ABCB4 gene

ATP binding cassette subfamily B member 4

Normal Function

The *ABCB4* gene (also known as *MDR3*) provides instructions for making a protein that helps move certain fats called phospholipids across the membranes of liver cells. The protein essentially flips the phospholipids from the inside to the outside of the cells. The protein then releases the phospholipids into a digestive fluid called bile. Outside the liver cells, in the bile duct, phospholipids attach (bind) to bile acids, which are the component of bile that digests fats. Large amounts of bile acids are potentially harmful to cells. When bile acids are bound to phospholipids, they are less toxic.

Health Conditions Related to Genetic Changes

Progressive familial intrahepatic cholestasis

Several variants (also called mutations) in the *ABCB4* gene have been found to cause a severe form of liver disease called progressive familial intrahepatic cholestasis type 3 (PFIC3). The signs and symptoms of PFIC3 often appear in early childhood. PFIC3 causes progressive liver disease, which often leads to liver failure. Affected individuals have a variant in both copies of the *ABCB4* gene. Variants that cause the cell to produce short, nonfunctional proteins or no proteins at all tend to be associated with more severe liver disease that appears earlier in life. *ABCB4* gene variants that cause PFIC3 impair the movement of phospholipids across cell membranes, leading to a lack of phospholipids to bind to bile acids. A buildup of free bile acids damages liver cells, which causes the signs and symptoms of liver disease.

Intrahepatic cholestasis of pregnancy

Pregnant people with variants in the *ABCB4* gene are at risk of developing a condition called intrahepatic cholestasis of pregnancy. Affected people typically develop impaired bile secretion and severe itching during the second half of pregnancy. These features usually disappear after the baby is born.

Many of the variants in the *ABCB4* gene that have been found in people with intrahepatic cholestasis of pregnancy cause the substitution of one protein building block (amino acid) for another. A few variants cause the cell to produce an abnormally short protein. Normally, enough protein is still available to move an adequate amount of

phospholipids out of liver cells to bind to bile acids. The added stress on the liver during pregnancy, however, contributes to the buildup of bile acids.

When there are not enough phospholipids to bind to bile acids, the bile acids can build up to toxic levels and impair liver function, including the regulation of bile flow. Problems with bile flow lead to the signs and symptoms of intrahepatic cholestasis of pregnancy. Additional factors, such as increased hormone levels during pregnancy, are thought to contribute to the risk of developing this complex disorder.

Other disorders

Variants in the *ABCB4* gene are also associated with a rare condition called low phospholipid-associated cholelithiasis (LPAC). This condition is characterized by the formation of small pebble-like deposits of cholesterol (known as gallstones) in the gallbladder or bile ducts. In people with LPAC, gallstones usually occur before age 40, which is young for the appearance of gallstones. In addition, affected individuals may have an accumulation of small crystals of cholesterol (microlithiasis) or a material called biliary sludge in the bile ducts of the liver. Biliary sludge is made up of solid particles that are usually dissolved in bile, including cholesterol crystals and calcium salts. The gallstones, cholesterol crystals, or biliary sludge can cause symptoms, such as pain, fever, nausea, or inflammation of the pancreas (pancreatitis), that can recur even after the gallbladder is removed.

It is thought that the variants in the *ABCB4* gene that are involved in LPAC impair the protein's ability to transfer phospholipids into bile. Because phospholipids help keep cholesterol dissolved in bile, the lack of phospholipids can result in the formation of gallstones or crystals from undissolved cholesterol.

Other Names for This Gene

- ABC21
- ATP-binding cassette, sub-family B (MDR/TAP), member 4
- ATP-binding cassette, subfamily B, member 4
- GBD1
- ICP3
- MDR3
- multidrug resistance 3
- P-glycoprotein 3
- PFIC-3
- PGY3

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ABCB4 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5244[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ABCB4%5BTIAB%5D%29+OR+%28MDR3%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- ATP-BINDING CASSETTE, SUBFAMILY B, MEMBER 4; ABCB4 (https://omim.org/entry/171060)
- GALLBLADDER DISEASE 1; GBD1 (https://omim.org/entry/600803)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/5244)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ABCB4[gene])

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Genomic Location

The *ABCB4* gene is found on chromosome 7 (https://medlineplus.gov/genetics/chromosome/7/).

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