

CDC73 gene

cell division cycle 73

Normal Function

The *CDC73* gene (also known as *HRPT2*) provides instructions for making a protein called parafibromin. This protein is found primarily in the nucleus of cells and is likely involved in regulating gene transcription, which is the first step in protein production. Parafibromin functions as a tumor suppressor, which means it keeps cells from growing and dividing (proliferating) too rapidly or in an uncontrolled way. When parafibromin is found outside the nucleus, it appears to be involved in the organization of the cell's structural framework (the cytoskeleton).

Health Conditions Related to Genetic Changes

Familial isolated hyperparathyroidism

Inherited mutations in the *CDC73* gene have been found in some families with familial isolated hyperparathyroidism, a condition characterized by overactivity of the parathyroid glands (primary hyperparathyroidism). These glands release a hormone that helps control the normal balance of calcium in the blood. Primary hyperparathyroidism disrupts this balance, which can lead to high blood calcium levels (hypercalcemia), kidney stones, thinning of the bones (osteoporosis), nausea, vomiting, high blood pressure (hypertension), weakness, and fatigue. Primary hyperparathyroidism is a characteristic feature of hyperparathyroidism-jaw tumor syndrome (described below); however, familial isolated hyperparathyroidism is diagnosed in people with hyperparathyroidism but not the other features of hyperparathyroidism-jaw tumor syndrome.

CDC73 gene mutations that cause familial isolated hyperparathyroidism likely result in decreased activity of the parafibromin protein. Reduced parafibromin activity can cause increased cell proliferation, leading to the formation of tumors involving the parathyroid glands. Parathyroid tumors in people with familial isolated hyperparathyroidism are usually noncancerous (benign). The tumors cause the glands to be overactive, and this overactivity leads to the signs and symptoms of the condition. The mutations associated with familial isolated hyperparathyroidism are thought to have a less severe effect on protein function than those that cause hyperparathyroidism-jaw tumor syndrome. Occasionally, individuals with familial isolated hyperparathyroidism later develop features of hyperparathyroidism-jaw tumor syndrome, although some never do. Familial

isolated hyperparathyroidism caused by *CDC73* gene mutations may be an early or mild form of hyperparathyroidism-jaw tumor syndrome.

Hyperparathyroidism-jaw tumor syndrome

More than 45 inherited mutations in the *CDC73* gene have been found to cause hyperparathyroidism-jaw tumor syndrome, which is a condition characterized by a type of benign tumor called a fibroma in the jaw and parathyroid tumors that cause hyperparathyroidism. Hyperparathyroidism disrupts the normal balance of calcium in the blood, which can lead to kidney stones, osteoporosis, nausea, vomiting, hypertension, weakness, and fatigue in people with hyperparathyroidism-jaw tumor syndrome.

Most of the *CDC73* gene mutations that cause this condition result in a parafibromin protein that is abnormally short and nonfunctional. Without functional parafibromin, cell proliferation is not properly regulated. Uncontrolled cell division resulting from the loss of parafibromin function can lead to the formation of tumors in the parathyroid glands, jaw, and other tissues in people with hyperparathyroidism-jaw tumor syndrome. Parathyroid tumors, which can be cancerous or noncancerous, interfere with the gland's normal function and lead to primary hyperparathyroidism in people with hyperparathyroidism-jaw tumor syndrome.

Parathyroid cancer

Mutations in the *CDC73* gene are found in up to 70 percent of cases of parathyroid cancer. In approximately one-third of affected individuals with changes in this gene, the mutation is inherited from a parent and is present in all of the body's cells (germline mutation). However, not everyone who inherits a mutation in the *CDC73* gene will ultimately develop parathyroid cancer. Other genetic and non-genetic factors also contribute to a person's cancer risk.

In the remaining two-thirds of individuals with *CDC73* gene mutations, the condition is associated with a mutation that occurs in parathyroid cells during their lifetime (somatic mutation). In individuals with either a germline or somatic *CDC73* gene mutation, a second mutation in the other copy of the *CDC73* gene must occur for parathyroid cancer to develop. Parathyroid cells with two altered copies of the *CDC73* gene produce no functional parafibromin. As a result, cells grow and divide unchecked, which can lead to parathyroid cancer.

A significantly increased risk of parathyroid cancer is a feature of hyperparathyroidism-jaw tumor syndrome and familial isolated hyperparathyroidism (both described above). Parathyroid cancer occurs in 15 percent of individuals with hyperparathyroidism-jaw tumor syndrome and in 1 percent of individuals with familial isolated hyperparathyroidism. It is unclear why some *CDC73* gene mutations cause isolated parathyroid cancer, others cause noncancerous tumors in the parathyroid glands and jaw, and still others cause only hyperparathyroidism.

Other Names for This Gene

- C1orf28
- CDC73_HUMAN
- cell division cycle 73, Paf1/RNA polymerase II complex component, homolog (S. cerevisiae)
- cell division cycle protein 73 homolog
- HRPT2
- hyperparathyroidism 2 protein
- hyrax
- HYX
- parafibromin

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CDC73 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=79577\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=79577[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28CDC73%5BTIAB%5D%29+OR+%28%28HRPT2%5BTIAB%5D%29+OR+%28parafibromin%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D%29>)

Catalog of Genes and Diseases from OMIM

- CELL DIVISION CYCLE 73; CDC73 (<https://omim.org/entry/607393>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/79577>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=CDC73\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=CDC73[gene]))

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Genomic Location

The *CDC73* gene is found on chromosome 1 (<https://medlineplus.gov/genetics/chromosome/1/>).

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