MEN1 Gene

Subjects: Genetics & Heredity
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menin 1

genes

1. Introduction

The *MEN1* gene provides instructions for making a protein called menin. This protein acts as a tumor suppressor, which means that it keeps cells from growing and dividing too fast or in an uncontrolled way. Although the exact function of menin is unclear, it is likely involved in several important cell functions. For example, it may play a role in copying and repairing DNA and regulating the controlled self-destruction of cells (apoptosis). The menin protein is present in the nucleus of many different types of cells and appears to be active in all stages of development.

Menin interacts with many other proteins, including several transcription factors. Transcription factors bind to specific areas of DNA and help control whether particular genes are turned on or off. Some of these genes likely play a role in cell growth and division. Researchers are working to identify the proteins that interact with menin and determine its specific role as a tumor suppressor.

2. Health Conditions Related to Genetic Changes

2.1. Familial isolated hyperparathyroidism

Mutations in the *MEN1* gene have been found in some cases of familial isolated hyperparathyroidism, a condition characterized by overactivity of the parathyroid glands (primary hyperparathyroidism). These glands help control the normal balance of calcium in the blood. This balance is disrupted in familial isolated hyperparathyroidism, which can lead to high blood calcium levels (hypercalcemia), kidney stones, thinning of bones, nausea and vomiting, high blood pressure (hypertension), weakness, and fatigue. Primary hyperparathyroidism is the most common sign of another condition called multiple endocrine neoplasia type 1 (described below); however, familial isolated hyperparathyroidism is diagnosed in people with hyperparathyroidism but not the other features of multiple endocrine neoplasia type 1.

Many of the mutations in the *MEN1* gene that are associated with familial isolated hyperparathyroidism change single protein building blocks (amino acids) in the menin protein. It is thought that these amino acid changes impair menin's ability to interact with other proteins. Without normal menin function, cells likely divide too frequently,

leading to the formation of tumors involving the parathyroid glands. Researchers speculate that the mutations that cause familial isolated hyperparathyroidism have a milder effect on the function of menin than the mutations that cause multiple endocrine neoplasia type 1. Occasionally, individuals with familial isolated hyperparathyroidism later develop features of multiple endocrine neoplasia type 1, although most never do. Familial isolated hyperparathyroidism caused by *MEN1* gene mutations may be an early or mild form of multiple endocrine neoplasia type 1.

2.2. Multiple endocrine neoplasia

More than 1,300 mutations in the *MEN1* gene have been found to cause multiple endocrine neoplasia type 1. Multiple endocrine neoplasia typically involves the development of tumors in two or more of the body's hormone-producing glands, called endocrine glands. These tumors can be noncancerous or cancerous. The most common endocrine glands affected in multiple endocrine neoplasia type 1 are the parathyroid glands, the pituitary gland, and the pancreas, although additional endocrine glands and other organs can also be involved.

Most of the *MEN1* gene mutations that cause multiple endocrine neoplasia type 1 lead to the production of an abnormally short, inactive version of menin or an unstable protein that is rapidly broken down. As a result of these mutations, one copy of the *MEN1* gene in each cell makes no functional protein. If the second copy of the *MEN1* gene is also altered, the cell has no working copies of the gene and does not produce any functional menin. For unknown reasons, a second mutation occurs most often in cells of the endocrine glands. Without menin, these cells can divide too frequently and form a tumor. Although menin appears to be necessary for preventing tumor formation, researchers have not determined how a lack of this protein leads to the specific tumors characteristic of multiple endocrine neoplasia type 1.

2.3. Other tumors

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 mutations in the *MEN1* gene have been identified in several types of nonhereditary (sporadic) tumors. Specifically, *MEN1* gene mutations have been found in a significant percentage of noncancerous tumors of the parathyroid glands (parathyroid adenomas); pancreatic tumors called nonfunctioning neuroendocrine tumors, gastrinomas, and insulinomas; and cancerous tumors of the major airways in the lungs (bronchi) called bronchial carcinoids. Many of these tumor types are also found in people who have multiple endocrine neoplasia type 1 (described above). As in multiple endocrine neoplasia, tumors occur only when both copies of the *MEN1* gene are inactivated in certain cells.

3. Other Names for This Gene

- MEAI
- MEN1_HUMAN
- menin
- multiple endocrine neoplasia I

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