TUBA1A Gene

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Tubulin alpha 1a.

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1. Normal Function

The *TUBA1A* gene provides instructions for making a protein called alpha-tubulin (α-tubulin). This protein is part of the tubulin family of proteins that form and organize structures called microtubules. Microtubules are rigid, hollow fibers that make up the cell's structural framework (the cytoskeleton). They are composed of α-tubulin and a similar protein called beta-tubulin (β-tubulin) that is produced from a different gene. Microtubules are necessary for cell division and movement.

Most cells produce α-tubulin, but the protein is found in highest amounts in the developing brain. During brain development, α-tubulin partners with β-tubulin to form microtubules that move nerve cells (neurons) to their proper location (neuronal migration). Microtubules form scaffolding within the cell. The tubulin proteins that make up the microtubule are moved from one end of a microtubule to the other end. This protein transfer propels the microtubules in a specific direction, moving the cell.

2. Health Conditions Related to Genetic Changes

2.1. Isolated Lissencephaly Sequence

Approximately 40 mutations in the *TUBA1A* gene have been found to cause isolated lissencephaly sequence (ILS). This condition is characterized by abnormal brain development that results in the brain having a smooth appearance (lissencephaly) instead of its normal folds and grooves. Individuals with ILS have severe neurological problems, including intellectual disability and recurrent seizures (epilepsy). Most of these mutations change single protein building blocks (amino acids) in the α-tubulin protein. The resulting abnormal α-tubulin cannot form microtubules or interact with other proteins. As a result, the overall function of microtubules is reduced. In the developing brain, this decrease in microtubule function impairs the normal migration of neurons and leads to a decrease in the formation of the brain's folds and grooves or a completely smooth appearance of the brain, resulting in the neurological problems characteristic of ILS.

2.2. Lissencephaly with Cerebellar Hypoplasia

At least 10 mutations in the *TUBA1A* gene have been found to cause lissencephaly with cerebellar hypoplasia (LCH). This condition affects brain development, resulting in lissencephaly and an unusually small and underdeveloped area of the brain called the cerebellum (cerebellar hypoplasia). The *TUBA1A* gene mutations that cause LCH change single amino acids in the α-tubulin protein. These altered proteins can still be incorporated into microtubules, but research suggests that these microtubules have decreased or abnormal function.

In the developing brain, impaired microtubule function prevents the normal migration of neurons. As a result, the normal folds and grooves of the brain do not form and the cerebellum and other brain structures do not develop properly. This impairment of brain development leads to intellectual disability, delayed overall development, movement problems, and other signs and symptoms of LCH.

3. Other Names for This Gene

- B-ALPHA-1
- TBA1A_HUMAN
- TUBA3

- tubulin alpha-1A chain
- tubulin alpha-3 chain
- tubulin B-alpha-1
- tubulin, alpha 1a
- tubulin, alpha, brain-specific

References

1. Bahi-Buisson N, Poirier K, Boddaert N, Saillour Y, Castelnau L, Philip N,Buyse G, Villard L, Joriot S, Marret S, Bourgeois M, Van Esch H, Lagae L, AmielJ, Hertz-Pannier L, Roubertie A, Rivier F, Pinard JM, Beldjord C, Chelly J.Refinement of cortical dysgeneses spectrum associated with TUBA1A mutations. JMed Genet. 2008 Oct;45(10):647-53. doi: 10.1136/jmg.2008.058073.
2. Jansen AC, Oostra A, Desprechins B, De Vlaeminck Y, Verhelst H, Régal L,Verloo P, Bockaert N, Keymolen K, Seneca S, De Meirleir L, Lissens W. TUBA1Amutations: from isolated lissencephaly to familial polymicrogyria. Neurology.2011 Mar 15;76(11):988-92. doi: 10.1212/WNL.0b013e31821043f5.
3. Kumar RA, Pilz DT, Babatz TD, Cushion TD, Harvey K, Topf M, Yates L, Robb S,Uyanik G, Mancini GM, Rees MI, Harvey RJ, Dobyns WB. TUBA1A mutations cause wide spectrum lissencephaly (smooth brain) and suggest that multiple neuronalmigration pathways converge on alpha tubulins. Hum Mol Genet. 2010 Jul15;19(14):2817-27. doi: 10.1093/hmg/ddq182.
4. Tian G, Jaglin XH, Keays DA, Francis F, Chelly J, Cowan NJ. Disease-associatedmutations in TUBA1A result in a spectrum of defects in the tubulin folding andheterodimer assembly pathway. Hum Mol Genet. 2010 Sep 15;19(18):3599-613. doi:10.1093/hmg/ddq276.