

## LDLRAP1 gene

low density lipoprotein receptor adaptor protein 1

### Normal Function

The *LDLRAP1* gene (also known as *ARH*) provides instructions for making a protein that helps remove cholesterol from the bloodstream. Cholesterol is a waxy, fat-like substance that is produced in the body and obtained from foods that come from animals.

The function of the LDLRAP1 protein is particularly important in the liver, which is the organ responsible for clearing most excess cholesterol from the body.

The LDLRAP1 protein interacts with a protein called a low-density lipoprotein receptor. This type of receptor attaches (binds) to particles called low-density lipoproteins (LDLs), which are the primary carriers of cholesterol in the blood. The receptors sit on the outer surface of cells, where they pick up LDLs circulating in the bloodstream. The LDLRAP1 protein appears to play a critical role in moving these receptors, together with their attached LDLs, from the cell surface to the interior of the cell. Once inside the cell, LDLs are broken down to release cholesterol. The cholesterol is then used by the cell, stored, or removed from the body.

### Health Conditions Related to Genetic Changes

#### Familial hypercholesterolemia

More than 20 mutations in the *LDLRAP1* gene have been shown to cause a form of familial hypercholesterolemia called autosomal recessive hypercholesterolemia. These mutations lead to the production of an abnormally small, nonfunctional version of the LDLRAP1 protein or prevent cells from making any of this protein. Without the LDLRAP1 protein, low-density lipoprotein receptors are unable to remove LDLs from the bloodstream effectively. Although the receptors can still bind normally to LDLs, these molecules are not properly transported into cells (particularly liver cells). As a result, many extra LDLs remain in the blood.

Because LDLs are major carriers of cholesterol in the blood, people with mutations in the *LDLRAP1* gene have very high blood levels of cholesterol. As the excess cholesterol circulates through the bloodstream, it is deposited abnormally in tissues such as the skin, tendons, and arteries that supply blood to the heart (coronary arteries).

A buildup of cholesterol in the walls of coronary arteries greatly increases a person's risk of having a heart attack.

## Other Names for This Gene

- ARH
- ARH\_HUMAN
- autosomal recessive hypercholesterolemia protein
- FHCB1
- FHCB2
- LDL receptor adaptor protein
- MGC34705

## Additional Information & Resources

### Tests Listed in the Genetic Testing Registry

- Tests of LDLRAP1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=26119\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=26119[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28LDLRAP1%5BTIAB%5D%29+OR+%28%28ARH%5BTIAB%5D%29+OR+%28autosomal+recessive+hypercholesterolemia+protein%5BTIAB%5D%29+OR+%28LDL+receptor+adaptor+protein%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+1440+days%22%5Bdp%5D>)

### Catalog of Genes and Diseases from OMIM

- LOW DENSITY LIPOPROTEIN RECEPTOR ADAPTOR PROTEIN 1; LDLRAP1 (<https://omim.org/entry/605747>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/26119>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=LDLRAP1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=LDLRAP1[gene]))

## References

- Garcia CK, Wilund K, Arca M, Zuliani G, Fellin R, Maioli M, Calandra S, Bertolini S, Cossu F, Grishin N, Barnes R, Cohen JC, Hobbs HH. Autosomal recessive hypercholesterolemia caused by mutations in a putative LDL receptor adaptor protein. *Science*. 2001 May 18;292(5520):1394-8. doi:10.1126/science.1060458. Epub 2001 Apr 26. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11326085>)

- Garuti R, Jones C, Li WP, Michaely P, Herz J, Gerard RD, Cohen JC, Hobbs HH. The modular adaptor protein autosomal recessive hypercholesterolemia (ARH) promotes low density lipoprotein receptor clustering into clathrin-coated pits. *J Biol Chem*. 2005 Dec 9;280(49):40996-1004. doi: 10.1074/jbc.M509394200. Epub 2005 Sep 22. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16179341>)
- Michaely P, Li WP, Anderson RG, Cohen JC, Hobbs HH. The modular adaptor protein ARH is required for low density lipoprotein (LDL) binding and internalization but not for LDL receptor clustering in coated pits. *J Biol Chem*. 2004 Aug 6;279(32):34023-31. doi: 10.1074/jbc.M405242200. Epub 2004 May 27. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15166224>)
- Sirinian MI, Belleudi F, Campagna F, Ceridono M, Garofalo T, Quagliarini F, Verna R, Calandra S, Bertolini S, Sorice M, Torrisi MR, Arca M. Adaptor protein ARH is recruited to the plasma membrane by low density lipoprotein (LDL) binding and modulates endocytosis of the LDL/LDL receptor complex in hepatocytes. *J Biol Chem*. 2005 Nov 18;280(46):38416-23. doi: 10.1074/jbc.M504343200. Epub 2005 Aug 29. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16129683>)
- Soutar AK, Naoumova RP, Traub LM. Genetics, clinical phenotype, and molecular cell biology of autosomal recessive hypercholesterolemia. *Arterioscler Thromb Vasc Biol*. 2003 Nov 1;23(11):1963-70. doi: 10.1161/01.ATV.0000094410.66558.9A. Epub 2003 Sep 4. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12958046>)
- Soutar AK, Naoumova RP. Autosomal recessive hypercholesterolemia. *Semin Vasc Med*. 2004 Aug;4(3):241-8. doi: 10.1055/s-2004-861491. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15630633>)
- Wilund KR, Yi M, Campagna F, Arca M, Zuliani G, Fellin R, Ho YK, Garcia JV, Hobbs HH, Cohen JC. Molecular mechanisms of autosomal recessive hypercholesterolemia. *Hum Mol Genet*. 2002 Nov 15;11(24):3019-30. doi: 10.1093/hmg/11.24.3019. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12417523>)

## Genomic Location

The *LDLRAP1* gene is found on chromosome 1 (<https://medlineplus.gov/genetics/chromosome/1/>).

**Last updated January 1, 2020**