HDAC4 gene

histone deacetylase 4

Normal Function

The *HDAC4* gene provides instructions for making an enzyme called histone deacetylase 4. This enzyme is part of a group of related enzymes, called histone deacetylases, that modify proteins called histones. Histones are structural proteins that attach (bind) to DNA and give chromosomes their shape.

By removing a molecule called an acetyl group from histones (a process called deacetylation), histone deacetylases cause the DNA within chromosomes to become tightly packed (compressed). As a result, proteins called transcription factors, which attach (bind) to specific regions of DNA and help control the activity of particular genes, cannot access the DNA. Through deacetylation of histones, histone deacetylase 4 is able to control (regulate) the activity of certain genes.

Histone deacetylase 4 appears to be particularly important for regulating the activity of genes involved in heart and skeletal development. This protein is also involved in nerve cell survival.

Health Conditions Related to Genetic Changes

2q37 deletion syndrome

2q37 deletion syndrome is caused by deletions of genetic material near the end of the long (q) arm of chromosome 2, at a location designated 2q37. The signs and symptoms of 2q37 deletion syndrome vary widely, but affected individuals generally have intellectual disability, behavioral problems, obesity, and skeletal abnormalities that often include unusually short fingers and toes (brachydactyly).

The chromosomal region that is deleted in 2q37 deletion syndrome varies among affected individuals and can contain many genes, but it always includes the *HDAC4* gene. As a result of the deletion, people with this condition have only one copy of the *HDAC4* gene in each cell instead of the usual two copies. Researchers believe that deletion of the *HDAC4* gene, and a reduction in the amount of histone deacetylase 4 produced, accounts for many of the features of 2q37 deletion syndrome. A shortage of histone deacetylase 4 enzyme likely disrupts the regulation of many genes and contributes to intellectual disability, behavioral problems, skeletal abnormalities, and

other features of 2q37 deletion syndrome.

Some people with a mutation in only the *HDAC4* gene have brachydactyly with no other health problems, while others have many features of 2q37 deletion syndrome. Researchers are studying why mutations in this gene can lead to a wide variety of signs and symptoms and what role the other genes on 2q37 play in the disorder.

Other Names for This Gene

- AHO3
- BDMR
- HA6116
- HD4
- HDAC-4
- HDAC-A
- HDACA
- histone deacetylase A
- KIAA0288

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of HDAC4 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=9759[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28HDAC4%5BTIAB%5D%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

- HISTONE DEACETYLASE 4; HDAC4 (https://omim.org/entry/605314)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/9759)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=HDAC4[gene])

References

- Jean-Marcais N, Decamp M, Gerard M, Ribault V, Andrieux J, Kottler ML, PlessisG. The first familial case of inherited 2q37.3 interstitial deletion withisolated skeletal abnormalities including brachydactyly type E and short stature.Am J Med Genet A. 2015 Jan;167A(1):185-9. doi: 10.1002/ajmg.a.36428. Epub 2014Nov 17. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25402011)
- Leroy C, Landais E, Briault S, David A, Tassy O, Gruchy N, Delobel B, GregoireMJ, Leheup B, Taine L, Lacombe D, Delrue MA, Toutain A, Paubel A, Mugneret F, Thauvin-Robinet C, Arpin S, Le Caignec C, Jonveaux P, Beri M, Leporrier N, MotteJ, Fiquet C, Brichet O, Mozelle-Nivoix M, Sabouraud P, Golovkine N, Bednarek N, Gaillard D, Doco-Fenzy M. The 2q37-deletion syndrome: an update of the clinicalspectrum including overweight, brachydactyly and behavioural features in 14 newpatients. Eur J Hum Genet. 2013 Jun;21(6):602-12. doi: 10.1038/ejhg.2012.230. Epub 2012 Oct 17. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23073310) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3658200/)
- Williams SR, Aldred MA, Der Kaloustian VM, Halal F, Gowans G, McLeod DR, Zondag S, Toriello HV, Magenis RE, Elsea SH. Haploinsufficiency of HDAC4 causesbrachydactyly mental retardation syndrome, with brachydactyly type E, developmental delays, and behavioral problems. Am J Hum Genet. 2010 Aug13;87(2):219-28. doi: 10.1016/j.ajhg.2010.07.011. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20691407) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2917703/)

Genomic Location

The *HDAC4* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chromosome/2/).

Last updated October 1, 2018