GPR101 Gene

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1. Introduction

The *GPR101* gene provides instructions for making a type of protein called a G protein-coupled receptor. G protein-coupled receptors are embedded in the outer membrane of cells, where they relay chemical signals from outside the cell to the interior of the cell. However, the specific function of the GPR101 protein is unknown. The protein is found primarily in the brain, and studies suggest that it has a role in the pituitary gland. This gland, located at the base of the brain, produces hormones that control many important body functions. One of these hormones, called growth hormone, helps direct normal growth of the body's bones and tissues. The GPR101 protein is predominantly expressed in the pituitary gland during development before birth and again at adolescence, stages when the body grows the most. The protein is thought to be involved in the growth of cells in the pituitary gland, in the release of growth hormone from the gland, or in both processes.

2. Health Conditions Related to Genetic Changes

2.1. X-linked acrogigantism

Genetic changes involving the *GPR101* gene cause a condition called X-linked acrogigantism (X-LAG), which is characterized by abnormally fast growth beginning in infancy or early childhood. Signs and symptoms of the condition result from enlargement (hyperplasia) of the gland or development of a noncancerous tumor in the gland (called a pituitary adenoma). The abnormal gland releases more growth hormone than normal, causing rapid growth in individuals with X-LAG.

X-LAG occurs when a small amount of genetic material on the X chromosome is abnormally copied (duplicated). The duplication, often referred to as an Xq26.3 microduplication, occurs on the long (q) arm of the chromosome at a location designated q26.3. Although several genes can be duplicated, only an extra copy of the *GPR101* gene is necessary to cause X-LAG. Duplication of the gene leads to an excess of GPR101 protein. It is unclear how extra GPR101 protein results in pituitary adenoma or hyperplasia or the release of excess growth hormone.

2.2. Other disorders

A variation in the *GPR101* gene is found in a small percentage of people with sporadic acromegaly, a condition that begins in adulthood and is characterized by overgrowth of the hands and feet, "coarse" facial features, heart problems, and other abnormalities. Sporadic acromegaly occurs in people with no history of overgrowth in their family. This variant leads to production of an altered GPR101 protein in which the protein building block (amino acid) glutamate is replaced with the amino acid aspartic acid at position 308 (written as Glu308Asp or E308D). Studies in the lab show that this alteration can lead to a small increase in the release of growth hormone and promote the growth and division (proliferation) of cells, although researchers are unsure exactly how it is associated with acromegaly in affected individuals.

While some studies found the E308D *GPR101* variant in a small percentage of people with sporadic acromegaly, other studies were unable to replicate this result, suggesting that the genetic change may not play a major role in development of the condition.

3. Other Names for This Gene

- GPCR6
- PAGH2

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