PIK3R1 Gene

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phosphoinositide-3-kinase regulatory subunit 1

genes

1. Introduction

The *PIK3R1* gene provides instructions for making a part (subunit) of an enzyme called phosphatidylinositol 3-kinase (PI3K). The primary function of the subunit is to regulate the enzyme's activity. Several slightly different versions of this regulatory subunit are produced from the *PIK3R1* gene; the most abundant of these is called p85α.

PI3K is a kinase, which means that it adds a cluster of oxygen and phosphorus atoms (a phosphate group) to other proteins through a process called phosphorylation. PI3K phosphorylates certain signaling molecules, which triggers a series of additional reactions that transmit chemical signals within cells. PI3K signaling is important for many cell activities, including cell growth and division, movement (migration) of cells, production of new proteins, transport of materials within cells, and cell survival. Studies suggest that PI3K signaling may be involved in the regulation of several hormones, including insulin, which helps control blood sugar levels. PI3K signaling may also play a role in the maturation of fat cells (adipocytes).

2. Health Conditions Related to Genetic Changes

2.1. Short stature, hyperextensibility, hernia, ocular depression, Rieger anomaly, and teething delay

At least seven mutations in the *PIK3R1* gene have been reported to cause a condition known as short stature, hyperextensibility, hernia, ocular depression, Rieger anomaly, and teething delay (often called SHORT syndrome). This condition is characterized by signs and symptoms affecting many parts of the body, including the skin, eyes, teeth, and joints. The most common mutation, which has been identified in at least 10 affected families, changes a single protein building block (amino acid) in the regulatory subunit of PI3K. Specifically, the amino acid arginine is replaced with the amino acid tryptophan at protein position 649 (written as Arg649Trp or R649W). Mutations in the *PIK3R1* gene alter the structure of the subunit, which reduces the ability of PI3K to participate in cell signaling. Because the mutations reduce the enzyme's activity, they are described as "loss-of-function" mutations.

Researchers are working to determine how *PIK3R1* gene mutations lead to the specific features of SHORT syndrome. PI3K's role in insulin activity may be related to insulin resistance and diabetes, which are problems with blood sugar regulation that are found in some people with SHORT syndrome. Abnormal adipocyte maturation might contribute to a lack of fatty tissue under the skin (lipoatrophy), which is another common feature of the condition. It is unclear how reduced PI3K signaling is associated with the other signs and symptoms of SHORT syndrome.

2.2. Cancers

Some gene mutations are acquired during a person's lifetime and are present only in certain cells. These changes, which are called somatic mutations, are not inherited. Somatic *PIK3R1* gene mutations have been identified in some cancers of the uterine lining (endometrial cancers) and in a form of brain cancer called glioblastoma. Less commonly, somatic mutations in the *PIK3R1* gene have been found in cancers of the colon, ovary, and breast.

Cancer-associated changes in the *PIK3R1* gene alter the regulatory subunit such that it can no longer control the activity of PI3K, which increases PI3K signaling dramatically. Because the genetic changes enhance the activity of the enzyme, they are classified as "gain-of-function" mutations. Increased PI3K signaling appears to promote the uncontrolled cell growth and division that is characteristic of cancerous tumors. It is unclear why these mutations seem to be more common in some types of cancer than in others.

3. Other Names for This Gene

- AGM7
- GRB1
- p85
- p85-ALPHA
- P85A_HUMAN
- phosphatidylinositol 3-kinase 85 kDa regulatory subunit alpha
- phosphatidylinositol 3-kinase regulatory subunit alpha
- phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 1 (p85 alpha)
- phosphatidylinositol 3-kinase-associated p-85 alpha
- phosphoinositide-3-kinase regulatory subunit
- phosphoinositide-3-kinase, regulatory subunit 1 (alpha)
- PI3-kinase subunit p85-alpha
- PI3K regulatory subunit alpha
- ptdIns-3-kinase regulatory subunit alpha

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