CDKN1B Gene

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cyclin dependent kinase inhibitor 1B

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1. Normal Function

The *CDKN1B* gene provides instructions for making a protein called p27. This protein is found in cells and tissues throughout the body. Within cells, p27 is located primarily in the nucleus, where it plays a critical role in controlling cell growth and division. It helps regulate the cell cycle, which is the cell's way of replicating itself in an organized, step-by-step fashion. Specifically, p27 normally blocks cells from entering the phase of the cell cycle when DNA is copied (replicated) in preparation for cell division. By blocking cell cycle progression, p27 prevents cells from dividing too quickly or at the wrong time. Based on this function, p27 is described as a tumor suppressor protein. Studies suggest that p27 is also involved in controlling cell differentiation, which is the process by which cells mature to carry out specific functions.

Because p27 plays such a key role in controlling cell division, its activity is tightly regulated. Regulation can occur through modification of the p27 protein's structure, its interaction with other proteins, or its localization within the cell. For example, when p27 is held (sequestered) in the fluid that surrounds the nucleus (the cytoplasm) instead of being transported into the nucleus, the protein is unavailable to block cell cycle progression. Researchers believe that p27 may have other functions in the cytoplasm, but these functions have not been well described.

2. Health Conditions Related to Genetic Changes

2.1. Multiple Endocrine Neoplasia

At least eight mutations in the *CDKN1B* gene have been found to cause a relatively rare form of multiple endocrine neoplasia called type 4. 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 4 are the parathyroid glands and the pituitary gland, although additional endocrine glands and other organs can also be involved.

Most of the *CDKN1B* gene mutations that cause multiple endocrine neoplasia type 4 change single protein building blocks (amino acids) in the p27 protein. Some mutations impair the protein's ability to interact with regulatory proteins, while others lead to the production of an unstable version of p27 that is quickly broken down. Still other mutations prevent p27 from moving from the cytoplasm into the nucleus. All of these mutations reduce the amount of functional p27 that is available in the nucleus to regulate the cell cycle. Cells with a shortage of functional p27 can divide too quickly or in an uncontrolled way, forming a tumor. It is unclear why these tumors occur primarily in endocrine glands; studies suggest that certain endocrine cells may be particularly dependent on the p27 protein to control cell division.

2.2. Other Tumors

Mutations in the *CDKN1B* gene have also been found to cause tumors in single endocrine glands, such as the pituitary gland or the parathyroid glands. These mutations are described as somatic; they are not inherited and are present only in tumor cells. Somatic *CDKN1B* gene mutations have been identified in sporadic (nonfamilial) pituitary adenomas and in sporadic parathyroid adenomas, which are noncancerous tumors of the parathyroid glands. Like the mutations that cause multiple endocrine neoplasia type 4, these genetic changes reduce the amount of functional p27 available to control cell division. As a result, cells become more likely to divide abnormally and form a tumor.

Apart from multiple endocrine neoplasia, the *CDKN1B* gene is rarely mutated in cancerous tumors. However, changes in regulation that reduce the amount or function of the p27 protein in the nucleus are found in many types of cancer. A shortage of p27 has been associated with more aggressive tumors and a poorer prognosis.

3. Other Names for This Gene

- CDKN4
- CDN1B_HUMAN
- cyclin-dependent kinase inhibitor 1B
- cyclin-dependent kinase inhibitor 1B (p27, Kip1)
- KIP1
- MEN1B
- MEN4
- P27KIP1

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