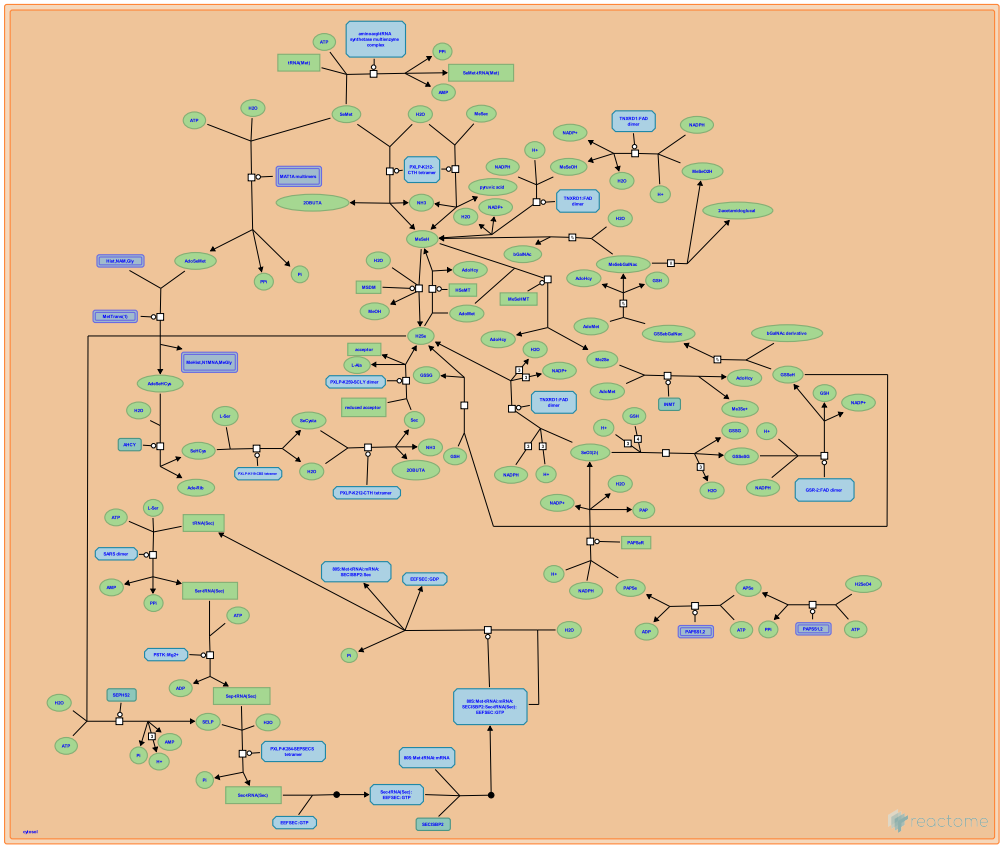
Selenoamino acid metabolism



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

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

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.

19/11/2024

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. ↗

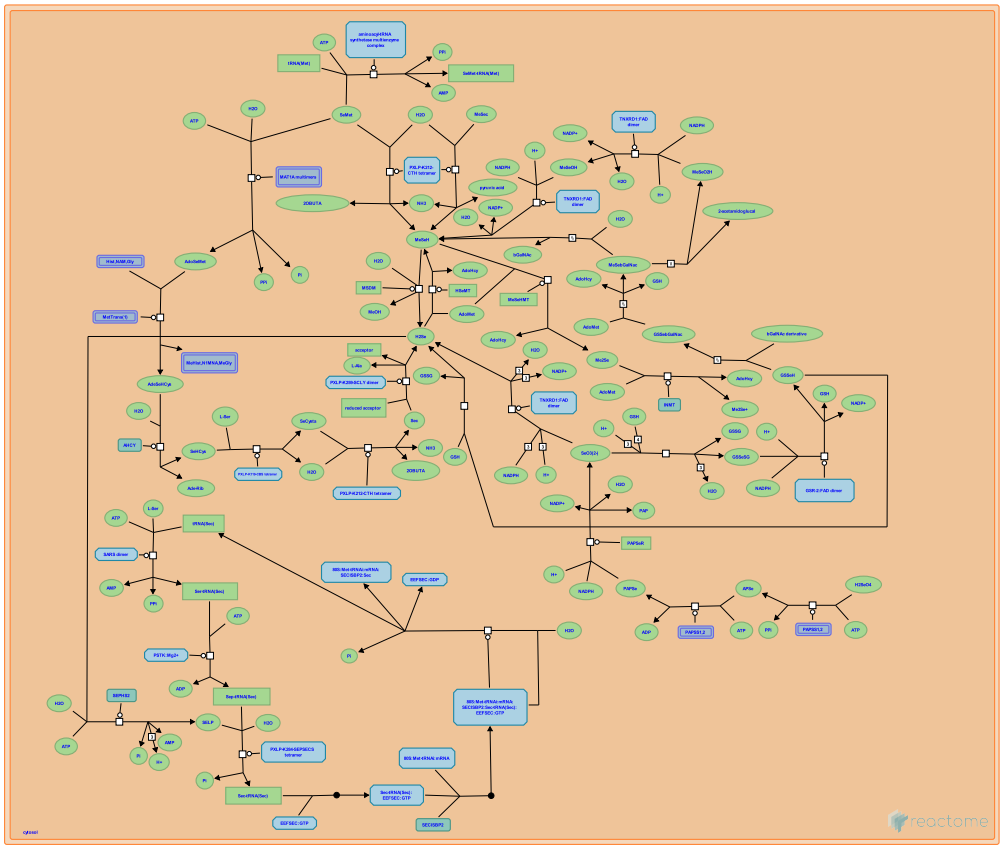
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Reactome database release: 90

This document contains 7 pathways and 1 reaction (see Table of Contents)

Selenoamino acid metabolism ↗

Stable identifier: R-HSA-2408522



Selenium (Se) is a trace element essential for the normal function of the body. Selenoamino acids are defined as those amino acids where selenium has been substituted for sulphur. Selenium and sulphur share many chemical properties and so the substitution of normal amino acids with selenoamino acids has little effect on protein structure and function. Both inorganic (selenite, SeO3(2-); and selenate, SeO4(2-)) and organic (selenocysteine, Sec; and selenomethionine, SeMet) forms of selenium can be introduced in the diet where they are transformed into the intermediate selenide (Se(2-)) and then utilized for the *de novo* synthesis of Sec through a phosphorylated intermediate in a tRNA-dependent fashion. The final step of Sec formation is catalyzed by O-phosphoseryl-tRNA:selenocysteinyl-tRNA synthase (SEPSECS) that converts phosphoseryl-tRNA(Sec) to selenocysteinyl-tRNA(Sec).

All nutritional selenium is metabolised into selenide directly or through methylselenol (MeSeH). Sec liberated from selenoproteins is transformed to Se(2-) by selenocysteine lyase (SCLY). SeMet liberated from general proteins and from free SeMet sources is transformed into Se(2-) either through MeSeH by cystathionine gamma-lyase (CTH) followed by demethylation (SeMet to CH3SeH to H2Se), or through Sec by SCLY after the trans-selenation pathway (SeMet to Sec to H2Se). MeSec is hydrolysed into MeSeH by CTH. Methylseleninic acid (MeSeO2H) is reduced to methylselenol. MeSeH is demethylated to Se(2-) for further utilization for selenoprotein synthesis or oxidised to selenite (SeO3(2-)) for excretion in the form of selenosugar. Additionally, MeSeH is further methylated to dimethylselenide (Me2Se) and trimethylselenonium (Me3Se+) for excretion.

Literature references

Broadley, MR., Bao, Y., Hurst, R., Collings, R., Fairweather-Tait, SJ., Hesketh, JE. et al. (2011). Selenium in human health and disease. *Antioxid. Redox Signal., 14*, 1337-83. ↗

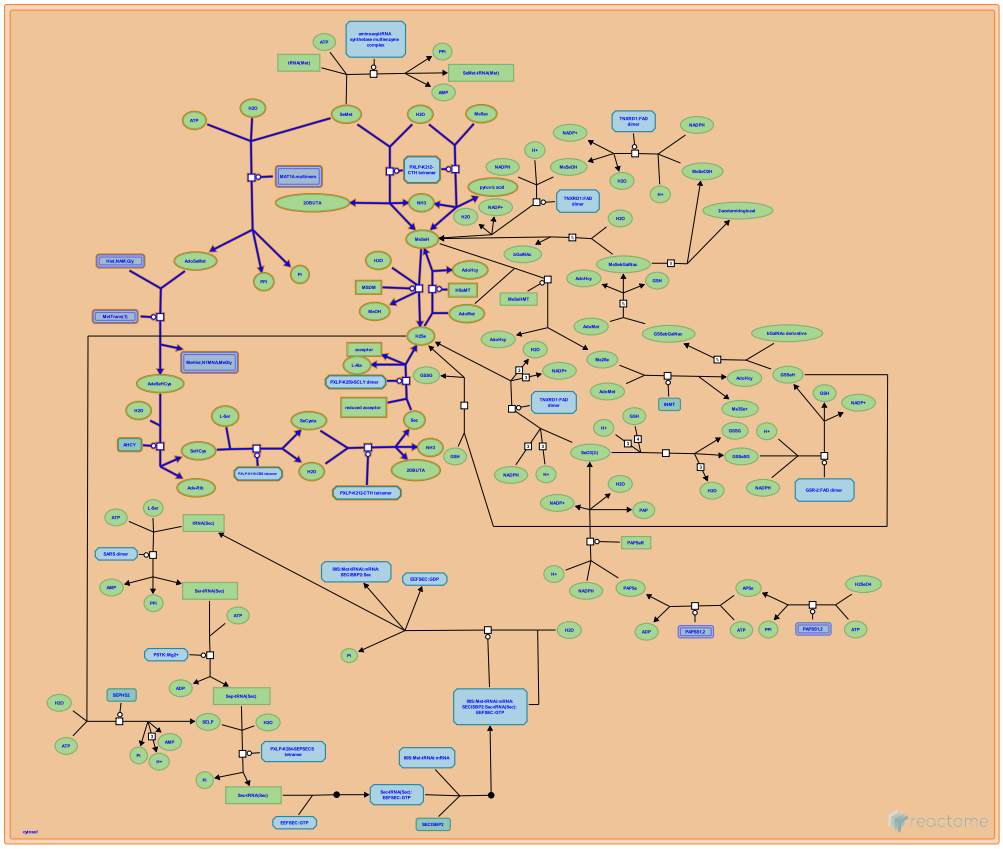
Editions

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

Metabolism of ingested SeMet, Sec, MeSec into H2Se ↗

Location: Selenoamino acid metabolism

Stable identifier: R-HSA-2408508



Inorganic (selenite, SeO3(2-); and selenate, SeO4(2-)) and organic (selenocysteine, Sec; and selenomethionine, SeMet) forms of selenium can introduced in the diet where they are transformed into the intermediate selenide (Se(2-)) through the trans-selenation pathway, selenocysteine lyase (SCLY), and cystathionine gamma-lyase (CTH).

Literature references

Esaki, N., Nakamura, T., Morino, Y., Soda, K., Tanaka, H., Suzuki, T. (1981). Enzymatic synthesis of selenocysteine in rat liver. *Biochemistry, 20*, 4492-6. ↗

Cooper, AJ., Sinha, R., Lee, JI., Pinto, JT., MacEwan, ME. (2011). Chemopreventive mechanisms of alpha-keto acid metabolites of naturally occurring organoselenium compounds. *Amino Acids, 41*, 29-41. ↗

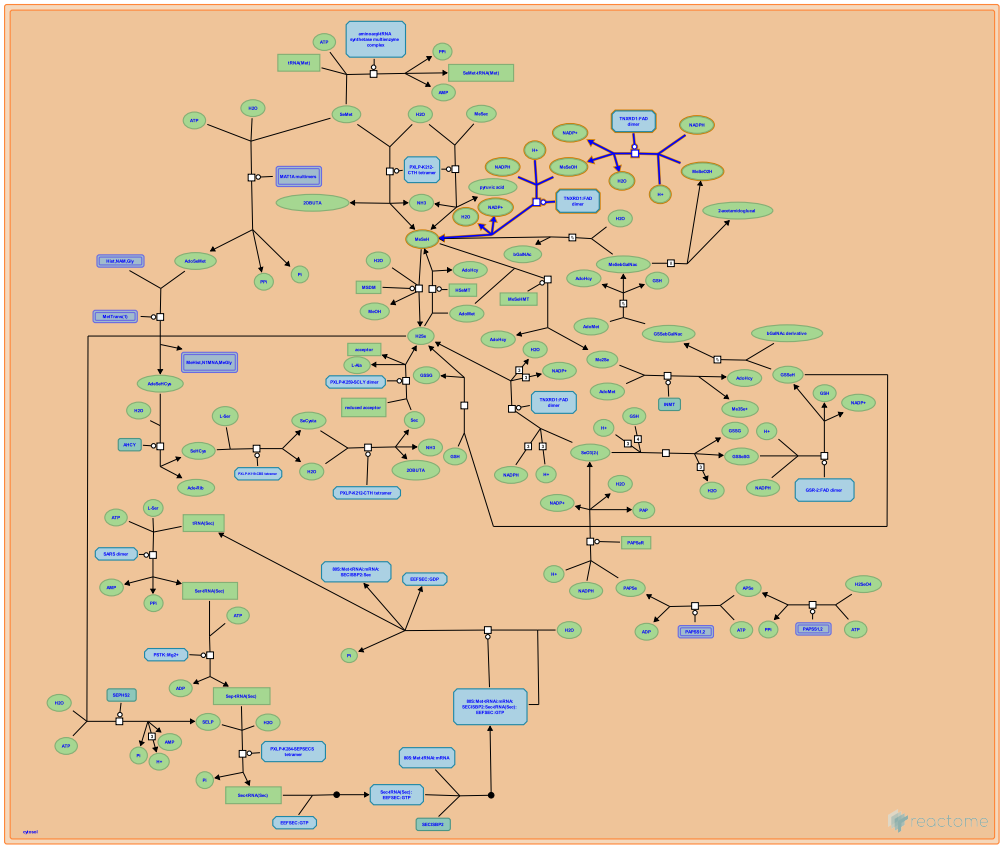
Editions

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

Metabolism of ingested MeSeO2H into MeSeH ↗

Location: Selenoamino acid metabolism

Stable identifier: R-HSA-5263617



Methylseleninic acid (MeSeO2H) is reduced to methylselenenic acid (MeSeOH) and then further reduced to methylselenol (MeSeH) by thioredoxin reductase (TXNRD1).

Literature references

Gross, JH., Gromer, S. (2002). Methylseleninate is a substrate rather than an inhibitor of mammalian thioredoxin reductase. Implications for the antitumor effects of selenium. *J. Biol. Chem., 277*, 9701-6. ↗

Lu, J., Berndt, C., Holmgren, A. (2009). Metabolism of selenium compounds catalyzed by the mammalian selenoprotein thioredoxin reductase. *Biochim. Biophys. Acta, 1790*, 1513-9. ↗

Editions

2014-05-06	Authored	Williams, MG.
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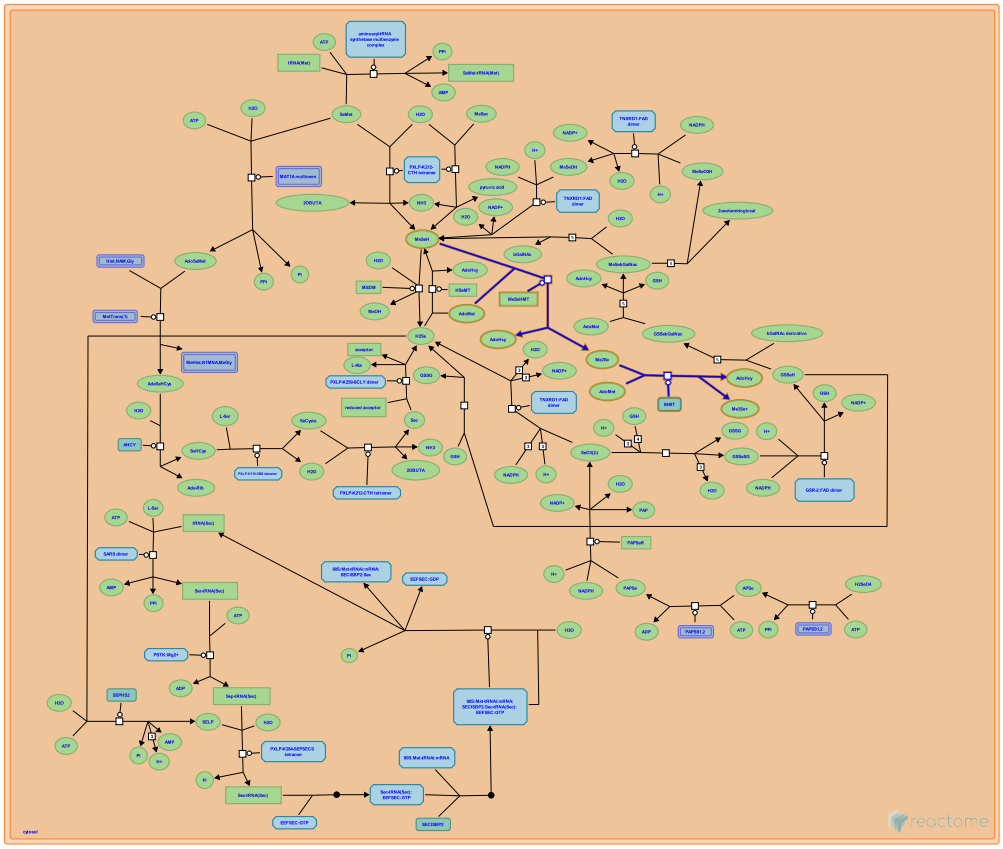
2015-08-30	Reviewed	Rush, MG.

Methylation of MeSeH for excretion ↗

Location: Selenoamino acid metabolism

Stable identifier: R-HSA-2408552



Methylselenol (MeSeH) is further methylated to dimethylselenide (Me2Se) and trimethylselenonium (Me3Se+) for excretion.

Literature references

Suzuki, KT., Ohta, Y. (2008). Methylation and demethylation of intermediates selenide and methylselenol in the metabolism of selenium. *Toxicol. Appl. Pharmacol., 226*, 169-77. ↗

Editions

2014-05-06	Authored	Williams, MG.
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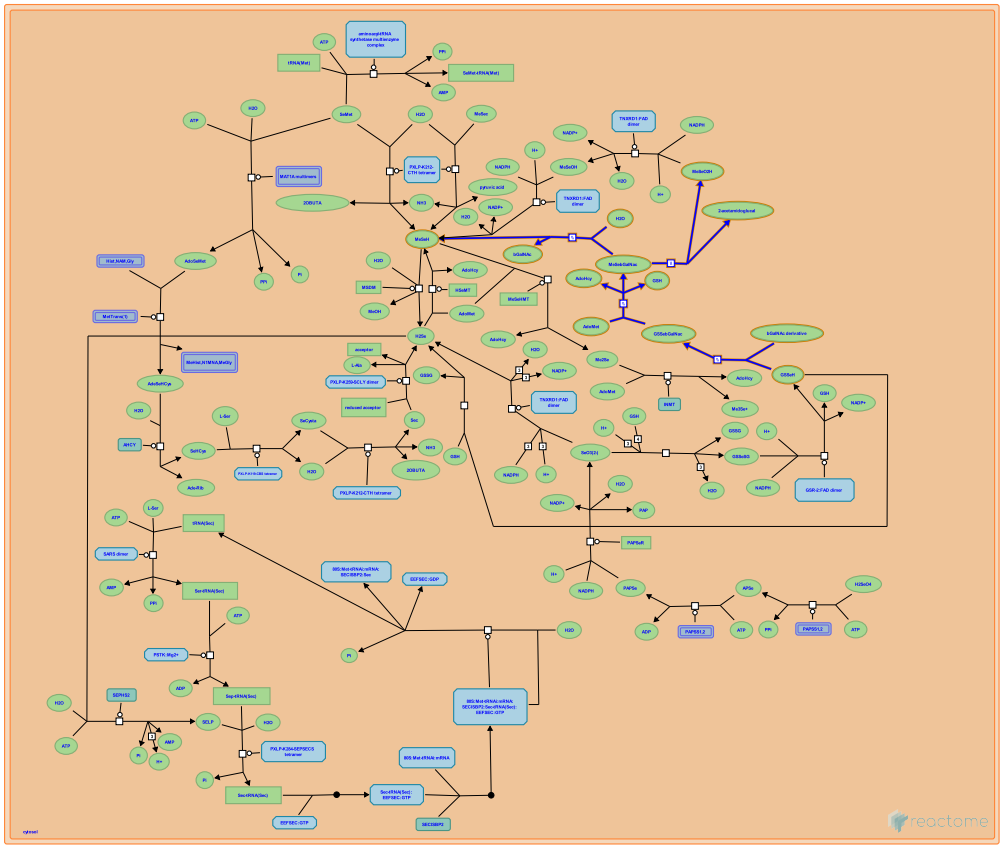
2015-08-30	Reviewed	Rush, MG.

Formation of selenosugars for excretion ↗

Location: Selenoamino acid metabolism

Stable identifier: R-HSA-2408499



Selenite (SeO3(2-)), potentially formed from oxidised H2Se, combines with glutathione (GSH) and 1beta-methylseleno-N-acetyl-D-galactosamine derivative to form selonosugars which are further metabolised and then excreted.

Literature references

Suzuki, KT., Suzuki, N., Somekawa, L. (2006). Distribution and reuse of 76Se-selenosugar in selenium-deficient rats. *Toxicol. Appl. Pharmacol., 216,* 303-8. ↗

Kobayashi, Y., Suzuki, KT., Ogra, Y., Takayama, H., Aimi, N., Ishiwata, K. (2002). Selenosugars are key and urinary metabolites for selenium excretion within the required to low-toxic range. *Proc. Natl. Acad. Sci. U.S.A., 99,* 15932-6. ↗

Editions

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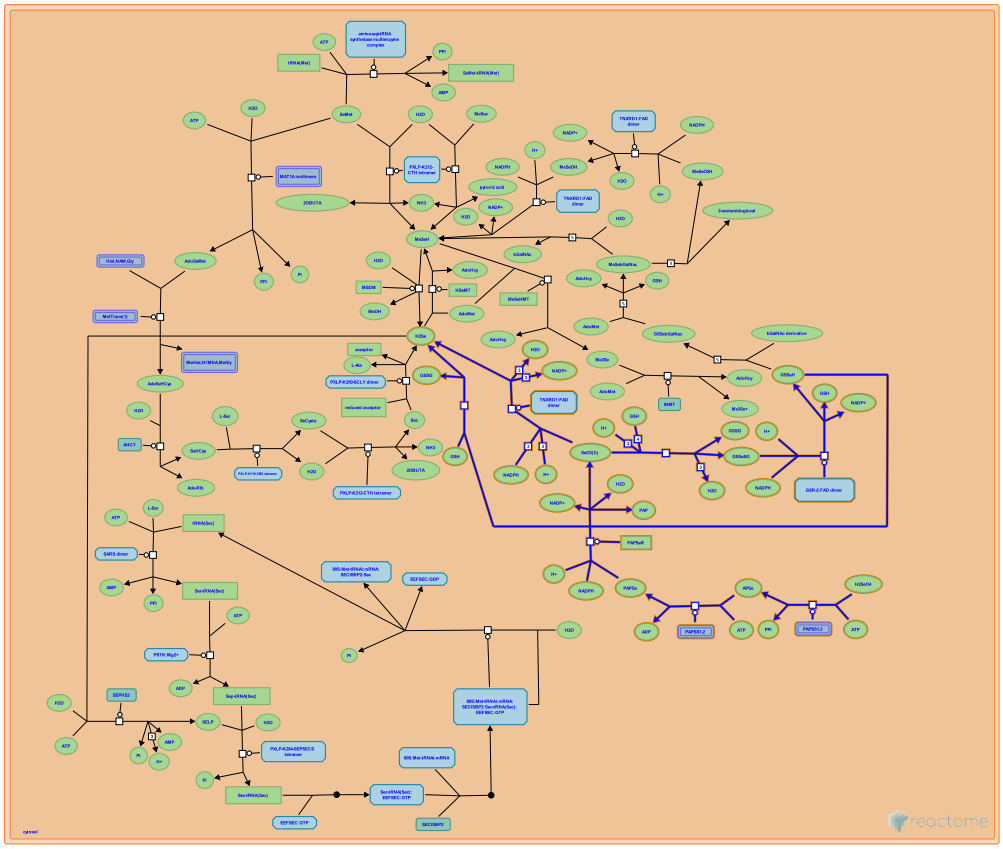
2015-08-29	Edited	D'Eustachio, P.
2015-08-30	Reviewed	Rush, MG.

Metabolism of ingested H2SeO4 and H2SeO3 into H2Se ↗

Location: Selenoamino acid metabolism

Stable identifier: R-HSA-2408550



Ingested selenic acid (H2SeO4) and selenite (SeO3(2-)) are reduced to hydrogen selenide (H2Se) through a combination of actions involving bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase 1 and 2 (PAPSS1/2), PAPSe reductase (PAPSeR), and thioredoxin reductase 1 (TXNRD1).

Literature references

Lu, J., Berndt, C., Holmgren, A. (2009). Metabolism of selenium compounds catalyzed by the mammalian selenoprotein thioredoxin reductase. *Biochim. Biophys. Acta, 1790*, 1513-9. ↗

Editions

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tRNA(Met) is selenomethionylated to SeMet-tRNA(Met) by multisynthetase complex ↗

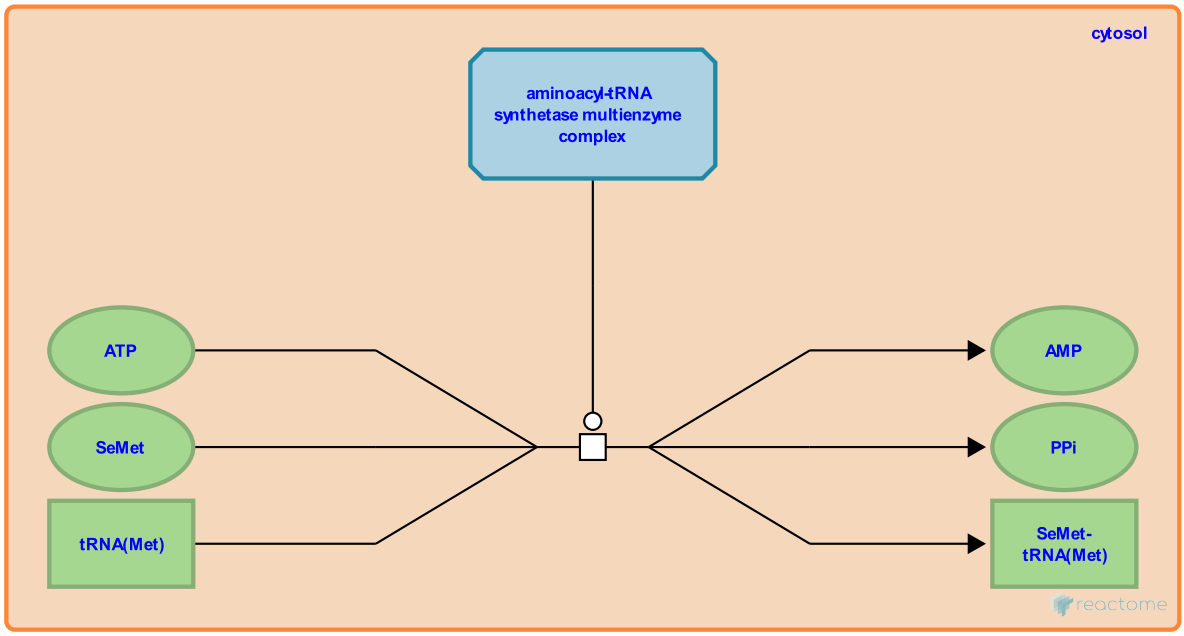
Location: Selenoamino acid metabolism

Stable identifier: R-HSA-2408546

Type: transition

Compartments: cytosol

Inferred from: tRNA(Met) is selenomethionylated to SeMet-tRNA(Met) by Mars (Vigna radiata var. radiata), tRNA(Met) is selenomethionylated to SeMet-tRNA(Met) by Mars (Triticum aestivum)



As a first step in the incorporation of selenomethionine into proteins, tRNA(Met) is converted into selenomethionyl-tRNA(Met) (SeMet-tRNA(Met)) by methionine-tRNA ligase (MARS) component of a multisynthetase complex comprised of a bifunctional glutamyl-prolyl-tRNA synthetase, the monospecific isoleucyl, leucyl, glutaminyl, methionyl, lysyl, arginyl, and aspartyl-tRNA synthetases as well as three auxiliary proteins, p18, p48 and p43. It is involved in the selenomethionylation of tRNA(Met) into selenomethionyl-tRNA(Met) (SeMet-tRNA(Met)). This reaction is inferred from the event in mung bean (Burnell 1981) and in wheat germ (Eustice et al. 1981).

Literature references

Kull, FJ., Eustice, DC., Shrift, A. (1981). Selenium toxicity: aminoacylation and Peptide bond formation with selenomethionine. *Plant Physiol., 67*, 1054-8. ↗

Burnell, JN. (1981). Methionyl-tRNA Synthetase from Phaseolus aureus: Purification and Properties. *Plant Physiol., 67* , 325-9. ↗

Editions

2014-05-06	Authored	Williams, MG.
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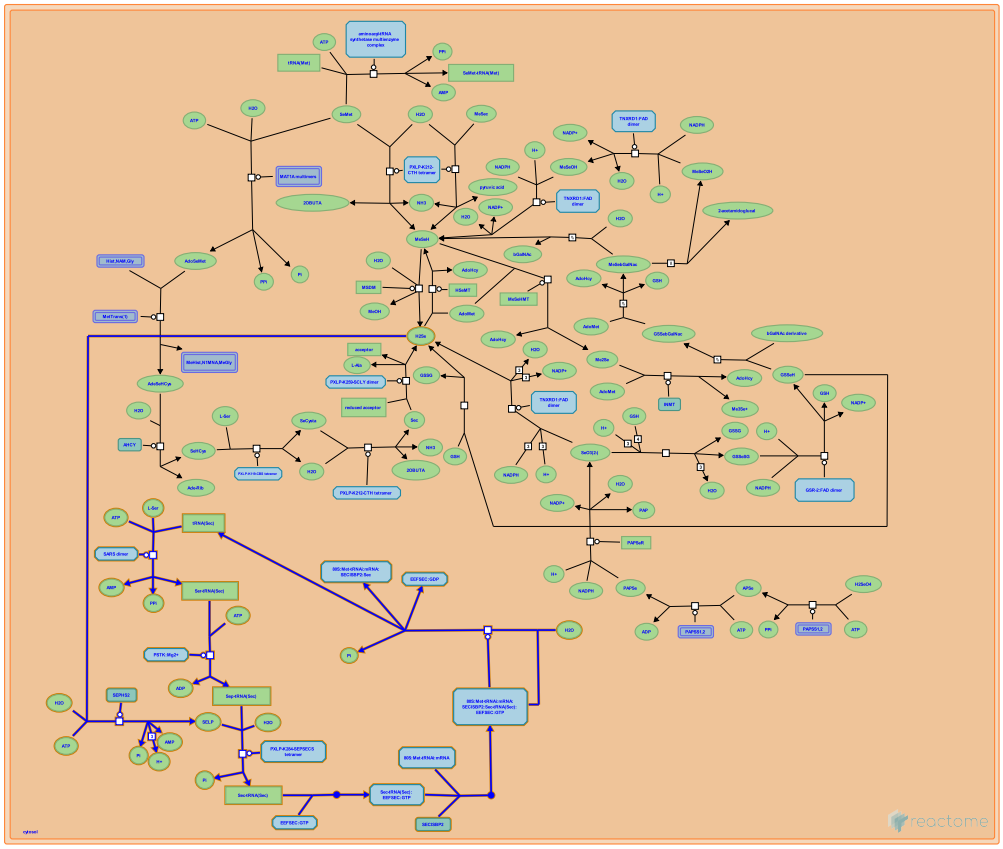
Selenocysteine synthesis ↗

Location: Selenoamino acid metabolism

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. ↗

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2014-05-06	Authored	Williams, MG.
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