ABCB11 gene
ATP binding cassette subfamily B member 11

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.

Health Conditions Related to Genetic Changes

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.

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.
Intrahepatic cholestasis of pregnancy

Women with a change in the \textit{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 \textit{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 \textit{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.

Chromosomal Location

Cytogenetic Location: 2q31.1, which is the long (q) arm of chromosome 2 at position 31.1

Molecular Location: base pairs 168,915,468 to 169,031,396 on chromosome 2 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)

Other Names for This Gene

- ABC16
- ABCBB_HUMAN
- ATP-binding cassette, sub-family B (MDR/TAP), member 11

Credit: Genome Decoration Page/NCBI
• bile salt export pump
• BRIC2
• BSEP
• PFIC-2
• PFIC2
• progressive familial intrahepatic cholestasis 2
• sister p-glycoprotein
• SPGP

Additional Information & Resources

Educational Resources
• Madame Curie Bioscience Database: Fat Absorption and Lipid Metabolism in Cholestasis
  https://www.ncbi.nlm.nih.gov/books/NBK6420/
• Madame Curie Bioscience Database: Genetics of Cholestatic Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK6475/#A20671
• The Human ATP-Binding Cassette (ABC) Transporter Superfamily: ABCB Genes
  https://www.ncbi.nlm.nih.gov/books/NBK3/#A179

Clinical Information from GeneReviews
• ATP8B1 Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1297

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ABCB11%5BTIAB%5D %29+OR+%28BSEP%29%29+AND+%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29+AND+english%5Blanguage%5D+AND+human%5Bhsa%5D+AND+%22last+1800+days%22+AND+ABC

Catalog of Genes and Diseases from OMIM
• ATP-BINDING CASSETTE, SUBFAMILY B, MEMBER 11
  http://omim.org/entry/603201

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ACB11.html
• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ABCB11%5Bgene%5D
• HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#/hgnc_id/HGNC:42

• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:8647

• NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/8647

• UniProt
  https://www.uniprot.org/uniprot/O95342

Sources for This Summary

• OMIM: ATP-BINDING CASSETTE, SUBFAMILY B, MEMBER 11
  http://omim.org/entry/603201

• Davit-Spraul A, Gonzales E, Baussan C, Jacquemin E. Progressive familial intrahepatic cholestasis. Orphanet J Rare Dis. 2009 Jan 8;4:1. doi: 10.1186/1750-1172-4-1. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19133130
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2647530/

• Dixon PH, van Mil SW, Chambers J, Strautnieks S, Thompson RJ, Lammert F, Kubitz R, Keitel V, Glantz A, Mattsson LA, Marschall HU, Molokhia M, Moore GE, Linton KJ, Williamson C. Contribution of variant alleles of ABCB11 to susceptibility to intrahepatic cholestasis of pregnancy. Gut. 2009 Apr;58(4):537-44. doi: 10.1136/gut.2008.159541. Epub 2008 Nov 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18987030

• Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. World J Gastroenterol. 2009 May 7;15(17):2049-66. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19418576
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2678574/

• Jansen PL, Sturm E. Genetic cholestasis, causes and consequences for hepatobiliary transport. Liver Int. 2003 Oct;23(5):315-22. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14708891

• Kagawa T, Watanabe N, Mochizuki K, Numari A, Ikeno Y, Itoh J, Tanaka H, Arias IM, Mine T. Phenotypic differences in PFIC2 and BRIC2 correlate with protein stability of mutant Bsep and impaired taurocholate secretion in MDCK II cells. Am J Physiol Gastrointest Liver Physiol. 2008 Jan;294(1):G58-67. Epub 2007 Oct 18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17947449

• Lam P, Pearson CL, Soroka CJ, Xu S, Mennone A, Boyer JL. Levels of plasma membrane expression in progressive and benign mutations of the bile salt export pump (Bsep/Abcb11) correlate with severity of cholestatic diseases. Am J Physiol Cell Physiol. 2007 Nov;293(5):C1709-16. Epub 2007 Sep 13.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17855769

• Lam P, Soroka CJ, Boyer JL. The bile salt export pump: clinical and experimental aspects of genetic and acquired cholestatic liver disease. Semin Liver Dis. 2010 May;30(2):125-33. doi: 10.1055/s-0030-1253222. Epub 2010 Apr 26. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20422495
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3008346/
• Meier Y, Pauli-Magnus C, Zanger UM, Klein K, Schaeffeler E, Nussler AK, Nussler N, Eichelbaum M, Meier PJ, Stieger B. Interindividual variability of canicular ATP-binding-cassette (ABC)-transporter expression in human liver. Hepatology. 2006 Jul;44(1):62-74. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16799996

• Meier Y, Zodan T, Lang C, Zimmermann R, Kullak-Ublick GA, Meier PJ, Stieger B, Pauli-Magnus C. Increased susceptibility for intrahepatic cholestasis of pregnancy and contraceptive-induced cholestasis in carriers of the 1331T>C polymorphism in the bile salt export pump. World J Gastroenterol. 2008 Jan 7;14(1):38-45. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18176959
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2673389/

• Pauli-Magnus C, Stieger B, Meier Y, Kullak-Ublick GA, Meier PJ. Enterohepatic transport of bile salts and genetics of cholestasis. J Hepatol. 2005 Aug;43(2):342-57. Review. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15975683

• Strautnieks SS, Bull LN, Knisely AS, Kocoshis SA, Dahl N, Arnell H, Sokal E, Dahan K, Childs S, Ling V, Tanner MS, Kagalwalla AF, Németh A, Pawlowska J, Baker A, Mieli-Vergani G, Freimer NB, Gardiner RM, Thompson RJ. A gene encoding a liver-specific ABC transporter is mutated in progressive familial intrahepatic cholestasis. Nat Genet. 1998 Nov;20(3):233-8. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9806540

• Strautnieks SS, Byrne JA, Pawlikowska L, Cebecauerová D, Rayner A, Dutton L, Meier Y, Antoniou A, Stieger B, Arnell H, Ozçay F, Al-Hussaini HF, Bassas AF, Verkade HJ, Fischler B, Németh A, Kotalová R, Shneider BL, Cielecka-Kuszyk J, McClean P, Whittington PF, Sokal E, Jirsa M, Wali SH, Jankowska I, Pawlowska J, Mieli-Vergani G, Knisely AS, Bull LN, Thompson RJ. Severe bile salt export pump deficiency: 82 different ABCB11 mutations in 109 families. Gastroenterology. 2008 Apr;134(4):1203-14. doi: 10.1053/j.gastro.2008.01.038. Epub 2008 Jan 18. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18395098

• Thompson R, Strautnieks S. BSEP: function and role in progressive familial intrahepatic cholestasis. Semin Liver Dis. 2001 Nov;21(4):545-50. Review. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11745042

• Vallejo M, Briz O, Serrano MA, Monte MJ, Marin JJ. Potential role of trans-inhibition of the bile salt export pump by progesterone metabolites in the etiopathogenesis of intrahepatic cholestasis of pregnancy. J Hepatol. 2006 Jun;44(6):1150-7. Epub 2005 Nov 7. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16458994

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/ABCB11

Reviewed: June 2012
Published: June 23, 2020

Lister Hill National Center for Biomedical Communications
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