LRP2 gene

LDL receptor related protein 2

Normal Function

The *LRP2* gene provides instructions for making a protein called megalin, which functions as a receptor. Receptor proteins have specific sites into which certain other proteins, called ligands, fit like keys into locks. Together, ligands and their receptors trigger signals that affect cell development and function. Megalin has many ligands involved in various body processes, including the absorption of vitamins A and D, immune functioning, stress response, and the transport of fats in the bloodstream.

Megalin is embedded in the membrane of cells that line the surfaces and cavities of the body (epithelial cells). The receptor helps move its ligands from the cell surface into the cell (endocytosis), and is also involved in transporting the ligands of a related receptor called cubulin. Megalin is active in the development and function of many parts of the body, including the brain and spinal cord (central nervous system), eyes, ears, lungs, intestine, reproductive system, and the small tubes in the kidneys where urine is formed (renal tubules).

Health Conditions Related to Genetic Changes

Donnai-Barrow syndrome

At least twelve *LRP2* gene mutations have been identified in people with Donnai-Barrow syndrome. These mutations are believed to result in the absence of functional megalin protein. The lack of functional megalin in the renal tubules causes megalin's various ligands to be excreted in the urine rather than being absorbed back into the bloodstream. The features of Donnai-Barrow syndrome are probably caused by the inability of megalin to help absorb these ligands, disruption of biochemical signaling pathways, or other effects of the nonfunctional megalin protein. However, it is unclear how these abnormalities result in the specific signs and symptoms of the disorder.

A condition previously classified as a separate disorder called facio-oculo-acoustico-renal (FOAR) syndrome has also been found to be caused by *LRP2* gene mutations. FOAR syndrome is now considered to be the same disorder as Donnai-Barrow syndrome.

Coloboma

Prostate cancer

Cancers

Certain common genetic variations (polymorphisms) in the *LRP2* gene may be associated with differences in the progression, recurrence, and severity of prostate cancer in affected men. Androgens, which are male sex hormones that contribute to the growth of cancerous (malignant) prostate tumors, are among megalin's ligands. A recent study suggests that prostate tumor cells may produce increased amounts of megalin and thereby absorb more androgens. *LRP2* gene polymorphisms that increase the activity of megalin may encourage more aggressive tumor growth, while polymorphisms that decrease the activity of megalin may tend to slow tumor growth.

Other disorders

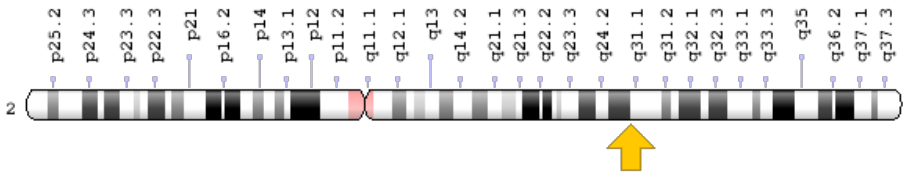
Certain *LRP2* gene polymorphisms have also been associated with increased levels of low-density lipoproteins (LDLs) and cholesterol in the blood. LDLs are the primary carriers of cholesterol in the blood. Cholesterol is a waxy, fat-like substance that is produced in the body and obtained from foods that come from animals. Increased LDL levels may result in excess cholesterol circulating through the bloodstream and accumulating on the walls of the blood vessels, increasing a person's risk of cardiovascular disease.

LDLs are among megalin's ligands, and researchers believe that variations in megalin function resulting from *LRP2* gene changes may influence LDL levels.

Chromosomal Location

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

Molecular Location: base pairs 169,127,109 to 169,362,597 on chromosome 2 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- calcium sensor protein
- DBS
- glycoprotein 330 (gp330)
- gp330

- Heymann nephritis antigen homolog
- low density lipoprotein receptor-related protein 2
- LRP2_HUMAN
- megalin

Additional Information & Resources

Clinical Information from GeneReviews

- Donnai-Barrow Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1878

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28LRP2%5BTIAB%5D%29+OR+%28megalin%5BTIAB%5D%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

- LOW DENSITY LIPOPROTEIN RECEPTOR-RELATED PROTEIN 2
  http://omim.org/entry/600073

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_LRP2.html
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:6694
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4036
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4036
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