

# Chromosome 6

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Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 6, one copy inherited from each parent, form one of the pairs.

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## 1. Introduction

Chromosome 6 spans about 171 million DNA building blocks (base pairs) and represents between 5.5 and 6 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 6 likely contains 1,000 to 1,100 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. 6q24-related transient neonatal diabetes mellitus

6q24-related transient neonatal diabetes mellitus, a type of diabetes that occurs in infants, is caused by the overactivity (overexpression) of certain genes in a region of the long (q) arm of chromosome 6 called 6q24. People inherit two copies of their genes, one from their mother and one from their father. Usually both copies of each gene are active, or "turned on," in cells. In some cases, however, only one of the two copies is normally turned on. Which copy is active depends on the parent of origin: some genes are normally active only when they are inherited from a person's father; others are active only when inherited from a person's mother. This phenomenon is known as genomic imprinting.

The 6q24 region includes paternally expressed imprinted genes, which means that normally only the copy of each gene that comes from the father is active. The copy of each gene that comes from the mother is inactivated (silenced) by a mechanism called methylation.

There are three ways that overexpression of paternally expressed imprinted genes in the 6q24 region can occur. About 40 percent of cases of 6q24-related transient neonatal diabetes mellitus are caused by a genetic change known as paternal uniparental disomy (UPD) of chromosome 6. In paternal UPD, people inherit both copies of the affected chromosome from their father instead of one copy from each parent. Paternal UPD causes people to have two active copies of paternally expressed imprinted genes, rather than one active copy from the father and one inactive copy from the mother.

Another 40 percent of cases of 6q24-related transient neonatal diabetes mellitus occur when the copy of chromosome 6 that comes from the father has a duplication of genetic material including the paternally expressed imprinted genes in the 6q24 region.

The third mechanism by which overexpression of genes in the 6q24 region can occur is by impaired silencing of the maternal copy of the genes (maternal hypomethylation). Approximately 20 percent of cases of 6q24-related transient neonatal diabetes mellitus are caused by maternal hypomethylation. Some people with this disorder have a genetic change in the maternal copy of the 6q24 region that prevents genes in that region from being silenced. Other affected individuals have a more generalized impairment of gene silencing involving many imprinted regions, called hypomethylation of imprinted loci (HIL). Because HIL can cause overexpression of many genes, this mechanism may account for the additional health problems that occur in some people with 6q24-related transient neonatal diabetes mellitus.

It is not well understood how overexpression of genes in the 6q24 region causes 6q24-related transient neonatal diabetes mellitus and why the condition improves after infancy. This form of diabetes is characterized by high blood sugar levels (hyperglycemia) resulting from a shortage of the hormone insulin. Insulin controls how much glucose (a type of sugar) is passed from the blood into cells for conversion to energy.

The protein produced from one gene in the 6q24 region may help control insulin secretion by beta cells in the pancreas. In addition, overexpression of this protein has been shown to stop the cycle of cell division and lead to the self-destruction of cells (apoptosis). Researchers suggest that overexpression of this gene may reduce the number of insulin-secreting beta cells or impair their function in affected individuals.

Lack of sufficient insulin results in the signs and symptoms of diabetes mellitus. In individuals with 6q24-related transient neonatal diabetes mellitus, these signs and symptoms are most likely to occur during times of physiologic stress, including the rapid growth of infancy, childhood illnesses, and pregnancy. Because insulin acts as a growth promoter during early development, a shortage of this hormone may account for the slow growth before birth (intrauterine growth retardation) seen in 6q24-related transient neonatal diabetes mellitus.

## 2.2. Other chromosomal conditions

Other changes in the number or structure of chromosome 6 can have a variety of effects, including delayed growth and development, intellectual disability, distinctive facial features, birth defects, and other health problems. Changes to chromosome 6 may include deletions or duplications of genetic material in the short (p) or long (q) arm of the chromosome in each cell, or a circular structure called ring chromosome 6. Ring chromosomes occur when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure.

## 2.3. Cancers

Duplications of genetic material in the short (p) arm of chromosome 6 have been associated with the growth and spread of several types of cancer. These duplications are somatic, which means they are acquired during a person's lifetime and are present only in certain cells. Researchers believe that some of the genes in the duplicated region on chromosome 6p are oncogenes. Oncogenes play roles in several critical cell functions, including cell division, the maturation of cells to carry out specific functions (cell differentiation), and the self-destruction of cells (apoptosis). When mutated, oncogenes have the potential to cause normal cells to become cancerous. The presence of extra copies of the oncogenes may allow cells to grow and divide in an uncontrolled way, leading to the progression and spread of cancer.

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