TUBB2B Gene

Subjects: Genetics & Heredity
Contributor: Hongliu Chen

Tubulin beta 2B class IIb.

genes

1. Normal Function

The *TUBB2B* gene provides instructions for making one version of a protein called beta-tubulin (β-tubulin). This protein is part of the tubulin family of proteins that form and organize cell structures called microtubules. Microtubules are rigid, hollow fibers that make up the cell's structural framework (the cytoskeleton). They are composed of β-tubulin and a similar protein called alpha-tubulin (α-tubulin) that is produced from a different gene. Microtubules grow and shrink as tubulin proteins are added to and removed from the ends of fibers. This process allows cells to move and change shape.

β-tubulin produced from the *TUBB2B* gene is found primarily in the brain and in nerve cells (neurons). In neurons, microtubules are integral for the cells' movement to the proper location in the brain and for a process called axon guidance, by which specialized extensions of neurons (axons) reach their correct positions. Once in the right location, axons relay messages to and from the brain to control muscle movement and detect sensations such as touch, pain, heat, and sound.

2. Health Conditions Related to Genetic Changes

2.1. Congenital Fibrosis of the Extraocular Muscles

At least one mutation in the *TUBB2B* gene has been found to cause a rare form of congenital fibrosis of the extraocular muscles (CFEOM) called CFEOM3 with polymicrogyria. Individuals with this condition are unable to move their eyes normally; they have difficulty looking up, and they have droopy eyelids (ptosis). In addition, affected individuals have a brain malformation called polymicrogyria, in which the surface of the brain develops too many folds, and the folds are unusually small. Individuals with this form of CFEOM3 typically have intellectual disability.

The *TUBB2B* gene mutation that causes CFEOM3 with polymicrogyria changes a single protein building block (amino acid) in the β-tubulin protein. It replaces the amino acid glutamate with the amino acid lysine at protein position 421 (written as Glu421Lys or E421K). Microtubules that contain the altered β-tubulin protein do not grow

and shrink as they should, which prevents axons from reaching their proper location. Nerves in the head and face (cranial nerves) that control muscles that surround the eyes (extraocular muscles) are particularly affected. Abnormal development of cranial nerves impairs the function of extraocular muscles, leading to the characteristic features of CFEOM such as restricted eye movement and droopy eyelids. It is unclear how the CFEOM-related change in the *TUBB2B* gene results in polymicrogyria.

2.2. Isolated Lissencephaly Sequence

2.3. Polymicrogyria

3. Other Disorders

Mutations in the *TUBB2B* gene have been identified in people with brain abnormalities affecting the surface of the brain (the cortex), which are classified as malformations of cortical development. These individuals do not have problems with extraocular muscles (described above). The brain abnormalities typically lead to intellectual disability in affected individuals. Brain malformations commonly associated with *TUBB2B* gene mutations result from abnormal development of the cortex and can include polymicrogyria (described above); reduced folding (simplified gyration); an abnormally smooth surface (lissencephaly), sometimes with an abnormally small head size (microlissencephaly); slits or clefts in one or both halves of the brain (schizencephaly); or other cortical abnormalities. In some affected individuals, a region of the brain called the cerebellum is particularly affected (cerebellar dysplasia). It is thought that mutations in the *TUBB2B* gene disrupt the movement of neurons and axons to their correct locations, altering brain development and leading to brain malformations.

3. Other Names for This Gene

- class IIb beta-tubulin
- TUBULIN, BETA, CLASS IIB
- TUBULIN, BETA-2B

References

1. Cederquist GY, Luchniak A, Tischfield MA, Peeva M, Song Y, Menezes MP, ChanWM, Andrews C, Chew S, Jamieson RV, Gomes L, Flaherty M, Grant PE, Gupta ML Jr,Engle EC. An inherited TUBB2B mutation alters a kinesin-binding site and causespolymicrogyria, CFEOM and axon dysinnervation. Hum Mol Genet. 2012 Dec15;21(26):5484-99. doi: 10.1093/hmg/dds393.
2. Di Donato N, Timms AE, Aldinger KA, Mirzaa GM, Bennett JT, Collins S, Olds C, Mei D, Chiari S, Carvill G, Myers CT, Rivière JB, Zaki MS; University ofWashington Center for Mendelian

Genomics, Gleeson JG, Rump A, Conti V, Parrini E,Ross ME, Ledbetter DH, Guerrini R, Dobyns WB. Analysis of 17 genes detectsmutations in 81% of 811 patients with lissencephaly. Genet Med. 2018Nov;20(11):1354-1364. doi: 10.1038/gim.2018.8.

3. Jaglin XH, Poirier K, Saillour Y, Buhler E, Tian G, Bahi-Buisson N,Fallet-Bianco C, Phan-Dinh-Tuy F, Kong XP, Bomont P, Castelnau-Ptakhine L, Odent S, Loget P, Kossorotoff M, Snoeck I, Plessis G, Parent P, Beldjord C, Cardoso C, Represa A, Flint J, Keays DA, Cowan NJ, Chelly J. Mutations in the beta-tubulingene TUBB2B result in asymmetrical polymicrogyria. Nat Genet. 2009Jun;41(6):746-52. doi: 10.1038/ng.380.
4. Romaniello R, Arrigoni F, Fry AE, Bassi MT, Rees MI, Borgatti R, Pilz DT,Cushion TD. Tubulin genes and malformations of cortical development. Eur J MedGenet. 2018 Dec;61(12):744-754. doi: 10.1016/j.ejmg.2018.07.012.
5. Romaniello R, Arrigoni F, Panzeri E, Poretti A, Micalizzi A, Citterio A,Bedeschi MF, Berardinelli A, Cusmai R, D'Arrigo S, Ferraris A, Hackenberg A,Kuechler A, Mancardi M, Nuovo S, Oehl-Jaschkowitz B, Rossi A, Signorini S,Tüttelmann F, Wahl D, Hehr U, Boltshauser E, Bassi MT, Valente EM, Borgatti R.Tubulin-related cerebellar dysplasia: definition of a distinct pattern ofcerebellar malformation. Eur Radiol. 2017 Dec;27(12):5080-5092. doi:10.1007/s00330-017-4945-2.12;:.