



## SNCA gene

synuclein alpha

### Normal Function

The *SNCA* gene provides instructions for making a small protein called alpha-synuclein. Alpha-synuclein is abundant in the brain, and smaller amounts are found in the heart, muscles, and other tissues. In the brain, alpha-synuclein is found mainly at the tips of nerve cells (neurons) in specialized structures called presynaptic terminals. Presynaptic terminals release chemical messengers, called neurotransmitters, from compartments known as synaptic vesicles. The release of neurotransmitters relays signals between neurons and is critical for normal brain function.

Although the function of alpha-synuclein is not well understood, studies suggest that it plays an important role in maintaining an adequate supply of synaptic vesicles in presynaptic terminals. It may also help regulate the release of dopamine, a neurotransmitter that is critical for controlling the start and stop of voluntary and involuntary movements. Alpha-synuclein may also play a role in the movement of structures called microtubules that help cells maintain their shape.

### Health Conditions Related to Genetic Changes

#### Dementia with Lewy bodies

At least six mutations in the *SNCA* gene have been found to cause dementia with Lewy bodies. This condition is characterized by intellectual decline (dementia); visual hallucinations; sudden changes in attention and mood; and movement problems characteristic of Parkinson disease (described below) such as rigidity of limbs, tremors, and impaired balance and coordination. A characteristic feature of this condition is Lewy bodies, which are abnormal clusters of alpha-synuclein protein in the brain. Lewy bodies also occur in Parkinson disease, but they tend to be more widespread in the brain in dementia with Lewy bodies.

In dementia with Lewy bodies, *SNCA* gene mutations lead to the production of an alpha-synuclein protein with an abnormal shape. The misshapen proteins cluster together, forming the main component of Lewy bodies. These protein clusters are present throughout the brain where they impair neuron function and ultimately cause cell death. Over time, the loss of neurons increasingly impairs intellectual and motor function and the regulation of emotions, resulting in the signs and symptoms of dementia with Lewy bodies.

## Parkinson disease

At least 30 mutations in the *SNCA* gene have been found to cause Parkinson disease, a condition characterized by progressive problems with movement and balance. *SNCA* gene mutations are associated with the early-onset form of the disorder, which typically appears before age 50. Other variations in the *SNCA* gene have been found to increase the risk of developing Parkinson disease, although they do not appear to be a direct cause of the disease.

Researchers have described two types of alterations of the *SNCA* gene in people with Parkinson disease. One type changes single protein building blocks (amino acids) used to make alpha-synuclein. In some cases, the amino acid alanine is replaced with the amino acid threonine at protein position 53 (written as Ala53Thr or A53T) or with the amino acid proline at position 30 (written as Ala30Pro or A30P). These alterations cause the alpha-synuclein protein to take on an incorrect 3-dimensional shape (misfold). In the other type of alteration, one of the two *SNCA* genes in each cell is inappropriately duplicated or triplicated. The extra copies of the *SNCA* gene lead to an excess of alpha-synuclein protein.

It is unclear how alterations in the *SNCA* gene cause Parkinson disease. This condition involves the selective death or impairment of neurons that produce dopamine. Misfolded or excess alpha-synuclein proteins may cluster together to form Lewy bodies and impair the function of these neurons in specific regions of the brain. Lewy bodies may disrupt the regulation of dopamine, which allows dopamine to accumulate to toxic levels and eventually kill neurons. Researchers also suspect that Lewy bodies stall or shut down the cell machinery that removes unneeded proteins. As a result, unneeded proteins may clog neurons and impair their functions. Symptoms of Parkinson disease appear when dopamine-producing neurons become impaired or die. The loss of these cells weakens communication between the brain and muscles, and ultimately the brain becomes unable to control muscle movement. The presence of Lewy bodies in a region of the brain called the substantia nigra, which controls balance and movement, are a characteristic feature of Parkinson disease.

## Multiple system atrophy

Several common variations in the *SNCA* gene have been found to increase the risk of multiple system atrophy, a progressive brain disorder that affects movement and balance and disrupts the function of the autonomic nervous system. The autonomic nervous system controls actions that are mostly involuntary, such as regulation of blood pressure.

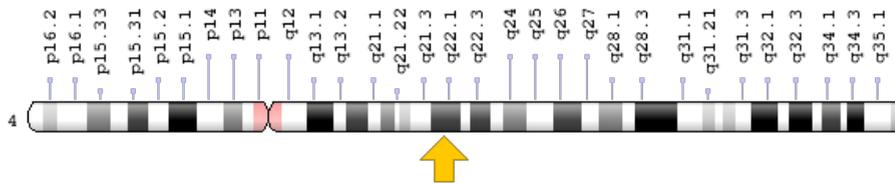
The identified gene variations each change a single DNA building block (nucleotide) in the *SNCA* gene. Researchers are working to determine whether these changes alter the function of alpha-synuclein and how they influence the risk of developing multiple system atrophy. Variations in the *SNCA* gene appear to affect disease risk in people of European descent; however, studies suggest that changes in this gene

are not associated with multiple system atrophy in the Chinese population or in South Koreans. It is unclear whether *SNCA* gene variations are a risk factor for this condition in people of other geographic and ethnic backgrounds.

### Chromosomal Location

Cytogenetic Location: 4q22.1, which is the long (q) arm of chromosome 4 at position 22.1

Molecular Location: base pairs 89,724,099 to 89,838,324 on chromosome 4 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

### Other Names for This Gene

- alpha-synuclein
- NACP
- nonA-beta component of AD amyloid
- PARK1
- PARK4
- PD1
- synuclein, alpha (non A4 component of amyloid precursor)
- SYUA\_HUMAN

### Additional Information & Resources

#### Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Composition of Synaptic Vesicles  
<https://www.ncbi.nlm.nih.gov/books/NBK28154/>
- Dementia: A NICE-SCIE Guideline on Supporting People With Dementia and Their Carers in Health and Social Care (2007): Dementia  
<https://www.ncbi.nlm.nih.gov/books/NBK55480/>

- Dementia: A NICE-SCIE Guideline on Supporting People With Dementia and Their Carers in Health and Social Care (2007): Diagnosis and Assessment  
<https://www.ncbi.nlm.nih.gov/books/NBK55453/#ch6.s32>
- Madame Curie Bioscience Database:  $\alpha$ -Synuclein Physiology and Membrane Binding  
<https://www.ncbi.nlm.nih.gov/books/NBK6143/>

#### Clinical Information from GeneReviews

- Parkinson Disease Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK1223>

#### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SNCA%5BTIAB%5D%29+OR+%28alpha-synuclein%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D>

#### Catalog of Genes and Diseases from OMIM

- SYNUCLEIN, ALPHA  
<http://omim.org/entry/163890>

#### Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
[http://atlasgeneticsoncology.org/Genes/GC\\_SNCA.html](http://atlasgeneticsoncology.org/Genes/GC_SNCA.html)
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=SNCA%5Bgene%5D>
- HGNC Gene Symbol Report  
[https://www.genenames.org/data/gene-symbol-report#!/hgnc\\_id/HGNC:11138](https://www.genenames.org/data/gene-symbol-report#!/hgnc_id/HGNC:11138)
- Monarch Initiative  
<https://monarchinitiative.org/gene/NCBIGene:6622>
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/6622>
- PDGene  
<http://www.pdgene.org/view?gene=SNCA>
- UniProt  
<https://www.uniprot.org/uniprot/P37840>

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