PLA2G6 Gene

Subjects: Genetics & Heredity
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phospholipase A2 group VI

genes

1. Introduction

The *PLA2G6* gene provides instructions for making a type of enzyme called an A2 phospholipase. This type of enzyme is involved in breaking down (metabolizing) fats called phospholipids. Phospholipid metabolism is important for many body processes, including helping to maintain the integrity of the cell membrane. Specifically, the A2 phospholipase produced from the *PLA2G6* gene, sometimes called PLA2 group VI, helps to regulate the levels of a compound called phosphatidylcholine, which is abundant in the cell membrane.

2. Health Conditions Related to Genetic Changes

2.1. Infantile neuroaxonal dystrophy

At least 50 mutations in the *PLA2G6* gene have been identified in people with infantile neuroaxonal dystrophy, a progressive neurological disorder that causes intellectual disability and movement problems. Mutations in the *PLA2G6* gene eliminate or severely impair the function of the PLA2 group VI enzyme. Impairment of PLA2 group VI enzyme function may disrupt cell membrane maintenance and contribute to the development of swellings called spheroid bodies in the axons, which are fibers that extend from nerve cells (neurons) and transmit impulses to muscles and other neurons. Although it is unknown how changes in this enzyme's function lead to the signs and symptoms of infantile neuroaxonal dystrophy, phospholipid metabolism problems have been seen in both this disorder and a similar disorder called pantothenate kinase-associated neurodegeneration. These disorders, as well as the more common Alzheimer disease and Parkinson disease, also are associated with changes in brain iron metabolism. Researchers are studying the links between phospholipid defects, brain iron, and damage to nerve cells, but have not determined how the iron accumulation that occurs in some individuals with infantile neuroaxonal dystrophy may contribute to the features of this disorder.

2.2. Other disorders

PLA2G6 gene mutations can also cause atypical neuroaxonal dystrophy and *PLA2G6*-related dystonia-parkinsonism, which are conditions in which deterioration of neurological function (neurodegeneration) occurs later

in life. The term *PLA2G6*-associated neurodegeneration (PLAN) is often used to include the entire spectrum of neurodegenerative disorders caused by mutations in *PLA2G6*.

Atypical neuroaxonal dystrophy (atypical NAD) is a disorder with signs and symptoms that are similar to those of infantile neuroaxonal dystrophy but that occur later and progress more slowly. Atypical NAD usually appears in early childhood but in some cases is not evident until the teenage years.

PLA2G6-related dystonia-parkinsonism is also caused by *PLA2G6* gene mutations and involves movement abnormalities that occur in adulthood. Dystonia is involuntary tensing of the muscles, and parkinsonism comprises a group of movement problems including unusually slow movement (bradykinesia), muscle rigidity, tremors, and an inability to hold the body upright and balanced (postural instability).

Both of these later-onset conditions are caused by *PLA2G6* gene mutations that are believed to have a less severe effect on PLA2 group VI enzyme function than the mutations that cause infantile neuroaxonal dystrophy.

3. Other Names for This Gene

- CaI-PLA2
- calcium-independent phospholipase A2
- cytosolic, calcium-independent phospholipase A2
- GVI
- INAD1
- iPLA2
- iPLA2beta
- NBIA2
- OTTHUMP00000028877
- PA2G6_HUMAN
- PARK14
- patatin-like phospholipase domain containing 9
- phospholipase A2, group VI
- phospholipase A2, group VI (cytosolic, calcium-independent)
- PLA2
- PNPLA9

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