UBE3A Gene

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Ubiquitin protein ligase E3A.

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1. Normal Function

The *UBE3A* gene provides instructions for making a protein called ubiquitin protein ligase E3A. Ubiquitin protein ligases are enzymes that target other proteins to be broken down (degraded) within cells. These enzymes attach a small molecule called ubiquitin to proteins that should be degraded. Cellular structures called proteasomes recognize and digest these ubiquitin-tagged proteins. Protein degradation is a normal process that removes damaged or unnecessary proteins and helps maintain the normal functions of cells.

Studies suggest that ubiquitin protein ligase E3A plays a critical role in the normal development and function of the nervous system. Studies suggest that it helps control (regulate) the balance of protein synthesis and degradation (proteostasis) at the junctions between nerve cells (synapses) where cell-to-cell communication takes place. Regulation of proteostasis is important for the synapses to change and adapt over time in response to experience, a characteristic called synaptic plasticity. Synaptic plasticity is critical for learning and memory.

People normally inherit two copies of the *UBE3A* gene, one from each parent. Both copies of the gene are turned on (active) in most of the body's tissues. In certain areas of the brain, however, only the copy inherited from a person's mother (the maternal copy) is active. This parent-specific gene activation results from a phenomenon known as genomic imprinting.

2. Health Conditions Related to Genetic Changes

2.1. Angelman Syndrome

A loss of *UBE3A* gene function in the brain likely causes many of the characteristic features of Angelman syndrome, a complex genetic disorder that primarily affects the nervous system. This loss of function results from a chromosomal change or gene mutation that affects the maternal copy of the gene.

Several different genetic mechanisms can turn off (inactivate) or delete the *UBE3A* gene. Most cases of Angelman syndrome (about 70 percent) occur when a segment of the maternal chromosome 15 containing this gene is deleted. In another 11 percent of cases, Angelman syndrome results from mutations within the *UBE3A* gene itself. Most of these mutations lead to the production of an abnormally short, nonfunctional version of ubiquitin protein ligase E3A. Because the copy of the gene inherited from a person's father (the paternal copy) is normally inactive in some areas of the brain, loss of the maternal copy prevents any of the enzyme from being produced in these brain regions. This lack of enzyme function likely causes the major signs and symptoms of Angelman syndrome.

Other abnormalities involving the region of chromosome 15 that contains the *UBE3A* gene can also cause Angelman syndrome. These chromosomal changes include rearrangements (translocations) of genetic material or a defect in the region of DNA that controls activation of the *UBE3A* gene. Like mutations within the gene, these chromosomal changes prevent any functional ubiquitin protein ligase E3A from being produced in certain parts of the brain.

3. Other Names for This Gene

- ANCR
- CTCL tumor antigen se37-2

- E6-AP
- E6AP ubiquitin-protein ligase
- EPVE6AP
- HPVE6A
- human papilloma virus E6-associated protein
- oncogenic protein-associated protein E6-AP
- UBE3A_HUMAN
- ubiquitin protein ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome)

References

1. Bittel DC, Kibiryeva N, Talebizadeh Z, Driscoll DJ, Butler MG. Microarrayanalysis of gene/transcript expression in Angelman syndrome: deletion versus UPD.Genomics. 2005 Jan;85(1):85-91.
2. Camprubí C, Guitart M, Gabau E, Coll MD, Villatoro S, Oltra S, Roselló M,Ferrer I, Monfort S, Orellana C, Martínez F. Novel UBE3A mutations causingAngelman syndrome: different parental origin for single nucleotide changes andmultiple nucleotide deletions or insertions. Am J Med Genet A. 2009Mar;149A(3):343-8. doi: 10.1002/ajmg.a.32659.
3. Clayton-Smith J, Laan L. Angelman syndrome: a review of the clinical andgenetic aspects. J Med Genet. 2003 Feb;40(2):87-95. Review.
4. Fang P, Lev-Lehman E, Tsai TF, Matsuura T, Benton CS, Sutcliffe JS, Christian SL, Kubota T, Halley DJ, Meijers-Heijboer H, Langlois S, Graham JM Jr, Beuten J, Willems PJ, Ledbetter DH, Beaudet AL. The spectrum of mutations in UBE3A causing Angelman syndrome. Hum Mol Genet. 1999 Jan;8(1):129-35.
5. Greer PL, Hanayama R, Bloodgood BL, Mardinly AR, Lipton DM, Flavell SW, KimTK, Griffith EC, Waldon Z, Maehr R, Ploegh HL, Chowdhury S, Worley PF, Steen J,Greenberg ME. The Angelman Syndrome protein Ube3A regulates synapse developmentby ubiquitinating arc. Cell. 2010 Mar 5;140(5):704-16. doi:10.1016/j.cell.2010.01.026.
6. Lalande M, Calciano MA. Molecular epigenetics of Angelman syndrome. Cell MolLife Sci. 2007 Apr;64(7-8):947-60. Review.
7. Louros SR, Osterweil EK. Perturbed proteostasis in autism spectrum disorders. J Neurochem. 2016 Dec;139(6):1081-1092. doi: 10.1111/jnc.13723.Review.
8. Matentzoglu K, Scheffner M. Ubiquitin ligase E6-AP and its role in humandisease. Biochem Soc Trans. 2008 Oct;36(Pt 5):797-801. doi: 10.1042/BST0360797.
9. Moncla A, Malzac P, Livet MO, Voelckel MA, Mancini J, Delaroziere JC, PhilipN, Mattei JF. Angelman syndrome resulting from UBE3A mutations in 14 patientsfrom eight families: clinical manifestations and genetic counselling. J MedGenet. 1999 Jul;36(7):554-60.
10. Noor A, Dupuis L, Mittal K, Lionel AC, Marshall CR, Scherer SW, Stockley T,Vincent JB, Mendoza-Londono R, Stavropoulos DJ. 15q11.2 Duplication Encompassing Only the UBE3A Gene Is Associated with Developmental Delay and NeuropsychiatricPhenotypes. Hum Mutat. 2015 Jul;36(7):689-93. doi: 10.1002/humu.22800.
11. Singhmar P, Kumar A. Angelman syndrome protein UBE3A interacts with primarymicrocephaly protein ASPM, localizes to centrosomes and regulates chromosomesegregation. PLoS One. 2011;6(5):e20397. doi: 10.1371/journal.pone.0020397.
12. Tan WH, Bacino CA, Skinner SA, Anselm I, Barbieri-Welge R, Bauer-Carlin A,Beaudet AL, Bichell TJ, Gentile JK, Glaze DG, Horowitz LT, Kothare SV, Lee HS,Nespeca MP, Peters SU, Sahoo T, Sarco D, Waisbren SE, Bird LM. Angelman syndrome:Mutations influence features in early childhood. Am J Med Genet A. 2011Jan;155A(1):81-90. doi: 10.1002/ajmg.a.33775.
13. Yi JJ, Berrios J, Newbern JM, Snider WD, Philpot BD, Hahn KM, Zylka MJ. AnAutism-Linked Mutation Disables Phosphorylation Control of UBE3A. Cell. 2015 Aug 13;162(4):795-807. doi: 10.1016/j.cell.2015.06.045.