

# Chromosome 11

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Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 11, one copy inherited from each parent, form one of the pairs.

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## 1. Introduction

Chromosome 11 spans about 135 million DNA building blocks (base pairs) and represents between 4 and 4.5 percent of the total DNA in cells.

Identifying genes on each chromosome is an active area of genetic research. Because researchers use different approaches to predict the number of genes on each chromosome, the estimated number of genes varies. Chromosome 11 likely contains 1,300 to 1,400 genes that provide instructions for making proteins. These proteins perform a variety of different roles in the body.

## 2. Health Conditions Related to Chromosomal Changes

### 2.1. Beckwith-Wiedemann syndrome

Beckwith-Wiedemann syndrome results from the abnormal regulation of genes on part of the short (p) arm of chromosome 11. The genes are located close together in a region designated 11p15.5 near one end of the chromosome.

People normally inherit one copy of chromosome 11 from each parent. For most genes on this chromosome, both copies of the gene are expressed, or "turned on," in cells. For some genes in the 11p15.5 region, however, only the copy inherited from a person's father (the paternally inherited copy) is expressed. For other genes, only the copy inherited from a person's mother (the maternally inherited copy) is expressed. These parent-specific differences in gene expression are caused by a phenomenon called genomic imprinting. Researchers have determined that changes in genomic imprinting disrupt the regulation of several genes located at 11p15.5, including *CDKN1C*, *H19*, *IGF2*, and *KCNQ1OT1*. Because these genes are involved in directing normal growth, problems with their regulation lead to overgrowth and the other characteristic features of Beckwith-Wiedemann syndrome.

About 20 percent of cases of Beckwith-Wiedemann syndrome are caused by a genetic change known as paternal uniparental disomy (UPD). Paternal UPD causes people to have two active copies of paternally inherited genes rather than one active copy from the father and one inactive copy from the mother. People with paternal UPD are also missing genes that are active only on the maternal copy of the chromosome. In Beckwith-Wiedemann syndrome, paternal UPD usually occurs early in embryonic development and affects only some of the body's cells. This phenomenon is called mosaicism. Mosaic paternal UPD leads to an imbalance in active paternal and maternal genes on chromosome 11, which underlies the signs and symptoms of the disorder.

About 1 percent of all people with Beckwith-Wiedemann syndrome have a chromosomal abnormality such as a rearrangement (translocation) involving 11p15.5 or abnormal copying (duplication) or deletion of genetic material in this region. Like the other genetic changes responsible for Beckwith-Wiedemann syndrome, these changes disrupt the normal regulation of genes in this part of chromosome 11.

### 2.2. Emanuel syndrome

Emanuel syndrome is caused by the presence of extra genetic material from chromosome 11 and chromosome 22 in each cell. In addition to the usual 46 chromosomes, people with Emanuel syndrome have an extra (supernumerary) chromosome consisting of a piece of chromosome 22 attached to a piece of chromosome 11. The extra chromosome is

known as a derivative 22 or der(22) chromosome.

People with Emanuel syndrome typically inherit the der(22) chromosome from an unaffected parent. The parent carries a chromosomal rearrangement between chromosomes 11 and 22 called a balanced translocation. No genetic material is gained or lost in a balanced translocation, so these chromosomal changes usually do not cause any health problems. As the translocation is passed to the next generation, it can become unbalanced. Individuals with Emanuel syndrome inherit an unbalanced translocation between chromosomes 11 and 22 in the form of a der(22) chromosome. These individuals have two normal copies of chromosome 11, two normal copies of chromosome 22, and extra genetic material from the der(22) chromosome.

As a result of the extra chromosome, people with Emanuel syndrome have three copies of some genes in each cell instead of the usual two copies. The excess genetic material disrupts the normal course of development, leading to intellectual disability and birth defects. Researchers are working to determine which genes are included on the der(22) chromosome and what role these genes play in development.

### **2.3. Ewing sarcoma**

A translocation involving chromosome 11 can cause a type of cancerous tumor known as Ewing sarcoma. These tumors develop in bones or soft tissues, such as nerves and cartilage. This translocation, t(11;22), fuses part of the *EWSR1* gene from chromosome 22 with part of the *FLI1* gene from chromosome 11, creating the *EWSR1/FLI1* fusion gene. This mutation is acquired during a person's lifetime and is present only in tumor cells. This type of genetic change, called a somatic mutation, is not inherited.

The protein produced from the *EWSR1/FLI1* fusion gene, called EWS/FLI, has functions of the protein products of both genes. The FLI protein, produced from the *FLI1* gene, attaches (binds) to DNA and regulates an activity called transcription, which is the first step in the production of proteins from genes. The FLI protein controls the growth and development of some cell types by regulating the transcription of certain genes. The EWS protein, produced from the *EWSR1* gene, also regulates transcription. The EWS/FLI protein has the DNA-binding function of the FLI protein as well as the transcription regulation function of the EWS protein. It is thought that the EWS/FLI protein turns the transcription of a variety of genes on and off abnormally. This dysregulation of transcription leads to uncontrolled growth and division (proliferation) and abnormal maturation and survival of cells, causing tumor development.

### **2.4. Jacobsen syndrome**

Jacobsen syndrome, which is also known as 11q terminal deletion disorder, is caused by a deletion of genetic material at the end (terminus) of the long (q) arm of chromosome 11. The size of the deletion varies among affected individuals, with most affected people missing from about 5 million to 16 million DNA building blocks (also written as 5 Mb to 16 Mb). In almost all affected people, the deletion includes the tip of chromosome 11. Larger deletions tend to cause more severe signs and symptoms than smaller deletions.

The features of Jacobsen syndrome are likely related to the loss of multiple genes on chromosome 11. Depending on its size, the deleted region can contain from about 170 to more than 340 genes. Many of these genes have not been well characterized. However, genes in this region appear to be critical for the normal development of many parts of the body, including the brain, facial features, and heart. Only a few genes have been studied as possible contributors to the specific features of Jacobsen syndrome; researchers are working to determine which additional genes may be associated with this condition.

### **2.5. Neuroblastoma**

About 35 percent of people with neuroblastoma have a deletion of genetic material on the long (q) arm of chromosome 11 at a position designated 11q23. Neuroblastoma is a type of cancerous tumor composed of immature nerve cells (neuroblasts). The 11q23 deletion can occur in the body's cells after conception, which is called a somatic mutation, or it can be inherited from a parent. This deletion is associated with a more severe form of neuroblastoma. Researchers believe the deleted region could contain a gene that keeps cells from growing and dividing too quickly or in an uncontrolled way, called a tumor suppressor gene. When tumor suppressor genes are deleted, cancer can occur. However, no tumor suppressor genes have been identified in the deleted region of chromosome 11. It is unknown how deletion of this region contributes to the formation or progression of neuroblastoma.

## 2.6. Potocki-Shaffer syndrome

Potocki-Shaffer syndrome is caused by the deletion of a segment of the short (p) arm of chromosome 11 at a position described as 11p11.2. This condition is also known as proximal 11p deletion syndrome. The characteristic features of Potocki-Shaffer syndrome include enlarged openings in the two bones that make up much of the top and sides of the skull (enlarged parietal foramina), multiple noncancerous bone tumors called osteochondromas, intellectual disability, delayed development, a distinctive facial appearance, and problems with vision. Occasionally, people with this condition have defects in the heart, kidneys, and urinary tract. The features of Potocki-Shaffer syndrome result from the loss of several genes on the short arm of chromosome 11. In particular, the deletion of a gene called *ALX4* causes enlarged parietal foramina in people with this condition, loss of the *EXT2* gene underlies the multiple osteochondromas, and deletion of the *PHF21A* gene is responsible for the intellectual disability and distinctive facial features. Researchers are working to find genes on the short arm of chromosome 11 that are associated with the other features of Potocki-Shaffer syndrome.

Another condition called WAGR syndrome (described below) is caused by a deletion of genetic material from the short arm of chromosome 11 at a position described as 11p13. Occasionally, a deletion is large enough to include the 11p11.2 and 11p13 regions. Individuals with such a deletion have signs and symptoms of both Potocki-Shaffer syndrome and WAGR syndrome.

## 2.7. Russell-Silver syndrome

Like Beckwith-Wiedemann syndrome, Russell-Silver syndrome can result from changes in genes in the 11p15.5 region. Specifically, Russell-Silver syndrome has been associated with changes in genomic imprinting that affect the regulation of the *H19* and *IGF2* genes on chromosome 11. The changes are different from those seen in Beckwith-Wiedemann syndrome and have the opposite effect on growth. Although both disorders can be caused by abnormal regulation of these genes, the changes that cause Russell-Silver syndrome lead to slow growth and short stature instead of overgrowth.

## 2.8. WAGR syndrome

WAGR syndrome is caused by a deletion of genetic material on the short (p) arm of chromosome 11 at a position described as 11p13. WAGR syndrome is a disorder that affects many body systems and is named for its main features: a childhood kidney cancer known as Wilms tumor, an eye problem called aniridia, genitourinary anomalies, and intellectual disability (formerly referred to as mental retardation). The signs and symptoms of WAGR syndrome are related to the loss of multiple genes from this part of the chromosome. The size of the deletion varies among affected individuals. Researchers have identified genes on the short arm of chromosome 11 that are associated with particular features of WAGR syndrome. A loss of the *PAX6* gene disrupts normal eye development, leading to aniridia and other eye problems, and may also affect the development of the brain. Deletion of the *WT1* gene is responsible for the genitourinary abnormalities and the increased risk of Wilms tumor in affected individuals. Researchers are working to identify additional genes deleted in people with WAGR syndrome and determine how their loss leads to the other features of the disorder.

## 2.9. Other chromosomal conditions

Other changes in the number or structure of chromosome 11 can have a variety of effects, including intellectual disability, delayed development, slow growth, distinctive facial features, and weak muscle tone (hypotonia). Changes involving chromosome 11 include an extra piece of the chromosome in each cell (partial trisomy 11), a missing segment of the chromosome in each cell (partial monosomy 11), and a circular structure called a ring chromosome 11. Ring chromosomes occur when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure.

## 2.10. Other cancers

Changes in chromosome 11 have been identified in other types of cancer. These chromosomal changes are somatic, which means they are acquired during a person's lifetime and are present only in certain cells. In some cases, translocations of genetic material between chromosome 11 and other chromosomes have been associated with cancers of blood-forming cells (leukemias) and cancers of immune system cells (lymphomas).

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