Chromosome 12

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Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 12, one copy inherited from each parent, form one of the pairs.

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1. Introduction

Chromosome 12 spans almost 134 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 12 likely contains 1,100 to 1,200 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. Pallister-Killian mosaic syndrome

Pallister-Killian mosaic syndrome is usually caused by the presence of an abnormal extra chromosome called an isochromosome 12p or i(12p). An isochromosome is a chromosome with two identical arms. Normal chromosomes have one long (q) arm and one short (p) arm, but isochromosomes have either two q arms or two p arms. Isochromosome 12p is a version of chromosome 12 made up of two p arms.

Cells normally have two copies of each chromosome, one inherited from each parent. In people with Pallister-Killian mosaic syndrome, cells have the two usual copies of chromosome 12, but some cells also have the isochromosome 12p. These cells have a total of four copies of all the genes on the p arm of chromosome 12. The extra genetic material from the isochromosome disrupts the normal course of development, causing the characteristic features of this disorder.

Although Pallister-Killian mosaic syndrome is usually caused by an isochromosome 12p, other, more complex chromosomal changes involving chromosome 12 are responsible for the disorder in rare cases.

2.2. PDGFRB-associated chronic eosinophilic leukemia

Translocations involving chromosome 12 are involved in a type of blood cell cancer called *PDGFRB*-associated chronic eosinophilic leukemia. This condition is characterized by an increased number of eosinophils, a type of white blood cell. The most common translocation that causes this condition fuses part of the *PDGFRB* gene from chromosome 5 with part of the *ETV6* gene from chromosome 12, written as t(5;12)(q31-33;p13). Translocations that fuse the *PDGFRB* gene with other genes can also cause *PDGFRB*-associated chronic eosinophilic leukemia, but these translocations are relatively uncommon. These translocations are acquired during a person's lifetime and are present only in cancer cells. This type of genetic change, called a somatic mutation, is not inherited.

The protein produced from the *ETV6-PDGFRB* fusion gene, called ETV6/PDGFRβ, functions differently than the proteins normally produced from the individual genes. The ETV6 protein normally turns off (represses) gene activity and the PDGFRβ protein plays a role in turning on (activating) signaling pathways. The ETV6/PDGFRβ protein is always turned on, activating signaling pathways and gene activity. When the *ETV6-PDGFRB* fusion gene mutation occurs in cells that develop into blood cells, the growth of eosinophils (and occasionally other white blood cells, such as neutrophils and mast cells) is poorly controlled, leading to *PDGFRB*-associated chronic eosinophilic leukemia. It is unclear why eosinophils are preferentially affected by this genetic change.

2.3. Other chromosomal conditions

Other changes in the number or structure of chromosome 12 can have a variety of effects on health and development. These effects include intellectual disability, slow growth, distinctive facial features, weak muscle tone (hypotonia), skeletal abnormalities, and heart defects.

Several different changes involving chromosome 12 have been reported, including an extra piece of the chromosome in each cell (partial trisomy 12), a missing segment of the chromosome in each cell (partial monosomy 12), and a circular structure called a ring chromosome 12. Ring chromosomes occur when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure.

2.4. Cancers

Changes in chromosome 12 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 certain cells. For example, rearrangements (translocations) of genetic material between chromosome 12 and other chromosomes are often found in certain cancers of blood-forming cells (leukemias) and cancers of immune system cells (lymphomas). Additionally, somatic mutations may lead to an extra copy of chromosome 12 (trisomy 12) in cancer cells, specifically a type of leukemia called chronic lymphocytic leukemia.

Translocations involving chromosome 12 have also been found in solid tumors such as lipomas and liposarcomas, which are made up of fatty tissue. In these tumors, the most common chromosome 12 rearrangements involve the long (q) arm in a region designated q13-q15. Abnormalities of chromosome 12 have been identified in at least two other rare tumors, angiomatoid fibrous histiocytomas and clear cell sarcomas. Angiomatoid fibrous histiocytomas occur primarily in adolescents and young adults and are usually found in the arms and legs (extremities). Clear cell sarcomas occur most often in young adults and tend to be associated with tendons and related structures called aponeuroses.

Researchers are working to determine which genes on chromosome 12 are disrupted by translocations, and they are studying how these chromosomal changes could contribute to the uncontrolled growth and division of tumor cells.

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