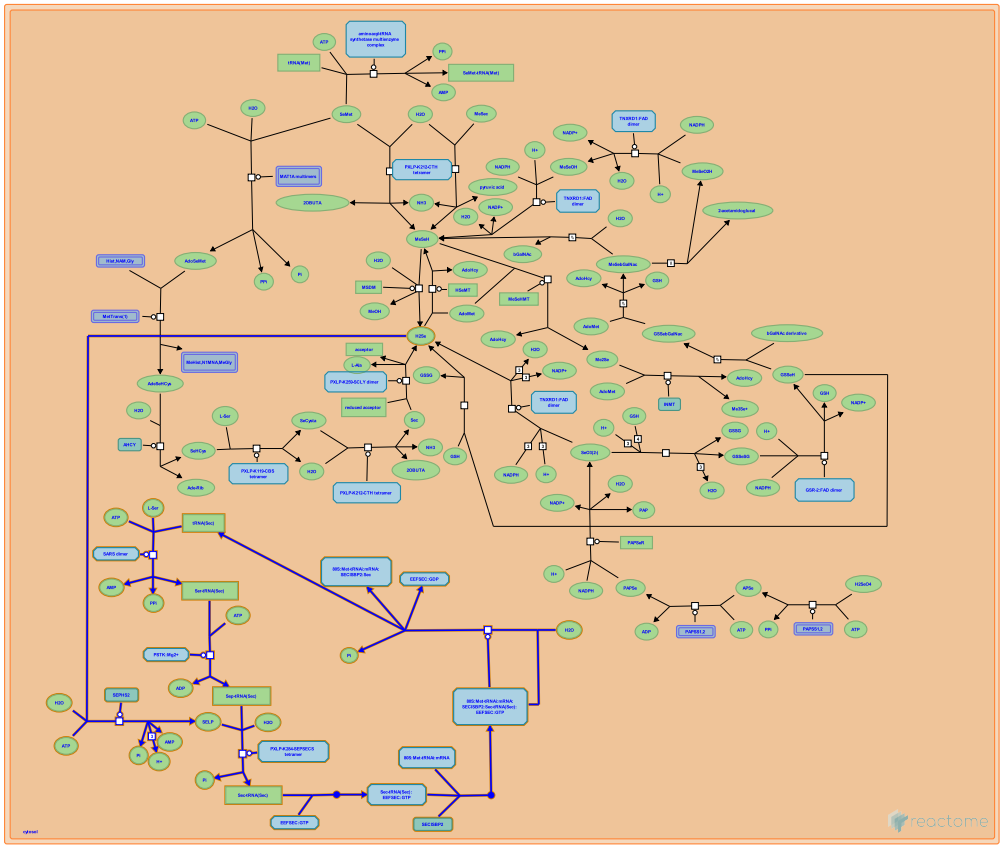
Selenocysteine synthesis



D'Eustachio, P., Jassal, B., Rush, MG., Williams, MG.

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

02/05/2024

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.
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. ↗

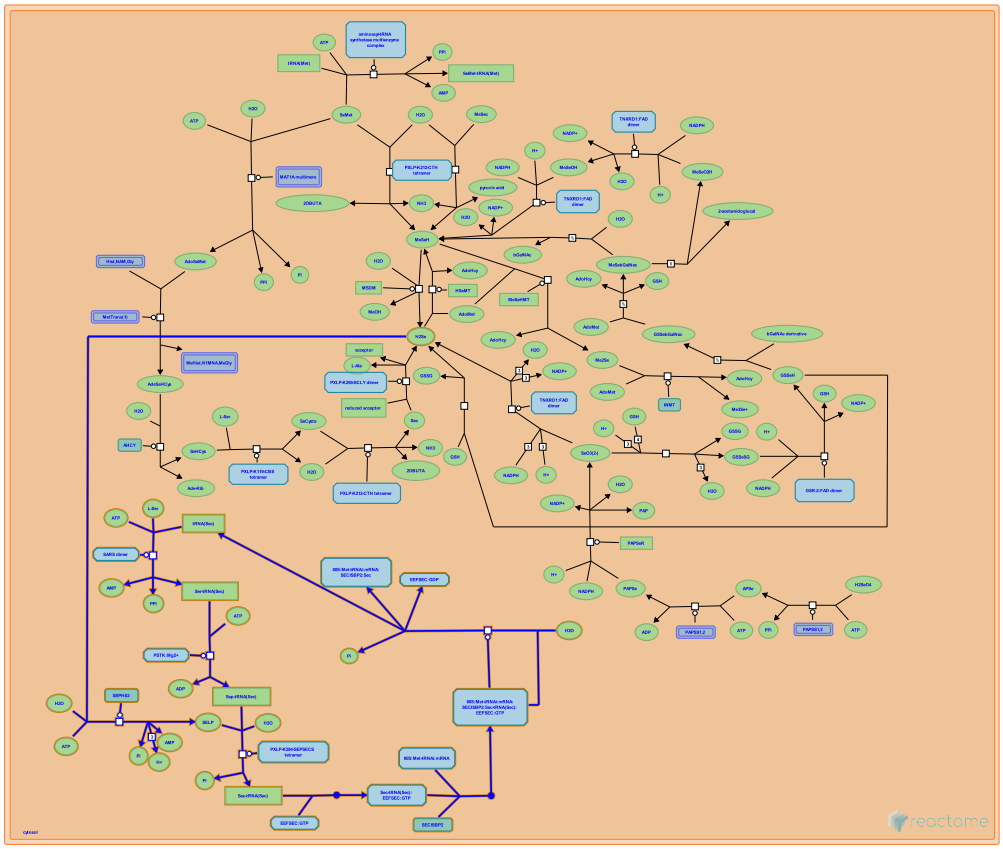
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Selenocysteine synthesis ↗

Stable identifier: R-HSA-2408557



Selenocysteine, the 21st genetically encoded amino acid, is the major form of the antioxidant trace element selenium in the human body. In eukaryotes and archaea its synthesis proceeds through a phosphorylated intermediate in a tRNA-dependent fashion. The final step of selenocysteine formation is catalyzed by O-phosphoseryl-tRNA:selenocysteinyl-tRNA synthase (SEPSECS) that converts phosphoseryl-tRNA(Sec) to selenocysteinyl-tRNA(Sec).

Literature references

Donovan, J., Copeland, PR. (2010). Threading the needle: getting selenocysteine into proteins. *Antioxid. Redox Signal. , 12*, 881-92. ↗

Palioura, S., Herkel, J., Simonovic, M., Lohse, AW., Söll, D. (2010). Human SepSecS or SLA/LP: selenocysteine formation and autoimmune hepatitis. *Biol. Chem., 391*, 771-6. ↗

Sheppard, K., Yuan, J., Devine, KM., Jester, B., Söll, D., Hohn, MJ. (2008). From one amino acid to another: tRNA-dependent amino acid biosynthesis. *Nucleic Acids Res., 36*, 1813-25. ↗

Editions

2014-05-06	Authored	Williams, MG.
2015-08-29	Edited	D'Eustachio, P.
2015-08-30	Reviewed	Rush, MG.

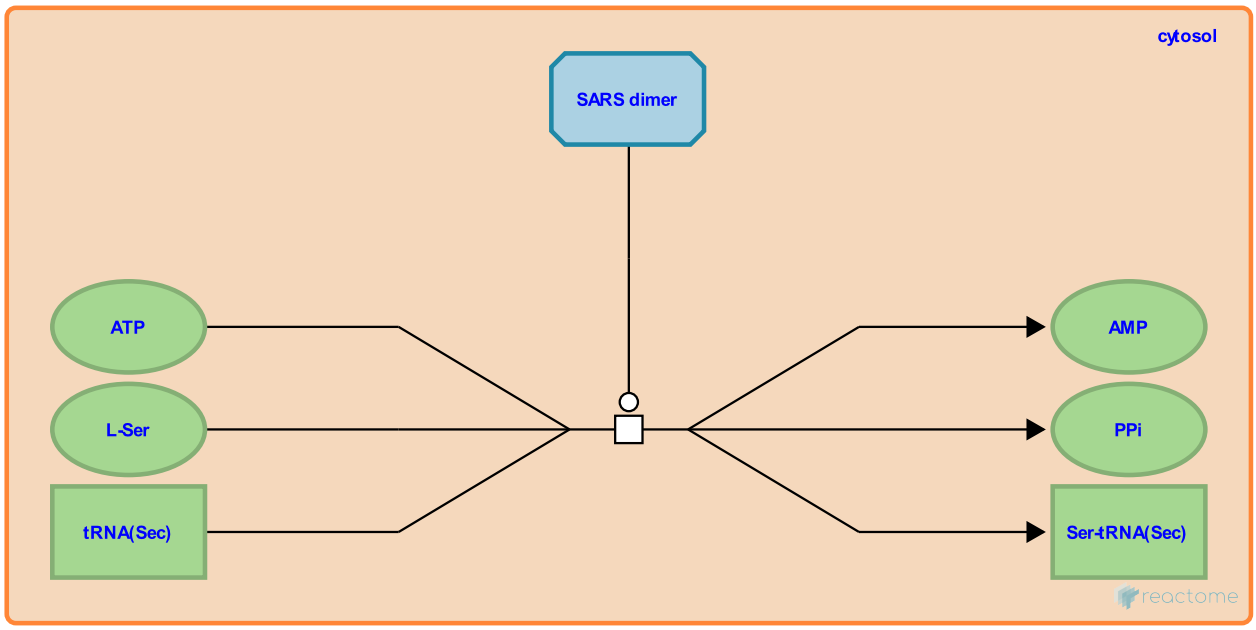
tRNA(Sec) is serylated to Ser-tRNA(Sec) by SARS dimer ↗

Location: Selenocysteine synthesis

Stable identifier: R-HSA-2408526

Type: transition

Compartments: cytosol



The synthetic cycle of selenocysteine (Sec) synthesis starts with misacylation (serylation) of the cognate transfer RNA (tRNA) for Sec, tRNASec, with serine (Ser) by Serine--tRNA ligase (SARS) homodimer. The structural homology of tRNASec and tRNASer enables SARS to form Ser-tRNASec (Vincent et al. 1997, Amberg et al. 1996, Heckl et al. 1998).

Followed by: Ser-tRNA(Sec) is phosphorylated to Sep-tRNA(Sec) by PSTK

Literature references

Hartlein, M., Vincent, C., Tarbouriech, N. (1997). Genomic organization, cDNA sequence, bacterial expression, and purification of human seryl-tRNA synthase. *Eur J Biochem, 250*, 77-84. ↗

Busch, K., Gross, HJ., Heckl, M. (1998). Minimal tRNA(Ser) and tRNA(Sec) substrates for human seryl-tRNA synthetase: contribution of tRNA domains to serylation and tertiary structure. *FEBS Lett., 427*, 315-9. ↗

Amberg, R., Gross, HJ., Mizutani, T., Wu, XQ. (1996). Selenocysteine synthesis in mammalia: an identity switch from tRNA(Ser) to tRNA(Sec). *J. Mol. Biol., 263*, 8-19. ↗

Editions

2014-05-06	Authored	Williams, MG.
2015-08-29	Edited	D'Eustachio, P.
2015-08-30	Reviewed	Rush, MG.

Ser-tRNA(Sec) is phosphorylated to Sep-tRNA(Sec) by PSTK ↗

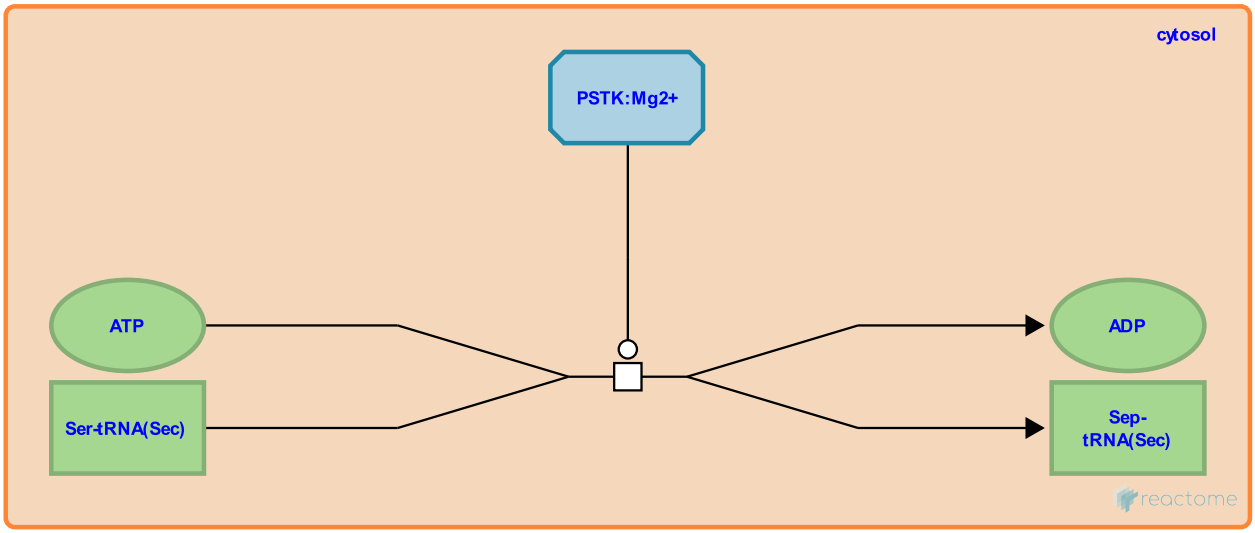
Location: Selenocysteine synthesis

Stable identifier: R-HSA-2408507

Type: transition

Compartments: cytosol

Inferred from: Ser-tRNA(Sec) is phosphorylated to Sep-tRNA(Sec) by Pstk (Mus musculus)



L-seryl-tRNA(Sec) kinase (PSTK) phosphorylates the serylated transfer RNA (tRNA) for Sec (Ser-tRNASec) to form Sep-tRNASec in the presence of ATP and Mg2+. PSTK exhibits a strict selectivity for Ser-tRNASec. It does not phosphorylate free Ser or Ser attached to its cognate tRNASer. This reaction involving PSTK is inferred from the equivalent reaction in mouse.

Preceded by: tRNA(Sec) is serylated to Ser-tRNA(Sec) by SARS dimer

Followed by: Sep-tRNA(Sec) is converted to Sec-tRNA(Sec) by PXLP-K284-SEPSECS tetramer

Literature references

Carlson, BA., Kryukov, GV., Berry, MJ., Hatfield, DL., Rao, M., Gladyshev, VN. et al. (2004). Identification and characterization of phosphoseryl-tRNA[Ser]Sec kinase. *Proc. Natl. Acad. Sci. U.S.A., 101*, 12848-53. ↗

Editions

2014-05-06	Authored	Williams, MG.
2015-08-29	Edited	D'Eustachio, P.
2015-08-30	Reviewed	Rush, MG.

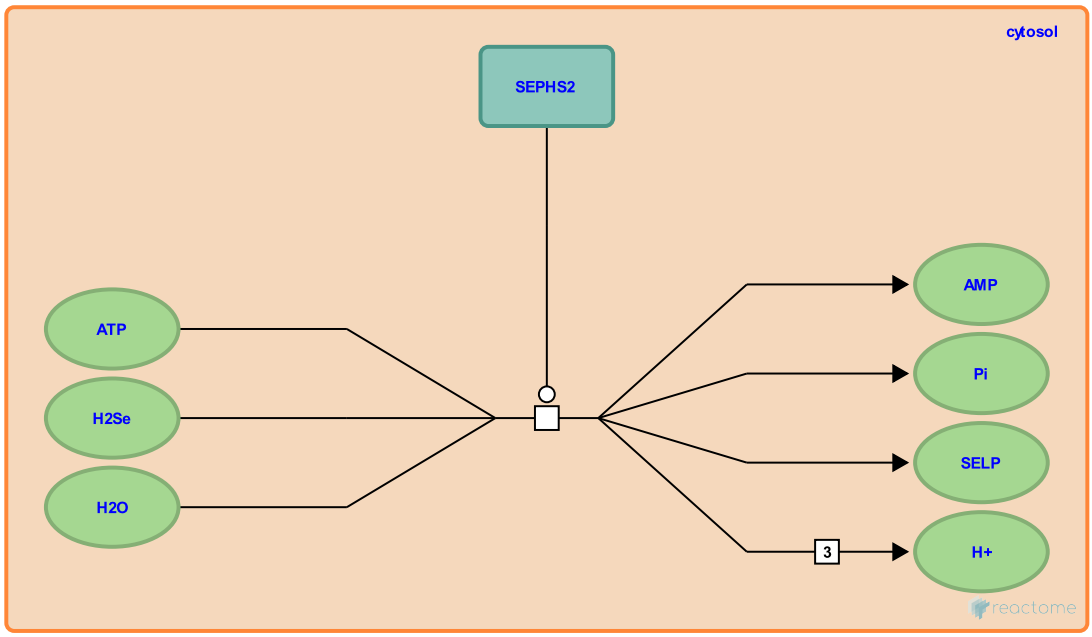
SEPHS2 phosphorylates H2Se to form SELP ↗

Location: Selenocysteine synthesis

Stable identifier: R-HSA-8959510

Type: transition

Compartments: cytosol



Selenoproteins are proteins that incorporate the nonstandard amino acid selenocysteine (Sec) in response to the UGA codon. Sec is synthesised in several steps from hydrogen selenide (H2Se), an intermediate formed from dietary sources of selenium. In the first step, cytosolic selenide water dikinase 2 (SEPHS2 aka SPS2) mediates the phosphorylation of H2Se using ATP as the phosphate donor, forming selenophosphate (SELP) (Tamura et al. 2004).

Literature references

Stadtman, TC., Tamura, T., Sakaguchi, H., Takahata, M., Tanaka, H., Yamamoto, S. et al. (2004). Selenophosphate synthetase genes from lung adenocarcinoma cells: Sps1 for recycling L-selenocysteine and Sps2 for selenite assimilation. *Proc. Natl. Acad. Sci. U.S.A., 101*, 16162-7. ↗

Editions

2017-01-26	Authored, Edited	Jassal, B.
2017-01-30	Reviewed	D'Eustachio, P.

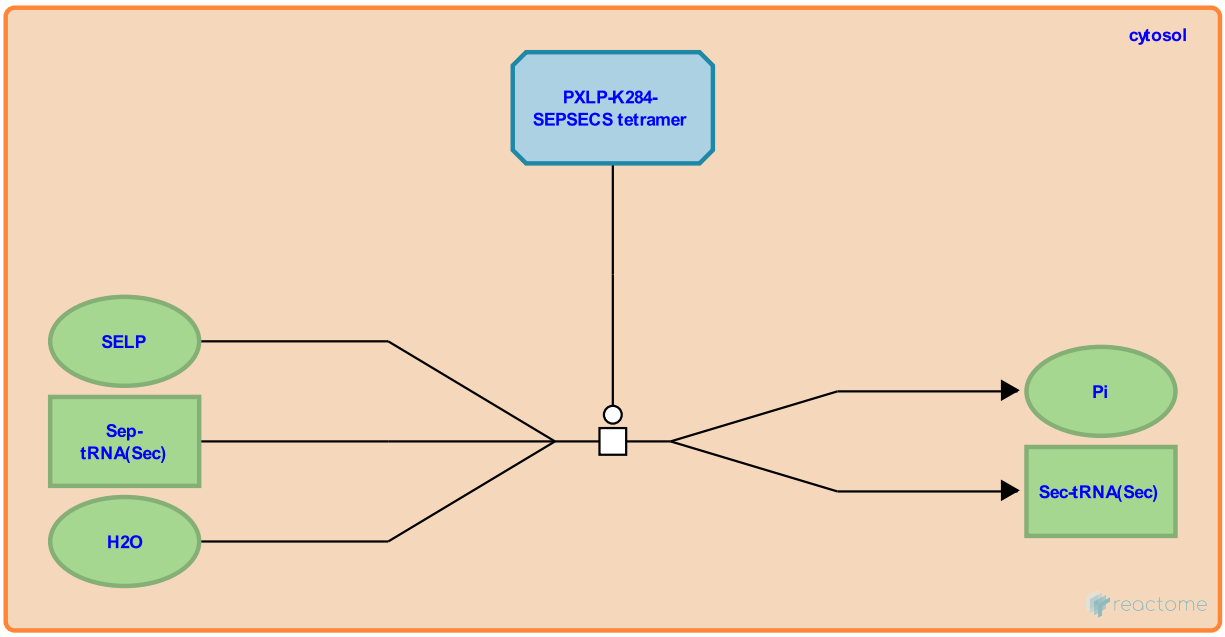
Sep-tRNA(Sec) is converted to Sec-tRNA(Sec) by PXLP-K284-SEPSECS tetramer ↗

Location: Selenocysteine synthesis

Stable identifier: R-HSA-2408555

Type: transition

Compartments: cytosol



O-phosphoseryl-tRNA(Sec) selenium transferase (SEPSECS) tetramer catalyses the transformation of phosphoserine (Sep) into selenocysteine (Sec) by using selenophosphate (SELP) as a selenium donor to convert the phosphoserylated transfer RNA (tRNA) for Sec (Sep-tRNASec) into Sec-tRNASec (Palioura et al. 2009, Yuan et al. 2006).

Preceded by: Ser-tRNA(Sec) is phosphorylated to Sep-tRNA(Sec) by PSTK

Followed by: Sec-tRNA(Sec) binds to EEFSEC:GTP

Literature references

Palioura, S., Cardoso, AM., Salazar, JC., Yuan, J., Whitman, WB., Su, D. et al. (2006). RNA-dependent conversion of phosphoserine forms selenocysteine in eukaryotes and archaea. *Proc. Natl. Acad. Sci. U.S.A., 103*, 18923-7. ↗

Palioura, S., Sherrer, RL., Steitz, TA., Simonovic, M., Söll, D. (2009). The human SepSecS-tRNASec complex reveals the mechanism of selenocysteine formation. *Science, 325*, 321-5. ↗

Editions

2014-05-06	Authored	Williams, MG.
2015-08-29	Edited	D'Eustachio, P.
2015-08-30	Reviewed	Rush, MG.

Sec-tRNA(Sec) binds to EEFSEC:GTP ↗

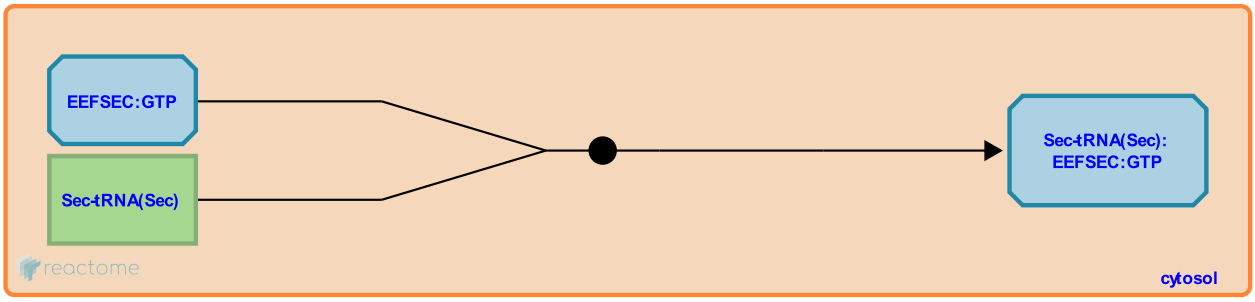
Location: Selenocysteine synthesis

Stable identifier: R-HSA-2408509

Type: binding

Compartments: cytosol

Inferred from: Sec-tRNA(Sec) binds to Eefsec:GTP (Mus musculus)



The final product, selenocysteinyl transfer RNA (tRNA) for Sec (Sec-tRNASec) binds to selenocysteine-specific elongation factor (EEFSEC) aka SelB complexed with GTP. This complex is now ready to be delivered to the 80S ribosome. This reaction is inferred from the equivalent reaction in mouse.

Preceded by: Sep-tRNA(Sec) is converted to Sec-tRNA(Sec) by PXLP-K284-SEPSECS tetramer

Followed by: Sec-tRNA(Sec):EEFSEC:GTP binds to 80S Ribosome

Literature references

Carlson, BA., Berry, MJ., Driscoll, DM., Tujebajeva, RM., Harney, JW., Hatfield, DL. et al. (2000). Decoding apparatus for eukaryotic selenocysteine insertion. *EMBO Rep., 1*, 158-63. ↗

Hubert, N., Yamada, K., Fagegaltier, D., Mizutani, T., Krol, A., Carbon, P. (2000). Characterization of mSelB, a novel mammalian elongation factor for selenoprotein translation. *EMBO J., 19*, 4796-805. ↗

Editions

2014-05-06	Authored	Williams, MG.
2015-08-29	Edited	D'Eustachio, P.
2015-08-30	Reviewed	Rush, MG.

Sec-tRNA(Sec):EEFSEC:GTP binds to 80S Ribosome

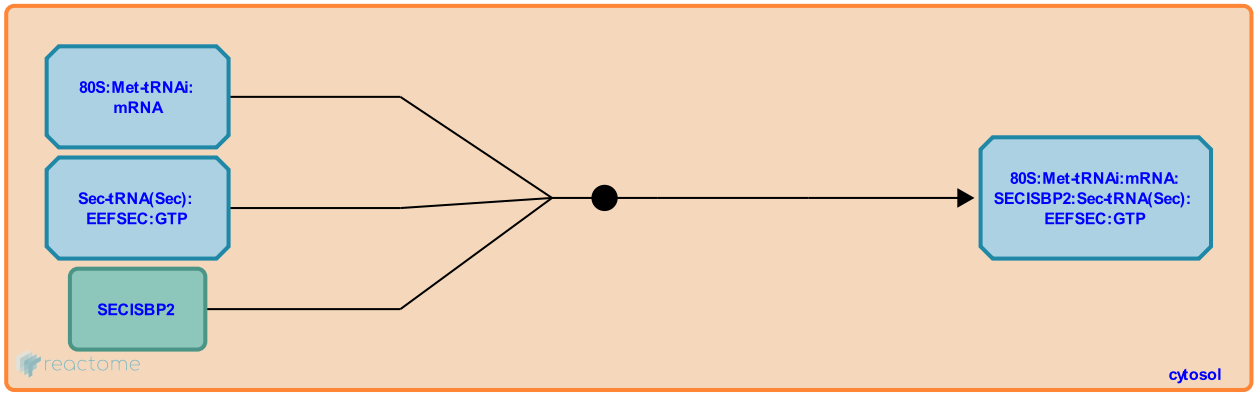
Location: Selenocysteine synthesis

Stable identifier: R-HSA-2408529

Type: binding

Compartments: cytosol

Inferred from: Sec-tRNA(Sec):Eefsec:GTP binds to Rpl30 (Rattus norvegicus)



The complex consisting of selenocysteinyl (Sec) transfer RNA (tRNA) for Sec (Sec-tRNASec), selenocysteine-specific elongation factor (EEFSEC) aka SelB, selenocysteine insertion sequence-binding protein 2 (SECISBP2) aka SBP2 and GTP interacts with the 80S ribosomal protein complex (80S:Met-tRNAi:mRNA). This reaction is inferred from events occurring in rats.

Preceded by: Sec-tRNA(Sec) binds to EEFSEC:GTP

Followed by: 80S:Met-tRNAi:mRNA:SECISBP2:Sec-tRNA(Sec):EEFSEC:GTP is hydrolysed to 80S:Met-tRNAi:mRNA:SECISBP2:Sec and EEFSEC:GDP by EEFSEC

Literature references

Chavatte, L., Driscoll, DM., Brown, BA. (2005). Ribosomal protein L30 is a component of the UGA-selenocysteine re-coding machinery in eukaryotes. *Nat. Struct. Mol. Biol., 12*, 408-16.

Editions

2014-05-06	Authored	Williams, MG.
2015-08-29	Edited	D'Eustachio, P.
2015-08-30	Reviewed	Rush, MG.

80S:Met-tRNAi:mRNA:SECISBP2:Sec-tRNA(Sec):EEFSEC:GTP is hydrolysed to 80S:Met-tRNAi:mRNA:SECISBP2:Sec and EEFSEC:GDP by EEFSEC ↗

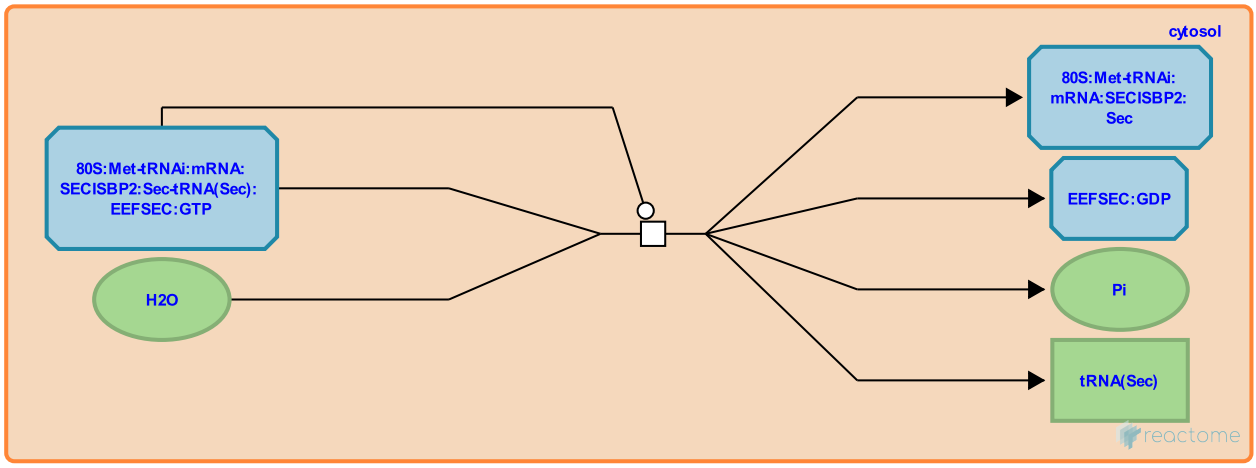
Location: Selenocysteine synthesis

Stable identifier: R-HSA-5333615

Type: transition

Compartments: cytosol

Inferred from: Rpl30:Met-tRNAi:mRNA:Secisbp2:Sec-tRNA(Sec):Eefsec:GTP is hydrolysed to Rpl30:Met-tRNAi:mRNA:Secisbp2:Sec and Eefsec:GDP by Eefsec (Rattus norvegicus)



The complex consisting of selenocysteinyl (Sec) transfer RNA (tRNA) for Sec (Sec-tRNASec), selenocysteine-specific elongation factor (EEFSEC) aka SelB, selenocysteine insertion sequence-binding protein 2 (SECISBP2) aka SBP2 and GTP interacts with the 80S ribosomal protein complex (80S:Met-tRNAi:mRNA). This triggers the hydrolysis of GTP (to GDP) by EEFSEC and delivery of Sec-tRNASec to the ribosomal A site. Before the Sec residue is inserted into the nascent polypeptide chain, EEFSEC:GDP is released. This reaction is inferred from events occurring in rats.

Preceded by: Sec-tRNA(Sec):EEFSEC:GTP binds to 80S Ribosome

Literature references

Chavatte, L., Driscoll, DM., Brown, BA. (2005). Ribosomal protein L30 is a component of the UGA-selenocysteine re-coding machinery in eukaryotes. *Nat. Struct. Mol. Biol., 12*, 408-16. ↗

Editions

2014-05-06	Authored	Williams, MG.
2015-08-29	Edited	D'Eustachio, P.
2015-08-30	Reviewed	Rush, MG.

Table of Contents