FOLR1 Gene

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Folate receptor 1

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1. 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.

2. Health Conditions Related to Genetic Changes

2.1 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.

3. 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

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