ABCB11 Gene

Subjects: Genetics & Heredity

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ATP binding cassette subfamily B member 11

genes

1. Normal Function

The *ABCB11* gene provides instructions for making a protein called the bile salt export pump (BSEP), which is found in the liver. Bile salts are a component of bile, which is used to digest fats. Bile salts are produced by liver cells and then transported out of the cell by BSEP to make bile. The release of bile salts from liver cells is critical for the normal secretion of bile.

2. Health Conditions Related to Genetic Changes

2.1 Benign recurrent intrahepatic cholestasis

Mutations in the *ABCB11* gene can cause benign recurrent intrahepatic cholestasis type 2 (BRIC2). People with BRIC2 have occasional episodes of impaired bile secretion that lead to severe itching (pruritus) and yellowing of the skin and whites of the eyes (jaundice). On occasion, people with BRIC2 have later been diagnosed with a more severe condition called progressive familial intrahepatic cholestasis type 2 (described below) when their symptoms worsened.

Affected individuals have a mutation in both copies of the *ABCB11* gene. Mutations in the *ABCB11* gene that cause BRIC2 lead to a 40 to 50 percent reduction of bile salt transport. The resulting buildup of bile salts in the liver leads to the signs and symptoms of BRIC2. It is unclear what causes the episodes to begin or end.

2.2 Progressive familial intrahepatic cholestasis

More than 100 mutations in the *ABCB11* gene have been found to cause a severe form of liver disease called progressive familial intrahepatic cholestasis type 2 (PFIC2) that usually leads to liver failure. Development of this condition requires a mutation in both copies of the *ABCB11* gene. Mutations in the *ABCB11* gene that cause PFIC2 result in a 70 percent reduction to complete absence of bile salt transport out of the liver. The lack of transport causes bile salts to build up in liver cells, leading to liver disease and its associated signs and symptoms.

Mutations that lead to the production of a short, nonfunctional protein or cause no protein to be produced tend to be associated with severe liver disease that appears earlier in life. People with no functional BSEP protein also seem to be at a greater risk of developing a type of liver cancer called hepatocellular carcinoma.

2.3 Intrahepatic cholestasis of pregnancy

Women with a change in the *ABCB11* gene are at risk of developing a condition called intrahepatic cholestasis of pregnancy. Affected women typically develop impaired bile secretion (cholestasis) and pruritus during the third trimester of pregnancy, and these features disappear after the baby is born. A common variation (polymorphism) in the *ABCB11* gene is found more often in women who develop this condition than women who do not. This variation leads to a change in a single protein building block (amino acid) in the BSEP protein. Specifically, the amino acid valine is replaced by the amino acid alanine at position 444 of the protein (written as V444A). This change leads to a reduction in the amount of BSEP protein in liver cells. In rare cases, an uncommon change (a mutation) in one copy of the *ABCB11* gene is found in women with intrahepatic cholestasis of pregnancy. A single mutation in this gene increases the risk of developing intrahepatic cholestasis of pregnancy. These mutations likely reduce the amount or function of the BSEP protein.

In women with either type of genetic change, enough BSEP function remains for sufficient bile secretion under most circumstances. Studies show that the hormones estrogen and progesterone (and products formed during their breakdown), which are elevated during pregnancy, further reduce the function of BSEP, resulting in impaired bile secretion and the signs and symptoms of intrahepatic cholestasis of pregnancy. Many factors, however, likely contribute to the risk of developing this complex disorder.

3. Other Names for This Gene

- ABC16
- ABCBB_HUMAN
- ATP-binding cassette, sub-family B (MDR/TAP), member 11
- bile salt export pump
- BRIC2
- BSEP
- PFIC-2
- PFIC2
- progressive familial intrahepatic cholestasis 2
- sister p-glycoprotein
- SPGP

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