UBE3A gene

ubiquitin protein ligase E3A

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.

Health Conditions Related to Genetic Changes

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

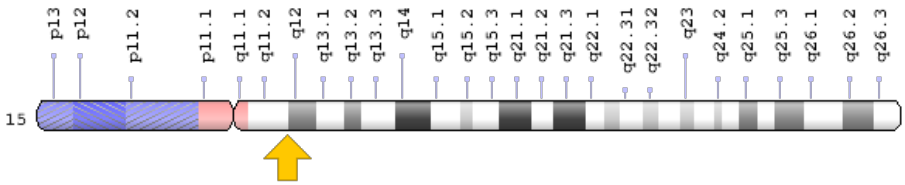
produced in these brain regions. This lack of enzyme function likely causes the major signs and symptoms of Angelman syndrome.

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.

Chromosomal Location

Cytogenetic Location: 15q11.2, which is the long (q) arm of chromosome 15 at position 11.2

Molecular Location: base pairs 25,333,728 to 25,439,381 on chromosome 15 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

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)

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Protein turnover is tightly regulated
  https://www.ncbi.nlm.nih.gov/books/NBK22397/

Clinical Information from GeneReviews

- Angelman Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1144

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28UBE3A%5BTIAB%5D%29+OR+%28ubiquitin+protein+ligase+E3A%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- UBIQUITIN-PROTEIN LIGASE E3A
  http://omim.org/entry/601623

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/UBE3AID42756ch15q11.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=UBE3A%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:12496
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:7337
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/7337
- UniProt
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