Chromosome 2

Description

Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 2, one copy inherited from each parent, form one of the pairs. Chromosome 2 is the second largest human chromosome, spanning about 243 million building blocks of DNA (base pairs) and representing almost 8 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 2 likely contains 1,200 to 1,300 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 2.

2q37 deletion syndrome

2q37 deletion syndrome is caused by a deletion of genetic material near the end of the long (q) arm of chromosome 2, at a location designated 2q37. The signs and symptoms of this condition vary widely, but affected individuals generally have intellectual disability, behavioral problems, obesity, and skeletal abnormalities that often include unusually short fingers and toes (brachydactyly).

Researchers are working to identify all of the genes that contribute to the features of 2q37 deletion syndrome. While the size of the deletion varies among affected individuals, it always contains a certain gene, called *HDAC4*. The loss of this gene is thought to account for many of the characteristic features of 2q37 deletion syndrome, such as intellectual disability, behavioral problems, and skeletal abnormalities. Researchers are studying what role the other genes on 2q37 play in this disorder.

MBD5-associated neurodevelopmental disorder

Loss (deletion) or gain (duplication) of a small piece of chromosome 2 at position q23.1 can cause *MBD5*-associated neurodevelopmental disorder (MAND). MAND is a condition that affects neurological and physical development from birth. Affected individuals often have intellectual disability, developmental delay, impaired speech, sleep problems, distinctive facial features, and mild hand and foot abnormalities. Most people with MAND also have features similar to autism spectrum disorder, a developmental condition that affects communication and social interaction.

The chromosomal changes that can cause MAND are known as 2q23.1 microdeletions or 2q23.1 microduplications. The deleted or duplicated segment varies in size but always contains the *MBD5* gene, and often additional genes. Most features of MAND are due to the loss or gain of one copy of the *MBD5* gene. The *MBD5* gene provides instructions for a protein that likely regulates the activity (expression) of genes, controlling the production of proteins that are involved in neurological functions such as learning, memory, and behavior.

Chromosome 2 deletions or duplications that cause MAND lead to an abnormal amount of MBD5 protein. Deletions prevent one copy of the *MBD5* gene in each cell from producing any functional protein, which reduces the total amount of this protein in cells. Duplications lead to an increase in the amount of MBD5 protein.

It is likely that any changes in MBD5 protein levels impair its regulation of gene expression, leading to the uncontrolled production of certain proteins. Proteins that play a role in neurological functions are particularly affected, which helps explain why MAND impacts brain development and behavior. An increase or decrease in MBD5 protein disrupts gene expression that is normally well-controlled by this protein, which is likely why duplications and deletions of this gene lead to the same signs and symptoms.

The cause of the skeletal abnormalities and other non-neurological features of MAND is unclear. It is also unknown whether the loss or gain of other genes in chromosome 2 deletions or duplications contribute to the features of MAND.

SATB2-associated syndrome

Genetic changes on the q arm of chromosome 2 have been found to cause *SATB2*-associated syndrome. Individuals with this condition have intellectual disability and severe speech problems. They may also have an opening in the roof of the mouth (cleft palate), dental abnormalities, or other abnormalities of the head and face (craniofacial anomalies).

Several types of genetic changes are involved in *SATB2*-associated syndrome, all of which affect a gene on chromosome 2 called *SATB2*. Some mutations remove genetic material from the long arm of chromosome 2. These deletions occur in regions designated 2q32 and 2q33, and the size of the deletion varies among affected individuals. They may be large, removing several genes from chromosome 2, including *SATB2*. Or they may be smaller, removing material from within the *SATB2* gene. Other mutations, such as those that change single DNA building blocks (nucleotides) in the *SATB2* gene, can also cause *SATB2*-associated syndrome.

These genetic changes disrupt the *SATB2* gene and are thought to reduce the amount of functional protein produced from it. The SATB2 protein directs development of the brain and craniofacial structures, and a reduction in this protein's function impairs their normal development, leading to the features of the condition.

The signs and symptoms of *SATB2*-associated syndrome are usually similar, regardless of the type of mutation that causes it. However, some individuals with large deletions have uncommon features of the condition, such as problems with the heart, genitals and urinary tract (genitourinary tract), skin, or hair. These features are thought to be related to loss of other genes near *SATB2* on the long arm of chromosome 2.

Other chromosomal conditions

Another chromosome 2 abnormality is known as a ring chromosome 2. A ring chromosome is formed when breaks occur at both ends of the chromosome and the broken ends join together to form a circular structure. Individuals with this chromosome abnormality often have developmental delay, small head size (microcephaly), slow growth before and after birth, heart defects, and distinctive facial features. The severity of symptoms typically depends on how many and which types of cells contain the ring chromosome 2.

Other changes involving the number or structure of chromosome 2 include an extra piece of the chromosome in each cell (partial trisomy 2) or a missing segment of the chromosome in each cell (partial monosomy 2). These changes can have a variety of effects on health and development, including intellectual disability, slow growth, characteristic facial features, weak muscle tone (hypotonia), and abnormalities of the fingers and toes.

Cancers

Changes in chromosome 2 have been identified in several types of cancer. These genetic changes are somatic, which means they are acquired during a person's lifetime and are present only in cells that give rise to the cancer. For example, a rearrangement (translocation) of genetic material between chromosomes 2 and 3 has been associated with cancers of a certain type of blood cell originating in the bone marrow (myeloid malignancies).

Trisomy 2, in which cells have three copies of chromosome 2 instead of the usual two copies, has been found in myelodysplastic syndrome. This disease affects the blood and bone marrow. People with myelodysplastic syndrome have a low number of red blood cells (anemia) and an increased risk of developing a form of blood cancer known as acute myeloid leukemia.

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+2%5BMAJR%5D%29+AND+%28Chromosome+2%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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