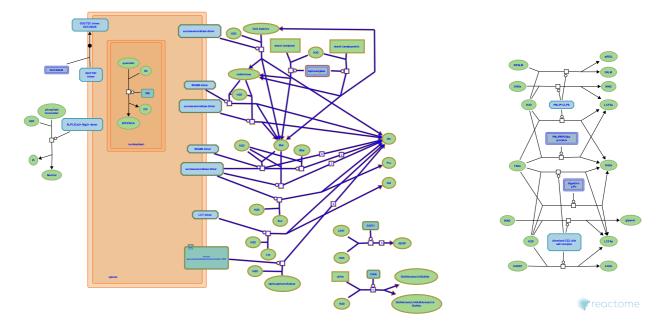


Digestion of dietary carbohydrate



Amiri, M., D'Eustachio, P., Jassal, B., Naim, HY., Nichols, BL.

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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 <u>Reactome Textbook</u>.

07/10/2024

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

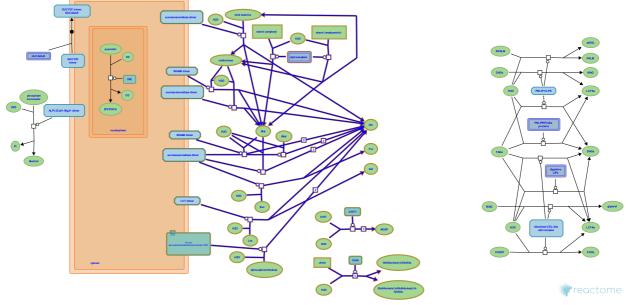
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This document contains 1 pathway and 13 reactions (see Table of Contents)

Digestion of dietary carbohydrate *¬*

Stable identifier: R-HSA-189085

Compartments: extracellular region, plasma membrane



Carbohydrate is a major component of the human diet, and includes starch (amylose and amylopectin) and disaccharides such as sucrose, lactose, maltose and, in small amounts, trehalose. The digestion of starch begins with the action of amylase enzymes secreted in the saliva and small intestine, which convert it to maltotriose, maltose, limit dextrins, and some glucose. Digestion of the limit dextrins and disaccharides, both dietary and starch-derived, to monosaccharides - glucose, galactose, and fructose - is accomplished by enzymes located on the luminal surfaces of enterocytes lining the microvilli of the small intestine (Van Beers et al. 1995).

Literature references

Büller, HA., Dekker, J., Einerhand, AW., Grand, RJ., Van Beers, EH. (1995). Intestinal brush border glycohydrolases: structure, function, and development. *Crit. Rev. Biochem. Mol. Biol.*, 30, 197-262. ↗

2006-11-03	Authored	D'Eustachio, P.
2007-01-16	Reviewed	Nichols, BL.
2007-01-18	Revised	D'Eustachio, P.

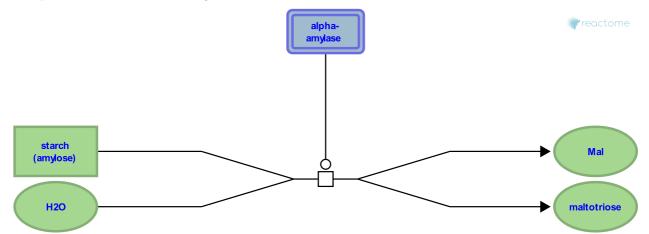
Digestion of linear starch (amylose) by extracellular amylase 7

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-188979

Type: transition

Compartments: extracellular region



Extracellular amylose starch, linear polymers of glucose joined by alpha-1,4 linkages, is digested by the endoglucosidase activity of alpha-amylases, yielding maltose, maltotriose, and longer maltosides. The human genome contains five functional alpha-amylase genes, encoding structurally closely related isoenzymes (Gumucio et al. 1988). Three of these genes encode proteins synthesized in the parotid glands and released into the saliva (amylase 1A, B, and C), and the other two encode proteins synthesized in the exocrine pancreas and released into the small intestine (amylase 2A and B). In the human body, starch digestion thus commences in the mouth, mediated by salivary amylases, and is continued in the small intestine, mediated by the pancreatic ones.

X-ray crystallographic studies of amylase 1A and 2A proteins show them to be monomers, complexed with single calcium and chloride ions (Ramasubbu et al. 1996; Brayer et al. 2000). Biochemical characterization of amylase 2A indicates that the enzyme efficiently cleaves poly-glucose chains so as to release maltose - a glucose disaccharide - from the reducing end of the chain (Braun et al. 1993; Brayer et al. 2000).

Followed by: maltose + H2O => 2 D-glucose (maltase-glucoamylase), maltotriose + H2O => maltose + D-glucose (sucrase-isomaltase), maltotriose + H2O => maltose + D-glucose (maltase-glucoamylase), maltose + H2O => 2 D-glucose (sucrase-isomaltase)

Literature references

- Caldwell, RM., Meisler, MH., Samuelson, LC., Wiebauer, K., Gumucio, DL. (1988). Concerted evolution of human amylase genes. *Mol Cell Biol*, *8*, 1197-205.
- Ramasubbu, N., Luo, Y., Paloth, V., Levine, MJ., Brayer, GD. (1996). Structure of human salivary alpha-amylase at 1.6 A resolution: implications for its role in the oral cavity. *Acta Crystallogr D Biol Crystallogr, 52*, 435-46.
- Braun, C., Wang, Y., Nguyen, NT., Brayer, GD., Overall, CM., Sidhu, G. et al. (2000). Subsite mapping of the human pancreatic alpha-amylase active site through structural, kinetic, and mutagenesis techniques. *Biochemistry*, 39, 4778-91.

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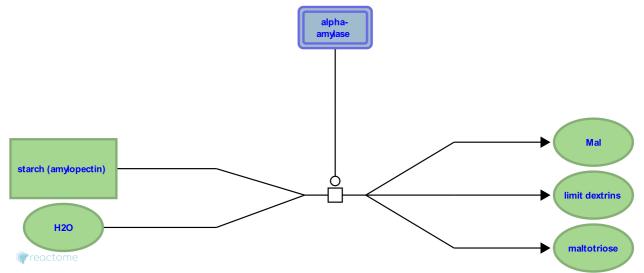
Digestion of branched starch (amylopectin) by extracellular amylase 7

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-191114

Type: transition

Compartments: extracellular region



The 1-4 linkages of extracellular amylopectin starch, a glucose polymer containing linear segments formed by alpha-1,4 linkages and a smaller number of alpha-1,6 linkages forming branch points, are digested by the endoglucosidase activity of alpha-amylases, yielding maltose, maltotriose, and longer maltosides from the alpha-1,4 linear segments and alpha-limit dextrins from the branch points. Alpha-limit dextrins are glucose (G) oligomers linked by 1-4 and 1-6 bonds. 1-6 branch points make up about 5% of all amylopectin glucose bonds - the exact fraction depends on the source of the starch. Mass spectroscopic analysis of alpha-limit dextrin shows it to be a mixture of maltosides and isomaltosides containing two to forty G residues, but the most common contain fewer than seven. Maltose (G2) is the shortest 1-4 maltoside produced by alpha-amylase. Isomaltose (G2) is the shortest 1-6 isomaltoside.

The human genome contains five functional alpha-amylase genes, encoding structurally closely related isoenzymes (Gumucio et al. 1988). Three of these genes encode proteins synthesized in the parotid glands and released into the saliva (amylase 1A, B, and C), and the other two encode proteins synthesized in the exocrine pancreas and released into the small intestine (amylase 2A and B). In the human body, starch digestion thus commences in the mouth, mediated by salivary amylases, and is continued in the small intestine, mediated by the pancreatic ones.

X-ray crystallographic studies of amylase 1A and 2A proteins show them to be monomers, complexed with single calcium and chloride ions (Ramasubbu et al. 1996; Brayer et al. 2000). Biochemical characterization of amylase 2A indicates that the enzyme efficiently cleaves poly-glucose chains so as to release maltose - a glucose disaccharide - from the reducing end of the chain (Braun et al. 1993; Brayer et al. 2000).

Followed by: maltose + H2O => 2 D-glucose (maltase-glucoamylase), maltotriose + H2O => maltose + D-glucose (sucrase-isomaltase), Digestion of 1-6 linkages of limit dextrins to yield maltose, maltotriose, longer maltosides, and glucose, maltotriose + H2O => maltose + D-glucose (maltase-glucoamylase), maltose + H2O => 2 D-glucose (sucrase-isomaltase)

Literature references

Caldwell, RM., Meisler, MH., Samuelson, LC., Wiebauer, K., Gumucio, DL. (1988). Concerted evolution of human amylase genes. *Mol Cell Biol*, *8*, 1197-205.

Ramasubbu, N., Luo, Y., Paloth, V., Levine, MJ., Brayer, GD. (1996). Structure of human salivary alpha-amylase at 1.6 A resolution: implications for its role in the oral cavity. *Acta Crystallogr D Biol Crystallogr, 52*, 435-46.

Braun, C., Wang, Y., Nguyen, NT., Brayer, GD., Overall, CM., Sidhu, G. et al. (2000). Subsite mapping of the human pancreatic alpha-amylase active site through structural, kinetic, and mutagenesis techniques. *Biochemistry*, 39, 4778-91. *¬*

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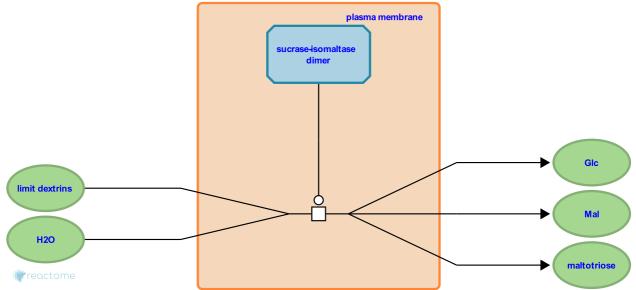
Digestion of 1-6 linkages of limit dextrins to yield maltose, maltotriose, longer maltosides, and glucose **7**

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-189053

Type: transition

Compartments: plasma membrane, extracellular region



The 1-6 linkages in extracellular limit dextrins are hydrolyzed by sucrase-isomaltase to yield maltose, maltotriose, longer maltosides, and glucose (Conklin et al. 1975; Nichols et al. 1998). In the body, this enzyme is found on the external face of enterocytes in microvilli of the small intestine (Hauri et al. 1985), and acts on limit dextrins generated by the hydrolysis of amylopectin starch.

Preceded by: Digestion of branched starch (amylopectin) by extracellular amylase

Followed by: maltose + H2O => 2 D-glucose (maltase-glucoamylase), maltotriose + H2O => maltose + D-glucose (sucrase-isomaltase), maltose + H2O => 2 D-glucose (sucrase-isomaltase), maltotriose + H2O => maltose + D-glucose (maltase-glucoamylase)

Literature references

- Hauri, HP., Fransen, JA., Bienz, D., Marxer, A., Sterchi, EE. (1985). Expression and intracellular transport of microvillus membrane hydrolases in human intestinal epithelial cells. *J Cell Biol, 101,* 838-51.
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2006-11-03	Authored, Edited	D'Eustachio, P.
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2007-01-18	Revised	D'Eustachio, P.

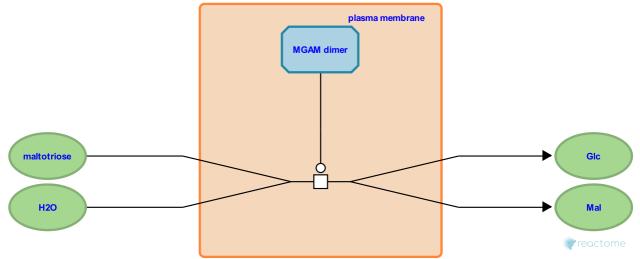
maltotriose + H2O => maltose + D-glucose (maltase-glucoamylase) 7

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-191116

Type: transition

Compartments: plasma membrane, extracellular region



Maltotriose is representative of linear glucose oligomers containing more than two residues. The 1-4 linkages of extracellular maltotriose are hydrolyzed to yield maltose and glucose in a reaction catalyzed by the exoglucosidase activity of maltase-glucoamylase (Nichols et al. 1998). In the body, this enzyme is found as a dimer on the external face of enterocytes in microvilli of the small intestine (Hauri et al. 1985), and acts on maltotriose derived directly from the diet and from the hydrolysis of starch. This reaction can also be catalyzed by sucrase-isomaltase, but maltase-glucoamylase is about a hundredfold more active.

Preceded by: Digestion of 1-6 linkages of limit dextrins to yield maltose, maltotriose, longer maltosides, and glucose, Digestion of branched starch (amylopectin) by extracellular amylase, Digestion of linear starch (amylose) by extracellular amylase

Followed by: maltose + H2O => 2 D-glucose (maltase-glucoamylase), maltose + H2O => 2 D-glucose (sucrase-isomaltase)

Literature references

Hauri, HP., Fransen, JA., Bienz, D., Marxer, A., Sterchi, EE. (1985). Expression and intracellular transport of microvillus membrane hydrolases in human intestinal epithelial cells. *J Cell Biol*, 101, 838-51.

Swallow, DM., Sterchi, EE., Hahn, D., Sen, P., Nichols, BL., Avery, S. (2003). The maltase-glucoamylase gene: common ancestry to sucrase-isomaltase with complementary starch digestion activities. *Proc Natl Acad Sci U S A*, 100, 1432-7. ↗

2006-11-03	Authored	D'Eustachio, P.
2007-01-16	Reviewed	Nichols, BL.
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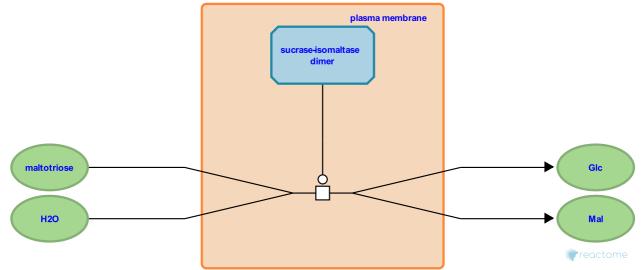
maltotriose + H2O => maltose + D-glucose (sucrase-isomaltase) 7

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-191101

Type: transition

Compartments: plasma membrane, extracellular region



Maltotriose is representative of linear glucose oligomers containing more than two residues. The 1-4 linkages of extracellular maltotriose are hydrolyzed to yield maltose and glucose in a reaction catalyzed by the exoglucosidase activity of sucrase-isomaltase (Nichols et al. 1998). In the body, this enzyme is found as a heterodimer on the external face of enterocytes in microvilli of the small intestine (Hauri et al. 1985), and acts on maltotriose derived directly from the diet and from the hydrolysis of starch, although with lower activity than maltase-glucoamylase.

Preceded by: Digestion of 1-6 linkages of limit dextrins to yield maltose, maltotriose, longer maltosides, and glucose, Digestion of branched starch (amylopectin) by extracellular amylase, Digestion of linear starch (amylose) by extracellular amylase

Followed by: maltose + H2O => 2 D-glucose (maltase-glucoamylase), maltose + H2O => 2 D-glucose (sucrase-isomaltase)

Literature references

- Hauri, HP., Fransen, JA., Bienz, D., Marxer, A., Sterchi, EE. (1985). Expression and intracellular transport of microvillus membrane hydrolases in human intestinal epithelial cells. *J Cell Biol*, 101, 838-51.
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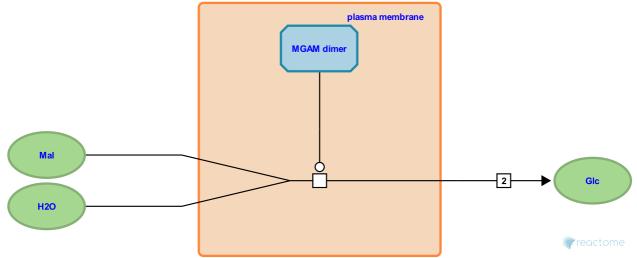
maltose + H2O => 2 D-glucose (maltase-glucoamylase) 7

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-189102

Type: transition

Compartments: plasma membrane, extracellular region



The alpha-1,4 linkages of extracellular maltose are hydrolyzed to yield glucose in a reaction catalyzed by maltaseglucoamylase (Nichols et al. 1998; Semenza et al. 2001). In the body, this enzyme is found as a dimer on the external face of enterocytes in microvilli of the small intestine (Hauri et al. 1985), and acts on maltose derived directly from the diet and from the hydrolysis of starch.

Preceded by: maltotriose + H2O => maltose + D-glucose (sucrase-isomaltase), Digestion of 1-6 linkages of limit dextrins to yield maltose, maltotriose, longer maltosides, and glucose, maltotriose + H2O => maltose + D-glucose (maltase-glucoamylase), Digestion of branched starch (amylopectin) by extracellular amylase, Digestion of linear starch (amylose) by extracellular amylase

Literature references

- Hauri, HP., Fransen, JA., Bienz, D., Marxer, A., Sterchi, EE. (1985). Expression and intracellular transport of microvillus membrane hydrolases in human intestinal epithelial cells. *J Cell Biol, 101*, 838-51.
- Swallow, DM., Sterchi, EE., Hahn, D., Sen, P., Nichols, BL., Avery, S. (2003). The maltase-glucoamylase gene: common ancestry to sucrase-isomaltase with complementary starch digestion activities. *Proc Natl Acad Sci U S A*, 100, 1432-7. ↗

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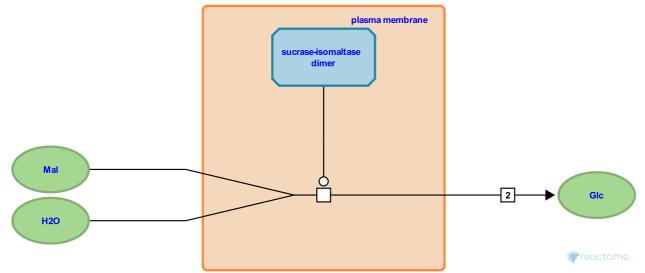
maltose + H2O => 2 D-glucose (sucrase-isomaltase) 7

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-191108

Type: transition

Compartments: plasma membrane, extracellular region



The alpha-1,4 linkages of extracellular maltose are hydrolyzed to yield glucose in a reaction catalyzed by sucrasemaltase (Nichols et al. 1998). In the body, this enzyme is found as a dimer on the external face of enterocytes in microvilli of the small intestine (Hauri et al. 1985), and acts on maltose derived directly from the diet and from the hydrolysis of starch.

Preceded by: maltotriose + H2O => maltose + D-glucose (sucrase-isomaltase), Digestion of 1-6 linkages of limit dextrins to yield maltose, maltotriose, longer maltosides, and glucose, maltotriose + H2O => maltose + D-glucose (maltase-glucoamylase), Digestion of branched starch (amylopectin) by extracellular amylase, Digestion of linear starch (amylose) by extracellular amylase

Literature references

Hauri, HP., Fransen, JA., Bienz, D., Marxer, A., Sterchi, EE. (1985). Expression and intracellular transport of microvillus membrane hydrolases in human intestinal epithelial cells. *J Cell Biol*, 101, 838-51.

Swallow, DM., Sterchi, EE., Hahn, D., Sen, P., Nichols, BL., Avery, S. (2003). The maltase-glucoamylase gene: common ancestry to sucrase-isomaltase with complementary starch digestion activities. *Proc Natl Acad Sci U S A*, 100, 1432-7. 7

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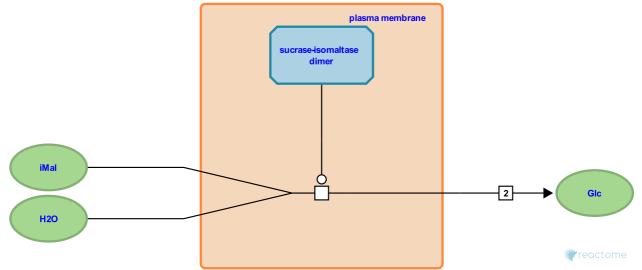
isomaltose + H2O => 2 D-glucose (sucrase-isomaltase) 7

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-5659861

Type: transition

Compartments: plasma membrane, extracellular region



The alpha-1,6 linkages of extracellular isomaltose are hydrolyzed to yield glucose in a reaction catalyzed by sucrasemaltase (Sim et al. 2010). In the body, this enzyme is found as a dimer on the external face of enterocytes in microvilli of the small intestine (Hauri et al. 1985). The predominant form of mature SI in the membrane is a dimer, as established from a variety of studies of the processing of the porcine enzyme (Cowell et al. 1986; Danielsen 1994) and crystallographic studies of the human one (Sim et al. 2010).

Literature references

- Rose, DR., Sim, L., Pinto, BM., Willemsma, C., Mohan, S., Naim, HY. (2010). Structural basis for substrate selectivity in human maltase-glucoamylase and sucrase-isomaltase N-terminal domains. J. Biol. Chem., 285, 17763-70.
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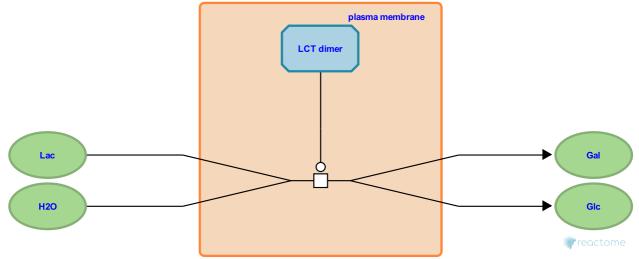
lactose + H2O => D-glucose + D-galactose ↗

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-189062

Type: transition

Compartments: plasma membrane, extracellular region



Extracellular lactose is hydrolyzed to yield molecules of glucose and galactose, in a reaction catalyzed by the lactase activity of lactase-phlorizin hydrolase associated with the plasma membrane. In the body, lactase-phlorzin hydrolase is found on the external face of enterocytes in microvilli of the small intestine (Hauri et al. 1985). Expression of the enzyme is developmentally regulated and subject to a genetic polymorphism: enzyme levels fall after weaning but the extent of the fall varies sharply between human populations (Grand et al. 2003; Swallow 2003). The lactase-phlorizin hydrolase polypeptide undergoes dimerization and two rounds of proteolytic cleavage in the course of its maturation and transport to the cell surface (Grunberg and Sterchi 1995; Wuthrich et al. 1996; Behrendt et al. 2010).

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- Hauri, HP., Fransen, JA., Bienz, D., Marxer, A., Sterchi, EE. (1985). Expression and intracellular transport of microvillus membrane hydrolases in human intestinal epithelial cells. *J Cell Biol, 101*, 838-51.

Montgomery, RK., Hirschhorn, JN., Grand, RJ., Chitkara, DK. (2003). Changing genes; losing lactase. Gut, 52, 617-9. 🛪

2006-11-03	Authored	D'Eustachio, P.
2007-01-16	Reviewed	Nichols, BL.
2015-02-15	Reviewed	Naim, HY., Amiri, M.

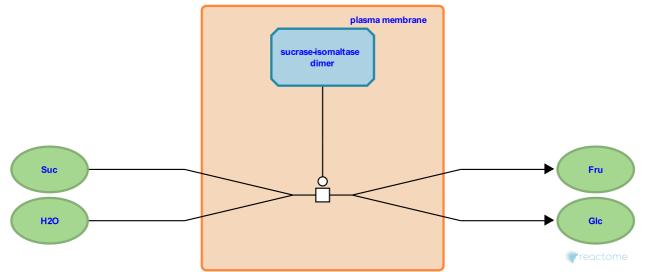
sucrose + H2O => glucose + fructose ↗

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-189069

Type: transition

Compartments: plasma membrane, extracellular region



Extracellular sucrose is hydrolyzed to yield glucose and fructose in a reaction catalyzed by the sucrase domain of sucrase-isomaltase (Conklin et al. 1975). In the body, this enzyme is found on the external face of enterocytes in microvilli of the small intestine (Hauri et al. 1985). The sucrase-isomaltase polypeptide is cleaved into its sucrase and isomaltase domains, which remain associated and, by analogy to the corresponding pig enzyme, are thought to dimerize (Cowell et al. 1986).

Literature references

- Hauri, HP., Fransen, JA., Bienz, D., Marxer, A., Sterchi, EE. (1985). Expression and intracellular transport of microvillus membrane hydrolases in human intestinal epithelial cells. *J Cell Biol, 101,* 838-51.
- Gray, GM., Conklin, KA., Yamashiro, KM. (1975). Human intestinal sucrase-isomaltase. Identification of free sucrase and isomaltase and cleavage of the hybrid into active distinct subunits. J Biol Chem, 250, 5735-41.

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trehalose + H2O => 2 D-glucose ↗

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-188985

Type: transition

Compartments: plasma membrane, extracellular region

Inferred from: trehalose + H2O => 2 D-glucose (Oryctolagus cuniculus)

	plasma membrane	
	Lp N-seryl- glycosylphosphatidylinositolethanolamine- TREH	
alpha,alpha- trehalose H20		2 Gic
H20		2 Gic

Extracellular trehalose, a disaccharide, is cleaved by trehalase associated with the plasma membrane to yield two molecules of glucose. Trehalase has been purified to homogeneity from rabbit intestine and shown to be a monomer attached to the plasma membrane by a GPI anchor (Galand 1984; Ruf et al. 1990). A human cDNA encoding a closely homologous protein has been cloned and its protein product has been shown to have trehalase activity in vitro (Ishihara et al. 1997). The human enzyme has not been characterized further, and so both the posttranslational modifications of the human enzyme and its activity in vivo have been inferred from the properties of the well studied rabbit enzyme.

Trehalase deficiency has been described in two isolated cases in Europe (Bergoz 1971; Madzarovovà-Nohejlova 1973) and at high frequency in a population of Greenland natives (Gudmand-Hoyer et al. 1988) but molecular defects responsible for the deficiency have not yet been described so it is not annotated in Reactome.

Literature references

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- von Kieckebusch, A., Mantei, N., Semenza, G., James, P., Ruf, J., Galand, G. et al. (1990). Rabbit small intestinal trehalase. Purification, cDNA cloning, expression, and verification of glycosylphosphatidylinositol anchoring. *J Biol Chem*, 265, 15034-9. *¬*
- Kobayashi, Y., Ishihara, R., Kino, M., Sasai-Takedatsu, M., Tokunaga, R., Taketani, S. (1997). Molecular cloning, sequencing and expression of cDNA encoding human trehalase. *Gene*, 202, 69-74. 🛪
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Madzarovovà-Nohejlova, J. (1973). Trehalase deficiency in a family. Gastroenterology, 65, 130-3. ↗

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2007-01-16	Reviewed	Nichols, BL.

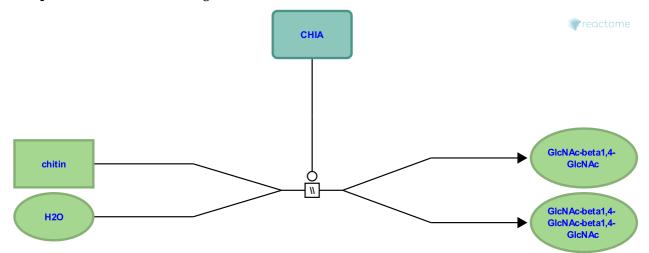
CHIA hydrolyses chitin 🛪

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-6786421

Type: omitted

Compartments: extracellular region



Chitin is a linear polymer made up of repeating units of the sugar N-acetylglucosamine (GlcNAc) and is the second most abundant polysaccharide in nature after cellulose. It is found in the cell walls of bacteria and fungi, the exoskeleton of crustaceans and insects, and the microfilarial sheath of parasitic nematodes. Chitinases are evolutionarily ancient enzymes that hydrolyse the chitin polymer into di- and trisaccharides. This process produces differentially sized chitin fragments that can trigger the release of type 2 cytokines, including interleukin IL-4, IL-5, IL-13 by CD4 T helper (Th2) and other immune cells which play critical roles in the pathogenesis of asthma and allergic responses. Humans express two active chitinases; acidic mammalian chitinase (CHIA, AMCase) and chitotriosidase (CHIT1). CHIA is a secreted enzyme that can randomly hydrolyse chitin (and chitotriose, not shown here) (Boot et al. 2001, Chou et al. 2006, Harti et al. 2008, Olland et al. 2009, Seibold et al. 2009).

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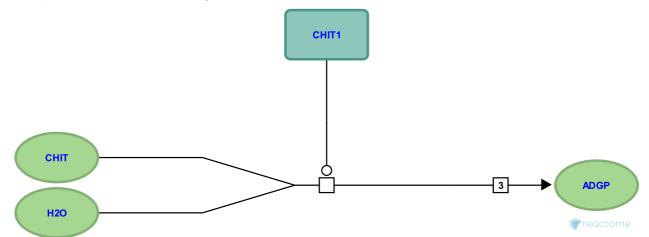
CHIT1 hydrolyses CHIT to 3xADGP ↗

Location: Digestion of dietary carbohydrate

Stable identifier: R-HSA-6786652

Type: transition

Compartments: extracellular region



Chitotriose (CHIT) is an amino trisaccharide comprising of three 2-amino-2-deoxy-beta-D-glucopyranose units. Chitotriosidase-1 (CHIT1) can mediate the hydrolysis of CHIT, as well as chitin and chitobiose (Renkema et al. 1995).

Literature references

Renkema, GH., Boot, RG., Donker-Koopman, WE., Muijsers, AO., Aerts, JM. (1995). Purification and characterization of human chitotriosidase, a novel member of the chitinase family of proteins. J. Biol. Chem., 270, 2198-202.

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