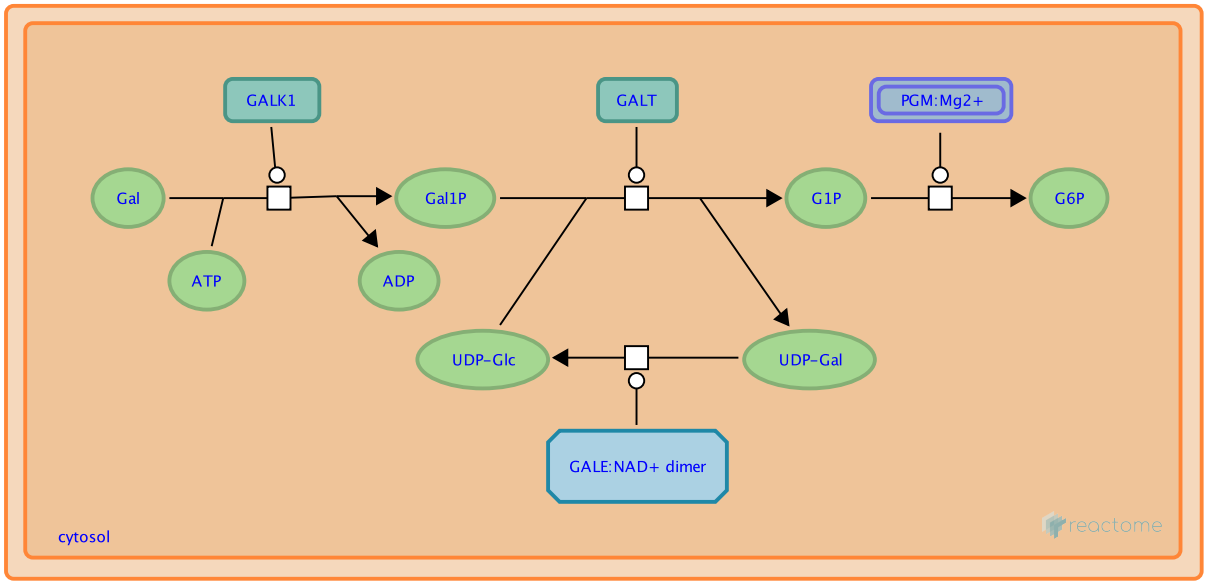
Galactose catabolism



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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.

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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. ↗

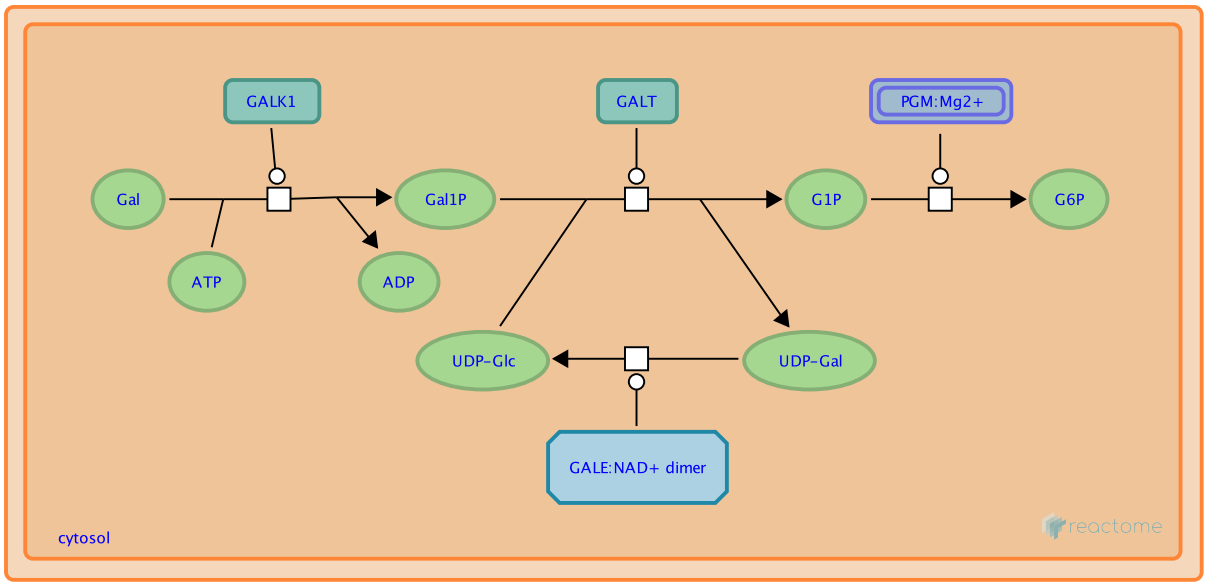
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Galactose catabolism ↗

Stable identifier: R-HSA-70370

Compartments: cytosol



The main sources of galactose in the human diet are milk and milk products. The disaccharide lactose from these sources is hydrolyzed in the intestine to its constituent monosaccharides, glucose and galactose. Galactose is metabolized primarily in the liver in a sequence of three reactions that yield one molecule of glucose 1-phosphate per molecule of galactose. First, it is phosphorylated to yield galactose 1-phosphate. Then, galactose 1-phosphate and UDP-glucose react to form UDP-galactose and glucose 1-phosphate, and UDP-galactose undergoes epimerization to form UDP-glucose. In a reaction shared with other pathways, glucose 1-phosphate can be converted into glucose 6-phosphate (Holton et al. 2001; Elsas and Lai 2001).

Literature references

Scriver, CR., Beaudet, AL., Sly, WS., Valle, D. (2001). Galactosemia, The Metabolic & Molecular Bases of Inherited Disease. *McGraw Hill*, 1553-1587.

Elsas, LJ., Lai, K. (2001). The molecular biology of galactosemia. *Genet Med, 1*, 40-8. ↗

Editions

2010-01-25	Revised	D'Eustachio, P.

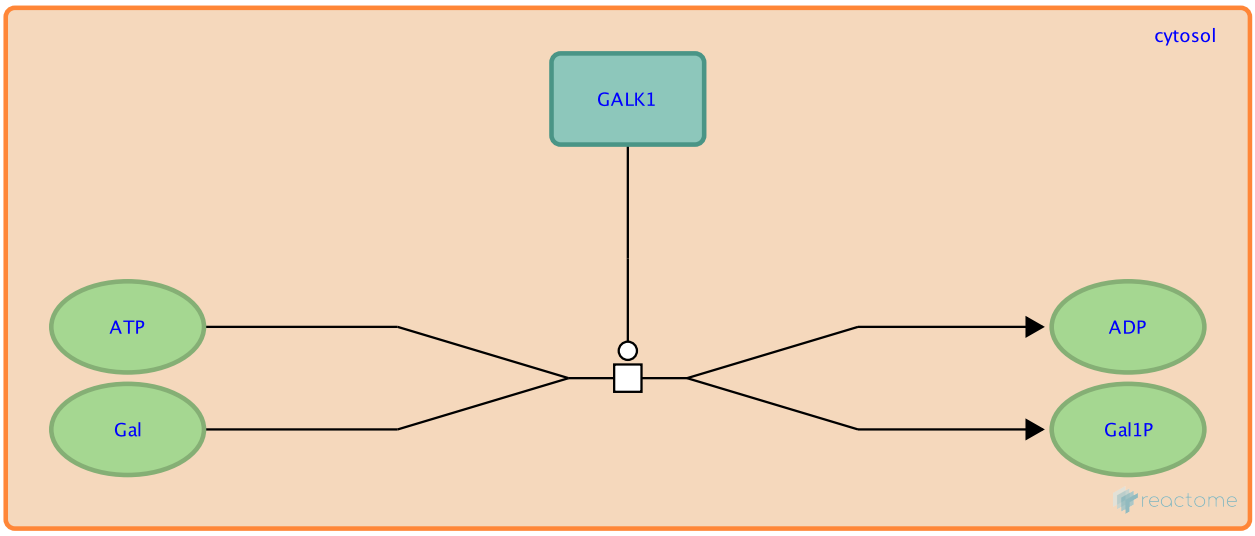
GALK1 phosphorylates Gal to Gal1P ↗

Location: Galactose catabolism

Stable identifier: R-HSA-70355

Type: transition

Compartments: cytosol



Cytosolic galactokinase (GALK1) catalyses the reaction of ATP and D-galactose to form ADP and D-galactose 1-phosphate (Ai at al. 1995).

Followed by: GALT transfers UMP from UDP-Glc to Gal1P to form UDP-Gal

Literature references

Ai, Y., Basu, M., Bergsma, DJ., Stambolian, D. (1995). Comparison of the enzymatic activities of human galactokinase GALK1 and a related human galactokinase protein GK2. *Biochem Biophys Res Commun, 212*, 687-91. ↗

Editions

2010-01-25	Revised	D'Eustachio, P.

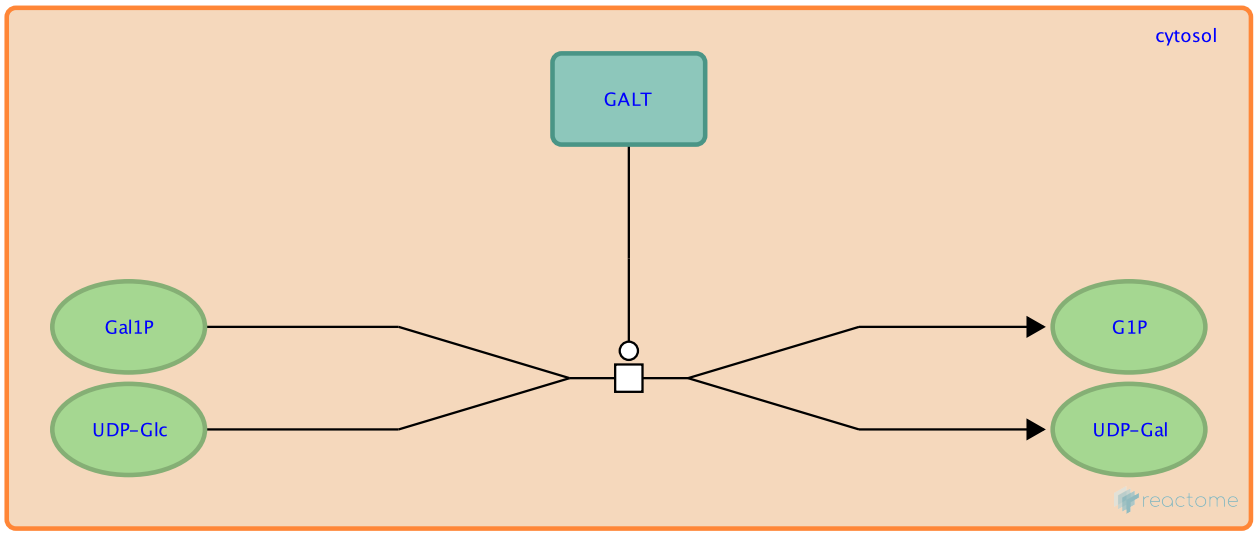
GALT transfers UMP from UDP-Glc to Gal1P to form UDP-Gal ↗

Location: Galactose catabolism

Stable identifier: R-HSA-70361

Type: transition

Compartments: cytosol



Cytosolic galactose-1-phosphate uridylyltransferase (GALT) catalyzes the reaction of alpha-D-galactose 1-phosphate and UDP glucose to form D-glucose 1-phosphate and UDP galactose (Reichardt & Woo 1991).

Preceded by: GALK1 phosphorylates Gal to Gal1P, GALE:NAD+ dimer reversibly epimerises UDP-Gal to UDP-Glc

Followed by: GALE:NAD+ dimer reversibly epimerises UDP-Gal to UDP-Glc, PGM:Mg2+ isomerise G1P to G6P

Literature references

Reichardt, JK., Packman, S., Woo, SL. (1991). Molecular characterization of two galactosemia mutations: correlation of mutations with highly conserved domains in galactose-1-phosphate uridyl transferase. *Am J Hum Genet, 49*, 860-7. ↗

Reichardt, JK., Woo, SL. (1991). Molecular basis of galactosemia: mutations and polymorphisms in the gene encoding human galactose-1-phosphate uridylyltransferase. *Proc. Natl. Acad. Sci. U.S.A., 88*, 2633-7. ↗

Editions

2010-01-25	Revised	D'Eustachio, P.

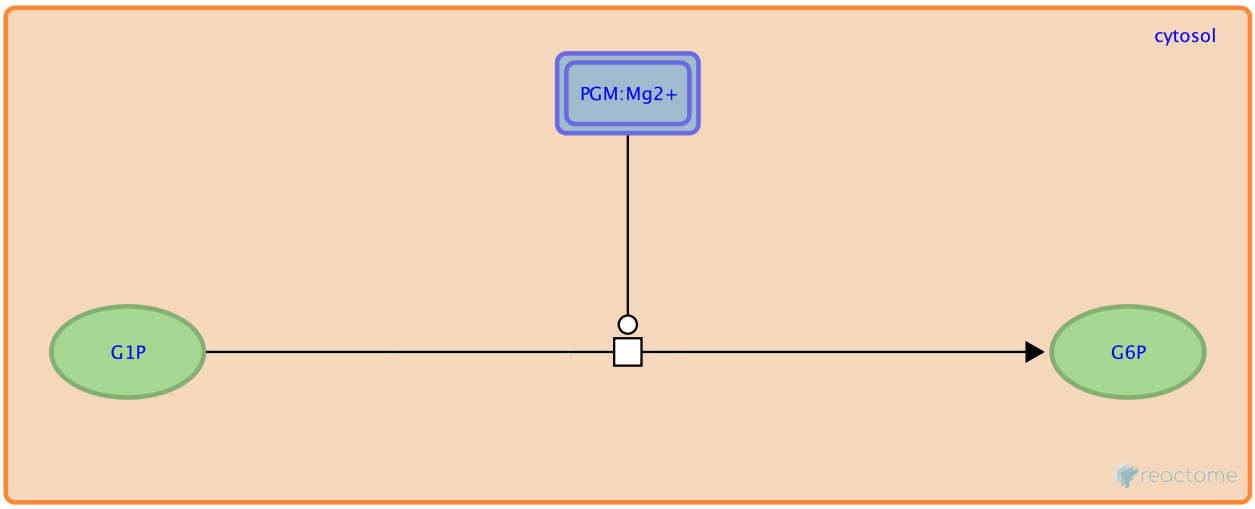
PGM:Mg2+ isomerise G1P to G6P ↗

Location: Galactose catabolism

Stable identifier: R-HSA-70427

Type: transition

Compartments: cytosol



Cytosolic phosphoglucomutase 1 (PGM1) catalyzes the reversible conversion of glucose 1-phosphate to glucose 6-phosphate. Two PGM isoenzymes, both monomers, have been identified. PGM1 is the major form found in most tissues except erythrocytes, where PGM2 is abundant (March et al. 1993; Parrington et al. 1968; Putt et al. 1993). PGM2 also has substantial phosphopentomutase activity and its primary physiological in normal tissues in vivo is not clear. Cytosolic glucose 1,6-bisphosphate synthase (PGM2L1) also possesses phosphoglucomutase activity (Maliekal et al. 2007, Veiga-da-Cunha et al. 2008).

Preceded by: GALT transfers UMP from UDP-Glc to Gal1P to form UDP-Gal

Literature references

March, RE., Putt, W., Hollyoake, M., Ives, JH., Lovegrove, JU., Hopkinson, DA. et al. (1993). The classical human phosphoglucomutase (PGM1) isozyme polymorphism is generated by intragenic recombination. *Proc Natl Acad Sci U S A, 90*, 10730-3. ↗

Maliekal, P., Sokolova, T., Vertommen, D., Veiga-da-Cunha, M., Van Schaftingen, E. (2007). Molecular identification of mammalian phosphopentomutase and glucose-1,6-bisphosphate synthase, two members of the alpha-D-phosphohexomutase family. *J Biol Chem, 282*, 31844-51. ↗

Veiga-da-Cunha, M., Vleugels, W., Maliekal, P., Matthijs, G., Van Schaftingen, E. (2008). Mammalian phosphomannomutase PMM1 is the brain IMP-sensitive glucose-1,6-bisphosphatase. *J. Biol. Chem., 283*, 33988-93. ↗

Editions

2010-01-22	Revised	D'Eustachio, P.
2017-01-12	Edited, Revised	Jassal, B.

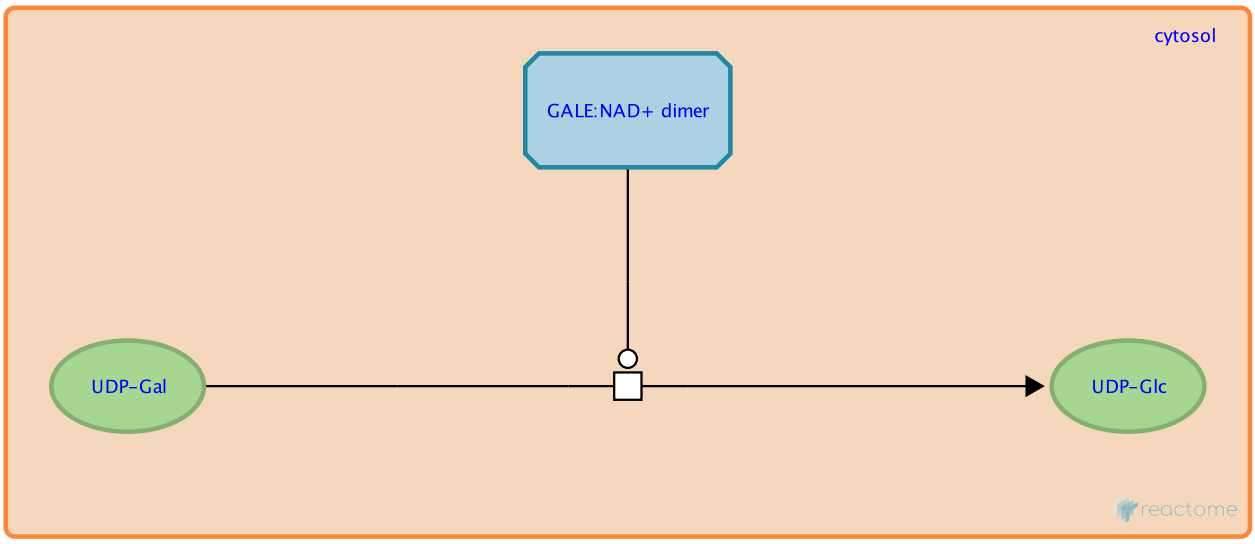
GALE:NAD+ dimer reversibly epimerises UDP-Gal to UDP-Glc ↗

Location: Galactose catabolism

Stable identifier: R-HSA-70369

Type: transition

Compartments: cytosol



Cytosolic UDP-galactose 4-epimerase catalyzes the interconversion of UDP-D-galactose and UDP-D-glucose (Schulz et al. 2004). The active form of the enzyme is a homodimer with one molecule of bound NAD+ per monomer (Thoden et al. 2000).

Preceded by: GALT transfers UMP from UDP-Glc to Gal1P to form UDP-Gal

Followed by: GALT transfers UMP from UDP-Glc to Gal1P to form UDP-Gal

Literature references

Schulz, JM., Watson, AL., Sanders, R., Ross, KL., Thoden, JB., Holden, HM. et al. (2004). Determinants of function and substrate specificity in human UDP-galactose 4'-epimerase. *J Biol Chem, 279*, 32796-803. ↗

Thoden, JB., Wohlers, TM., Fridovich-Keil, JL., Holden, HM. (2000). Crystallographic evidence for Tyr 157 functioning as the active site base in human UDP-galactose 4-epimerase. *Biochemistry, 39*, 5691-701. ↗

Editions

2010-01-25	Revised	D'Eustachio, P.

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