ATP6V0A2 gene

ATPase H+ transporting V0 subunit a2

Normal Function

The *ATP6V0A2* gene provides instructions for making one part, the a2 subunit, of a large protein complex (a group of proteins that work together). This protein complex is known as a vacuolar H+-ATPase (V-ATPase). A V-ATPase acts as a pump to move positively charged hydrogen atoms (protons) across cell membranes.

V-ATPases are embedded in the membranes surrounding cells, where they transport protons into and out of cells. This movement of protons helps regulate the relative acidity (pH) of cells and their surrounding environment. Tight control of pH is necessary for most biological reactions to proceed properly.

Within cells, V-ATPases help regulate the pH of particular cell compartments. These compartments include endosomes and lysosomes, which digest and recycle materials that the cell no longer needs. Studies suggest that V-ATPases are also involved in the movement (trafficking) of small sac-like structures called vesicles. Vesicles transport many types of molecules within cells.

V-ATPases also play a key role in a complex process called glycosylation, in which proteins are modified by adding sugar molecules. Glycosylation is necessary for the normal function of many different kinds of proteins. V-ATPases regulate the pH of a cellular structure called the Golgi apparatus, where glycosylation occurs.

Health Conditions Related to Genetic Changes

Cutis laxa

More than 40 variants (also known as mutations) in the *ATP6V0A2* gene have been identified in people with cutis laxa. *ATP6V0A2* variants cause a form of the disorder called autosomal recessive cutis laxa type 2A (ARCL2A), which is characterized by loose, sagging skin; distinctive facial features; and larger than normal spaces (fontanelles) between the skull bones that close later than usual. Some affected individuals also have delayed development, intellectual disability, seizures, or problems with movement that can worsen over time. Variants in this gene also cause a related condition called wrinkly skin syndrome, which typically has milder features.

Variants in the *ATP6V0A2* gene prevent the cell from producing a functional a2 subunit,

which disrupts the normal function of V-ATPases. It is unclear how these genetic changes cause the signs and symptoms of cutis laxa. Researchers suspect that changes in V-ATPase function may disrupt the normal glycosylation of proteins, including several that are involved in the assembly and maintenance of elastic fibers. Elastic fibers are slender bundles of proteins that provide strength and flexibility to connective tissue (tissue that supports the body's joints and organs). People with cutis laxa have a reduced density of elastic fibers, which weakens connective tissue in the skin, lungs, and other organs. These defects in connective tissue underlie many of the major features of the disorder.

Because problems with glycosylation underlie ARCL2A, the condition is classified as a congenital disorder of glycosylation.

Other Names for This Gene

- A2V-ATPase
- ATP6a2
- ATP6N1D
- ATPase, H+ transporting, lysosomal V0 subunit a2
- J6B7
- Stv1
- TJ6
- TJ6M
- TJ6s
- Vph1
- VPP2_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ATP6V0A2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=23545[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ATP6V0A2%5BTIAB%5D%29+OR+%28%28V-ATPase%5BTIAB%5D%29+AND+%28a2%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- ATPase, H+ TRANSPORTING, LYSOSOMAL, V0 SUBUNIT A2; ATP6V0A2 (https://omim.org/entry/611716)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/23545)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ATP6V0A2[gene])

References

- Guillard M, Dimopoulou A, Fischer B, Morava E, Lefeber DJ, Kornak U, WeversRA. Vacuolar H+-ATPase meets glycosylation in patients with cutis laxa. BiochimBiophys Acta. 2009 Sep;1792(9):903-14. doi: 10.1016/j.bbadis.2008.12.009. Epub2009 Jan 8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19171192)
- Hucthagowder V, Morava E, Kornak U, Lefeber DJ, Fischer B, Dimopoulou A, Aldinger A, Choi J, Davis EC, Abuelo DN, Adamowicz M, Al-Aama J, Basel-VanagaiteL, Fernandez B, Greally MT, Gillessen-Kaesbach G, Kayserili H, Lemyre E, Tekin M,Turkmen S, Tuysuz B, Yuksel-Konuk B, Mundlos S, Van Maldergem L, Wevers RA, UrbanZ. Loss-of-function mutations in ATP6V0A2 impair vesicular trafficking,tropoelastin secretion and cell survival. Hum Mol Genet. 2009 Jun15;18(12):2149-65. doi: 10.1093/hmg/ddp148. Epub 2009 Mar 25. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19321599) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2685755/)
- Kornak U, Reynders E, Dimopoulou A, van Reeuwijk J, Fischer B, Rajab A, BuddeB, Nurnberg P, Foulquier F; ARCL Debre-type Study Group; Lefeber D, Urban Z, Gruenewald S, Annaert W, Brunner HG, van Bokhoven H, Wevers R, Morava E, MatthijsG, Van Maldergem L, Mundlos S. Impaired glycosylation and cutis laxa caused bymutations in the vesicular H+-ATPase subunit ATP6V0A2. Nat Genet. 2008Jan;40(1):32-4. doi: 10.1038/ng.2007.45. Epub 2007 Dec 23. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18157129)
- Marshansky V, Futai M. The V-type H+-ATPase in vesicular trafficking:targeting, regulation and function. Curr Opin Cell Biol. 2008 Aug;20(4):415-26.doi: 10.1016/j.ceb.2008.03.015. Epub 2008 May 27. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18511251)
- Marshansky V. The V-ATPase a2-subunit as a putative endosomal pH-sensor. Biochem Soc Trans. 2007 Nov;35(Pt 5):1092-9. doi: 10.1042/BST0351092. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17956287)
- Morava E, Lefeber DJ, Urban Z, de Meirleir L, Meinecke P, Gillessen KaesbachG, Sykut-Cegielska J, Adamowicz M, Salafsky I, Ranells J, Lemyre E, van ReeuwijkJ, Brunner HG, Wevers RA. Defining the phenotype in an autosomal recessive cutislaxa syndrome with a combined congenital defect of glycosylation. Eur J HumGenet. 2008 Jan;16(1):28-35. doi: 10.1038/sj.ejhg.5201947. Epub 2007 Oct 31. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17971833)

Genomic Location

The *ATP6V0A2* gene is found on chromosome 12 (https://medlineplus.gov/genetics/chromosome/12/).

Last updated August 5, 2021