UBA1 gene

ubiquitin like modifier activating enzyme 1

Normal Function

The *UBA1* gene provides instructions for making the ubiquitin-activating enzyme E1. This enzyme is necessary for the ubiquitin-proteasome system, which targets damaged or unneeded proteins to be broken down (degraded) within cells. Protein degradation helps maintain the proper balance of protein production and breakdown (protein homeostasis). Old proteins need to be removed to make way for new proteins to allow cells to function and survive. The ubiquitin-proteasome system acts as the cell's quality control system by disposing of damaged, misshapen, and excess proteins.

Ubiquitin-activating enzyme E1 is responsible for the first step in the ubiquitin-proteasome system; it turns on (activates) a small protein called ubiquitin. With the assistance of other proteins, the active ubiquitin attaches to a protein that is to be broken down. When a chain of ubiquitin proteins is attached to a protein, the protein is recognized and destroyed by a complex of enzymes called a proteasome.

Health Conditions Related to Genetic Changes

VEXAS syndrome

Variants (also called mutations) in the *UBA1* gene have been found to cause VEXAS syndrome. This condition is characterized by episodes of fever and abnormal inflammation affecting many parts of the body, particularly the skin, joints, and blood vessels. The *UBA1* gene variants that cause VEXAS syndrome are somatic, which means that they occur after birth during a person's lifetime. These variants occur only in certain immune cells and blood-forming cells in the bone marrow.

Most cases of VEXAS syndrome are caused by genetic variants that change the protein building block (amino acid) methione at position 41 in the ubiquitin-activating enzyme E1 to another amino acid. These variants lead to the production of an abnormally short enzyme with reduced function. As a result, damaged or unneeded proteins build up inside cells instead of being broken down, which may contribute to abnormal activation of immune cells or cell damage and death. This protein buildup also disrupts protein homeostasis. Old proteins must be removed before cells can make new proteins. If these damaged or unneeded proteins are not broken down, they can impair normal cell functions by stopping the production of new proteins. When *UBA1* gene variants occur

in immune cells or blood cells, they lead to abnormal inflammation, impaired blood cell development, and other features of VEXAS syndrome.

X-linked infantile spinal muscular atrophy

Variants in the *UBA1* gene have been reported to cause X-linked infantile spinal muscular atrophy. This condition is characterized by severe muscle weakness that begins at birth or in early infancy. Weakness in the chest muscles that control breathing often causes death from respiratory failure in early childhood.

UBA1 gene variants that cause X-linked infantile spinal muscular atrophy are inherited and present in all cells in the body. They all change one DNA building block (nucleotide) in an area of the gene known as exon 15. These variants reduce the activity, function, or production of the enzyme. This shortage of functional enzyme allows damaged or unneeded proteins to build up inside cells instead of being broken down, which may damage cells and contribute to cell death. This buildup also disrupts protein homeostasis. If damaged or unneeded proteins are not broken down, they can impair normal cell functions by stopping the production of new proteins. An imbalance in protein production and breakdown can ultimately lead to cell death. Specialized nerve cells that control muscle movement (motor neurons) are particularly susceptible to disruptions in cell function, likely due to their large size. Loss of these cells causes many of the signs and symptoms of X-linked infantile spinal muscular atrophy.

Other Names for This Gene

- GXP1
- SMAX2
- UBA1, ubiquitin-activating enzyme E1 homolog A
- UBA1_HUMAN
- UBA1A
- UBE1
- UBE1X
- ubiquitin-activating enzyme E1
- ubiquitin-like modifier activating enzyme 1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of UBA1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7317[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28UBA1%5BTIAB%5D%29+OR

+%28%28UBA1A%5BTIAB%5D%29+OR+%28UBE1%5BTIAB%5D%29+OR+%28ubiquitin-activating+enzyme+E1%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-LIKE MODIFIER-ACTIVATING ENZYME 1; UBA1 (https://omim.org/entry/314370)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7317)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=UBA1[gene])

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Genomic Location

The *UBA1* gene is found on the X chromosome (https://medlineplus.gov/genetics/chromosome/x/).

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