

## 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. However, in nerve cells (neurons) in the brain and spinal cord (the central nervous system), 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 variant (also known as a 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 10 to 20

percent of cases, Angelman syndrome results from variants within the *UBE3A* gene itself. Most of these variants 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 most 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 variants within the gene, these chromosomal changes prevent any functional ubiquitin protein ligase E3A from being produced in certain parts of the brain.

### Other disorders

Variants in the *UBE3A* gene have been found in a small number of individuals with a variety of neurological problems, including intellectual disability, seizures, and autism spectrum disorder. Unlike variants involved in Angelman syndrome, which reduce the function of ubiquitin protein ligase E3A in cells, these rare variants increase the function of the protein. It is not clear how excess ubiquitin protein ligase E3A activity affects development and contributes to the neurological features in people with these variants.

### **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**

#### Tests Listed in the Genetic Testing Registry

- Tests of UBE3A ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7337\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7337[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?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%29%29%29>)

### Catalog of Genes and Diseases from OMIM

- UBIQUITIN-PROTEIN LIGASE E3A; UBE3A (<https://omim.org/entry/601623>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/7337>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=UBE3A\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=UBE3A[gene]))

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3143/)

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## Genomic Location

The *UBE3A* gene is found on chromosome 15 (<https://medlineplus.gov/genetics/chromo>

some/15/).

**Last updated May 17, 2022**