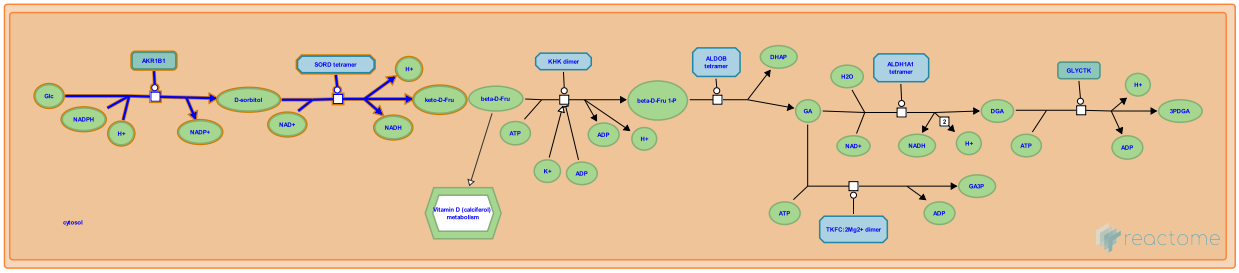
Fructose biosynthesis



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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. ↗

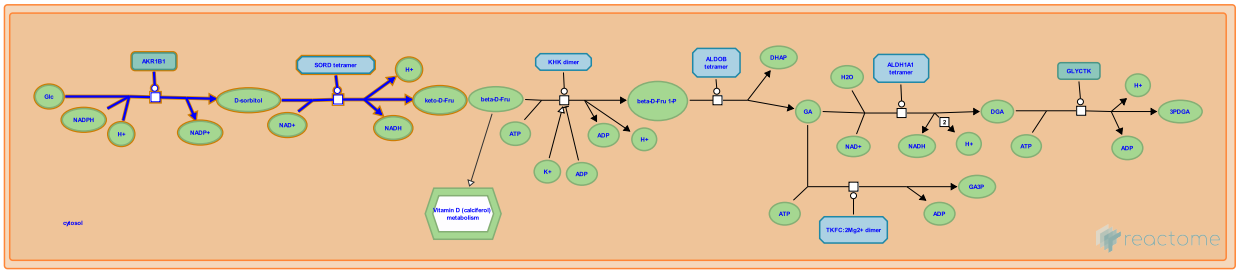
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Fructose biosynthesis ↗

Stable identifier: R-HSA-5652227



The conversion of glucose to fructose via sorbitol was demonstrated by Hers (1960) in the seminal vesicles of sheep, has since been demonstrated as well in human epididymal tissue (Frenette et al. 2006), and appears to be the physiological source of the abundant fructose found in seminal fluid. The enzymes of the pathway are likewise abundant in the eye lens and in neurons, where their physiological role is less clear but where they appear to play a central role in diabetic tissue damage (Oates 2008).

Literature references

Oates, PJ. (2008). Aldose reductase, still a compelling target for diabetic neuropathy. *Curr Drug Targets, 9*, 14-36. ↗

Hers, HG. (1960). [The mechanism of the formation of seminal fructose and fetal fructose]. *Biochim. Biophys. Acta, 37* , 127-38. ↗

Sullivan, R., Thabet, M., Frenette, G. (2006). Polyol pathway in human epididymis and semen. *J. Androl., 27*, 233-9. ↗

Editions

2014-11-29	Authored, Edited	D'Eustachio, P.
2015-01-29	Reviewed	Jassal, B.
2015-08-28	Authored	Ribeiro, JM., Cameselle, JC.

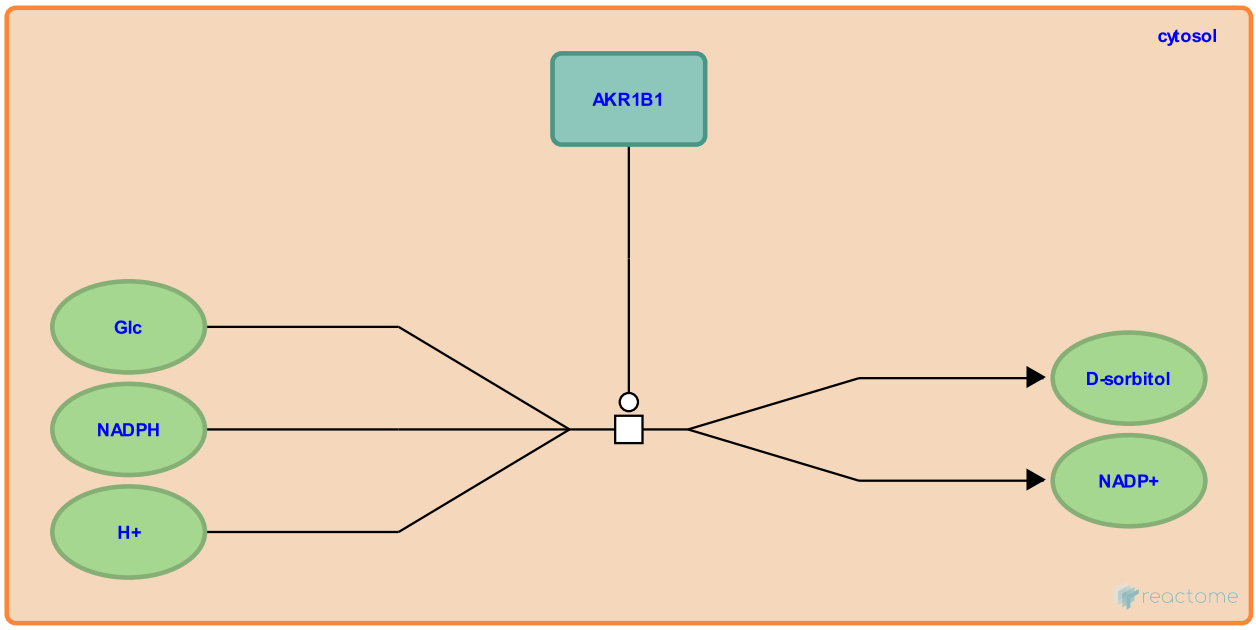
AKR1B1 reduces Glc to D-sorbitol ↗

Location: Fructose biosynthesis

Stable identifier: R-HSA-5652172

Type: transition

Compartments: cytosol



Cytosolic AKR1B1 (aldose reductase) catalyzes the reaction of glucose (Glc) and NADPH + H+ to form D-sorbitol and NADP+. This reaction was first described by Hers (1960) in sheep seminal vesicles; the human enzyme was identified by Nishimura et al. (1990) and is a potential target for treatment of diabetic neuropathy (Oates, 2008). The active enzyme is a monomer (Ruiz et al. 2004) whose amino-terminal methionine residue has been removed (Jacquinod et al. 1993). Under physiological conditions, formation of D-sorbitol is strongly favored (Grimshaw 1992).

Followed by: SORD oxidizes D-sorbitol to Fru

Literature references

Van Dorsselaer, A., Andriantomanga, V., Barth, P., Biellmann, JF., Kieffer, S., Reymann, JM. et al. (1993). Sequence of pig lens aldose reductase and electrospray mass spectrometry of non-covalent and covalent complexes. *Eur. J. Biochem., 218*, 893-903. ↗

Hers, HG. (1960). [Aldose reductase]. *Biochim. Biophys. Acta, 37*, 120-6. ↗

Grimshaw, CE. (1992). Aldose reductase: model for a new paradigm of enzymic perfection in detoxification catalysts. *Biochemistry, 31*, 10139-45. ↗

Oates, PJ. (2008). Aldose reductase, still a compelling target for diabetic neuropathy. *Curr Drug Targets, 9*, 14-36. ↗

Morjana, N., Carper, D., Flynn, TG., Kokai, Y., Lyons, C., Nishimura, C. et al. (1990). Cloning and expression of human aldose reductase. *J. Biol. Chem., 265*, 9788-92. ↗

Editions

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2015-01-29	Reviewed	Jassal, B.
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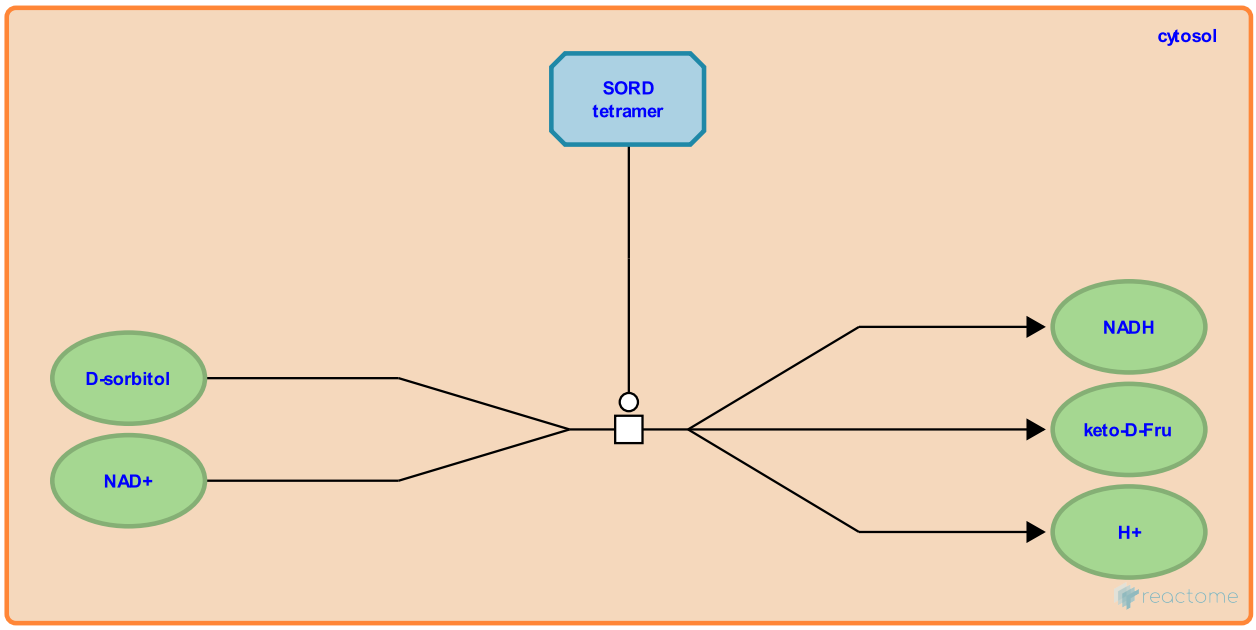
SORD oxidizes D-sorbitol to Fru ↗

Location: Fructose biosynthesis

Stable identifier: R-HSA-5652195

Type: transition

Compartments: cytosol



Cytosolic SORD (sorbitol dehydrogenase) catalyzes the reaction of D-sorbitol and NAD+ to form fructose (Fru) and NADH + H+. This reaction was first described by Hers (1960) in sheep seminal vesicles; the human enzyme was identified by O'Brien et al. (1983). The active enzyme is a tetramer with four associated Zn2+ ions (Pauly et al. 2003) whose amino-terminal methionine residue has been removed (Karlsson et al. 1989).

Preceded by: AKR1B1 reduces Glc to D-sorbitol

Literature references

Adams, PD., Cunningham, D., Kamath, A., Mcguire, D., Chrunyk, B., Madura, R. et al. (2003). X-ray crystallographic and kinetic studies of human sorbitol dehydrogenase. *Structure, 11*, 1071-85. ↗

Edwards, MR., Schofield, PJ., O'Brien, MM. (1983). Polyol-pathway enzymes of human brain. Partial purification and properties of sorbitol dehydrogenase. *Biochem. J., 211*, 81-90. ↗

Höög, JO., Karlsson, C., Jörnvall, H., Maret, W., Auld, DS. (1989). Variability within mammalian sorbitol dehydrogenases. The primary structure of the human liver enzyme. *Eur. J. Biochem., 186*, 543-50. ↗

Hers, HG. (1960). [The mechanism of the formation of seminal fructose and fetal fructose]. *Biochim. Biophys. Acta, 37* , 127-38. ↗

Editions

2014-11-29	Authored, Edited	D'Eustachio, P.
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2015-08-28	Authored	Ribeiro, JM., Cameselle, JC.
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