Chromosome 8

Description

Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 8, one copy inherited from each parent, form one of the pairs. Chromosome 8 spans more than 146 million DNA building blocks (base pairs) and represents between 4.5 and 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 8 likely contains about 700 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 8.

8p11 myeloproliferative syndrome

Translocations of genetic material between chromosome 8 and other chromosomes can cause 8p11 myeloproliferative syndrome. This condition is characterized by an increased number of white blood cells (myeloproliferative disorder) and the development of lymphoma, a blood-related cancer that causes tumor formation in the lymph nodes. The myeloproliferative disorder usually develops into another form of blood cancer called acute myeloid leukemia. The most common translocation involved in this condition, written as t(8;13)(p11;q12), fuses part of the *FGFR1* gene on chromosome 8 with part of the *ZMYM2* gene on chromosome 13. The translocations are found only in cancer cells.

The protein produced from the normal *FGFR1* gene can turn on (activate) cellular signaling that helps the cell respond to its environment, for example by stimulating cell growth. The protein produced from the fused gene, regardless of the partner gene involved, leads to constant FGFR1 signaling. The uncontrolled signaling promotes continuous cell growth and division (proliferation), leading to cancer.

Core binding factor acute myeloid leukemia

A type of blood cancer known as core binding factor acute myeloid leukemia (CBF-AML) is associated with a rearrangement (translocation) of genetic material between chromosomes 8 and 21. This rearrangement is associated with approximately 7 percent of acute myeloid leukemia cases in adults. The translocation, written as t(8;21), fuses part of the *RUNX1T1* gene (also known as *ETO*) from chromosome 8 with part of the *RUNX1* gene from chromosome 21. 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 function 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 activates genes involved in blood cell development. The normal ETO protein, produced from the *RUNX1T1* gene, turns off (represses) gene activity. The fusion protein forms CBF and attaches to DNA, but instead of activating genes that stimulate the development of blood cells, it represses those genes. 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.

Recombinant 8 syndrome

Recombinant 8 syndrome is caused by a rearrangement of genetic material on chromosome 8. This condition is characterized by heart and urinary tract abnormalities, moderate to severe intellectual disability, abnormal muscle tone, and a distinctive facial appearance. The chromosomal rearrangement that causes recombinant 8 syndrome is a deletion of a piece of the short (p) arm and a duplication of a piece of the long (q) arm. This chromosome abnormality is written rec(8)dup(8q)inv(8)(p23.1q22.1). On the recombinant 8 chromosome, there is one copy of each of the genes instead of the usual two on the section of chromosome 8p that is deleted; and there are three copies each of the genes on the section of chromosome 8q that is duplicated. The signs and symptoms of recombinant 8 syndrome are related to the loss and addition of genetic material on these regions of chromosome 8. While the regions affected in recombinant chromosome 8 includes hundreds of genes, researchers are working to determine which genes play a role in the signs and symptoms of this condition.

Trichorhinophalangeal syndrome type II

Trichorhinophalangeal syndrome type II (TRPS II) is caused by a deletion of genetic material on the long (q) arm of chromosome 8. TRPS II is a condition that causes bone and joint malformations; distinctive facial features; intellectual disability; and abnormalities of the skin, hair, teeth, sweat glands, and nails. The signs and symptoms of TRPS II are related to the loss of multiple genes from this part of the chromosome. The size of the deletion varies among affected individuals; studies suggest that larger deletions tend to result in a greater number of features than smaller deletions.

The *TRPS1*, *EXT1*, and *RAD21* genes are missing in people with TRPS II. Researchers

have determined that the loss of the *EXT1* gene is responsible for multiple benign (noncancerous) bone tumors called osteochondromas seen in people with TRPS II. Loss of the *TRPS1* gene is thought to cause the other bone and facial abnormalities. Deletion of the *RAD21* gene may contribute to intellectual disability. The loss of other genes from this region of chromosome 8 likely contributes to the additional features of this condition.

Other chromosomal conditions

Trisomy 8 occurs when cells have three copies of chromosome 8 instead of the usual two copies. Full trisomy 8, which occurs when all of the body's cells contain an extra copy of chromosome 8, is not compatible with life. A similar but less severe condition called mosaic trisomy 8 occurs when only some of the body's cells have an extra copy of chromosome 8. The signs and symptoms of mosaic trisomy 8 vary widely and can include intellectual disability, absence of the tissue connecting the left and right halves of the brain (corpus callosum), skeletal defects, heart problems, kidney and liver malformations, and facial abnormalities. Trisomy 8 mosaicism is also associated with an increased risk of acute myeloid leukemia.

Another chromosomal condition called inversion duplication 8p is caused by a rearrangement of genetic material on the short (p) arm of chromosome 8. This rearrangement results in an abnormal duplication and an inversion of a segment of the chromosome. An inversion involves the breakage of a chromosome in two places; the resulting piece of DNA is reversed and reinserted into the chromosome. People with inversion duplication 8p typically have severe intellectual disability, a thin or absent corpus callosum, weak muscle tone (hypotonia), abnormal curvature of the spine (scoliosis), and minor facial abnormalities. Some individuals with this condition may also have heart defects, underdeveloped kidneys, or eye abnormalities. Older individuals usually develop abnormal muscle stiffness (spasticity). The signs and symptoms of inversion duplication 8p tend to depend on the size and location of the chromosome segment involved. For example, inclusion of chromosome region 8p21 is thought to be associated with more severe symptoms.

Other cancers

Translocations between chromosome 8 and other chromosomes have been associated with other types of cancer. For example, Burkitt lymphoma (a cancer of white blood cells called B cells that occurs most often in children and young adults) can be caused by a translocation between chromosomes 8 and 14. This translocation, written t(8;14)(q24; q32), leads to continuous cell division without control or order, which likely contributes to the development of Burkitt lymphoma. Less frequently, Burkitt lymphoma can be caused by translocations between chromosomes 8 and 2 or chromosomes 8 and 22.

Additional Information & Resources

Additional NIH Resources

- National Human Genome Research Institute: Chromosome Abnormalities (https://w

ww.genome.gov/about-genomics/fact-sheets/Chromosome-Abnormalities-Fact-Sheet)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=(Chromosomes,+Human,+Pair+8%5BMAJR%5D)+AND+(Chromosome+8%5BTI%5D)+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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