

FOLR1 gene

folate receptor alpha

Normal Function

The *FOLR1* gene provides instructions for making a protein called folate receptor alpha. This protein helps regulate transport of the B-vitamin folate into cells. Folate (also called vitamin B9) is needed for many processes, including the production and repair of DNA, regulation of gene activity (expression), and protein production. Folate from food is absorbed in the intestines and then released in a form called 5-methyl-tetrahydrofolate (5-MTHF) into the bloodstream, where it can be taken in by cells in various tissues.

Folate receptor alpha is found within the cell membrane, where it attaches (binds) to 5-MTHF, allowing the vitamin to be brought into the cell. Folate receptor alpha is produced in largest amounts in the brain, specifically in an area of the brain called the choroid plexus. This region releases cerebrospinal fluid (CSF), which surrounds and protects the brain and spinal cord. Folate receptor alpha is thought to play a major role in transporting folate from the bloodstream into brain cells. It transports folate across the choroid plexus and into the CSF, ultimately reaching the brain. In the brain, folate is needed for making chemical messengers called neurotransmitters and a fatty substance called myelin, which insulates nerve fibers and promotes the rapid transmission of nerve impulses. Both of these substances play essential roles in transmitting signals in the nervous system.

Health Conditions Related to Genetic Changes

Cerebral folate transport deficiency

At least 11 mutations in the *FOLR1* gene have been found to cause cerebral folate transport deficiency, a disorder characterized by neurological problems that begin around age 2. Most of these mutations change single protein building blocks (amino acids) in folate receptor alpha. *FOLR1* gene mutations result in a lack of protein or malfunctioning protein. Without folate receptor alpha in brain cells, 5-MTHF in the bloodstream cannot be transported into the CSF and passed to the brain. A shortage (deficiency) of folate in the brain impairs normal cell functions such as the production of DNA, proteins, and neurotransmitters. Folate deficiency affects the stability of myelin, leading to impaired production or increased breakdown of this tissue, a condition known as leukodystrophy. These brain abnormalities caused by a lack of folate lead to the intellectual disability, movement problems, and recurrent seizures (epilepsy) typical of

cerebral folate transport deficiency.

Other Names for This Gene

- adult folate-binding protein
- FBP
- folate binding protein
- folate receptor 1 (adult)
- folate receptor alpha
- folate receptor, adult
- FOLR
- FR-alpha
- KB cells FBP

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of FOLR1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2348\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2348[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28FOLR1%5BTIAB%5D%29+OR+%28folate+receptor+alpha%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

- FOLATE RECEPTOR, ALPHA; FOLR1 (<https://omim.org/entry/136430>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/2348>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=FOLR1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=FOLR1[gene]))

References

- Cario H, Bode H, Debatin KM, Opladen T, Schwarz K. Congenital null mutations of the FOLR1 gene: a progressive neurologic disease and its treatment. *Neurology*. 2009 Dec 15;73(24):2127-9. doi: 10.1212/WNL.0b013e3181c679df. No

abstractavailable. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20018644>)

- Grapp M, Wrede A, Schweizer M, Huwel S, Galla HJ, Snaidero N, Simons M, Buckers J, Low PS, Urlaub H, Gartner J, Steinfeld R. Choroid plexus transcytosis and exosome shuttling deliver folate into brain parenchyma. *Nat Commun*. 2013;4:2123. doi: 10.1038/ncomms3123. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23828504>)
- Perez-Duenas B, Toma C, Ormazabal A, Muchart J, Sanmarti F, Bombau G, Serrano M, Garcia-Cazorla A, Cormand B, Artuch R. Progressive ataxia and myoclonic epilepsy in a patient with a homozygous mutation in the FOLR1 gene. *J Inher Metab Dis*. 2010 Dec;33(6):795-802. doi: 10.1007/s10545-010-9196-1. Epub 2010 Sep 21. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20857335>)
- Steinfeld R, Grapp M, Kraetzner R, Dreha-Kulaczewski S, Helms G, Dechent P, Wevers R, Grosso S, Gartner J. Folate receptor alpha defect causes cerebral folate transport deficiency: a treatable neurodegenerative disorder associated with disturbed myelin metabolism. *Am J Hum Genet*. 2009 Sep;85(3):354-63. doi:10.1016/j.ajhg.2009.08.005. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19732866>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2771535/>)
- Watkins D, Rosenblatt DS. Update and new concepts in vitamin responsive disorders of folate transport and metabolism. *J Inher Metab Dis*. 2012 Jul;35(4):665-70. doi: 10.1007/s10545-011-9418-1. Epub 2011 Nov 23. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22108709>)

Genomic Location

The *FOLR1* gene is found on chromosome 11 (<https://medlineplus.gov/genetics/chromosome/11/>).

Last updated September 1, 2014