LRRK2 Gene

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Leucine rich repeat kinase 2

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1. Introduction

The *LRRK2* gene provides instructions for making a protein called dardarin. The *LRRK2* gene is active in the brain and other tissues throughout the body.

One segment of the dardarin protein is called a leucine-rich region because it contains a large amount of a protein building block (amino acid) known as leucine. Proteins with leucine-rich regions appear to play a role in activities that require interactions with other proteins, such as transmitting signals or helping to assemble the cell's structural framework (cytoskeleton). Other parts of the dardarin protein are also thought to be involved in protein-protein interactions.

Additional studies indicate that dardarin has an enzyme function known as kinase activity. Proteins with kinase activity assist in the transfer of a phosphate group (a cluster of oxygen and phosphorus atoms) from the energy molecule ATP to amino acids in certain proteins. This phosphate transfer is called phosphorylation, and it is an essential step in turning on and off many cell activities. Dardarin also has a second enzyme function referred to as a GTPase activity. This activity is associated with a region of the protein called the ROC domain. The ROC domain may help control the overall shape of the dardarin protein.

2. Health Conditions Related to Genetic Changes

2.1. Parkinson Disease

Researchers have identified more than 100 *LRRK2* gene mutations in families with late-onset Parkinson disease (the most common form of the disorder, which appears after age 50). These mutations replace single amino acids in the dardarin protein, which affects the protein's structure and function. It is unclear how *LRRK2* gene mutations lead to the movement and balance problems characteristic of Parkinson disease.

A mutation that replaces the amino acid arginine with the amino acid glycine at protein position 1441 (written as Arg1441Gly or R1441G) is a relatively common cause of Parkinson disease in the Basque region between France and Spain. The protein name dardarin comes from the Basque word "dardara," which means tremor, a characteristic feature of Parkinson disease.

Studies of several different populations from around the world revealed a common *LRRK2* gene mutation in 3 to 7 percent of familial Parkinson disease cases. This mutation replaces the amino acid glycine with the amino acid serine at protein position 2019 (written as Gly2019Ser or G2019S). The incidence of the Gly2019Ser mutation in familial cases is highest among Arabs from North Africa and people of Ashkenazi (eastern and central European) Jewish ancestry, and it is lowest in Asian and northern European populations. This particular mutation has also been reported in 1 to 3 percent of sporadic Parkinson disease cases, in which there is no family history of the disease.

Studies in Chinese and Japanese populations have identified an *LRRK2* gene mutation that occurs more frequently in people with Parkinson disease than in people without the disease. This mutation replaces the amino acid glycine with the amino acid arginine at protein position 2385 (written as Gly2385Arg or G2385R). This mutation appears to increase the risk of Parkinson disease among people in these populations.

3. Other Names for This Gene

- DRDN
- leucine-rich repeat kinase 2
- LRRK2_HUMAN
- PARK8
- RIPK7
- ROCO2

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