ZMPSTE24 gene

zinc metallopeptidase STE24

Normal Function

The *ZMPSTE24* gene provides instructions for making a protein that acts as a protease, which is an enzyme that cuts (cleaves) other proteins. The ZMPSTE24 protein cuts an immature version of the lamin A protein (prelamin A) at a particular location; this cleavage is an essential step in the maturation of lamin A.

Mature lamin A is a component of the nuclear envelope, which is the membrane that surrounds the nucleus in cells. The nuclear envelope regulates the movement of molecules into and out of the nucleus, and researchers believe it may play a role in regulating the activity of certain genes.

Health Conditions Related to Genetic Changes

Mandibuloacral dysplasia

At least four mutations in the *ZMPSTE24* gene cause a form of mandibuloacral dysplasia called mandibuloacral dysplasia with type B lipodystrophy (MADB). This condition is characterized by a variety of signs and symptoms, which can include bone abnormalities, mottled or patchy skin coloring, and loss of fatty tissue under the skin affecting all parts of the body (type B lipodystrophy). *ZMPSTE24* gene mutations that cause MADB lead to a reduction of functional ZMPSTE24 protein. As a result, prelamin A is not processed efficiently, and it builds up in cells. In addition, there is a shortage of mature lamin A. Some researchers speculate that these changes damage the nucleus, making cells more fragile. It is not known how the effects of *ZMPSTE24* gene mutations relate to the specific signs and symptoms of MADB.

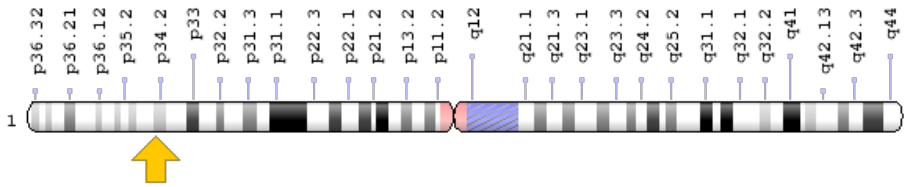
Other disorders

Mutations in the *ZMPSTE24* gene that completely eliminate the function of the ZMPSTE24 protein have been identified in newborns with a disorder called lethal restrictive dermopathy. Infants with this disorder have tight, rigid skin; underdeveloped lungs; and other abnormalities. They do not usually survive past the first week of life. Without any functional ZMPSTE24 protein, prelamin A accumulates and mature lamin A is absent; however, it is unclear how these changes lead to the severe signs and symptoms of lethal restrictive dermopathy.

Chromosomal Location

Cytogenetic Location: 1p34.2, which is the short (p) arm of chromosome 1 at position 34.2

Molecular Location: base pairs 40,258,050 to 40,294,184 on chromosome 1 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CAAX prenyl protease 1 homolog
- FACE-1
- FACE1
- FACE1_HUMAN
- farnesylated proteins-converting enzyme 1
- HGPS
- prenyl protein-specific endoprotease 1
- PRO1
- STE24
- Ste24p
- zinc metalloproteinase Ste24 homolog

Additional Information & Resources

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28ZMPSTE24%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

- RESTRICTIVE DERMOPATHY, LETHAL
  http://omim.org/entry/275210
- ZINC METALLOPROTEINASE STE24
  http://omim.org/entry/606480

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ZMPSTE24.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ZMPSTE24%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:12877
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:10269
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/10269
- UniProt
  https://www.uniprot.org/uniprot/O75844

Sources for This Summary

- Ahmad Z, Zackai E, Medne L, Garg A. Early onset mandibuloacral dysplasia due to compound heterozygous mutations in ZMPSTE24. Am J Med Genet A. 2010 Nov;152A(11):2703-10. doi: 10.1002/ajmg.a.33664.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20814950
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2965306/
- Barrowman J, Michaelis S. ZMPSTE24, an integral membrane zinc metalloprotease with a connection to progeroid disorders. Biol Chem. 2009 Aug;390(8):761-73. doi: 10.1515/BC.2009.080. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19453269
- Barrowman J, Wiley PA, Hudon-Miller SE, Hrycyna CA, Michaelis S. Human ZMPSTE24 disease mutations: residual proteolytic activity correlates with disease severity. Hum Mol Genet. 2012 Sep 15;21(18):4084-93. doi: 10.1093/hmg/dds233. Epub 2012 Jun 19.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22718200
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3428156/

- Ben Yaou R, Navarro C, Quijano-Roy S, Bertrand AT, Massart C, De Sandre-Giovannoli A, Cadiñanos J, Mamchaoui K, Butler-Browne G, Estournet B, Richard P, Barois A, Lévy N, Bonne G. Type B mandibuloacral dysplasia with congenital myopathy due to homozygous ZMPSTE24 missense mutation. Eur J Hum Genet. 2011 Jun;19(6):647-54. doi: 10.1038/ejhg.2010.256. Epub 2011 Jan 26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21267004
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3110044/
- OMIM: ZINC METALLOPROTEINASE STE24
  http://omim.org/entry/606480

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/ZMPSTE24

Reviewed: August 2013
Published: May 14, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services