



## Leptin receptor deficiency

Leptin receptor deficiency is a condition that causes severe obesity beginning in the first few months of life. Affected individuals are of normal weight at birth, but they are constantly hungry and quickly gain weight. The extreme hunger leads to chronic excessive eating (hyperphagia) and obesity. Beginning in early childhood, affected individuals develop abnormal eating behaviors such as fighting with other children over food, hoarding food, and eating in secret.

People with leptin receptor deficiency also have hypogonadotropic hypogonadism, which is a condition caused by reduced production of hormones that direct sexual development. Affected individuals experience delayed puberty or do not go through puberty, and they may be unable to conceive children (infertile).

### Frequency

Leptin receptor deficiency is a rare cause of obesity. Its prevalence is unknown.

### Causes

Leptin receptor deficiency is caused by mutations in the *LEPR* gene. This gene provides instructions for making a protein called the leptin receptor, which is involved in the regulation of body weight. The leptin receptor protein is found on the surface of cells in many organs and tissues of the body including a part of the brain called the hypothalamus. The hypothalamus controls hunger and thirst as well as other functions such as sleep, moods, and body temperature. It also regulates the release of many hormones that have functions throughout the body.

The leptin receptor is turned on (activated) by a hormone called leptin that attaches (binds) to the receptor, fitting into it like a key into a lock. Normally, the body's fat cells release leptin in proportion to their size. As fat cells become larger, they produce more leptin. This rise in leptin indicates that fat stores are increasing. In the hypothalamus, the binding of leptin to its receptor triggers a series of chemical signals that affect hunger and help produce a feeling of fullness (satiety).

*LEPR* gene mutations that cause leptin receptor deficiency prevent the receptor from responding to leptin, leading to the excessive hunger and weight gain associated with this disorder. Because hypogonadotropic hypogonadism occurs in leptin receptor deficiency, researchers suggest that leptin receptor signaling is also involved in regulating the body's response to hormones that control sexual development, and that this response is affected by *LEPR* gene mutations. However, the mechanism of this effect is unknown.

## **Inheritance Pattern**

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## **Other Names for This Condition**

- congenital deficiency of the leptin receptor
- leptin receptor-related monogenic obesity
- obesity due to leptin receptor gene deficiency
- obesity, morbid, due to leptin receptor deficiency
- obesity, morbid, nonsyndromic 2

## **Diagnosis & Management**

### Genetic Testing Information

- What is genetic testing?  
[/primer/testing/genetictesting](#)
- Genetic Testing Registry: Leptin receptor deficiency  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3554225/>

### Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22leptin+receptor+deficiency%22>

### Other Diagnosis and Management Resources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development: How Are Obesity and Overweight Diagnosed?  
<https://www.nichd.nih.gov/health/topics/obesity/conditioninfo/diagnosed>
- Genetics of Obesity Study  
<https://www.goos.org.uk/home>
- National Heart, Lung, and Blood Institute: Overweight and Obesity  
<https://www.nhlbi.nih.gov/health-topics/kawasaki-disease>

## **Additional Information & Resources**

### Health Information from MedlinePlus

- Encyclopedia: Appetite - Increased  
<https://medlineplus.gov/ency/article/003134.htm>
- Encyclopedia: Hypogonadotropic Hypogonadism  
<https://medlineplus.gov/ency/article/000390.htm>
- Encyclopedia: Hypothalamus  
<https://medlineplus.gov/ency/article/002380.htm>
- Health Topic: Obesity  
<https://medlineplus.gov/obesity.html>

### Additional NIH Resources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development: How Are Obesity and Overweight Diagnosed?  
<https://www.nichd.nih.gov/health/topics/obesity/conditioninfo/diagnosed>
- National Heart, Lung, and Blood Institute: Overweight and Obesity  
<https://www.nhlbi.nih.gov/health-topics/kawasaki-disease>
- National Institute of Diabetes and Digestive and Kidney Diseases: Active at Any Size!  
<https://www.niddk.nih.gov/health-information/weight-management/staying-active-at-any-size>

### Educational Resources

- Centers for Disease Control and Prevention: Obesity and Genetics  
<https://www.cdc.gov/genomics/resources/diseases/obesity/>
- MalaCards: leptin receptor deficiency  
[https://www.malacards.org/card/leptin\\_receptor\\_deficiency](https://www.malacards.org/card/leptin_receptor_deficiency)
- Orphanet: Obesity due to leptin receptor gene deficiency  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=179494](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=179494)
- TeensHealth: Dealing With Feelings When You're Overweight  
<https://kidshealth.org/en/teens/feelings-overweight.html>
- TeensHealth: Delayed Puberty  
<https://kidshealth.org/en/teens/delayed-puberty.html>

### Patient Support and Advocacy Resources

- Obesity Action Coalition  
<https://www.obesityaction.org/>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28leptin+receptor+deficiency%5BTIAB%5D%29+OR+%28%28leptin+receptor%5BTI%5D%29+AND+%28obesity%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>

### Catalog of Genes and Diseases from OMIM

- LEPTIN RECEPTOR DEFICIENCY  
<http://omim.org/entry/614963>

### Medical Genetics Database from MedGen

- Leptin receptor deficiency  
<https://www.ncbi.nlm.nih.gov/medgen/767139>

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Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/leptin-receptor-deficiency>

Reviewed: July 2016

Published: June 11, 2019

Lister Hill National Center for Biomedical Communications  
U.S. National Library of Medicine  
National Institutes of Health  
Department of Health & Human Services