Defective ABCG8 causes gallbladder disease 4 and sitosterolemia

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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**


Reactome database release: 73

This document contains 1 pathway and 1 reaction (see Table of Contents)
Defective ABCG8 causes gallbladder disease 4 and sitosterolemia

**Stable identifier:** R-HSA-5679090

**Diseases:** atherosclerosis, cholelithiasis, lipid metabolism disorder

ATP-binding cassette sub-family G member 8 (ABCG8 aka sterolin-2), is a "half transporter", that forms a complex with another half transporter ABCG5 in the endoplasmic reticulum. This complex translocates to the plasma membrane to mediate the ATP-dependent intestinal absorption and facilitation of biliary secretion of cholesterol and phytosterols (eg sitosterol). Defects in either of these half transporters result in loss of enterocyte discrimination between cholesterol and sitosterol causing sterol accumulation and predisposition for atherosclerosis. Defects in ABCG8 are the cause of gallbladder disease 4 (GBD4; MIM:611465), one of the major digestive diseases. Gallstones are composed of cholesterol (cholelithiasis) and are the common manifestations of GBD in western countries (Buch et al. 2007, Rudkowska & Jones 2008, Jakulj et al. 2010). Defects in ABCG8 also cause sitosterolemia (MIM:210250), characterised by unrestricted intestinal absorption of both cholesterol and plant-derived sterols causing hypercholesterolemia and premature coronary atherosclerosis. Patients with sitosterolemia absorb between 15 and 60% of ingested sitosterol, and they excrete only a fraction into the bile (Berge et al. 2000, Othman et al. 2013, Yu et al. 2014).

**Literature references**


Defective ABCG8 (in ABCG5:ABCG8) does not transport sterols from cytosol to extracellular region

Location: Defective ABCG8 causes gallbladder disease 4 and sitosterolemia

Stable identifier: R-HSA-5679101

Type: transition

Compartments: plasma membrane, cytosol, extracellular region

Diseases: cholelithiasis, lipid metabolism disorder, atherosclerosis

ATP-binding cassette sub-family G member 8 (ABCG8 aka sterolin-2), is a "half transporter", that forms a complex with another half transporter ABCG5 in the endoplasmic reticulum. This complex translocates to the plasma membrane to mediate the ATP-dependent intestinal absorption and facilitation of biliary secretion of cholesterol and phytosterols (e.g., sitosterol). Defects in either of these half transporters result in loss of enterocyte discrimination between cholesterol and sitosterol causing sterol accumulation and predisposition for atherosclerosis. Defects in ABCG8 are the cause of gallbladder disease 4 (GBD4; MIM:611465) and sitosterolemia (MIM:210250). A mutation causing GBD4 is D19H (Buch et al. 2007). Mutations causing sitosterolemia include W361*, G574R, Y658*, R263Q and P231T (Berge et al. 2000).

Literature references

