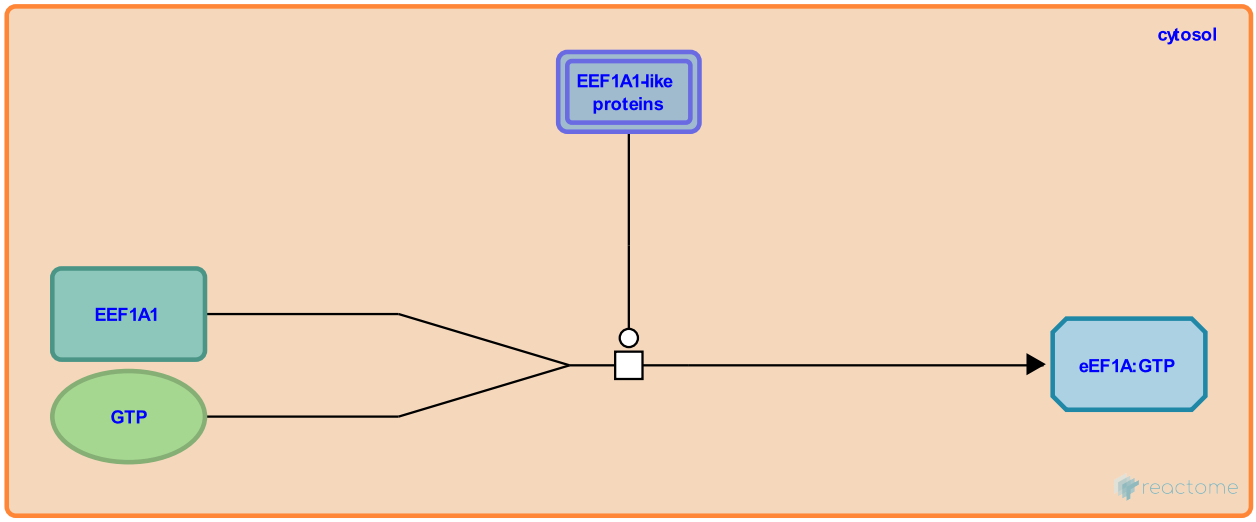
Location: Eukaryotic Translation Elongation

Stable identifier: R-HSA-156909

Type: transition

Compartments: cytosol

Inferred from: reEF1A complexes with GTP (Oryctolagus cuniculus)



The cycle of elongation starts with an empty ribosomal A-site and the peptidyl-tRNA in the P-site. eEF1A is activated by GTP binding and allows for the subsequent binding of aminoacyl-tRNA (aa-tRNA).This process is illustrated below with a GTP molecule in white and eEF1A protein in yellow.

Followed by: eEF1A:GTP:aminoacyl tRNA ternary complex formation.

Editions

2005-03-12	Authored	Gopinathrao, G.

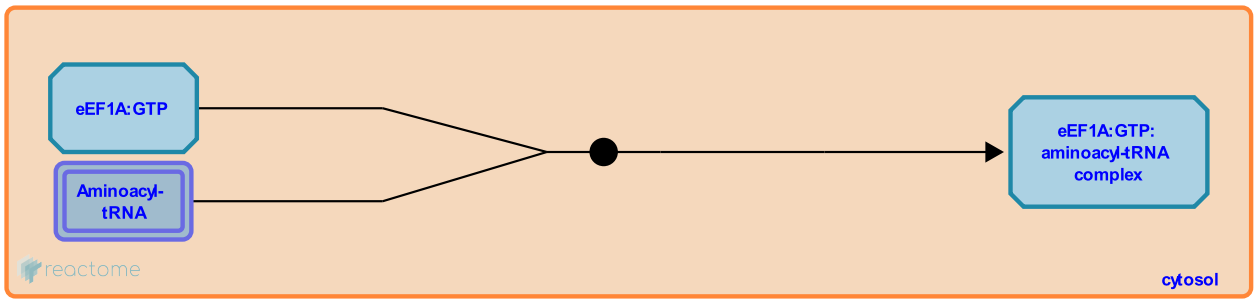
eEF1A:GTP:aminoacyl tRNA ternary complex formation. ↗

Location: Eukaryotic Translation Elongation

Stable identifier: R-HSA-156908

Type: binding

Compartments: cytosol



The binding of eEF1A:GTP to aminoacyl tRNA (aa-tRNA) results in the formation of a ternary complex (eEF1A:GTP:aa-tRNA). Human eEF1A and rabbit eEF1A are 100% identical, and prokaryotic homologue of eEF1A (EF-Tu) shows 59% identity in the GTP-binding domain.This process is illustrated below with: a GTP molecule in white and eEF1A protein in yellow.

Preceded by: eEF1A complexes with GTP, Regeneration of eEF1A:GTP by eEF1B activity

Editions

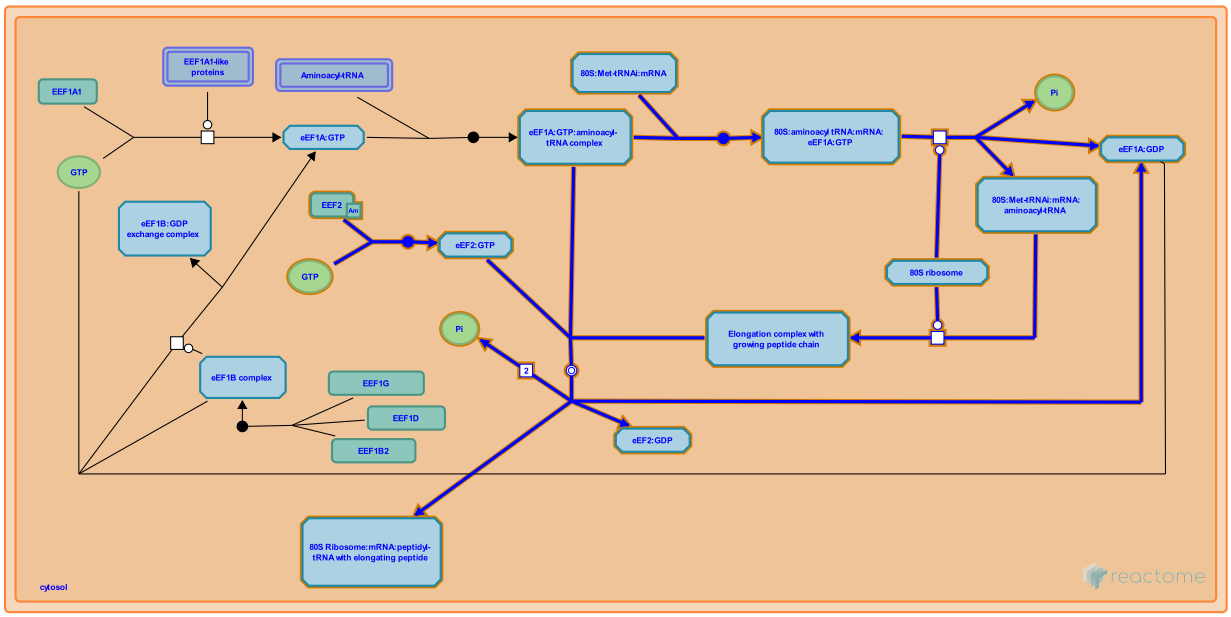
2005-03-12	Authored	Gopinathrao, G.

Peptide chain elongation ↗

Location: Eukaryotic Translation Elongation

Stable identifier: R-HSA-156902

Compartments: cytosol



The mechanism of a peptide bond requires the movement of three protons. First the deprotonation of the ammonium ion generates a reactive amine, allowing a nucleophilic attack on the carbonyl group. This is followed by the loss of a proton from the reaction intermediate, only to be taken up by the oxygen on the leaving group (from the end of the amino acid chain bound to the tRNA in the P-site). The peptide bond formation results in the net loss of one water molecule, leaving a deacylated-tRNA in the P-site, and a nascent polypeptide chain one amino acid larger in the A-site.
For the purpose of illustration, the figures used in the section show one amino acid being added to a peptidyl-tRNA with a growing peptide chain.

Literature references

Lorsch, JR., Green, R. (2002). The path to perdition is paved with protons. *Cell, 110*, 665-8. ↗

Editions

2005-03-13	Authored	Gopinathrao, G.

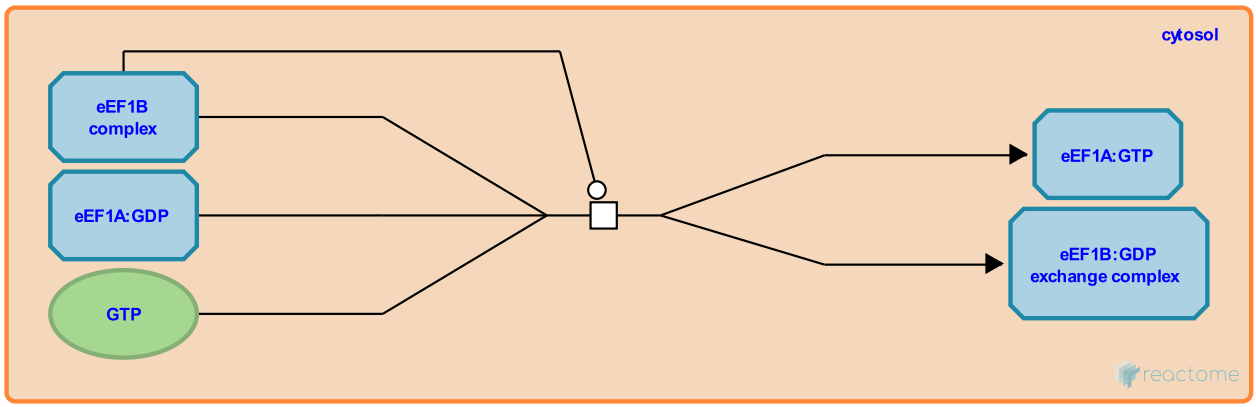
Regeneration of eEF1A:GTP by eEF1B activity ↗

Location: Eukaryotic Translation Elongation

Stable identifier: R-HSA-156913

Type: transition

Compartments: cytosol



The eEF1B complex binds to eEF1A and regulates its activity by catalyzing the release of GDP. Subsequently, GTP is able to bind eEF1A allowing the formation of the ternary complex (eEF1A-GTP-aa-tRNA).In metazoans eEF1 protein family is composed of four subunits: eEF1A and eEF1B alpha, beta, and gamma (formerly EF-1alpha, EF-1beta, EF-1delta, and EF-1gamma, respectively). Both eEF1B alpha and eEF1B beta function as nucleotide exchange proteins. eEF1B gamma associates with eEF1B alpha and stimulates its exchange activity.
This process is illustrated below with a GTP molecule in white and eEF1A protein in yellow.The three subunits of eEF1B are also shown.

Preceded by: Formation of eEF1B complex

Followed by: eEF1A:GTP:aminoacyl tRNA ternary complex formation.

Literature references

Canters, GW., Kriek, J., Dijk, J., Hard, K., Moller, W., Siegal, G. et al. (1999). The solution structure of the guanine nucleotide exchange domain of human elongation factor 1beta reveals a striking resemblance to that of EF-Ts from Escherichia coli. *Structure Fold Des, 7*, 217-26. ↗

Editions

2005-03-12	Authored	Gopinathrao, G.

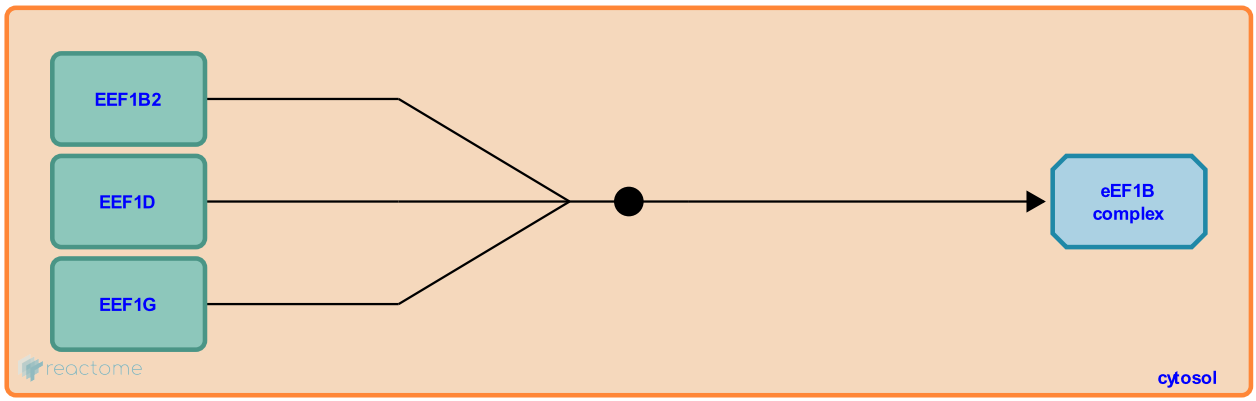
Formation of eEF1B complex ↗

Location: Eukaryotic Translation Elongation

Stable identifier: R-HSA-156910

Type: binding

Compartments: cytosol



At the beginning of this reaction, 1 molecule of 'eEF1B alpha', 1 molecule of 'eEF1B gamma', and 1 molecule of 'eEF1B beta' are present. At the end of this reaction, 1 molecule of 'eEF1B complex' is present. This reaction takes place in the 'cytosol' (Veremieva et al. 2011).

Followed by: Regeneration of eEF1A:GTP by eEF1B activity

Literature references

El'skaya, A., Veremieva, M., Negrutskii, B., Khoruzhenko, A., Zaicev, S. (2011). Unbalanced expression of the translation complex eEF1 subunits in human cardioesophageal carcinoma. *Eur. J. Clin. Invest., 41*, 269-76. ↗

Table of Contents