

## Chromosome 9

### Description

Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 9, one copy inherited from each parent, form one of the pairs. Chromosome 9 is made up of about 141 million DNA building blocks (base pairs) and represents approximately 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 9 likely contains 800 to 900 genes that provide instructions for making proteins. These proteins perform a variety of different roles in the body.

### Health Conditions Related to Chromosomal Changes

The following chromosomal conditions are associated with changes in the structure or number of copies of chromosome 9.

#### 9q22.3 microdeletion

9q22.3 microdeletion is a chromosomal change in which a small piece of the long (q) arm of chromosome 9 is deleted in each cell. Affected individuals are missing at least 352,000 base pairs, also written as 352 kilobases (kb), in the q22.3 region of chromosome 9. This 352-kb segment is known as the minimum critical region because it is the smallest deletion that has been found to cause the signs and symptoms related to 9q22.3 microdeletions. These signs and symptoms include delayed development, intellectual disability, certain physical abnormalities, and the characteristic features of a genetic condition called Gorlin syndrome (also known as nevoid basal cell carcinoma syndrome). 9q22.3 microdeletions can also be much larger; the largest reported deletion included 20.5 million base pairs (20.5 Mb).

People with a 9q22.3 microdeletion are missing two to more than 270 genes on chromosome 9. All known 9q22.3 microdeletions include the *PTCH1* gene. Researchers believe that many of the features associated with 9q22.3 microdeletions, particularly the signs and symptoms of Gorlin syndrome, result from a loss of the *PTCH1* gene. Other signs and symptoms related to 9q22.3 microdeletions probably result from the loss of additional genes in the q22.3 region. Researchers are working to determine which missing genes contribute to the other features associated with the deletion.

## Bladder cancer

Deletions of part or all of chromosome 9 are commonly found in bladder cancer. Bladder cancer is a disease in which certain cells in the bladder become abnormal and multiply uncontrollably to form a tumor. Bladder cancer may cause blood in the urine, pain during urination, frequent urination, the feeling of needing to urinate without being able to, or lower back pain.

Bladder cancer is generally divided into two types, non-muscle invasive bladder cancer (NMIBC) and muscle-invasive bladder cancer (MIBC), based on where in the bladder the tumor is located. Many cases of NMIBC tumors have a chromosome 9 deletion, which typically occurs early in tumor formation. These chromosomal changes are seen only in cancer cells. Research shows that several genes that control cell growth and division are located on chromosome 9. Many of these genes are tumor suppressors, which means they normally help prevent cells from growing and dividing in an uncontrolled way. It is likely that a loss of one or more of these genes plays a role in the early development and progression of bladder cancer.

## Chronic myeloid leukemia

A rearrangement (translocation) of genetic material between chromosomes 9 and 22 causes a type of cancer of blood-forming cells called chronic myeloid leukemia. This slow-growing cancer leads to an overproduction of abnormal white blood cells. Common features of the condition include excessive tiredness (fatigue), fever, weight loss, and an enlarged spleen.

The translocation involved in this condition, written as t(9;22), fuses part of the *ABL1* gene from chromosome 9 with part of the *BCR* gene from chromosome 22, creating an abnormal fusion gene called *BCR-ABL1*. The abnormal chromosome 22, containing a piece of chromosome 9 and the fusion gene, is commonly called the Philadelphia chromosome. The translocation is acquired during a person's lifetime and is present only in the abnormal blood cells. This type of genetic change, called a somatic mutation, is not inherited.

The protein produced from the *BCR-ABL1* gene signals cells to continue dividing abnormally and prevents them from self-destructing, which leads to overproduction of the abnormal cells.

The Philadelphia chromosome also has been found in some cases of rapidly progressing blood cancers known as acute leukemias. It is likely that the form of blood cancer that develops is influenced by the type of blood cell that acquires the mutation and other genetic changes that occur. The presence of the Philadelphia chromosome provides a target for molecular therapies.

## Kleefstra syndrome

Most people with Kleefstra syndrome, a disorder with signs and symptoms involving many parts of the body, are missing a sequence of about 1 million DNA building blocks (base pairs) on one copy of chromosome 9 in each cell. The deletion occurs near the

end of the long (q) arm of the chromosome at a location designated q34.3, a region containing a gene called *EHMT1*. Some affected individuals have shorter or longer deletions in the same region.

The loss of the *EHMT1* gene from one copy of chromosome 9 in each cell is believed to be responsible for the characteristic features of Kleeftstra syndrome in people with the 9q34.3 deletion. However, the loss of other genes in the same region may lead to additional health problems in some affected individuals.

The *EHMT1* gene provides instructions for making an enzyme called euchromatic histone methyltransferase 1. Histone methyltransferases are enzymes that modify proteins called histones. Histones are structural proteins that attach (bind) to DNA and give chromosomes their shape. By adding a molecule called a methyl group to histones, histone methyltransferases can turn off (suppress) the activity of certain genes, which is essential for normal development and function. A lack of euchromatic histone methyltransferase 1 enzyme impairs proper control of the activity of certain genes in many of the body's organs and tissues, resulting in the abnormalities of development and function characteristic of Kleeftstra syndrome.

### Other chromosomal conditions

Other changes in the structure or number of copies of chromosome 9 can have a variety of effects. Intellectual disability, delayed development, distinctive facial features, and an unusual head shape are common features. Changes to chromosome 9 include an extra piece of the chromosome in each cell (partial trisomy), a missing segment of the chromosome in each cell (partial monosomy), and a circular structure called a ring chromosome 9. A ring chromosome occurs when both ends of a broken chromosome are reunited. Rearrangements (translocations) of genetic material between chromosome 9 and other chromosomes can also lead to extra or missing chromosome segments.

### Other cancers

Changes in the structure of chromosome 9 have been found in many types of cancer. These changes, which occur only in cells that give rise to cancer, usually involve a loss of part of the chromosome or a rearrangement of chromosomal material. For example, a loss of part of the long (q) arm of chromosome 9 has been identified in some types of brain tumor. In addition, chromosomal rearrangements that fuse the *ABL1* gene with genes other than *BCR* have been found in a small number of acute leukemias. The exact mechanisms by which these genetic changes lead to cancer are not completely understood, although it is likely that the proteins produced from them promote uncontrolled growth of cells.

## **Additional Information & Resources**

### Additional NIH Resources

- National Human Genome Research Institute: Chromosome Abnormalities (<https://www.nih.gov/genetics>)

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28Chromosomes,+Human,+Pair+9%5BMAJR%5D%29+AND+%28Chromosome+9%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>)

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