MTRR gene

5-methyltetrahydrofolate-homocysteine methyltransferase reductase

Normal Function

The *MTRR* gene provides instructions for making an enzyme called methionine synthase reductase. This enzyme is required for the proper function of another enzyme called methionine synthase. Methionine synthase helps process amino acids, which are the building blocks of proteins. Specifically, it converts the amino acid homocysteine to another amino acid called methionine. After a period of being turned on (active), methionine synthase turns off (becomes inactive). Methionine synthase reductase reactivates methionine synthase so the enzyme can continue to produce methionine.

Health Conditions Related to Genetic Changes

Homocystinuria

At least 20 mutations in the *MTRR* gene have been identified in people with homocystinuria. Some of these mutations change single amino acids in methionine synthase reductase. Other mutations lead to an abnormally small, nonfunctional version of the enzyme. All these mutations prevent the enzyme from functioning normally. Without methionine synthase reductase, methionine synthase cannot convert homocysteine 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 *MTRR* gene may be associated with an increased risk of various health problems before birth. The variant (written as A66G) replaces a building block of DNA (nucleotide) called adenine with the nucleotide guanine at a specific location in the *MTRR* gene. This variant is associated with birth defects that occur during the development of the brain and spinal cord (neural tube defects). This variant may also increase the risk of having a child with Down syndrome, a condition characterized by intellectual disability and associated health problems. Researchers have not determined why there may be a connection between the A66G variant of the *MTRR* gene and the risk of neural tube defects or Down syndrome. Many factors play a part in determining the risk of these disorders.

Other Names for This Gene

- cblE
- methionine synthase reductase
- MSR
- MTRR_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of MTRR (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4552[geneid])

Scientific Articles on PubMed

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

- DOWN SYNDROME (https://omim.org/entry/190685)
- NEURAL TUBE DEFECTS, SUSCEPTIBILITY TO; NTD (https://omim.org/entry/182940)
- METHIONINE SYNTHASE REDUCTASE; MTRR (https://omim.org/entry/602568)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4552)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=MTRR[gene])

References

- 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/12375236) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC 385102/)

- 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)
- Hobbs CA, Sherman SL, Yi P, Hopkins SE, Torfs CP, Hine RJ, Pogribna M, RozenR, James SJ. Polymorphisms in genes involved in folate metabolism as maternalrisk factors for Down syndrome. Am J Hum Genet. 2000 Sep;67(3):623-30. doi:10.1086/303055. Epub 2000 Aug 7. Citation on PubMed (https://pubmed.ncbi.nl m.nih.gov/10930360) or Free article on PubMed Central (https://www.ncbi.nlm.nih.g ov/pmc/articles/PMC1287522/)
- Vilaseca MA, Vilarinho L, Zavadakova P, Vela E, Cleto E, Pineda M, Coimbra E, Suormala T, Fowler B, Kozich V. CblE type of homocystinuria: mild clinicalphenotype in two patients homozygous for a novel mutation in the MTRR gene. JInherit Metab Dis. 2003;26(4):361-9. doi: 10.1023/a:1025159103257. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12971424)
- Wilson A, Leclerc D, Rosenblatt DS, Gravel RA. Molecular basis for methioninesynthase reductase deficiency in patients belonging to the cblE complementationgroup of disorders in folate/cobalamin metabolism. Hum Mol Genet. 1999Oct;8(11):2009-16. doi: 10.1093/hmg/8.11.2009. Citation on PubMed (https://p ubmed.ncbi.nlm.nih.gov/10484769)
- Zavadakova P, Fowler B, Zeman J, Suormala T, Pristoupilova K, Kozich V,Zavad&# x27;akova P. CblE type of homocystinuria due to methionine synthase reductasedeficiency: clinical and molecular studies and prenatal diagnosis in twofamilies. J Inherit Metab Dis. 2002 Oct;25(6):461-76. doi:10.1023/a: 1021299117308. Erratum In: J Inherit Metab Dis. 2003;26(1):95. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12555939)

Genomic Location

The *MTRR* gene is found on chromosome 5 (https://medlineplus.gov/genetics/chromoso me/5/).

Last updated July 1, 2011