

## Genetic test results

A clinical geneticist or genetic counsellor will explain which piece (or pieces) of genetic material have been duplicated. The information given will include the location and size of the piece of DNA that has been duplicated as well as the known significance of any genes included in the change, and whether the same or a similar change has been seen before in another person.

Chromosomal duplications are commonly identified using a genetic test called **microarray analysis** (such as **array CGH**). The results of this test are likely to read something like the following example:

**arr[hg19] 16p11.2 [29653028-30190538]x3 dn**

**arr** The analysis used microarray technology

**hg19** This is the reference DNA sequence that the base pair numbers refer to, in this case **human genome build 19**

**16p11.2** The analysis revealed a DNA change on the **p** arm of chromosome **16** in band **11.2**

**[29653028-30190538]** The DNA change is identified by its base pair numbers (the points where the chromosomal change has occurred).

In this example, the DNA change lies between **base pairs (bp) 29653028** and **30190538**.

This region covers 537,510 base pairs (≈0.5 Mb)

**x3** There are 3 copies of the piece of DNA specified. Since there should be 2 copies of chromosome 16, this indicates that the DNA change is a duplication

**dn** The duplication occurred *de novo* (as a 'new event'). The parents' chromosomes have been checked and no duplication has been found in this region of chromosome 16

If a duplication in a person is identified as *de novo*, it is very unlikely to recur in any sibling of that person. If a test result is followed by **mat**, the duplication has been inherited from the mother (**maternal**); if it is followed by **pat**, the duplication has been inherited from the father (**paternal**).

Genetic test results may also contain a list of **morbid** genes. These are genes known to cause symptoms if they do not function as expected. Unless the duplication directly disrupts a gene sequence, the genes within the duplication may be able to perform their usual role, but have increased activity due to increased copy number and this may cause symptoms. Some genes are also **imprinted**, which means one copy is usually switched off. These genes, and other genes, may be more sensitive to copy number changes (i.e. are '**dose-sensitive**').

## Why did this happen and can it happen again?

Duplications can be inherited from an unaffected or affected parent or happen as a new event (*de novo*). Chromosome sections can be duplicated during the formation of eggs or sperm or during the complicated replication process that is needed to produce new cells as we grow and develop. Sometimes similar duplications occur in unrelated people due to regions of repetitive DNA. It is important to know that nothing could have been done to prevent the duplication from happening. It was a natural event that no lifestyle, dietary or environmental factors are known to cause. There is nothing that anyone did before, during or after pregnancy to cause the duplication.

If a child has inherited the duplication, the chances of having another child with the same duplication is about 50%. If the duplication is *de novo*, the chances are estimated at less than 1%. Your genetics centre should be able to offer counselling to all family members, including individuals with the duplication or microduplication, regarding the chances of having a(nother) child with the same change.

## Inform Network Support



**Rare Chromosome Disorder Support Group,**

The Stables, Station Road West,  
Oxted, Surrey. RH8 9EE. UK.

Tel +44(0)1883 723356

[info@rarechromo.org](mailto:info@rarechromo.org)

[www.rarechromo.org](http://www.rarechromo.org)

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This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. This booklet was compiled by Unique (AP) and reviewed by Dr. Gregory Costain, Division of Clinical and Metabolic Genetics, The Hospital for Sick Children, Toronto, Canada.

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Understanding Chromosome & Gene Disorders

# Duplications and microduplications

[rarechromo.org](http://rarechromo.org)

## What are duplications and microduplications?

A chromosomal duplication is the duplication of a piece of genetic material from a chromosome. Duplications can vary in size and those that are too small to be seen under the microscope are sometimes called microduplications.

## What are chromosomes?

Our bodies are made up of many different types of cells, most of which contain our chromosomes. Chromosomes come in pairs; one member of each pair is usually inherited from each parent. Most cells have 23 pairs of chromosomes (a total of 46). Eggs and sperm, however, have a single copy of each chromosome pair; when a sperm fertilises an egg at conception, the number of chromosomes is restored to 46.

We usually have 22 chromosome pairs called **autosomes**, numbered 1-22 roughly according to decreasing size, and two **sex chromosomes** that determine the characteristics associated with biological sex. Males commonly have one X and one Y chromosome (XY), and females usually have two X chromosomes (XX).

Chromosomes can't be seen with the naked eye but if cells are prepared in a specific way, the chromosomes can be stained and viewed under a microscope. This image shows the chromosomes present in a typical male (XY) cell.



Chromosomes pairs 1-22, X and Y (male)

## How will a duplication affect me or my child?

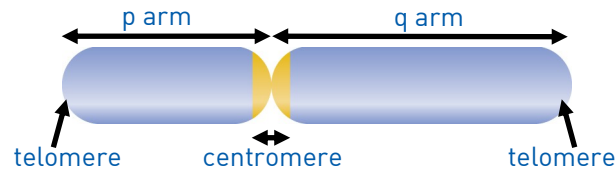
Effects of chromosomal duplications vary greatly between individuals and are dependent on which chromosome is affected and what additional genetic material is present. Duplications can affect intellectual abilities and/or cause physical and functional changes to our bodies. Duplications thought to cause symptoms are called **pathogenic**, those thought to have no ill effect are called **benign**. There are also many duplications of **uncertain significance** that may be reclassified as benign or pathogenic when we've learnt more about them.

## Duplication location

Chromosomal duplications are often described by their location on a specific chromosome; which 'arm' they are on and which 'band' they are in.

### What are chromosome arms?

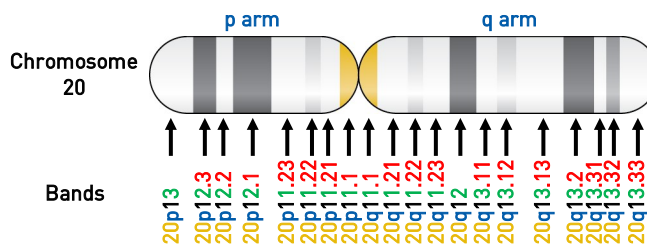
Each chromosome consists of two 'arms' joined together at a constricted part of the chromosome called the **centromere**. The shorter arm is called the 'p' arm, and the longer arm is known as the 'q' arm.



The tips of the arms are called **telomeres**. If a piece of chromosome is duplicated at the tip of a chromosome it's called a **terminal** duplication. If a piece of chromosome is duplicated within one of the arms, it's called an **interstitial** duplication; those closer to the centromere are called **proximal** duplications, those closer to the arm tips are called **distal** duplications.

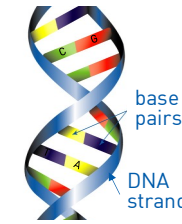
### What are chromosome bands?

Each of our chromosomes can be identified as a series of **bands** visualised by specific laboratory staining techniques. The bands on each chromosome arm are numbered starting at the centromere (which has been assigned the number 10) and finishing at the telomere. Duplications are described by their band location on a chromosome arm. Descriptions start with the **number of the chromosome** e.g. chromosome 20 (as shown in the image below). followed by the arm letter, **p** or **q**. The number of the **region** e.g. 1 is then noted, followed by the **band** number e.g. 3, then any smaller **sub-bands** such as **.2** or an even smaller division of a sub-band e.g. **.33**.



## What's in a duplication?

Chromosomes are made from incredibly long pieces of tightly packaged **DNA** (deoxyribonucleic acid). DNA exists as a double stranded structure (called a **double helix**, as shown in the image below).



A single strand of DNA is made from building blocks called **nucleotides**, each containing one of four **bases**: **G** (guanine), **A** (adenine), **T** (thymine), or **C** (cytosine). Two strands of DNA coil around each other and are held together by bonds between the base pairs **A** and **T** or **G** and **C**.

DNA can be thought of as a sequence of letters (bases) but unlike an alphabet, the sequence only uses 4 letters (**G, A, T, C**). Within these long sequences, there are regions that code for our **genes**, which are the 'instructions' that our bodies use to function, grow and develop. We have over 20,000 genes and each one has a distinct role in different parts of the body at different stages of development.

Due to advances in genetic technologies, pieces of duplicated DNA can now be easily identified, together with their size, location and most importantly, gene content. When we try to assess what possible effects a duplication may have, we look at which genes (or sequences of DNA that control the activity of genes) are affected.

## Duplication size

The size of a duplication is measured in **bases** or **base pairs** (**bp**). The first base pair of each chromosome is at the tip (telomere) of the p arm, and the last is at the tip of the q arm. Since DNA sequences are so long, they are often measured in megabases (Mb's; 1 Mb = 1 million base pairs) or kilobases (kb's; 1 kb = 1000 bp). Duplications smaller than 5 Mb (that's 5,000,000 base pairs) are sometimes known as microduplications.

Duplications can vary in size from one base pair (known as a **sequence variant**) to an entire chromosome (known as **polysomy**). But the majority of duplications currently identified using standard technologies are between a few hundred kb and a few Mb. Such duplications are commonly known as **copy number variants** (CNVs) since the usual copy number of the duplicated piece of DNA has been increased. Duplications can include one or multiple additional copies of a specific sequence of DNA.