Chromosome 1

Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 1, one copy inherited from each parent, form one of the pairs. Chromosome 1 is the largest human chromosome, spanning about 249 million DNA building blocks (base pairs) and representing approximately 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 1 likely contains 2,000 to 2,100 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 1.

1p36 deletion syndrome

1p36 deletion syndrome is caused by a deletion of genetic material from a specific region in the short (p) arm of chromosome 1. The signs and symptoms of this disorder, which include intellectual disability, distinctive facial features, and structural abnormalities in several body systems, are probably related to the loss of multiple genes in this region. The size of the deletion varies among affected individuals.

1q21.1 microdeletion

1q21.1 microdeletion is a chromosomal change in which a small piece of the long (q) arm of chromosome 1 is deleted in each cell. Most commonly, affected individuals are missing about 1.35 million DNA building blocks (base pairs), also written as 1.35 megabases (Mb), in the q21.1 region. However, the exact size of the deleted region varies. The loss of multiple genes from this region probably contributes to the various signs and symptoms that can be associated with a 1q21.1 microdeletion. Related features can include delayed development, intellectual disability, physical abnormalities, and neurological and psychiatric problems; however, some individuals with a 1q21.1 microdeletion have no obvious signs or symptoms.

1q21.1 microduplication

A 1q21.1 microduplication is a copied (duplicated) segment of genetic material at position q21.1 on one of the two copies of chromosome 1 in each cell. Some people with a 1q21.1 microduplication have developmental delay, intellectual disability, or features of autism spectrum disorders characterized by impaired communication

and socialization skills. Affected individuals may also have psychiatric disorders such as schizophrenia, malformations of the heart, or other neurological or physical features. Other individuals with 1q21.1 microduplications have no identified physical, intellectual, or behavioral problems.

1q21.1 microduplications most often involve the same segment of about 1.35 million base pairs that is missing in 1q21.1 microdeletions (described above). In other cases, individuals have a shorter or longer duplicated segment within the q21.1 region of chromosome 1. Extra copies of genes in the duplicated segment likely contribute to the signs and symptoms that occur in some individuals with 1q21.1 microduplications; researchers are working to determine which specific genes are involved and how they relate to these features. Because some people with a 1q21.1 microduplication have no apparent features of the condition, additional genetic or environmental factors are thought to be involved in the development of signs and symptoms.

Neuroblastoma

Deletions within region 1p36 have also been associated with another condition called neuroblastoma. Neuroblastoma is a type of cancerous tumor composed of immature nerve cells (neuroblasts). These deletions are somatic mutations, which means they occur during a person's lifetime and are present only in the cells that become cancerous. About 25 percent of people with neuroblastoma have a deletion of 1p36.1-1p36.3, which is associated with a more severe form of neuroblastoma. Researchers believe the deleted region could contain a gene that keeps cells from growing and dividing too quickly or in an uncontrolled way, called a tumor suppressor gene. When tumor suppressor genes are deleted, cancer can occur. Researchers have identified several possible tumor suppressor genes in the deleted region of chromosome 1, and more research is needed to understand what role these genes play in neuroblastoma development.

Thrombocytopenia-absent radius syndrome

A deletion in the 1q21.1 region of chromosome 1 is involved in most cases of thrombocytopenia-absent radius (TAR) syndrome. TAR syndrome is characterized by the absence of a bone called the radius in each forearm and a shortage (deficiency) of blood cells involved in clotting (platelets).

The deletion in chromosome 1 involved in TAR syndrome eliminates at least 200,000 DNA building blocks (200 kilobases, or 200 kb) from the long (q) arm of the chromosome, including a gene called *RBM8A*. Most people with TAR syndrome have the deletion in one copy of chromosome 1, which removes one copy of the *RBM8A* gene, and a mutation in the other copy of the *RBM8A* gene in each cell. The *RBM8A* gene provides instructions for making a protein called RNA-binding motif protein 8A. This protein is believed to be involved in a number of important cellular functions involving the production of other proteins.

RBM8A gene mutations that cause TAR syndrome reduce the amount of RNA-binding motif protein 8A in cells. The deletion on chromosome 1 eliminates one

copy of the *RBM8A* gene in each cell and the RNA-binding motif protein 8A that would have been produced from it. The reduced total amount of RNA-binding motif protein 8A is thought to cause problems in the development of certain tissues, but it is unknown how it causes the specific signs and symptoms of TAR syndrome. No cases have been reported in which individuals have deletions on both copies of chromosome 1 that include both copies of the *RBM8A* gene; studies indicate that the complete loss of RNA-binding motif protein 8A is not compatible with life.

Researchers sometimes refer to the deletion in chromosome 1 associated with TAR syndrome as the 200-kb deletion to distinguish it from another chromosomal abnormality called a 1q21.1 microdeletion (described above). People with a 1q21.1 microdeletion are missing a different, larger DNA segment in the chromosome 1q21.1 region near the area where the 200-kb deletion occurs. The chromosomal change related to 1q21.1 microdeletion is often called the recurrent distal 1.35-Mb deletion.

Other cancers

Changes in the structure of chromosome 1 are associated with other forms of cancer and conditions related to cancer. These changes are typically somatic, which means they are acquired during a person's lifetime and are present only in tumor cells.

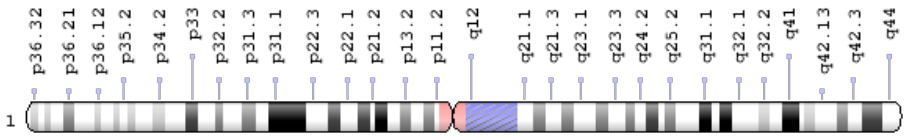
Deletions in the short (p) arm of the chromosome have been identified in tumors of the brain and kidney. Duplications in the long (q) arm of the chromosome have been reported in a disorder called myelodysplastic syndrome, which is a disease of the blood and bone marrow. People with this condition have a low number of red blood cells (anemia) and an increased risk of developing leukemia.

Other chromosomal conditions

Other changes in the number or structure of chromosome 1 can have a variety of effects, including delayed growth and development, distinctive facial features, birth defects, and other health problems. Changes to chromosome 1 may include an extra segment of the short (p) or long (q) arm of the chromosome in each cell (partial trisomy 1p or 1q), a missing segment of the short or long arm of the chromosome in each cell (partial monosomy 1p or 1q), or a circular structure called ring chromosome 1. Ring chromosomes occur when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure.

Chromosome Diagram

Geneticists use diagrams called idiograms as a standard representation for chromosomes. Idiograms show a chromosome's relative size and its banding pattern, which is the characteristic pattern of dark and light bands that appears when a chromosome is stained with a chemical solution and then viewed under a microscope. These bands are used to describe the location of genes on each chromosome.



Credit: Genome Decoration Page/NCBI

Additional Information & Resources

MedlinePlus

- Encyclopedia: Chromosome
  https://medlineplus.gov/ency/article/002327.htm

Additional NIH Resources

- National Human Genome Research Institute: Chromosome Abnormalities
  https://www.genome.gov/11508982/

GeneReviews

- 1p36 Deletion Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1191
- 1q21.1 Recurrent Microdeletion
  https://www.ncbi.nlm.nih.gov/books/NBK52787
- Thrombocytopenia Absent Radius Syndrome
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OMIM

- MENTAL RETARDATION, AUTOSOMAL DOMINANT 22
  http://omim.org/entry/612337
- NEUROBLASTOMA, SUSCEPTIBILITY TO
  http://omim.org/entry/256700

Research Resources

- Cancer Genetics Web
  http://www.cancerindex.org/geneweb/clinkc01.htm
- Database of Genomic Variants
  http://projects.tcag.ca/variation/cgi-bin/tbrowse/tbrowse?so
  urce=hg17&table=Locus&show=table&keyword=&flop=AND&fcol=_C19
  &fcomp==&fkwd=chr1&cols=
- Ensembl Human Map View
  http://www.ensembl.org/Homo_sapiens/Location/Chromosome?chr=1;r=1:
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