YWHAE Gene

Subjects: Genetics & Heredity
Contributor: Peter Tang

Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein epsilon

Keywords: genes

1. Normal Function

The *YWHAE* gene provides instructions for making the 14-3-3 epsilon (ε) protein, which is part of the large 14-3-3 protein family. Proteins in this family attach (bind) to other proteins involved in cell signaling. 14-3-3 proteins either turn on (activate) or turn off (inactivate) these other proteins. The 14-3-3ε protein helps to regulate a variety of processes including cell division and sensitivity to insulin, a hormone that helps control blood sugar levels.

The 14-3-3ε protein is active in tissues throughout the body, although its function is sometimes unclear. In the brain, this protein is involved in directing the movement of nerve cells (neuronal migration) by binding to other proteins involved in this process. It is thought that the 14-3-3ε protein is critical for proper neuronal migration and normal brain development.

2. Health Conditions Related to Genetic Changes

2.1. Miller-Dieker syndrome

The characteristic signs and symptoms of Miller-Dieker syndrome are caused by a deletion of genetic material near the end of the short (p) arm of chromosome 17. The chromosomal region that is typically deleted contains multiple genes, including the *YWHAE* gene. As a result of the deletion, people with this condition have only one copy of the *YWHAE* gene in each cell instead of the usual two copies.

A deletion of one copy of the *YWHAE* gene in each cell reduces the amount of 14-3-3ε protein by about half. A shortage of 14-3-3ε protein increases the severity of lissencephaly (a problem with brain development in which the surface of the brain is abnormally smooth) in people with Miller-Dieker syndrome.

2.2. Schizophrenia

2.3. Other disorders

A deletion that only involves the *YWHAE* gene can also cause health problems. People with a *YWHAE* gene deletion are missing one copy of the gene in each cell, which reduces the amount of 14-3-3ε protein that is produced by about half. A deficiency (shortage) of this protein is thought to cause short stature; intellectual disability; and distinctive facial features including a prominent forehead, wide nasal bridge, and small jaw. People with a *YWHAE* gene deletion do not have lissencephaly but tend to have other brain abnormalities.

3. Other Names for This Gene

- 14-3-3 epsilon
- 14-3-3E
- 1433E_HUMAN
- KCIP-1
- mitochondrial import stimulation factor L subunit
- protein kinase C inhibitor protein-1

- tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon
- tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide
- tyrosine 3/tryptophan 5 -monooxygenase activation protein, epsilon polypeptide

References

1. Jin DY, Lyu MS, Kozak CA, Jeang KT. Function of 14-3-3 proteins. Nature. 1996 Jul 25;382(6589):308.
2. Mignon-Ravix C, Cacciagli P, El-Waly B, Moncla A, Milh M, Girard N, Chabrol B,Philip N, Villard L. Deletion of YWHAE in a patient with periventricularheterotopias and pronounced corpus callosum hypoplasia. J Med Genet. 2010Feb;47(2):132-6. doi: 10.1136/jmg.2009.069112.
3. Nagamani SC, Zhang F, Shchelochkov OA, Bi W, Ou Z, Scaglia F, Probst FJ,Shinawi M, Eng C, Hunter JV, Sparagana S, Lagoe E, Fong CT, Pearson M, Doco-FenzyM, Landais E, Mozelle M, Chinault AC, Patel A, Bacino CA, Sahoo T, Kang SH,Cheung SW, Lupski JR, Stankiewicz P. Microdeletions including YWHAE in theMiller-Dieker syndrome region on chromosome 17p13.3 result in facialdysmorphisms, growth restriction, and cognitive impairment. J Med Genet. 2009Dec;46(12):825-33. doi: 10.1136/jmg.2009.067637.
4. Ogihara T, Isobe T, Ichimura T, Taoka M, Funaki M, Sakoda H, Onishi Y, Inukai K, Anai M, Fukushima Y, Kikuchi M, Yazaki Y, Oka Y, Asano T. 14-3-3 protein bindsto insulin receptor substrate-1, one of the binding sites of which is in thephosphotyrosine binding domain. J Biol Chem. 1997 Oct 3;272(40):25267-74.
5. Tak H, Jang E, Kim SB, Park J, Suk J, Yoon YS, Ahn JK, Lee JH, Joe CO.14-3-3epsilon inhibits MK5-mediated cell migration by disrupting F-actinpolymerization. Cell Signal. 2007 Nov;19(11):2379-87.
6. Toyo-oka K, Shionoya A, Gambello MJ, Cardoso C, Leventer R, Ward HL, Ayala R, Tsai LH, Dobyns W, Ledbetter D, Hirotsune S, Wynshaw-Boris A. 14-3-3epsilon isimportant for neuronal migration by binding to NUDEL: a molecular explanation forMiller-Dieker syndrome. Nat Genet. 2003 Jul;34(3):274-85.