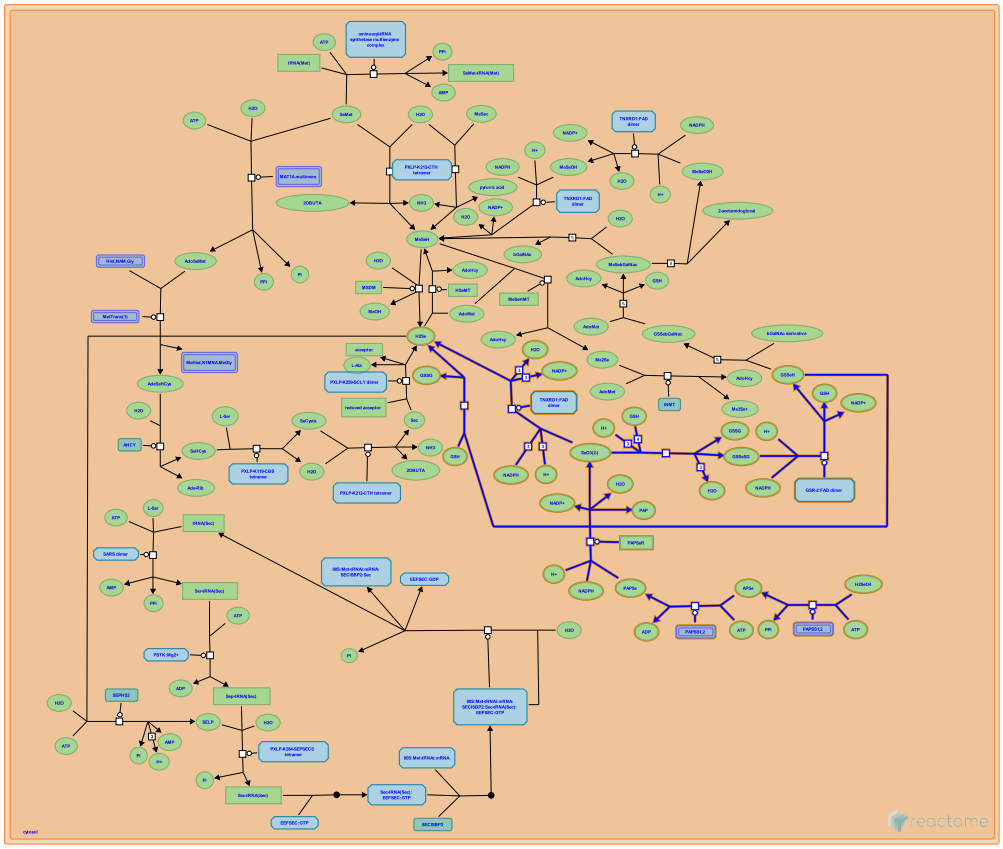
Metabolism of ingested H2SeO4 and H2SeO3 into H2Se



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.

21/05/2024

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. ↗

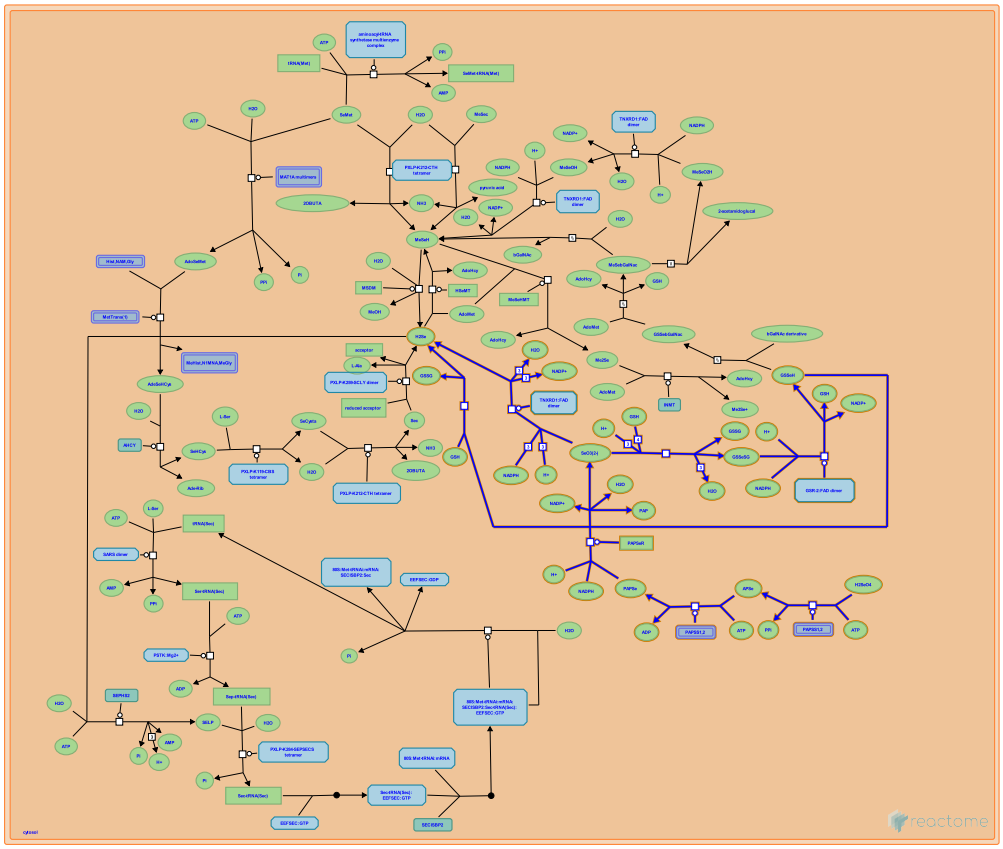
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Metabolism of ingested H2SeO4 and H2SeO3 into H2Se ↗

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

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

H2SeO4 is converted to APSe by PAPSS1,2 ↗

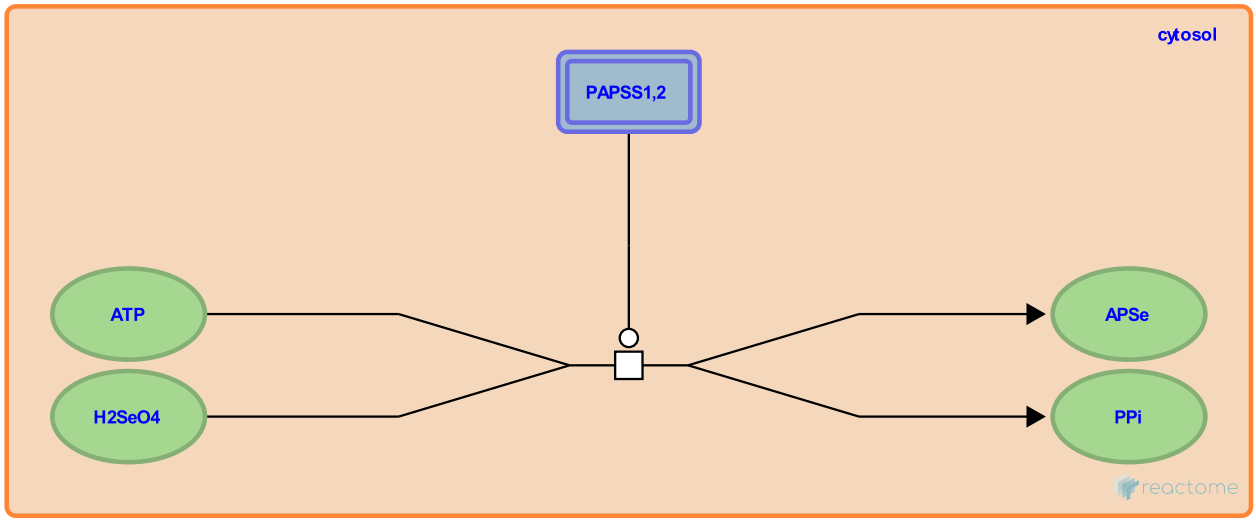
Location: Metabolism of ingested H2SeO4 and H2SeO3 into H2Se

Stable identifier: R-HSA-2408525

Type: transition

Compartments: cytosol

Inferred from: H2SeO4 is converted to APSe by PAPSS1,2 (Rattus norvegicus)



Bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthases 1 and 2 (PAPSS1,2) (Venkatachalam et al. 1998, Xu et al. 2000) are involved in transforming adenosine triphosphate (ATP) and selenic acid (H2SeO4) into adenylylselenate (APSe) and diphosphate via its ATP sulphurylase domain. This reaction is inferred from the event in rat (Yu et al. 1989).

Followed by: APSe is phosphorylated to PAPSe by PAPSS1,2

Literature references

Venkatachalam, KV., Akita, H., Strott, CA. (1998). Molecular cloning, expression, and characterization of human bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase and its functional domains. *J Biol Chem, 273*, 19311-20. ↗

Xu, JP., Kim, UJ., Freimuth, RR., Mitchell, S., Moon, E., Otterness, DM. et al. (2000). Human 3'-phosphoadenosine 5'-phosphosulfate synthetase 1 (PAPSS1) and PAPSS2: gene cloning, characterization and chromosomal localization . *Biochem. Biophys. Res. Commun., 268*, 437-44. ↗

Chen, LJ., Segel, IH., Yu, M., Martin, RL., Jain, S. (1989). Rat liver ATP-sulfurylase: purification, kinetic characterization, and interaction with arsenate, selenate, phosphate, and other inorganic oxyanions. *Arch. Biochem. Biophys., 269*, 156-74. ↗

Editions

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

APSe is phosphorylated to PAPSe by PAPSS1,2 ↗

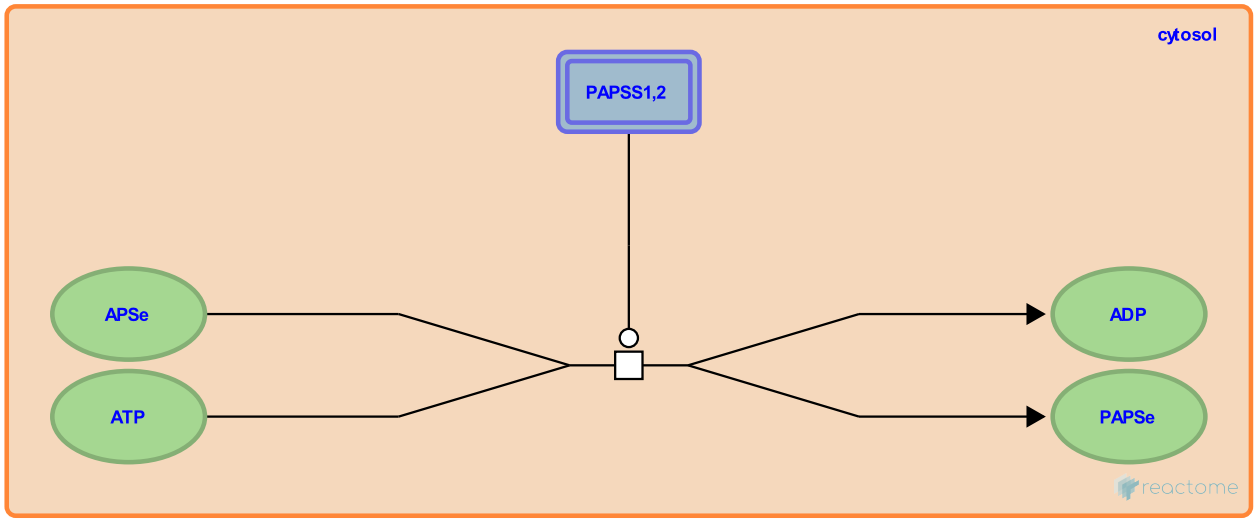
Location: Metabolism of ingested H2SeO4 and H2SeO3 into H2Se

Stable identifier: R-HSA-2408540

Type: transition

Compartments: cytosol

Inferred from: APSe is phosphorylated to PAPSe by Kaps (Penicillium chrysogenum)



Bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthases 1 and 2 (PAPSS1,2) (Venkatachalam et al. 1998, Xu et al. 2000) are involved in phosphorylating adenylylselenate (APSe) into 3'-phosphoadenylyl selenate (PAPSe) via its APS kinase domain. This reaction is inferred from the event in Penicillium chrysogenum involving APS kinase (Kaps) (Yu et al. 1989).

Preceded by: H2SeO4 is converted to APSe by PAPSS1,2

Followed by: PAPSe is reduced to SeO3(2-) by PAPSe reductase

Literature references

Venkatachalam, KV., Akita, H., Strott, CA. (1998). Molecular cloning, expression, and characterization of human bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase and its functional domains. *J Biol Chem, 273*, 19311-20. ↗

Xu, JP., Kim, UJ., Freimuth, RR., Mitchell, S., Moon, E., Otterness, DM. et al. (2000). Human 3'-phosphoadenosine 5'-phosphosulfate synthetase 1 (PAPSS1) and PAPSS2: gene cloning, characterization and chromosomal localization . *Biochem. Biophys. Res. Commun., 268*, 437-44. ↗

Chen, LJ., Segel, IH., Yu, M., Martin, RL., Jain, S. (1989). Rat liver ATP-sulfurylase: purification, kinetic characterization, and interaction with arsenate, selenate, phosphate, and other inorganic oxyanions. *Arch. Biochem. Biophys., 269*, 156-74. ↗

Editions

2014-05-06	Authored	Williams, MG.
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PAPSe is reduced to SeO3(2-) by PAPSe reductase ↗

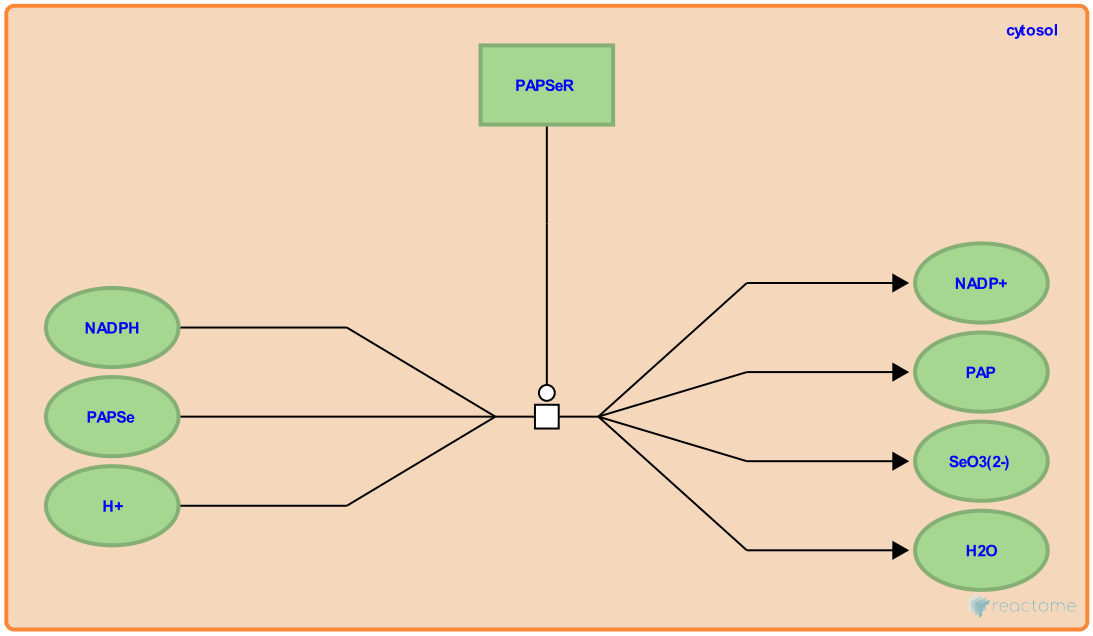
Location: Metabolism of ingested H2SeO4 and H2SeO3 into H2Se

Stable identifier: R-HSA-2408548

Type: transition

Compartments: cytosol

Inferred from: PAPSe is reduced to SeO3(2-) by MET16 (Saccharomyces cerevisiae)



A yet to be identified enzyme with 3'-phosphoadenylyl selenate reductase (PAPSeR) activity is involved in the reduction of 3'-phosphoadenylyl selenate (PAPSe) into selenite (SeO3(2-)) and adenosine 3',5'-bismonophosphate (PAP). This reaction is inferred from the event in yeast (Banszky et al. 2003).

Preceded by: APSe is phosphorylated to PAPSe by PAPSS1,2

Followed by: SeO3(2-) is reduced to H2Se by TXNRD1, SeO3(2-) combines with GSH to form GSSeSG and GSSG

Literature references

Bánszky, L., Maráz, A., Simonics, T. (2003). Sulphate metabolism of selenate-resistant Schizosaccharomyces pombe mutants. *J. Gen. Appl. Microbiol., 49*, 271-8. ↗

Editions

2014-05-06	Authored	Williams, MG.
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SeO3(2-) is reduced to H2Se by TXNRD1 ↗

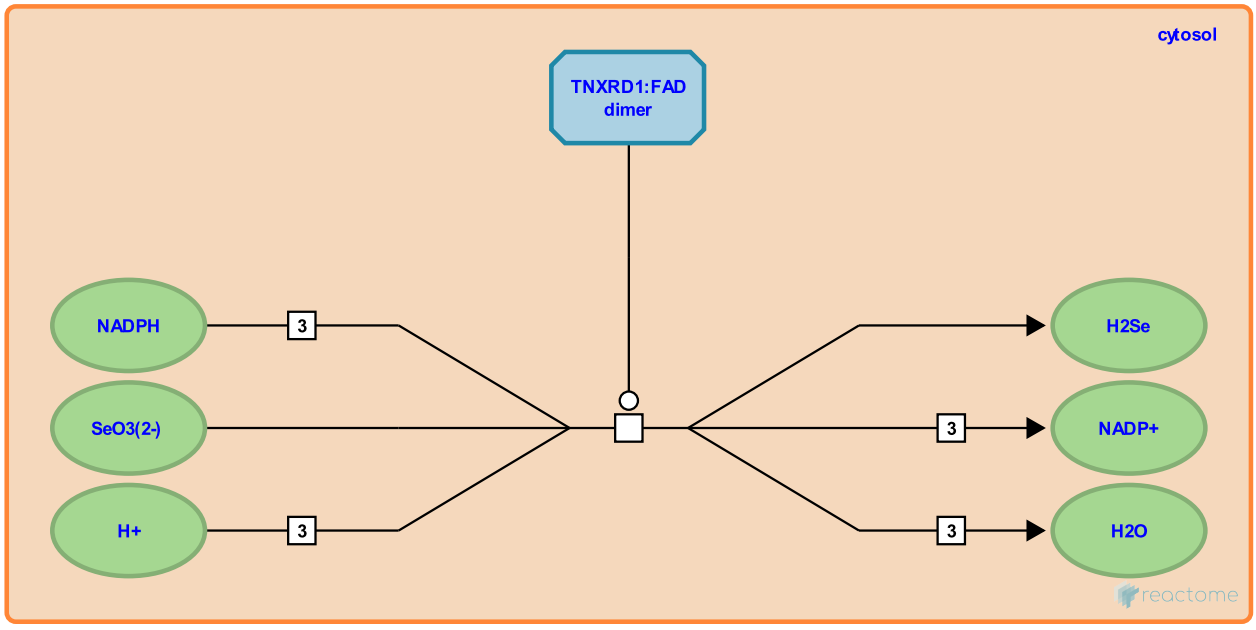
Location: Metabolism of ingested H2SeO4 and H2SeO3 into H2Se

Stable identifier: R-HSA-2408558

Type: transition

Compartments: cytosol

Inferred from: SeO3(2-) is reduced to H2Se by TXNRD1 (Bos taurus)



Thioredoxin reductase 1 (TXNRD1) homodimer (Sun et al. 1999) is involved in the reduction of selenite (SeO3(2-)) into hydrogen selenide (H2Se). This reaction is inferred from the event in cow (Kumar et al. 1992).

Preceded by: PAPSe is reduced to SeO3(2-) by PAPSe reductase

Literature references

Björnstedt, M., Holmgren, A., Kumar, S. (1992). Selenite is a substrate for calf thymus thioredoxin reductase and thioredoxin and elicits a large non-stoichiometric oxidation of NADPH in the presence of oxygen. *Eur. J. Biochem. , 207*, 435-39. ↗

Jeang, KT., Zappacosta, F., Wu, Y., Sun, QA., Hatfield, DL., Lee, BJ. et al. (1999). Redox regulation of cell signaling by selenocysteine in mammalian thioredoxin reductases. *J. Biol. Chem., 274*, 24522-30. ↗

Editions

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

SeO3(2-) combines with GSH to form GSSeSG and GSSG ↗

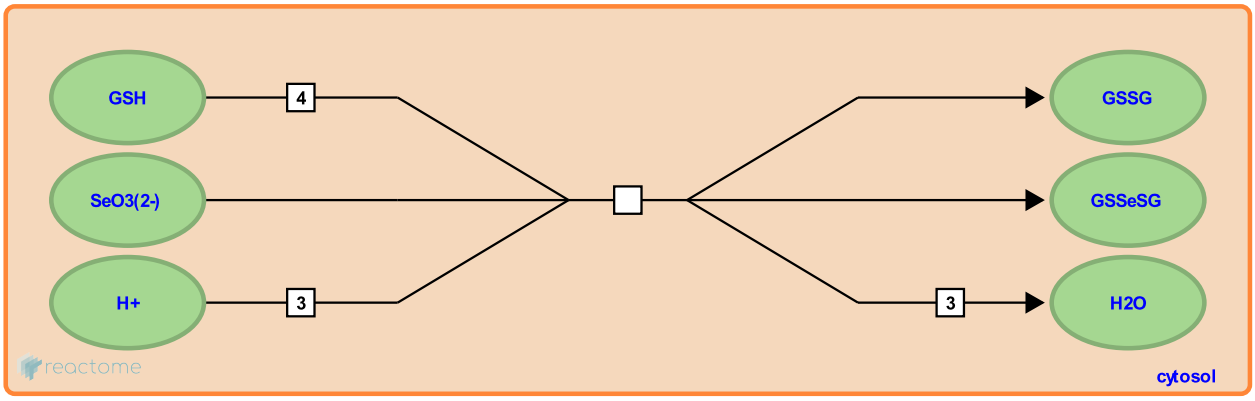
Location: Metabolism of ingested H2SeO4 and H2SeO3 into H2Se

Stable identifier: R-HSA-2408556

Type: transition

Compartments: cytosol

Inferred from: SeO3(2-) combines with GSH to form GSSeSG and GSSG (Rattus norvegicus)



Selenite (SeO3(2-)) and reduced glutathione (GSH) spontaneously react to form selenodiglutathione (GSSeSG) and glutathione disulfide (GSSG). This has been proposed to be the major form of entry of selenium compounds into metabolism. This reaction is inferred from the event in rat (Bjornstedt et al. 1992).

Preceded by: GSSeSG is reduced to GSSeH and GSH by GSR, PAPSe is reduced to SeO3(2-) by PAPSe reductase

Followed by: GSSeSG is reduced to GSSeH and GSH by GSR

Literature references

Björnstedt, M., Holmgren, A., Kumar, S. (1992). Selenodiglutathione is a highly efficient oxidant of reduced thioredoxin and a substrate for mammalian thioredoxin reductase. *J. Biol. Chem., 267*, 8030-4. ↗

Editions

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GSSeSG is reduced to GSSeH and GSH by GSR ↗

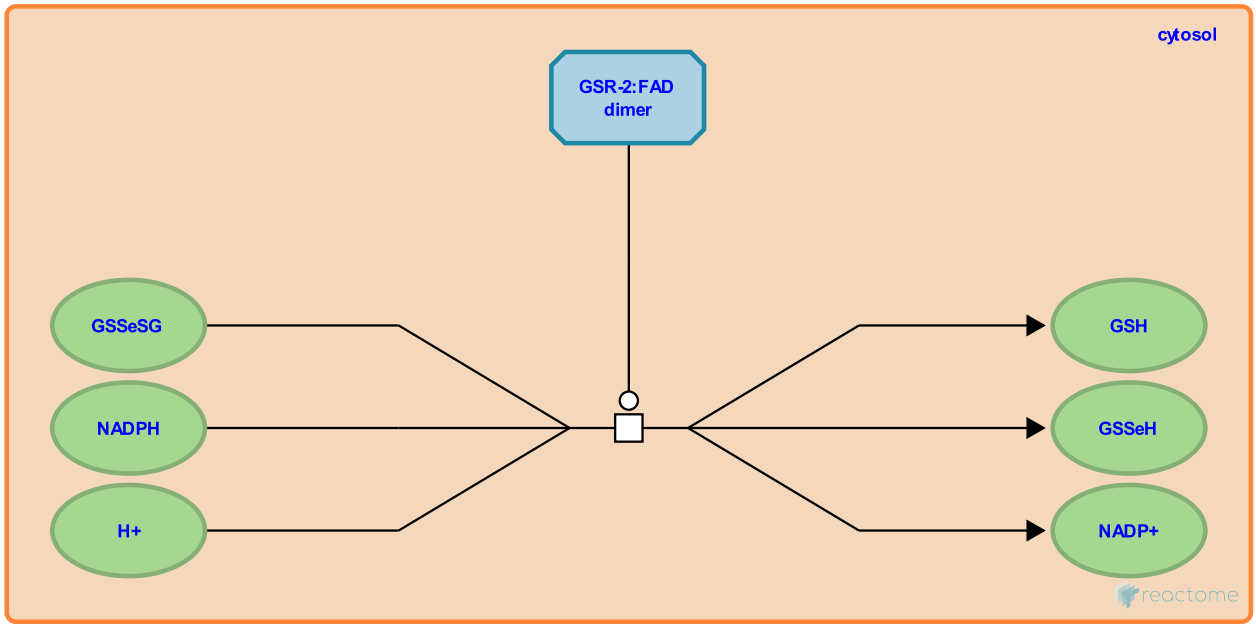
Location: Metabolism of ingested H2SeO4 and H2SeO3 into H2Se

Stable identifier: R-HSA-2408542

Type: transition

Compartments: cytosol

Inferred from: GSSeSG is reduced to GSSeH and GSH by Gsr (Rattus norvegicus)



Glutathione reductase (GSR) homodimer is involved in the reduction of selenodiglutathione (GSSeSG) into gluthathioselenol (GSSeH) and reduced glutathione (GSH). This reaction is inferred from the event in rat (Bjornstedt et al. 1992).

Preceded by: SeO3(2-) combines with GSH to form GSSeSG and GSSG

Followed by: GSSeH condenses with GSH to form H2Se and GSSG, SeO3(2-) combines with GSH to form GSSeSG and GSSG

Literature references

Björnstedt, M., Holmgren, A., Kumar, S. (1992). Selenodiglutathione is a highly efficient oxidant of reduced thioredoxin and a substrate for mammalian thioredoxin reductase. *J. Biol. Chem., 267*, 8030-4. ↗

Editions

2014-05-06	Authored	Williams, MG.
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GSSeH condenses with GSH to form H2Se and GSSG ↗

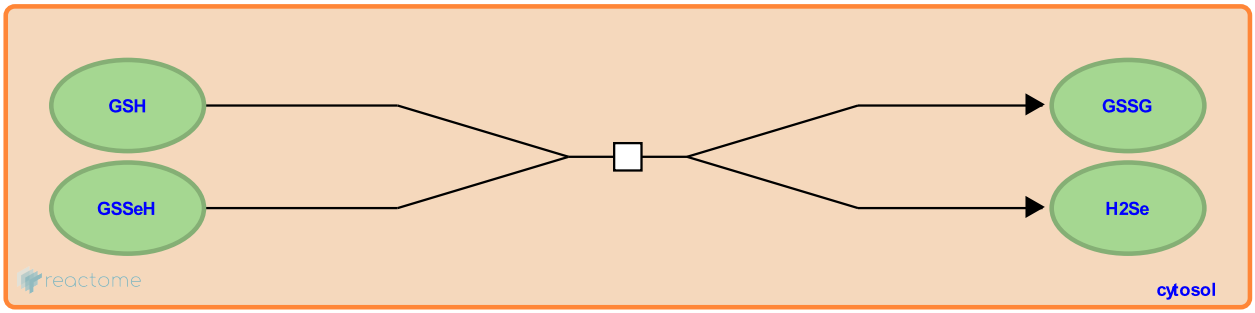
Location: Metabolism of ingested H2SeO4 and H2SeO3 into H2Se

Stable identifier: R-HSA-2408500

Type: transition

Compartments: cytosol

Inferred from: GSSeH condenses with GSH to form H2Se and GSSG (Rattus norvegicus)



Gluthathioselenol (GSSeH) and reduced glutathione (GSH) condense to form hydrogen selenide (H2Se) and glutathione disulfide (GSSG). This reaction is inferred from the event in rat (Bjornstedt et al. 1992).

Preceded by: GSSeSG is reduced to GSSeH and GSH by GSR

Literature references

Björnstedt, M., Holmgren, A., Kumar, S. (1992). Selenodiglutathione is a highly efficient oxidant of reduced thioredoxin and a substrate for mammalian thioredoxin reductase. *J. Biol. Chem., 267*, 8030-4. ↗

Editions

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

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