CUBN gene

cubilin

Normal Function

The *CUBN* gene provides instructions for making a protein called cubilin. This protein is involved in the uptake of vitamin B12 (also called cobalamin) from food into the body. Vitamin B12, which cannot be made in the body and can only be obtained from food, is essential for the formation of DNA and proteins, the production of cellular energy, and the breakdown of fats. This vitamin is involved in the formation of red blood cells and maintenance of the brain and spinal cord (central nervous system).

The cubilin protein is primarily found associated with kidney cells and cells that line the small intestine. Cubilin is anchored to the outer membrane of these cells by its attachment to another protein called amnionless. Cubilin can interact with molecules and proteins passing through the small intestine and kidneys, including vitamin B12. During digestion, vitamin B12 is released from food. As the vitamin passes through the small intestine, cubilin attaches (binds) to it. Amnionless helps transfer the cubilin-vitamin B12 complex into the intestinal cell. From there, the vitamin is released into the blood and transported throughout the body. In the kidneys, cubilin and amnionless are involved in the reabsorption of certain proteins that would otherwise be released in urine.

Health Conditions Related to Genetic Changes

Imerslund-Gräsbeck syndrome

At least 35 mutations in the *CUBN* gene have been found to cause a condition called Imerslund-Gräsbeck syndrome. This condition is characterized by low levels of vitamin B12 in the body, which leads to a blood disorder known as megaloblastic anemia. About half of affected individuals also have excess protein in their urine (proteinuria), and some have neurological problems.

The most common *CUBN* gene mutation, which is found in people of Finnish heritage, changes a single protein building block (amino acid) in the cubilin protein; the amino acid proline is replaced by the amino acid leucine at position 1297 (written as Pro1297Leu or P1297L). The protein alteration impairs cubilin's ability to bind to vitamin B12. Instead of being taken up into intestinal cells, the vitamin is released from the body. A shortage of this essential vitamin impairs the proper development of red blood cells,

leading to megaloblastic anemia. In addition, low levels of vitamin B12 can affect the central nervous system, causing neurological problems.

Other *CUBN* gene mutations prevent cubilin from attaching to the amnionless protein or lead to a reduction in the amount or function of the cubilin protein. These changes impair cubilin's function in the kidneys as well as in the small intestine. Without amnionless function in the kidneys, proteins are not reabsorbed into the body and are instead released in the urine, leading to proteinuria. Individuals with these mutations develop megaloblastic anemia and proteinuria.

Other Names for This Gene

- 460 kDa receptor
- cubilin (intrinsic factor-cobalamin receptor)
- cubilin precursor
- gp280
- IFCR
- intestinal intrinsic factor receptor
- intrinsic factor-vitamin B12 receptor
- MGA1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CUBN (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=8029[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28CUBN%5BTIAB%5D%29+OR+%28cubilin%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+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- CUBILIN; CUBN (https://omim.org/entry/602997)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/8029)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=CUBN[gene])

References

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- Kristiansen M, Aminoff M, Jacobsen C, de La Chapelle A, Krahe R, Verroust PJ, Moestrup SK. Cubilin P1297L mutation associated with hereditary megaloblasticanemia 1 causes impaired recognition of intrinsic factor-vitamin B(12) bycubilin. Blood. 2000 Jul 15;96(2):405-9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10887099)
- Watkins D, Rosenblatt DS. Lessons in biology from patients with inborn errorsof vitamin B12 metabolism. Biochimie. 2013 May;95(5):1019-22. doi:10.1016/j.biochi.2013.01.013. Epub 2013 Feb 10. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23402785)

Genomic Location

The *CUBN* gene is found on chromosome 10 (https://medlineplus.gov/genetics/chromosome/10/).

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