# C9orf72 Gene

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chromosome 9 open reading frame 72

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## 1. Normal Function

The *C9orf72* gene provides instructions for making a protein that is found in various tissues. The protein is abundant in nerve cells (neurons) in the outer layers of the brain (cerebral cortex) and in specialized neurons in the brain and spinal cord that control movement (motor neurons). The C9orf72 protein is thought to be located at the tip of the neuron in a region called the presynaptic terminal. This area is important for sending and receiving signals between neurons.

The C9orf72 protein likely plays a role in many processes involving the chemical cousin of DNA, known as RNA. This protein is thought to influence the production of RNA from genes, the production of proteins from RNA, and the transport of RNA within the cell.

The *C9orf72* gene contains a segment of DNA made up of a series of six DNA building blocks (nucleotides), four guanines followed by two cytosines (written as GGGGCC). This segment (known as a hexanucleotide repeat) can occur once or be repeated multiple times in a row; estimates suggest repeats of up to 30 times have no negative effect on gene function.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Amyotrophic Lateral Sclerosis

Mutations in the *C9orf72* gene have been found to cause amyotrophic lateral sclerosis (ALS), a condition characterized by progressive muscle weakness, a loss of muscle mass, and an inability to control movement. These mutations affect the GGGGCC segment of the gene. When this series of nucleotides is repeated too many times, it can cause ALS. This type of mutation is called a hexanucleotide repeat expansion. Although it is not clear exactly how many hexanucleotide repeats are needed to cause disease, researchers believe that having more than about 30 repeats can lead to ALS.

It is unclear whether the hexanucleotide repeat expansion reduces C9orf72 protein function or leads to the production of a protein with abnormal function that disrupts RNA and protein production in the cell, resulting in the formation of protein clumps (aggregates). In ALS, the large size of motor neurons is thought to make these cells vulnerable to impairments in normal cell function. Disruptions in C9orf72 protein function may lead to premature motor neuron cell death, resulting in the signs and symptoms of ALS.

Some people with ALS caused by *C9orf72* gene mutations also develop a condition called frontotemporal dementia (FTD), which is a progressive brain disorder that affects personality, behavior, and language. It is unclear why some people with *C9orf72* gene mutations develop FTD and others do not. Individuals who develop both conditions are diagnosed as having ALS-FTD.

## 3. Other Names for This Gene

- CI072_HUMAN
- MGC23980
- uncharacterized protein C9orf72

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