Intestinal saccharidase deficiencies

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02/05/2021
**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**


Reactome database release: 76

This document contains 1 pathway and 5 reactions (see Table of Contents)
Intestinal saccharidase deficiencies

**Stable identifier:** R-HSA-5659898

**Diseases:** intestinal disaccharidase deficiency

Defects 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**


**Editions**

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Defective SI does not hydrolyze Mal

Location: Intestinal saccharidase deficiencies

Stable identifier: R-HSA-5659922

Type: transition

Compartments: extracellular region, plasma membrane

Diseases: intestinal disaccharidase deficiency

Mutations that disrupt the catalytic activity or strongly interfere with proper folding, glycosylation and transport of SI (sucrase-isomaltase) block the cleavage of maltose (Mal) to glucose in the gut lumen. Affected individuals can develop severe diarrhea; this symptom is managed by excluding indigestible sugars from the diet (Gray et al. 1976; Ritz et al. 2003; Semenza et al. 1965). A variety of SI mutant alleles have been described. Three missense mutations that are associated with severe loss of SI activity in vivo are annotated here (Alfalah et al. 2009; Ouwendijk et al. 1996; Sander et al. 2006; Spodsberg et al. 2001). All missense mutant alleles that have been characterized to date encode proteins that fail to reach the luminal plasma membrane or cannot associate stably with it; one missense mutation not annotated here encodes a polypeptide that undergoes an intracellular cleavage and is secreted as the active enzyme (Jacob et al. 2000).

Literature references


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Defective SI does not hydrolyze iMal

**Location:** Intestinal saccharidase deficiencies

**Stable identifier:** R-HSA-5659879

**Type:** transition

**Compartments:** extracellular region, plasma membrane

**Diseases:** intestinal disaccharidase deficiency

**Inferred from:** Defective SI does not hydrolyze Mal (Homo sapiens)

Mutations that disrupt the catalytic activity or strongly interfere with proper folding, glycosylation and transport of SI (sucrase-isomaltase) are inferred to block the cleavage of isomaltose (iMal) to glucose, based on the experimentally demonstrated failure of these SI mutant proteins to hydrolyze maltose (e.g., Sander et al. 2006) and the broad substrate specificity of the normal enzyme (Sim et al. 2010).

**Literature references**


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Defective SI does not hydrolyze Suc

**Location:** Intestinal saccharidase deficiencies

**Stable identifier:** R-HSA-5659926

**Type:** transition

**Compartments:** extracellular region, plasma membrane

**Diseases:** intestinal disaccharidase deficiency

**Inferred from:** Defective SI does not hydrolyze Mal (Homo sapiens)

Mutations that disrupt the catalytic activity or strongly interfere with proper folding, glycosylation and transport of SI (sucrase-isomaltase) are inferred to block the cleavage of sucrose (Suc) to glucose and fructose, based on the experimentally demonstrated failure of these SI mutant proteins to hydrolyze maltose (e.g., Sander et al. 2006) and the broad substrate specificity of the normal enzyme (Sim et al. 2010).

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Defective SI does not hydrolyze maltotriose

**Location:** Intestinal saccharidase deficiencies

**Stable identifier:** R-HSA-5659899

**Type:** transition

**Compartments:** extracellular region, plasma membrane

**Diseases:** intestinal disaccharidase deficiency

**Inferred from:** Defective SI does not hydrolyze Mal (Homo sapiens)

Mutations that disrupt the catalytic activity or strongly interfere with proper folding, glycosylation and transport of SI (sucrase-isomaltase) are inferred to block the cleavage of maltotriose to maltose and glucose, based on the experimentally demonstrated failure of these SI mutant proteins to hydrolyze maltose (e.g., Sander et al. 2005) and the broad substrate specificity of the normal enzyme (Sim et al. 2010).

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Defective LCT does not hydrolyze Lac

Location: Intestinal saccharidase deficiencies

Stable identifier: R-HSA-5658001

Type: transition

Compartments: extracellular region, plasma membrane

Diseases: lactose intolerance

Mutations that disrupt the catalytic activity of LCT (lactase) block the cleavage of lactose (Lac) to galactose and glucose in the gut lumen and cause lactose intolerance in nursing infants. Affected individuals can develop severe diarrhea; the disease can be effectively managed by complete exclusion of lactose from the diet. A variety of LCT mutant alleles have been described. Two missense mutations that are associated with severe loss of lactase activity in vivo are annotated here (Kuokkanen et al. 2006; Torniainen et al. 2009).

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