

PNPLA3 gene

patatin like phospholipase domain containing 3

Normal Function

The *PNPLA3* gene provides instructions for making a protein called adiponutrin, which is found in fat cells (adipocytes) and liver cells (hepatocytes). The liver is a part of the digestive system that helps break down food, store energy, and remove waste products, including toxins. The function of the adiponutrin protein is not well understood, but it is thought to help regulate the development of adipocytes and the production and breakdown of fats (lipogenesis and lipolysis) in hepatocytes and adipocytes. Studies indicate that the activity (expression) of the *PNPLA3* gene decreases during periods without food (fasting) and increases after eating, suggesting that the amount of adiponutrin protein produced is regulated as needed to help process and store fats in the diet.

Health Conditions Related to Genetic Changes

Non-alcoholic fatty liver disease

A particular variation in the *PNPLA3* gene has been associated with an increased risk of developing non-alcoholic fatty liver disease (NAFLD). NAFLD is a buildup of excessive fat in the liver that can lead to liver damage resembling the damage caused by alcohol abuse, but that occurs in people who do not drink heavily. In some cases NAFLD leads to inflammation of the liver (non-alcoholic steatohepatitis, also known as NASH) and permanent liver damage (cirrhosis).

The *PNPLA3* gene variation associated with NAFLD changes the protein building block (amino acid) isoleucine to the amino acid methionine at protein position 148, written as Ile148Met or I148M. Research suggests that the altered protein leads to increased production and decreased breakdown of fats in the liver. Studies are ongoing to determine how this and other genetic changes contribute to the development of NAFLD and its complications.

Other disorders

The I148M variation of the *PNPLA3* gene has also been associated with the worsening of other liver diseases, such as a viral infection called hepatitis C. The variation also increases the risk of liver damage in people with alcohol use disorder. The mechanism

of this effect is not well understood, but the altered protein appears to increase fibrosis of the liver in people with these conditions.

Other Names for This Gene

- acylglycerol O-acyltransferase
- adiponutrin
- ADPN
- C22orf20
- calcium-independent phospholipase A2-epsilon
- dJ796I17.1
- FLJ22012
- iPLA(2)epsilon
- iPLA2-epsilon
- iPLA2epsilon
- patatin-like phospholipase domain-containing protein 3

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PNPLA3 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=80339\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=80339[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28PNPLA3%5BTI%5D%29+OR+%28patatin+like+phospholipase+domain+containing+3%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>)

Catalog of Genes and Diseases from OMIM

- PATATIN-LIKE PHOSPHOLIPASE DOMAIN-CONTAINING PROTEIN 3; PNPLA3 (<https://omim.org/entry/609567>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/80339>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=PNPLA3\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=PNPLA3[gene]))

References

- Baulande S, Lasnier F, Lucas M, Pairault J. Adiponutrin, a transmembraneprotein corresponding to a novel dietary- and obesity-linked mRNA specifically expressed in the adipose lineage. *J Biol Chem*. 2001 Sep 7;276(36):33336-44. doi:10.1074/jbc.M105193200. Epub 2001 Jun 28. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11431482>)
- Caligiuri A, Gentilini A, Marra F. Molecular Pathogenesis of NASH. *Int J MolSci*. 2016 Sep 20;17(9):1575. doi: 10.3390/ijms17091575. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/27657051>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5037841/>)
- Chen LZ, Xin YN, Geng N, Jiang M, Zhang DD, Xuan SY. PNPLA3 I148M variant innonalcoholic fatty liver disease: demographic and ethnic characteristics and therole of the variant in nonalcoholic fatty liver fibrosis. *World J Gastroenterol*. 2015 Jan 21;21(3):794-802. doi: 10.3748/wjg.v21.i3.794. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25624712>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4299331/>)
- Dongiovanni P, Donati B, Fares R, Lombardi R, Mancina RM, Romeo S, Valenti L. PNPLA3 I148M polymorphism and progressive liver disease. *World J Gastroenterol*. 2013 Nov 7;19(41):6969-78. doi: 10.3748/wjg.v19.i41.6969. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24222941>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3819533/>)
- Krawczyk M, Portincasa P, Lammert F. PNPLA3-associated steatohepatitis: towards a gene-based classification of fatty liver disease. *Semin Liver Dis*. 2013 Nov; 33(4):369-79. doi: 10.1055/s-0033-1358525. Epub 2013 Nov 12. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24222094>)
- Romeo S, Kozlitina J, Xing C, Pertsemlidis A, Cox D, Pennacchio LA, Boerwinkle E, Cohen JC, Hobbs HH. Genetic variation in PNPLA3 confers susceptibility tonalcoholic fatty liver disease. *Nat Genet*. 2008 Dec;40(12):1461-5. doi:10.1038/ng.257. Epub 2008 Sep 25. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18820647>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2597056/>)
- Severson TJ, Besur S, Bonkovsky HL. Genetic factors that affect nonalcoholicfatty liver disease: A systematic clinical review. *World J Gastroenterol*. 2016 Aug 7;22(29): 6742-56. doi: 10.3748/wjg.v22.i29.6742. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/27547017>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4970479/>)
- Yu J, Marsh S, Hu J, Feng W, Wu C. The Pathogenesis of Nonalcoholic Fatty Liver Disease: Interplay between Diet, Gut Microbiota, and Genetic Background. *Gastroenterol Res Pract*. 2016;2016:2862173. doi: 10.1155/2016/2862173. Epub 2016 May 9. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/27247565>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4876215/>)

Genomic Location

The *PNPLA3* gene is found on chromosome 22 (<https://medlineplus.gov/genetics/chromosome/22/>).

Last updated November 1, 2016