ITPR1 Gene

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Inositol 1,4,5-trisphosphate receptor type 1

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1. Introduction

The *ITPR1* gene provides instructions for making a protein that is part of a channel that controls the flow of positively charged calcium atoms (calcium ions) within cells. Four ITPR1 protein molecules join together in a complex (a homotetramer) to form the channel. In response to certain signals, the ITPR1 channel releases calcium ions from storage in a cell structure called the endoplasmic reticulum into the surrounding cell fluid (the cytoplasm). Proper regulation of calcium ion concentration inside cells is important for the development and function of various tissues and organs.

2. Health Conditions Related to Genetic Changes

2.1. Gillespie Syndrome

At least 13 *ITPR1* gene mutations have been identified in people with Gillespie syndrome, a disorder that involves eye abnormalities, weak muscle tone from birth (congenital hypotonia), problems with balance and coordinating movements (ataxia), and mild to moderate intellectual disability. The *ITPR1* gene mutations that cause Gillespie syndrome likely result in a protein with an altered structure. It is thought that calcium channel homotetramers made with the altered proteins are unstable. A shortage of normal ITPR1 channels impairs the cell's ability to regulate the concentration of calcium ions. However, the specific connection between these changes and the signs and symptoms of Gillespie syndrome is unclear.

2.2. Other Disorders

Mutations in the *ITPR1* gene have been identified in people with spinocerebellar ataxia type 15 (SCA15), spinocerebellar ataxia type 29 (SCA29), and less commonly, in other forms of spinocerebellar ataxia. These conditions lead to movement problems that worsen over time. The mutations associated with these disorders likely impair regulation of calcium levels in cells, leading to the signs and symptoms of spinocerebellar ataxia.

Researchers are working to understand why some people with *ITPR1* gene mutations have only movement problems while others also have the eye problems and intellectual disability characteristic of Gillespie syndrome (described above). Studies indicate that *ITPR1* gene mutations that cause the spinocerebellar ataxias affect different regions of the protein than do the mutations that cause Gillespie syndrome. The mutations may also differ in the degree to which they destabilize the homotetramer structure of the calcium channel. These factors could account for the different patterns of signs and symptoms among Gillespie syndrome and the various spinocerebellar ataxias.

3. Other Names for This Gene

- IP3R
- IP3R1

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