OPA3 Gene

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OPA3, outer mitochondrial membrane lipid metabolism regulator

genes

1. Introduction

The *OPA3* gene provides instructions for making a protein whose exact function is unknown. The OPA3 protein is found in structures called mitochondria, which are the energy-producing centers of cells. The OPA3 protein is thought to play a role in the organization of the shape and structure of the mitochondria and in controlled cell death (apoptosis).

2. Health Conditions Related to Genetic Changes

2.1. Autosomal dominant optic atrophy and cataract

At least four mutations in the *OPA3* gene have been found to cause autosomal dominant optic atrophy and cataract. This condition causes slowly worsening vision in both eyes that often begins at birth. The severity of the vision loss varies widely, even among affected members of the same family. People with this condition have degeneration (atrophy) of the optic nerves, which carry information from the eyes to the brain, and clouding of the lenses of the eyes (cataracts). Some affected individuals have additional features such as hearing loss or movement problems.

Mutations in the *OPA3* gene that cause autosomal dominant optic atrophy and cataract occur in one copy of the gene in each cell. A mutation that has been found in multiple people with autosomal dominant optic atrophy and cataract results in the production of a protein with the building block (amino acid) glutamine replaced with the amino acid glutamic acid at position 105 (written as Gln105Glu or Q105E).

This and other *OPA3* gene mutations that cause autosomal dominant optic atrophy and cataract lead to abnormal mitochondrial function. The mitochondria become misshapen and disorganized and have reduced energy-producing capabilities. Cells that contain these poorly functioning mitochondria seem to be more susceptible to apoptosis, particularly those with high energy demands, such as a type in the eye called retinal ganglion cells. Specialized extensions of retinal ganglion cells, called axons, form the optic nerves, so when retinal ganglion cells die, the optic nerves atrophy and cannot transmit visual information to the brain. Loss of retinal ganglion cells and

optic nerve atrophy contribute to vision impairment in people with autosomal dominant optic atrophy and cataracts. It is likely that nerve cells in other parts of the body are similarly affected by dysfunctional mitochondria, resulting in movement problems and hearing loss in some individuals with this condition.

2.2. Costeff syndrome

At least five mutations in the *OPA3* gene have been found to cause Costeff syndrome. This condition is characterized by vision loss due to optic nerve atrophy, delayed development, and movement problems. Costeff syndrome is caused by mutations in both copies of the *OPA3* gene in each cell, leading to a complete loss of OPA3 protein function. An *OPA3* gene mutation that causes Costeff syndrome in the Iraqi Jewish population (written as 143-1G>C) alters the way the *OPA3* gene's instructions are put together to make the protein, which results in a lack of functional protein. Cells without any functional OPA3 protein have abnormally shaped mitochondria with reduced energy-producing capabilities. Nerve cells in the brain and retinal ganglion cells that make up optic nerves have high energy demands and may be particularly dependent on energy production in the mitochondria for survival. It is likely that dysfunctional mitochondria and reduced energy production result in the death of these cell types more readily than other cell types.

3. Other Names for This Gene

- FLJ22187
- FLJ25932
- MGA3
- MGC75494
- OPA3 protein
- OPA3_HUMAN
- optic atrophy 3 (autosomal recessive, with chorea and spastic paraplegia)

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