VCP gene

valosin containing protein

Normal Function

The *VCP* gene provides instructions for making an enzyme called valosin-containing protein. This enzyme is found throughout the body and has a wide variety of functions within cells. It is involved in cell division, joining (fusing) membranes within cells, reassembling cell structures after cells have divided, preventing the self-destruction of cells (apoptosis), and repairing damaged DNA.

Valosin-containing protein is part of the ubiquitin-proteasome system, which is the machinery that breaks down (degrades) unneeded proteins within cells. This system provides quality control by disposing of damaged, misshapen, and excess proteins. It also regulates the level of proteins involved in several critical cell activities, such as the timing of cell division and growth. Researchers believe that most of the functions of valosin-containing protein are directly or indirectly related to the ubiquitin-proteasome system.

Health Conditions Related to Genetic Changes

Inclusion body myopathy with early-onset Paget disease and frontotemporal dementia

Many variants (also known as mutations) in the *VCP* gene have been identified in people who have inclusion body myopathy with early-onset Paget disease and frontotemporal dementia (IBMPFD). This rare disease causes muscle weakness (myopathy) and can also include a painful bone condition called Paget disease of bone and a brain condition called frontotemporal dementia that worsens over time.

The variants associated with IBMPFD each change a single protein building block (amino acid) in valosin-containing protein. Changes in the structure of this enzyme impair its ability to break down other proteins as part of the ubiquitin-proteasome system. As a result, excess and abnormal proteins build up in muscle, bone, and brain cells. The proteins form clumps (aggregates) that interfere with the normal functions of these cells. It remains unclear how damage to muscle, bone, and brain cells leads to the specific features of IBMPFD.

Amyotrophic lateral sclerosis

MedlinePlus Genetics provides information about Amyotrophic lateral sclerosis

Charcot-Marie-Tooth disease

MedlinePlus Genetics provides information about Charcot-Marie-Tooth disease

Other Names for This Gene

- 15S Mg(2+)-ATPase p97 subunit
- CDC48
- IBMPFD
- MGC131997
- MGC148092
- MGC8560
- p97
- TER ATPase
- TERA
- TERA_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of VCP (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7415[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28VCP%5BTI%5D%29+OR+%28valosin-containing+protein%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

Catalog of Genes and Diseases from OMIM

- VALOSIN-CONTAINING PROTEIN; VCP (https://omim.org/entry/601023)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7415)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=VCP[gene])

References

- Guinto JB, Ritson GP, Taylor JP, Forman MS. Valosin-containing protein and thepathogenesis of frontotemporal dementia associated with inclusion body myopathy.Acta Neuropathol. 2007 Jul;114(1):55-61. doi: 10.1007/s00401-007-0224-7. Epub2007 Apr 25. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17457594)
- Ju JS, Miller SE, Hanson PI, Weihl CC. Impaired protein aggregate handling andclearance underlie the pathogenesis of p97/VCP-associated disease. J Biol Chem.2008 Oct 31;283(44):30289-99. doi: 10.1074/jbc.M805517200. Epub 2008 Aug 20. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18715868) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2573070/)
- Korb M, Peck A, Alfano LN, Berger KI, James MK, Ghoshal N, Healzer E, Henchcliffe C, Khan S, Mammen PPA, Patel S, Pfeffer G, Ralston SH, Roy B, SeeleyWW, Swenson A, Mozaffar T, Weihl C, Kimonis V; VCP Standards of Care WorkingGroup. Development of a standard of care for patients with valosin-containingprotein associated multisystem proteinopathy. Orphanet J Rare Dis. 2022 Jan29;17(1):23. doi: 10.1186/s13023-022-02172-5. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/35093159)
- Meyer H, Weihl CC. The VCP/p97 system at a glance: connecting cellularfunction to disease pathogenesis. J Cell Sci. 2014 Sep 15;127(Pt 18):3877-83.doi: 10.1242/jcs.093831. Epub 2014 Aug 21. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25146396) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4163641/)
- Nalbandian A, Donkervoort S, Dec E, Badadani M, Katheria V, Rana P, Nguyen C, Mukherjee J, Caiozzo V, Martin B, Watts GD, Vesa J, Smith C, Kimonis VE. Themultiple faces of valosin-containing protein-associated diseases: inclusion bodymyopathy with Paget's disease of bone, frontotemporal dementia, and amyotrophiclateral sclerosis. J Mol Neurosci. 2011 Nov;45(3):522-31. doi:10.1007/s12031-011-9627-y. Epub 2011 Sep 3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21892620)
- Song C, Wang Q, Li CC. Characterization of the aggregation-prevention activityof p97/valosin-containing protein. Biochemistry. 2007 Dec 25;46(51):14889-98.doi: 10.1021/bi700499j. Epub 2007 Nov 29. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18044963)
- Watts GD, Thomasova D, Ramdeen SK, Fulchiero EC, Mehta SG, Drachman DA, WeihlCC, Jamrozik Z, Kwiecinski H, Kaminska A, Kimonis VE. Novel VCP mutations ininclusion body myopathy associated with Paget disease of bone and frontotemporaldementia. Clin Genet. 2007 Nov;72(5):420-6. doi:10.1111/j.1399-0004.2007.00887.x. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17935506)
- Watts GD, Wymer J, Kovach MJ, Mehta SG, Mumm S, Darvish D, Pestronk A, WhyteMP, Kimonis VE. Inclusion body myopathy associated with Paget disease of bone andfrontotemporal dementia is caused by mutant valosin-containing protein. NatGenet. 2004 Apr;36(4):377-81. doi: 10.1038/ng1332. Epub 2004 Mar 21. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15034582)

Genomic Location

The *VCP* gene is found on chromosome 9 (https://medlineplus.gov/genetics/chromosome/9/).

Last updated April 1, 2018