PLAGL1 Gene

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PLAG1 like zinc finger 1

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1. Introduction

The *PLAGL1* gene provides instructions for making a member of a protein family called zinc finger proteins. Zinc finger proteins are involved in many cellular functions. These proteins each contain one or more short regions called zinc finger domains, which include a specific pattern of protein building blocks (amino acids) and one or more charged atoms of zinc (zinc ions).

Zinc finger proteins attach (bind) primarily to DNA. In most cases, they attach to regions near certain genes and turn the genes on and off as needed. Proteins that bind to DNA and regulate the activity of particular genes are known as transcription factors. Some zinc finger proteins can also bind to other molecules, including RNA (a chemical cousin of DNA) and proteins.

The PLAGL1 protein helps regulate the cell's process for replicating itself in an organized, step-by-step fashion (cell cycle), and is involved in the self-destruction of cells (apoptosis). It is also important in fetal growth. The PLAGL1 protein helps control another protein called the pituitary adenylate cyclase-activating polypeptide receptor (PACAP1). One of the functions of the PACAP1 protein is to stimulate insulin secretion by beta cells in the pancreas. Insulin controls how much glucose (a type of sugar) is passed from the blood into cells for conversion to energy.

PLAGL1 is a paternally expressed imprinted gene, which means that normally only the copy of the gene that comes from the father is active. The copy of the gene that comes from the mother is inactivated (silenced) by a mechanism called methylation.

2. Health Conditions Related to Genetic Changes

2.1. 6q24-related transient neonatal diabetes mellitus

6q24-related transient neonatal diabetes mellitus, a type of diabetes that occurs in infants, is caused by the overactivity (overexpression) of the *PLAGL1* gene. There are three ways that overexpression of the *PLAGL1* gene can occur. About 40 percent of cases of 6q24-related transient neonatal diabetes mellitus are caused by a genetic change known as paternal uniparental disomy (UPD) of chromosome 6. In paternal UPD, people inherit both copies of a chromosome from their father instead of one copy from each parent. Paternal UPD causes people to have two active copies of paternally expressed imprinted genes, rather than one active copy from the father and one inactive copy from the mother.

Another 40 percent of cases of 6q24-related transient neonatal diabetes mellitus occur when the copy of chromosome 6 that comes from the father has a duplication of genetic material including the *PLAGL1* gene.

The third mechanism by which overexpression of the *PLAGL1* gene can occur is by impaired silencing of the maternal copy of the gene (maternal hypomethylation). Approximately 20 percent of cases of 6q24-related transient neonatal diabetes mellitus are caused by maternal hypomethylation. Some people with this disorder have a genetic change in the maternal copy of the 6q24 region that prevents genes in that region from being silenced. Other affected individuals have a more generalized impairment of gene silencing involving many imprinted regions, called hypomethylation of imprinted loci (HIL). HIL results from mutations in other genes.

It is not well understood how overexpression of the *PLAGL1* gene causes 6q24-related transient neonatal diabetes mellitus and why the condition improves after infancy. Researchers suggest that *PLAGL1* overexpression may reduce the number of insulin-secreting beta cells or impair their function in affected individuals. Lack of sufficient insulin results in the

impaired blood sugar control associated with diabetes mellitus. In individuals with 6q24-related transient neonatal diabetes mellitus, these signs and symptoms are most likely to occur during times of physiologic stress, including the rapid growth of infancy, childhood illnesses, and pregnancy. Because insulin acts as a growth promoter during early development, a shortage of this hormone may account for the slow prenatal growth seen in 6q24-related transient neonatal diabetes mellitus.

2.2. Cancers

Excessive silencing (hypermethylation) of the *PLAGL1* gene has been identified in various cancerous tumors, including ovarian cancer and cancers of immune system cells (lymphomas). *PLAGL1* gene hypermethylation results in decreased production of the PLAGL1 protein. A shortage of the PLAGL1 protein likely impairs its role in regulating the cell cycle and interferes with apoptosis. As a result, cells may grow and divide too quickly or in an uncontrolled way, leading to cancer.

3. Other Names for This Gene

- lost on transformation 1
- LOT-1
- LOT1
- MGC126275
- MGC126276
- PLAG-like 1
- PLAL1_HUMAN
- pleiomorphic adenoma gene-like 1
- pleiomorphic adenoma-like protein 1
- ZAC
- ZAC1

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