LCAT gene

lecithin-cholesterol acyltransferase

Normal Function

The *LCAT* gene provides instructions for making an enzyme called lecithin-cholesterol acyltransferase (LCAT). This enzyme plays a role in removing cholesterol from the blood and tissues. Cholesterol is a waxy, fat-like substance that is produced in the body and obtained from foods that come from animals (particularly egg yolks, meat, poultry, fish, and dairy products). The body needs this substance to build cell membranes, make certain hormones, and produce compounds that aid in fat digestion. Too much cholesterol, however, increases a person's risk of developing heart disease, and can also lead to buildup of cholesterol in other tissues.

The LCAT enzyme helps transport cholesterol out of the blood and tissues by a process called cholesterol esterification. This process results in a form of cholesterol that is more efficiently carried by molecules called lipoproteins, which transport the cholesterol to the liver. Once in the liver, the cholesterol is redistributed to other tissues or removed from the body. The enzyme has two major functions, called alpha- and beta-LCAT activity. Alpha-LCAT activity helps attach cholesterol to a lipoprotein called high-density lipoprotein (HDL). Beta-LCAT activity helps attach cholesterol to other lipoproteins called very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL).

Health Conditions Related to Genetic Changes

Complete LCAT deficiency

More than 70 mutations in the *LCAT* gene have been identified in people with complete LCAT deficiency, a disorder that primarily causes corneal clouding and kidney problems. Individuals with complete LCAT deficiency have mutations in both copies of the *LCAT* gene in each cell. Most of these mutations change single amino acids in the LCAT enzyme sequence. Others add or delete small amounts of genetic material in the *LCAT* gene. The mutations either prevent the production of LCAT or impair both alpha-LCAT and beta-LCAT activity, reducing the enzyme's ability to attach cholesterol to lipoproteins. Impairment of this mechanism for reducing cholesterol in the body leads to cholesterol deposits in the corneas, kidneys, and other tissues and organs. These deposits cause the signs and symptoms of complete LCAT deficiency.

Fish-eye disease

At least 18 mutations in the *LCAT* gene have been identified in people with fish-eye disease, also called partial LCAT deficiency. This disorder causes clouding of the clear covering of the eyes (corneas). Individuals with fish-eye disease have mutations

in both copies of the *LCAT* gene in each cell. Most of these mutations change single protein building blocks (amino acids) in the LCAT sequence. The mutations impair alpha-LCAT activity, reducing the enzyme's ability to attach cholesterol to HDL. Impairment of this mechanism for reducing cholesterol in the body leads to cholesterol deposits in the corneas that gradually cause them to become cloudy.

Other disorders

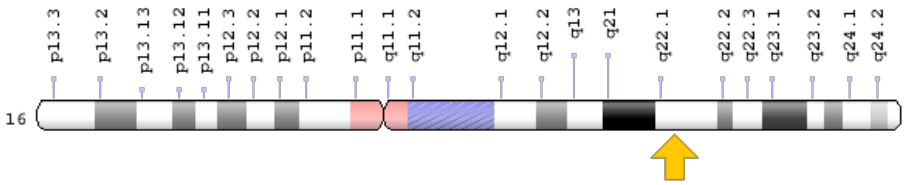
People with one *LCAT* gene mutation in each cell may have an increased risk of atherosclerosis, which is an accumulation of cholesterol-rich fatty deposits and scar-like tissue in the lining of the arteries that can impede blood flow and lead to heart attacks, strokes, and other health problems. A single *LCAT* gene mutation likely reduces alpha-LCAT activity and binding of cholesterol to HDL, leading to less efficient transport of cholesterol from the blood and resulting in the development of atherosclerosis.

Atherosclerosis also occurs in some people with fish-eye disease or complete LCAT deficiency. However, because atherosclerosis is very common in the general population and both fish-eye disease and complete LCAT deficiency are very rare, it is difficult to determine whether affected individuals are at increased risk of atherosclerosis.

Chromosomal Location

Cytogenetic Location: 16q22.1, which is the long (q) arm of chromosome 16 at position 22.1

Molecular Location: base pairs 67,939,750 to 67,944,120 on chromosome 16 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- LCAT_HUMAN
- phosphatidylcholine-sterol acyltransferase
- phosphatidylcholine-sterol acyltransferase precursor
- phospholipid-cholesterol acyltransferase

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database: Fat Absorption and Lipid Metabolism in Cholestasis
  https://www.ncbi.nlm.nih.gov/books/NBK6420/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28LCAT%5BTIAB%5D%29+OR+%28lecithin-cholesterol+acyltransferase%5BTIAB%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+1080+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- ATHEROSCLEROSIS SUSCEPTIBILITY
  http://omim.org/entry/108725
- LECITHIN:CHOLESTEROL ACYLTRANSFERASE
  http://omim.org/entry/606967

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_LCAT.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=LCAT%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:6522
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:3931
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3931
- UniProt
  https://www.uniprot.org/uniprot/P04180

Sources for This Summary

- Calabresi L, Pisciotta L, Costantin A, Frigerio I, Eberini I, Alessandrini P, Arca M, Bon GB, Boscutti G, Busnach G, Frascà G, Gesualdo L, Gigante M, Lupattelli G, Montali A, Pizzolitto S, Rabbone I, Rolleri M, Ruotolo G, Sampietro T, Sessa A, Vaudo G, Cantafora A, Veglia F, Calandra S, Bertolini S, Franceschini G. The molecular basis of lecithin:cholesterol acyltransferase deficiency syndromes: a comprehensive study of molecular and biochemical findings in 13 unrelated Italian families. Arterioscler Thromb Vasc Biol. 2005 Sep;25(9):1972-8. Epub 2005 Jun 30.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15994445
- Duivenvoorden R, Holleboom AG, van den Bogaard B, Nederveen AJ, de Groot E, Hutten BA, Schimmel AW, Hovingh GK, Kastelein JJ, Kuivenhoven JA, Stroes ES. Carriers of lecithin cholesterol acyltransferase gene mutations have accelerated atherogenesis as assessed by carotid 3.0-T magnetic resonance imaging [corrected]. J Am Coll Cardiol. 2011 Dec 6;58(24):2481-7. doi: 10.1016/j.jacc.2010.11.092. Erratum in: J Am Coll Cardiol. 2012 Jan 10;59(2):196.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22133847
- OMIM: LECITHIN:CHOLESTEROL ACYLTRANSFERASE
  http://omim.org/entry/606967
- Reshetnyak Y, Tchedre KT, Nair MP, Pritchard PH, Lacko AG. Structural differences between wild-type and fish eye disease mutant of lecithin:cholesterol acyltransferase. J Biomol Struct Dyn. 2006 Aug;24(1):75-82.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16780378
- Roshan B, Ganda OP, Desilva R, Ganim RB, Ward E, Haessler SD, Polisecki EY, Asztalos BF, Schaefer EJ. Homozygous lecithin:cholesterol acyltransferase (LCAT) deficiency due to a new loss of function mutation and review of the literature. J Clin Lipidol. 2011 Nov-Dec;5(6):493-9. doi: 10.1016/j.jacl.2011.07.002. Epub 2011 Aug 23. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22108153
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4565181/
- Savel J, Lafitte M, Pucheu Y, Pradeau V, Tabarin A, Couffinhal T. Very low levels of HDL cholesterol and atherosclerosis, a variable relationship--a review of LCAT deficiency. Vasc Health Risk Manag. 2012;8:357-61. doi: 10.2147/VHRM.S29985. Epub 2012 Jun 5. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22701329
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3373316/
- van den Bogaard B, Holleboom AG, Duivenvoorden R, Hutten BA, Kastelein JJ, Hovingh GK, Kuivenhoven JA, Stroes ES, van den Born BJ. Patients with low HDL-cholesterol caused by mutations in LCAT have increased arterial stiffness. Atherosclerosis. 2012 Dec;225(2):481-5. doi: 10.1016/j.atherosclerosis.2012.09.022. Epub 2012 Sep 27.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23078883

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