

Digestion



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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. 7
- 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. *¬*

Reactome database release: 77

This document contains 3 pathways and 3 reactions (see Table of Contents)

Digestion 才

Stable identifier: R-HSA-8935690



Dietary carbohydrates, fats, and proteins must be broken down to their constituent monosaccharides, fatty acids and sterols, and amino acids, respectively, before they can be absorbed in the intestine.

Dietary lipids such as long-chain triacylglycerols and cholesterol esters are hydrolyzed in the stomach and small intestine to yield long-chain fatty acids, monoacylglycerols, glycerol and cholesterol through the action of a variety of lipases, and are then absorbed into enterocytes.

Carbohydrates include 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.

Dietary protein is hydrolyzed to dipeptides and amino acids by the action of pepsin in the stomach and an array of intestinal hydrolases. All of these enzymes are released in inactive (proenzyme) forms and activated by proteolytic cleavage within the gastrointestinal lumen (Van Beers et al. 1995; Yamada 2015).

Literature references

Yamada, T. (2015). Yamada's Textbook of Gastroenterology. Wiley-Blackwell, 3440.

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

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Digestion of dietary lipid *对*

Location: Digestion

Stable identifier: R-HSA-192456

Compartments: extracellular region



Dietary lipids such as long-chain triacylglycerols and cholesterol esters are digested in the stomach and small intestine to yield long-chain fatty acids, monoacylglycerols, glycerol and cholesterol through the action of a variety of lipases, and are then absorbed into enterocytes.

Literature references

Lombardo, D. (2001). Bile salt-dependent lipase: its pathophysiological implications. *Biochim Biophys Acta, 1533*, 1-28 . 7

Lowe, ME. (2002). The triglyceride lipases of the pancreas. J Lipid Res, 43, 2007-16.

Editions

2007-02-03

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D'Eustachio, P.

Digestion of dietary carbohydrate 7

Location: Digestion

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

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

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2007-01-18	Revised	D'Eustachio, P.

ALPI dimer hydrolyses phosphate monoesters 7

Location: Digestion

Stable identifier: R-HSA-8878787

Type: transition

Compartments: extracellular region, plasma membrane



Alkaline phosphatases (ALPs) are ubiquitous membrane-bound glycoproteins that catalyse the hydrolysis of phosphate monoesters in alkaline conditions (Sharma et al. 2014). To date, little is known about the physiological function of ALPs in most tissues. In humans, four isozymes exist, named from their tissue localisations. One isozyme, intestinal-type alkaline phosphatase (ALPI, IAP), possesses alkaline phosphatase activity but has no specific physiological substrate defiend for it yet. It may be involved in the hydrolysis of pro-drugs in the intestine (Lowe et al. 1990).

Literature references

Hua, JC., Berger, J., Pan, YC., Hulmes, JD., Udenfriend, S. (1986). Partial sequencing of human adult, human fetal, and bovine intestinal alkaline phosphatases: comparison with the human placental and liver isozymes. *Proc. Natl. Acad. Sci. U.S.A., 83*, 2368-72. 7

Sharma, U., Pal, D., Prasad, R. (2014). Alkaline phosphatase: an overview. Indian J Clin Biochem, 29, 269-78. 🛪

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GUCY2C trimer binds GUCA2A,B ↗

Location: Digestion

Stable identifier: R-HSA-8936214

Type: binding

Compartments: extracellular region, plasma membrane



Heat-stable enterotoxin receptor (GUCY2C, STAR) is the receptor for the endogenous peptides guanylin (GUCA2A) and uroguanylin (GUCA2B) and E.coli heat-stable enterotoxin. GUCY2C is an integral membrane protein composed of an extracellular ligand-binding domain, an intracellular domain and a guanylyl cyclase catalytic domain and functions in trimeric form (Vijayachandra et al. 2000). Once activated by its ligands, GUCY2C mediates fluid-ion homeostasis, intestinal inflammation, and cell proliferation in a cGMP-dependent manner (Arshad et al. 2013). In the intestine, salt and fluid secretion is stimulated by E.coli heat-stable enterotoxins through activation of CUCY2C. The endogenous peptides GUCA2A and GUCA2B have structural similarity to these bacterial enterotoxins and function as mediators of Cl-and water secretion in the intestine (Hamra et al. 1993, Forte et al. 1993, Basu et al. 2010).

Literature references

- Hamra, FK., Forte, LR., Eber, SL., Pidhorodeckyj, NV., Krause, WJ., Freeman, RH. et al. (1993). Uroguanylin: structure and activity of a second endogenous peptide that stimulates intestinal guanylate cyclase. *Proc. Natl. Acad. Sci. U.S.A., 90*, 10464-8. 7
- Forte, LR., Eber, SL., Turner, JT., Freeman, RH., Fok, KF., Currie, MG. (1993). Guanylin stimulation of Cl- secretion in human intestinal T84 cells via cyclic guanosine monophosphate. J. Clin. Invest., 91, 2423-8. ↗
- Vijayachandra, K., Guruprasad, M., Bhandari, R., Manjunath, UH., Somesh, BP., Srinivasan, N. et al. (2000). Biochemical characterization of the intracellular domain of the human guanylyl cyclase C receptor provides evidence for a catalytically active homotrimer. *Biochemistry*, *39*, 16075-83.
- Kuhn, M., Raida, M., Adermann, K., Schulz-Knappe, P., Gerzer, R., Heim, JM. et al. (1993). The circulating bioactive form of human guanylin is a high molecular weight peptide (10.3 kDa). *FEBS Lett.*, 318, 205-9.
- Basu, N., Arshad, N., Visweswariah, SS. (2010). Receptor guanylyl cyclase C (GC-C): regulation and signal transduction. *Mol. Cell. Biochem.*, 334, 67-80. *¬*

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PIR oxygenates quercetin *↗*

Location: Digestion

Stable identifier: R-HSA-8953398

Type: transition

Compartments: nucleoplasm



Quercetin is an abundant flavonoid found in edible vegetables, grains and fruits and is used as an ingredient in supplements, beverages, or foods. Pirin (PIR) is a highly conserved nuclear protein (Wendler et al. 1997) which possesses quercetinase activity, transforming quercetin to 2-protocatechuoylphloroglucinol carboxylic acid (2PCPGCA) and carbon monoxide (CO) (Adams & Jia 2005). Quercetin supplements have been promoted for the treatment of a wide spectrum of diseases including cancer but there is insufficient evidence to draw any conclusive proof of its beneficial effects to date (Miles et al. 2014).

Literature references

- Wendler, WM., Kremmer, E., Förster, R., Winnacker, EL. (1997). Identification of pirin, a novel highly conserved nuclear protein. J. Biol. Chem., 272, 8482-9. ↗
- Adams, M., Jia, Z. (2005). Structural and biochemical analysis reveal pirins to possess quercetinase activity. J. Biol. Chem., 280, 28675-82. 🛪

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