IGF2 gene

insulin like growth factor 2

Normal Function

The *IGF2* gene provides instructions for making a protein called insulin-like growth factor 2. This protein plays an essential role in growth and development before birth. Studies suggest that insulin-like growth factor 2 promotes the growth and division (proliferation) of cells in many different tissues. Although the *IGF2* gene is highly active during fetal development, it is much less active after birth.

In most cases, people receive one copy of each gene from the egg cell and one copy from the sperm cell. Both copies are usually active, or "turned on," in cells. However, the activity of the *IGF2* gene depends on whether the gene comes from the sperm cell or the egg cell. In most cases, only the *IGF2* gene from the sperm cell is active. This parent-specific difference in gene activation is called genomic imprinting.

A nearby region of DNA regulates the genomic imprinting of the *IGF2* gene and another gene, called *H19,* that is important for growth and development. This region is known as an imprinting center or imprinting control region. In a process known as methylation, small molecules called methyl groups are added to the imprinting center to regulate the activity of the *IGF2* and *H19* genes. Typically, only the copy of the *IGF2* imprinting center that is derived from the sperm cell is methylated.

Health Conditions Related to Genetic Changes

Beckwith-Wiedemann syndrome

Beckwith-Wiedemann syndrome, a growth disorder that affects many parts of the body, can result from changes that affect the *IGF2* imprinting center. In some people with this condition, both copies of the *IGF2* imprinting center are methylated. Because this region controls the genomic imprinting of the *IGF2* and *H19* genes, this abnormality disrupts the regulation of both genes. Specifically, this abnormal methylation of the *IGF2* imprinting center leads to increased *IGF2* gene activity and decreased *H19* gene activity, which causes the overgrowth seen in people with Beckwith-Wiedemann syndrome.

In a few cases, Beckwith-Wiedemann syndrome has been caused by deletions of a small amount of DNA from the *IGF2* imprinting center. These deletions impair the imprinting center’s ability to regulate the activity of the *IGF2* and *H19* genes.

Prostate cancer

MedlinePlus Genetics provides information about Prostate cancer

Silver-Russell syndrome

Changes in methylation are responsible for most cases of Silver-Russell syndrome, a disorder that is characterized by slow growth before and after birth.

In people with Silver-Russell syndrome, the *IGF2* imprinting center from the sperm cell often has fewer methyl groups than it should (hypomethylation). Hypomethylation of the imprinting center impairs its ability to regulate genes and leads to decreased *IGF2* gene activity and increased *H19* gene activity, which causes the slow growth seen in people with Silver-Russell syndrome.

Rarely, variants (also called mutations) in the *IGF2* gene cause Silver-Russell syndrome.

Wilms tumor

Methylation changes have also been found in some cases of Wilms tumor, a rare form of kidney cancer that occurs almost exclusively in children.

In some people with Wilms tumor, both copies of the *IGF2* imprinting center are methylated. This change leads to a decrease in *H19* gene activity and an increase in *IGF2* gene activity in kidney cells. This causes cells to produce more insulin-like growth factor 2 protein, which likely stimulates the growth of tumor cells in the kidney and prevents damaged cells from being destroyed. As this mechanism is similar to the one that causes Beckwith-Wiedemann syndrome, some children who have Beckwith-Wiedemann syndrome will also develop Wilms tumor.

In most cases of Wilms tumor, abnormal methylation and subsequent changes in *IGF2* and *H19* gene activity are acquired during a person's lifetime (somatic) and are present only in the kidneys.

Other cancers

Increased activity of the *IGF2* gene has been associated with many types of cancer. Normally, the *IGF2* gene undergoes genomic imprinting, and only the copy derived from the sperm cell is active. In some cancers, however, the *IGF2* gene from both the egg cell and the sperm cell are active, increasing the amount of insulin-like growth factor 2 that cells can produce. This phenomenon, known as loss of imprinting (LOI), occurs during a person's lifetime in cells that ultimately give rise to cancer. An increased amount of insulin-like growth factor 2 may stimulate the growth of tumor cells and prevent damaged cells from being destroyed.

Loss of imprinting of the *IGF2* gene has been identified in several types of cancer. In some cases, these cancers occur without any other related health problems, in other cases they occur in people with Beckwith-Wiedemann syndrome. These types of cancer

include cancer of blood-forming cells (leukemia), a cancer of muscle tissue called rhabdomyosarcoma, a form of liver cancer called hepatoblastoma, and cancers of the breast, prostate, lung, and colon.

Other Names for This Gene

- C11orf43
- GRDF
- IGF-2
- IGF-II
- insulin-like growth factor 2
- insulin-like growth factor II
- pp9974
- somatomedin A

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of IGF2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3481[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28IGF2%5BTIAB%5D%29+OR+%28insulin-like+growth+factor+2%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- INSULIN-LIKE GROWTH FACTOR II; IGF2 (https://omim.org/entry/147470)
- H19/IGF2-IMPRINTING CONTROL REGION (https://omim.org/entry/616186)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3481)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=IGF2[gene])

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Genomic Location

The *IGF2* gene is found on chromosome 11 (https://medlineplus.gov/genetics/chromosome/11/).

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