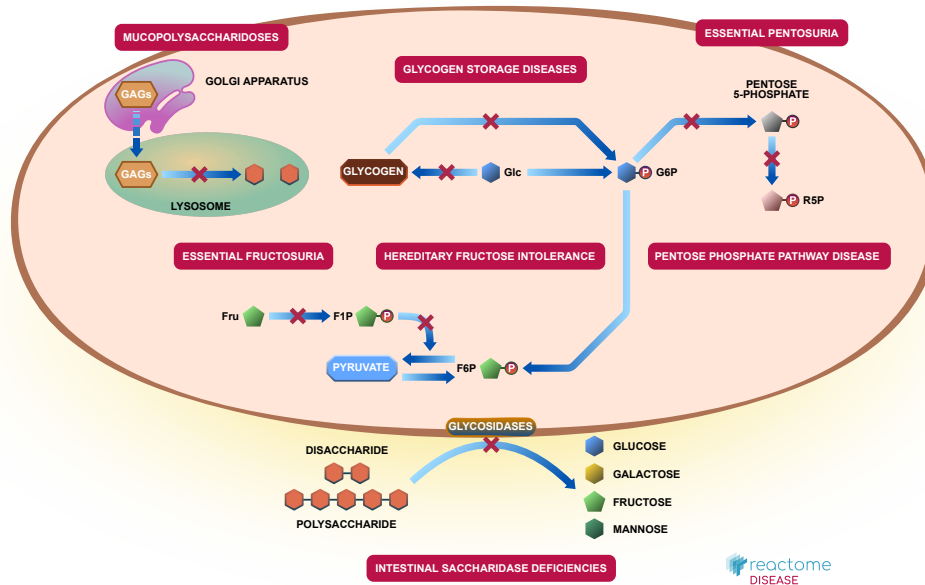


Diseases of carbohydrate metabolism



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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](https://reactome.org/textbook/).

30/04/2024

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.

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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. [↗](#)
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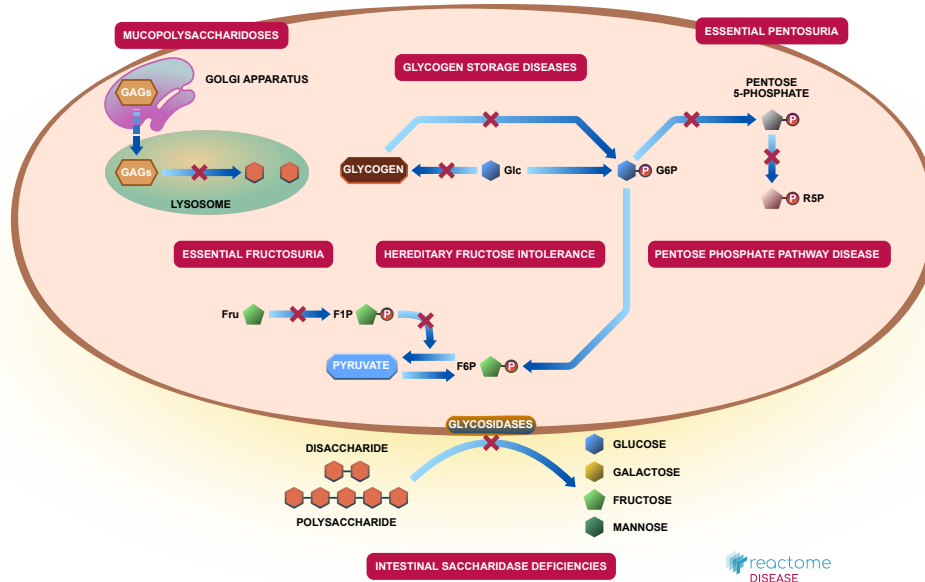
Reactome database release: 88

This document contains 8 pathways ([see Table of Contents](#))

Diseases of carbohydrate metabolism ↗

Stable identifier: R-HSA-5663084

Diseases: carbohydrate metabolic disorder



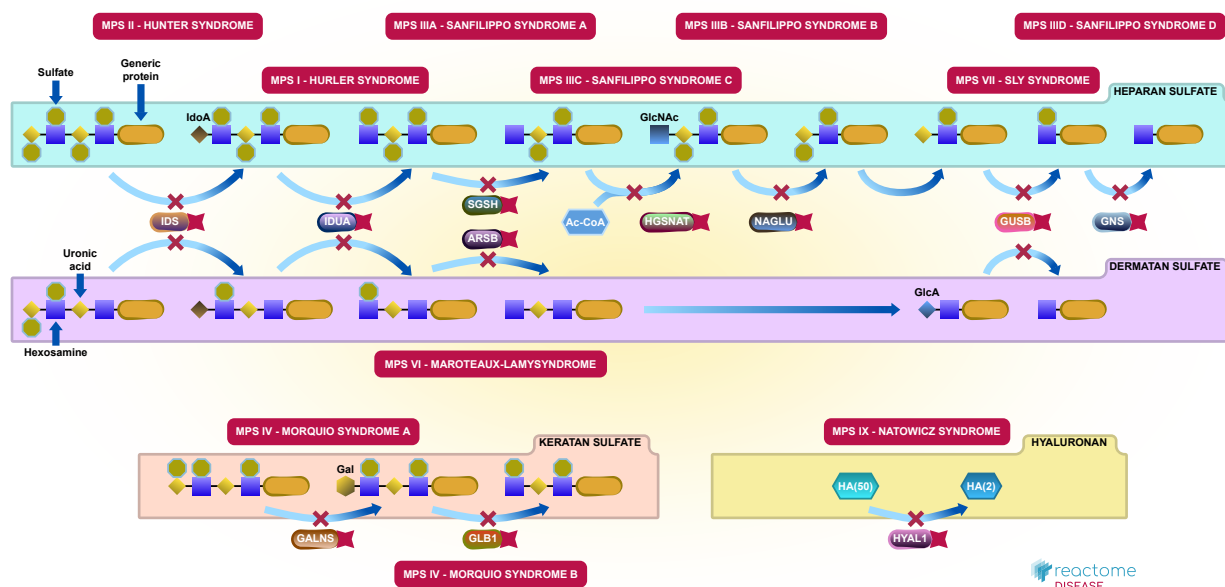
The processes by which dietary carbohydrate is digested to monosaccharides and these are taken up from the gut lumen into cells where they are oxidized to yield energy or consumed in biosynthetic processes are a central part of human metabolism and defects in them can lead to serious disease. Defects annotated here affect saccharide digestion in the gut lumen, fructose metabolism, and the pentose phosphate pathway. In addition, the defect in glucuronate catabolism that leads to essential pentosuria, a benign phenotype that is one of Garrod's original four inborn errors of metabolism, is annotated.

Mucopolysaccharidoses ↗

Location: Diseases of carbohydrate metabolism

Stable identifier: R-HSA-2206281

Diseases: mucopolysaccharidosis



The mucopolysaccharidoses (MPS) are a group of rare, inherited lysosomal storage disorders caused by deficiencies of enzymes catalyzing the stepwise degradation of glycosaminoglycans (GAGs, originally called mucopolysaccharides) (Neufeld & Muenzer in Scriver et al. 2001). Catabolism of the GAGs dermatan sulfate, heparan sulfate, heparin, keratan sulfate, chondroitin sulfate or hyaluronan may be blocked at one or more steps, resulting in lysosomal accumulation of GAG fragments of varying size. Over time these collect in the cells, blood and connective tissues ultimately resulting in progressive irreversible cellular damage which affects appearance, physical abilities, organ and system function, vision, and usually mental development (Lehman et al. 2011, Ashworth et al. 2006). Life expectancy is also reduced. There are 11 known enzyme deficiencies that give rise to 7 distinct MPS. These disorders are biochemically characterized by elevated levels of partially or undegraded GAGs in lysosomes, blood, urine and cerebro-spinal fluid (Muenzer 2011, Coutinho et al. 2012). The MPS are part of the lysosomal storage disease family, a group of about 50 genetic disorders caused by deficient lysosomal proteins (Ballabio & Gieselmann 2009).

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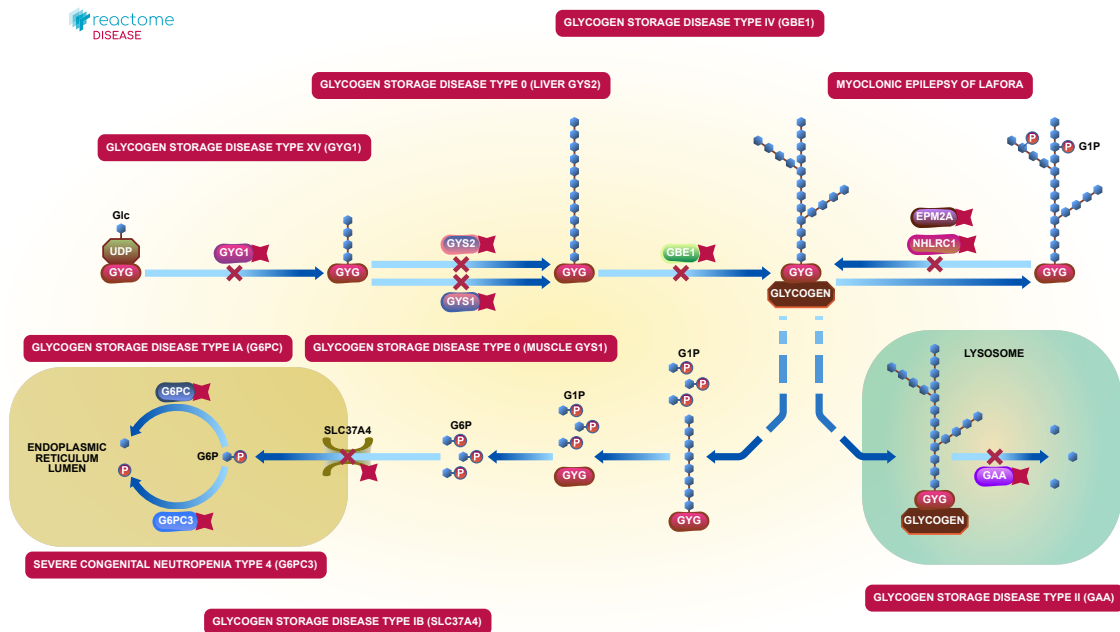
2012-04-26	Authored, Edited	Jassal, B.
2012-08-27	Reviewed	Coutinho, MF., Matos, L., Alves, S.
2012-08-28	Reviewed	Ashworth, J.

Glycogen storage diseases ↗

Location: Diseases of carbohydrate metabolism

Stable identifier: R-HSA-3229121

Diseases: glycogen storage disease



The regulated turnover of glycogen plays a central, tissue-specific role in the maintenance of blood glucose levels and in the provision of glucose to tissues such as muscle and brain in response to stress. Defects in the enzymes involved in glycogen turnover are associated with abnormal responses to fasting and exercise that can differ widely in their presentation and severity. Additional symptoms can be the result of accumulation of abnormal products of glycogen metabolism (Hauk et al. 1959; Hers 1964; Shin 2006). Annotations are provided here for diseases due to deficiencies of GYS1 and GYS2 (glycogen synthase 1 and 2; glycogen storage disease type 0 (GSD type 0), of G6PC3 (glucose-6-phosphatase, GSD type Ia) and the SLC37A4 transporter (GSD type Ib), of GAA (lysosomal acid alpha-glucosidase, GSD type II), of GBE1 (glycogen branching enzyme, GSD type IV), and of GYG1 (glycogenin 1, GSD XV). Two additional diseases, myoclonic epilepsy of Lafora (Roach et al. 2012) and severe congenital neutropenia type 4 (Boztug et al. 2009), are included as they are due to defects in enzymes of glycogen metabolism.

Literature references

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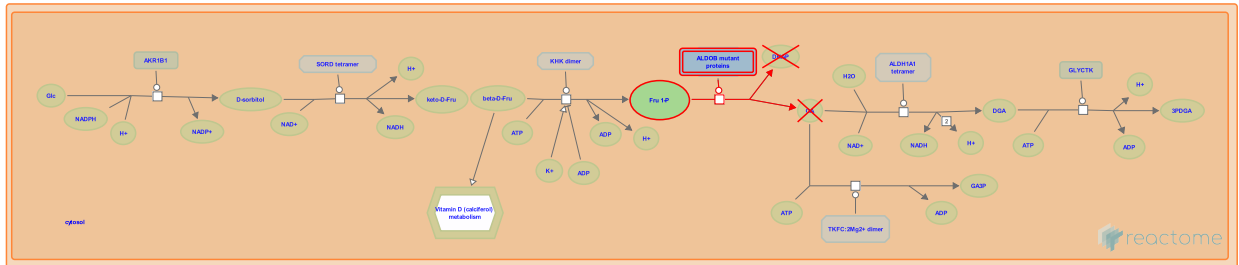
2013-07-19	Authored, Edited	D'Eustachio, P.
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Hereditary fructose intolerance [↗](#)

Location: Diseases of carbohydrate metabolism

Stable identifier: R-HSA-5657560

Diseases: hereditary fructose intolerance syndrome



Deficiencies in aldolase B arising from mutations in the aldolase B gene (ALDOB) prevent the cleavage of fructose 1-phosphate to glyceraldehyde (GA) and dihydroxyacetone phosphate (DHAP), leading to hereditary fructose intolerance (HFI). This autosomal recessive disorder is potentially fatal, but can be managed by exclusion of fructose from the diet (Cox et al. 1988; Tolan 1995).

Literature references

Tolan, DR. (1995). Molecular basis of hereditary fructose intolerance: mutations and polymorphisms in the human aldolase B gene. *Hum Mutat*, 6, 210-8. [↗](#)

Cross, NC., Cox, TM., Tolan, DR. (1988). Catalytic deficiency of human aldolase B in hereditary fructose intolerance caused by a common missense mutation. *Cell*, 53, 881-5. [↗](#)

Editions

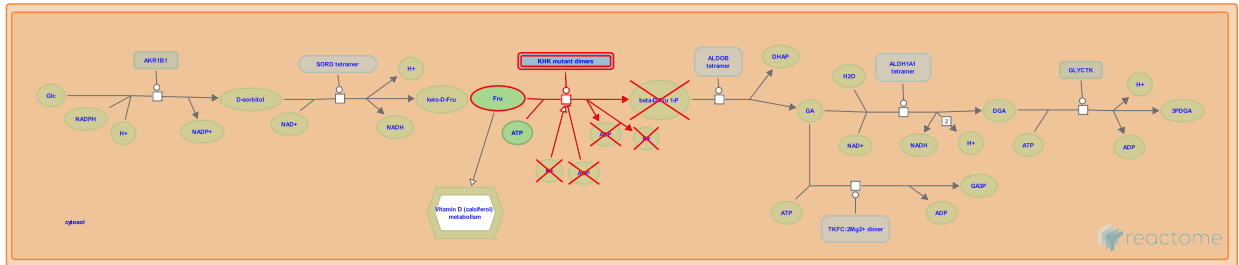
2015-01-29	Authored, Edited	D'Eustachio, P.
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Essential fructosuria [↗](#)

Location: Diseases of carbohydrate metabolism

Stable identifier: R-HSA-5657562

Diseases: carbohydrate metabolic disorder



Deficiencies in KHK (ketoHexokinase) are associated with essential fructosuria (Bonthon et al. 1994).

Literature references

Donaldson, IA., Brady, N., Steinmann, B., Bonthon, DT. (1994). Molecular basis of essential fructosuria: molecular cloning and mutational analysis of human ketoHexokinase (fructokinase). *Hum Mol Genet*, 3, 1627-31. [↗](#)

Editions

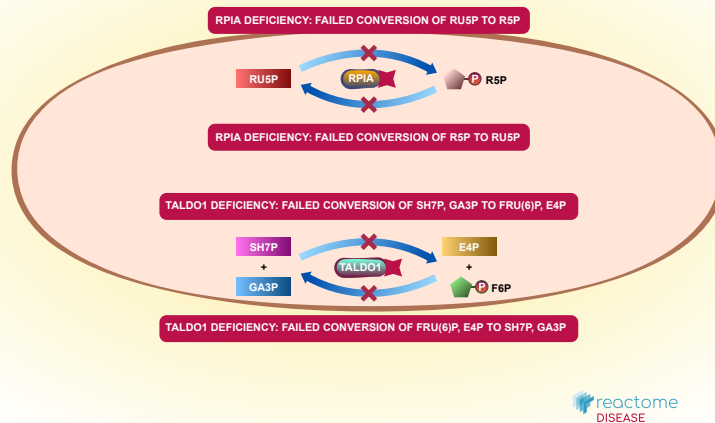
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Pentose phosphate pathway disease ↗

Location: Diseases of carbohydrate metabolism

Stable identifier: R-HSA-6791465

Diseases: carbohydrate metabolic disorder



Mutant forms of two enzymes of the pentose phosphate pathway have been associated with disease in humans. A mutation in ribose-5-phosphate isomerase (RPIA), which normally mediates the reversible interconversion of D-ribulose-5-phosphate and ribose-5-phosphate, has been associated with a slowly progressive leukoencephalopathy, and mutations in transaldolase 1 (TALDO1), which normally mediates the reversible interconversion of D-fructose 6-phosphate and D-erythrose-4-phosphate to form sedoheptulose-7-phosphate and D-glyceraldehyde-3-phosphate, have been associated with congenital liver disease (Wamelink et al. 2008).

Literature references

Wamelink, MM., Struys, EA., Jakobs, C. (2008). The biochemistry, metabolism and inherited defects of the pentose phosphate pathway: a review. *J Inherit Metab Dis*, 31, 703-17. ↗

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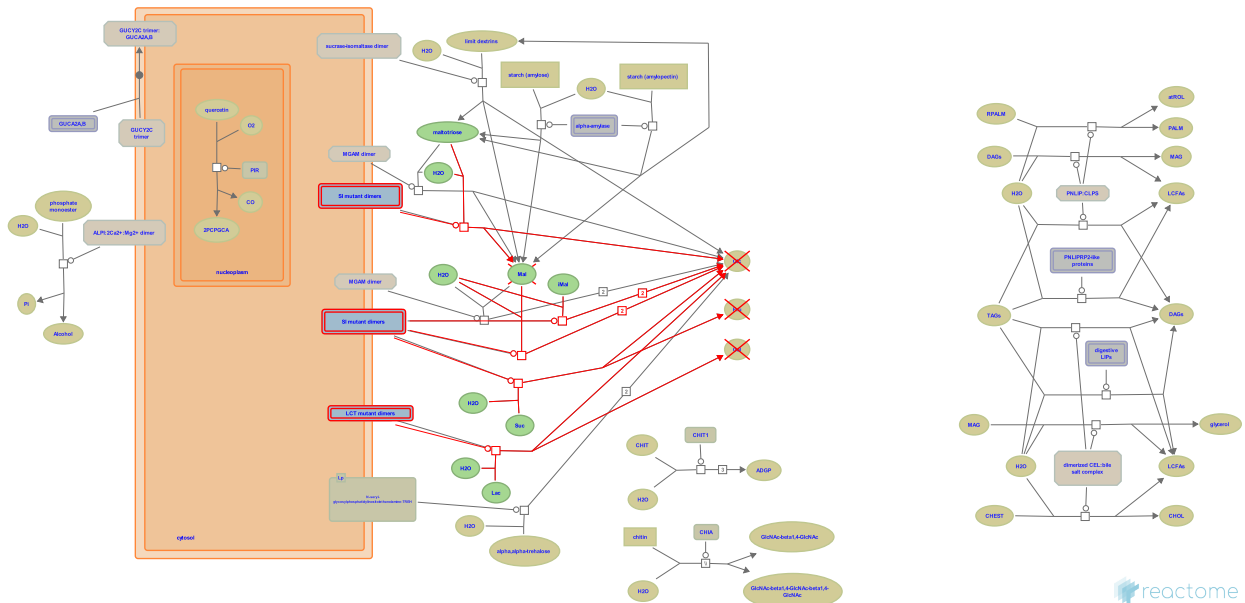
2015-02-24	Authored, Edited	D'Eustachio, P.
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Intestinal saccharidase deficiencies ↗

Location: Diseases of carbohydrate metabolism

Stable identifier: R-HSA-5659898

Diseases: intestinal disaccharidase deficiency



Defects in in two enzymes required for intestinal digestion of dietary carbohydrate, lactase (LCT, a domain of lactase-phlorizin hydrolase protein) and sucrase-isomaltase (SI), are annotated here. The first affects nursing infants; the second affects individuals after weaning.

The disaccharide lactose is a major constituent of human breast milk. To be taken up from the gut in the nursing infant, this sugar must first be hydrolyzed by LCT present on the external face of enterocytes in microvilli of the small intestine. Mutations that disrupt LCT activity are associated with acute illness in newborn children as lactose fermentation by gut bacteria leads to severe diarrhea. The condition is effectively treated by feeding affected infants a lactose-free formula. This congenital disease is distinct from the down-regulation of LCT expression after weaning in many human populations that is associated with a milder form of lactose intolerance in adults (Jarvela et al. 2009).

The starch in a post-weaning diet is digested by amylases to di- and oligosaccharides that must be further digested to monosaccharides in order to be taken up from the lumen of the small intestine into endothelial cells of the intestinal brush border. If they are not digested, a process in which enterocyte-associated SI plays a central role, they remain in the gut lumen and are fermented by gut bacteria, leading to osmotic and fermentative diarrhea (Naim et al. 2012; Van Beers et al. 1995).

Literature references

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