Selenoamino acid metabolism

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


Reactome database release: 67

This document contains 8 pathways (see Table of Contents)

https://www.reactome.org
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

### Editions

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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-)) through the trans-selenation pathway, selenocysteine lyase (SCLY), and cystathionine gamma-lyase (CTH).

**Literature references**


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


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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


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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 selenosugars which are further metabolised and then excreted.

Literature references


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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).

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SeMet incorporation into proteins

Location: Selenoamino acid metabolism

Stable identifier: R-HSA-2408517

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.

Literature references


Editions

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

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