MTR gene

5-methyltetrahydrofolate-homocysteine methyltransferase

Normal Function

The *MTR* gene provides instructions for making an enzyme called methionine synthase. This enzyme plays a role in processing amino acids, the building blocks of proteins. Specifically, methionine synthase carries out a chemical reaction that converts the amino acid homocysteine to another amino acid called methionine. The body uses methionine to make proteins and other important compounds. To function properly, methionine synthase requires methylcobalamin (a form of vitamin B12) and another enzyme called methionine synthase reductase, which is produced from the *MTRR* gene.

Health Conditions Related to Genetic Changes

Homocystinuria

More than 20 mutations in the *MTR* gene have been identified in people with homocystinuria. Many of these mutations lead to the production of an abnormally small, nonfunctional version of methionine synthase. Other mutations change single amino acids in the enzyme. One of the most common mutations replaces the amino acid proline with the amino acid leucine at position 1173 (written as Pro1173Leu or P1173L), resulting in an enzyme with reduced function. Without functional methionine synthase, homocysteine cannot be converted to methionine. As a result, homocysteine builds up in the bloodstream, and the amount of methionine is reduced. Some of the excess homocysteine is excreted in urine. Researchers have not determined how altered levels of homocysteine and methionine lead to the health problems associated with homocystinuria.

Other disorders

A specific version (variant) of the *MTR* gene has been associated with various health problems before birth. The variant (written as A2756G) replaces one building block of DNA (nucleotide) called adenine with the nucleotide guanine at a certain location in the *MTR* gene. This variant has been associated with an increased risk of birth defects that occur during the development of the brain and spinal cord (neural tube defects). Some studies have suggested that the variant also increases the risk of having a child with Down syndrome, which is a condition characterized by intellectual disability and associated health problems, but other studies found no increased risk. Researchers do

not know why there may be a connection between the A2756G variant of the *MTR* gene and the risk of neural tube defects or Down syndrome. Many factors play a part in determining the risk of these complex disorders.

Other Names for This Gene

- 5-methyltetrahydrofolate-homocysteine methyltransferase 1
- 5-Methyltetrahydrofolate-Homocysteine S-Methyltransferase
- cblG
- cobalamin-dependent methionine synthase
- Homocysteine-methyl tetrahydrofolate methyltransferase
- METH_HUMAN
- Methionine Synthase
- Tetrahydropteroylglutamate Methyltransferase

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of MTR (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4548[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28MTR%5BTIAB%5D%29+OR+%285-methyltetrahydrofolate-homocysteine+methyltransferase%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

- 5-METHYLTETRAHYDROFOLATE-HOMOCYSTEINE S-METHYLTRANSFERASE; MTR (https://omim.org/entry/156570)
- DOWN SYNDROME (https://omim.org/entry/190685)
- NEURAL TUBE DEFECTS, SUSCEPTIBILITY TO; NTD (https://omim.org/entry/182940)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4548)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=MTR[gene])

References

- Bosco P, Gueant-Rodriguez RM, Anello G, Barone C, Namour F, Caraci F, RomanoA, Romano C, Gueant JL. Methionine synthase (MTR) 2756 (A --> G) polymorphism,double heterozygosity methionine synthase 2756 AG/methionine synthase reductase(MTRR) 66 AG, and elevated homocysteinemia are three risk factors for having achild with Down syndrome. Am J Med Genet A. 2003 Sep 1;121A(3):219-24. doi:10.1002/ajmg.a.20234. Citation on PubMed (https://pubmed.ncbi.nlm. nih.gov/12923861)
- Carmel R, Green R, Rosenblatt DS, Watkins D. Update on cobalamin, folate, andhomocysteine. Hematology Am Soc Hematol Educ Program. 2003:62-81. doi:10. 1182/asheducation-2003.1.62. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov /14633777)
- Doolin MT, Barbaux S, McDonnell M, Hoess K, Whitehead AS, Mitchell LE.Maternal genetic effects, exerted by genes involved in homocysteineremethylation, influence the risk of spina bifida. Am J Hum Genet. 2002Nov;71(5):1222-6. doi: 10.1086/ 344209. Epub 2002 Oct 9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/123 75236) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles /PMC385102/)
- Gueant-Rodriguez RM, Rendeli C, Namour B, Venuti L, Romano A, Anello G, BoscoP, Debard R, Gerard P, Viola M, Salvaggio E, Gueant JL. Transcobalamin andmethionine synthase reductase mutated polymorphisms aggravate the risk of neuraltube defects in humans. Neurosci Lett. 2003 Jul 3;344(3):189-92. doi:10.1016/ s0304-3940(03)00468-3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/1281 2837)
- Watkins D, Ru M, Hwang HY, Kim CD, Murray A, Philip NS, Kim W, Legakis H, WaiT, Hilton JF, Ge B, Dore C, Hosack A, Wilson A, Gravel RA, Shane B, Hudson TJ,Rosenblatt DS. Hyperhomocysteinemia due to methionine synthase deficiency, cblG:structure of the MTR gene, genotype diversity, and recognition of a commonmutation, P1173L. Am J Hum Genet. 2002 Jul;71(1):143-53. doi: 10.1086/ 341354.Epub 2002 May 30. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12 068375) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/article s/PMC384971/)

Genomic Location

The *MTR* gene is found on chromosome 1 (https://medlineplus.gov/genetics/chromoso me/1/).

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