

PRKN gene

parkin RBR E3 ubiquitin protein ligase

Normal Function

The *PRKN* gene, one of the largest human genes, provides instructions for making a protein called parkin. Parkin plays a role in the cell machinery that breaks down (degrades) unneeded proteins by tagging damaged and excess proteins with molecules called ubiquitin. Ubiquitin serves as a signal to move unneeded proteins into specialized cell structures known as proteasomes, where the proteins are degraded. The ubiquitin-proteasome system acts as the cell's quality control system by disposing of damaged, misshapen, and excess proteins. This system also regulates the availability of proteins that are involved in several critical cell activities, such as the timing of cell division and growth. Because of its activity in the ubiquitin-proteasome system, parkin belongs to a group of proteins called E3 ubiquitin ligases.

Parkin appears to be involved in the maintenance of mitochondria, the energy-producing centers in cells. However, little is known about its role in mitochondrial function. Research suggests that parkin may help trigger the destruction of mitochondria that are not working properly.

Studies of the structure and activity of parkin have led researchers to propose several additional activities for this protein. Parkin may act as a tumor suppressor protein, which means it prevents cells from growing and dividing too rapidly or in an uncontrolled way. Parkin may also regulate the supply and release of sacs called synaptic vesicles from nerve cells. Synaptic vesicles contain chemical messengers that transmit signals from one nerve cell to another.

Health Conditions Related to Genetic Changes

Parkinson's disease

Researchers have identified more than 200 *PRKN* gene mutations that cause Parkinson's disease, a condition characterized by progressive problems with movement and balance. Mutations in this gene are associated with the juvenile form of Parkinson's disease, which appears before age 20, and some cases of the more common, late-onset form that begins after age 50.

Some *PRKN* gene mutations lead to an abnormally small parkin protein that is

nonfunctional and is rapidly broken down (degraded) within cells. Other mutations insert, delete, or change DNA building blocks (nucleotides) in the *PRKN* gene, leading to a defective version of the parkin protein or preventing the production of this protein. The *PRKN* gene mutations associated with Parkinson's disease usually lead to a loss of parkin activity.

It is unclear how *PRKN* gene mutations cause Parkinson's disease. The loss of parkin activity probably disturbs the ubiquitin-proteasome system, which allows unneeded proteins to accumulate. A buildup of these proteins could disrupt normal cell activities such as the supply and release of synaptic vesicles, particularly those that contain a chemical messenger called dopamine. As parkin is normally abundant in the brain, its loss could lead to the impairment or death of nerve cells, including those that produce dopamine. Loss of dopamine-producing nerve cells is a characteristic feature of Parkinson's disease.

Mutations in the *PRKN* gene may also disrupt the regulation of mitochondria. Researchers speculate that mitochondrial dysfunction in dopamine-producing nerve cells may play an important role in causing the signs and symptoms of Parkinson's disease.

Leprosy

Studies suggest that common variations (polymorphisms) in the *PRKN* gene (and a neighboring gene called *PACRG*) can increase the risk of contracting Hansen disease, also known as leprosy. This disease affects the nerves and skin and is caused by the bacterium *Mycobacterium leprae*. It remains unclear how *PRKN* polymorphisms increase susceptibility to Hansen disease. Researchers believe that the ubiquitin-proteasome system may play a role in controlling infection. Polymorphisms in the *PRKN* gene may subtly alter parkin's function, making the ubiquitin-proteasome system less efficient.

Lung cancer

The *PRKN* gene spans part of a region on chromosome 6 known as FRA6E. This region is known as a fragile area because it is unstable and prone to breakage and rearrangement. Changes involving the FRA6E region have been reported in several forms of human cancer, including lung cancer. In some cancerous tumors, segments of the FRA6E region, including part or all of the *PRKN* gene, are abnormally deleted or duplicated. These genetic changes are described as somatic because they occur only in tumor cells and are not inherited. As a result of these alterations, parkin activity is reduced or absent in these cells. Because parkin is thought to act as a tumor suppressor, a shortage of this protein's function could allow cells to grow and divide in an uncontrolled manner, leading to tumor formation.

Ovarian cancer

Changes involving the FRA6E region (described above) have also been reported in ovarian cancer. These changes include abnormal deletion or duplication of segments of

the FRA6E region, including part or all of the *PRKN* gene. As a result of these somatic alterations, parkin activity is reduced or absent in affected cells. Because parkin is thought to act as a tumor suppressor, a shortage of this protein's function could allow cells to grow and divide in an uncontrolled manner, leading to tumor formation.

Cancers

Deletion or duplication of segments of the FRA6E region that involve the *PRKN* gene have also been found in glioblastoma (a form of brain cancer) and colorectal cancer. As a result of these somatic alterations, parkin activity is reduced or absent in tumor cells. Because parkin is thought to act as a tumor suppressor, a shortage of this protein's function could allow cells to grow and divide in an uncontrolled manner, leading to tumor formation.

Other Names for This Gene

- AR-JP
- PARK2
- parkin
- Parkinson disease (autosomal recessive, juvenile) 2, parkin
- parkinson protein 2, E3 ubiquitin protein ligase (parkin)
- PDJ
- PRKN2_HUMAN
- ubiquitin E3 ligase

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PRKN ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5071\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5071[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28PARK2%5BTIAB%5D%29+OR+%28parkin+AND+protein%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+720+days%22%5Bdp%5D%29%29%29>)

Catalog of Genes and Diseases from OMIM

- PARKIN RBR E3 UBIQUITIN PROTEIN LIGASE; PRKN (<https://omim.org/entry/602544>)
- LEPROSY, SUSCEPTIBILITY TO, 2; LPRS2 (<https://omim.org/entry/607572>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/5071>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=PRKN\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=PRKN[gene]))

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Genomic Location

The *PRKN* gene is found on chromosome 6 (<https://medlineplus.gov/genetics/chromosome/6/>).

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