Chromosome 21

Description

Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 21, one copy inherited from each parent, form one of the pairs. Chromosome 21 is the smallest human chromosome, spanning about 48 million base pairs (the building blocks of DNA) and representing 1.5 to 2 percent of the total DNA in cells.

In 2000, researchers working on the Human Genome Project announced that they had determined the sequence of base pairs that make up this chromosome. Chromosome 21 was the second human chromosome to be fully sequenced.

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 21 likely contains 200 to 300 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 21.

Core binding factor acute myeloid leukemia

A genetic rearrangement (translocation) involving chromosome 21 is associated with a type of blood cancer known as core binding factor acute myeloid leukemia (CBF-AML). This rearrangement occurs in approximately 7 percent of acute myeloid leukemia cases in adults. The translocation, written as t(8;21), fuses part of the *RUNX1* gene from chromosome 21 with part of the *RUNX1T1* gene (also known as *ETO*) from chromosome 8. This mutation is acquired during a person's lifetime and is present only in certain cells. This type of genetic change, called a somatic mutation, is not inherited.

The fusion protein produced from the t(8;21) translocation, called RUNX1-ETO, retains some functions of the two individual proteins. The normal RUNX1 protein, produced from the *RUNX1* gene, is part of a protein complex called core binding factor (CBF) that attaches (binds) to DNA and turns on genes involved in blood cell development. The normal ETO protein, produced from the *RUNX1T1* gene, turns off gene activity.

The RUNX1-ETO fusion protein forms CBF and attaches to DNA, but instead of turning on genes that stimulate the development of blood cells, it turns those genes off. This change in gene activity blocks the maturation (differentiation) of blood cells and leads to the production of abnormal, immature white blood cells called myeloid blasts. While t(8; 21) is important for leukemia development, one or more additional genetic changes are typically needed for the myeloid blasts to develop into cancerous leukemia cells.

Down syndrome

Down syndrome is a chromosomal condition that is associated with intellectual disability, a characteristic facial appearance, and weak muscle tone (hypotonia) in infancy. This condition is most often caused by trisomy 21. Trisomy 21 means that each cell in the body has three copies of chromosome 21 instead of the usual two copies.

Less commonly, Down syndrome occurs when part of chromosome 21 becomes attached (translocated) to another chromosome during the formation of reproductive cells (eggs and sperm) or very early in fetal development. Affected people have two copies of chromosome 21 plus extra material from chromosome 21 attached to another chromosome, resulting in three copies of genetic material from chromosome 21. Affected individuals with this genetic change are said to have translocation Down syndrome.

In a very small percentage of cases, Down syndrome results from an extra copy of chromosome 21 in only some of the body's cells. In these people, the condition is called mosaic Down syndrome.

Researchers believe that having extra copies of genes on chromosome 21 disrupts the course of normal development, causing the characteristic features of Down syndrome and the increased risk of health problems associated with this condition.

Other chromosomal conditions

Other changes in the number or structure of chromosome 21 have a variety of effects on health and development. Chromosome 21 abnormalities can cause intellectual disability, delayed development, and characteristic facial features. In some cases, the signs and symptoms are similar to those of Down syndrome (described above).

Changes involving chromosome 21 can include a missing segment of the chromosome in each cell (partial monosomy 21) and a circular structure called ring chromosome 21. A ring chromosome occurs when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure.

Other cancers

Translocations of genetic material between chromosome 21 and other chromosomes have been associated with several types of cancer. For example, acute lymphoblastic leukemia (a type of blood cancer most often diagnosed in childhood) has been associated with a translocation between chromosomes 12 and 21.

Additional Information & Resources

Additional NIH Resources

- National Human Genome Research Institute: Chromosome Abnormalities (https://www.genome.gov/about-genomics/fact-sheets/Chromosome-Abnormalities-Fact-Sheet)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Chromosomes,+Human,+Pair+21%5BMAJR%5D%29+AND+%28Chromosome+21%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

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