MITF gene

melanocyte inducing transcription factor

Normal Function

The *MITF* gene provides instructions for making a protein called melanocyte inducing transcription factor. This protein plays a role in the development, survival, and function of certain types of cells. To carry out this role, the protein attaches to specific areas of DNA and helps control the activity of particular genes. On the basis of this action, the protein is called a transcription factor.

Melanocyte inducing transcription factor helps control the development and function of pigment-producing cells called melanocytes. Within these cells, this protein controls production of the pigment melanin, which contributes to hair, eye, and skin color. Melanocytes are also found in the inner ear and play an important role in hearing. Additionally, melanocyte inducing transcription factor regulates the development of specialized cells in the eye called retinal pigment epithelial cells. These cells nourish the retina, the part of the eye that detects light and color. Some research indicates that melanocyte inducing transcription factor also regulates the development of cells that break down and remove bone (osteoclasts) and cells that play a role in allergic reactions (mast cells).

The structure of melanocyte inducing transcription factor includes three critically important regions. Two of the regions, called the helix-loop-helix motif and the leucine-zipper motif, are critical for protein interactions. These motifs allow molecules of melanocyte inducing transcription factor to interact with each other or with other proteins that have a similar structure, creating a two-protein unit (dimer) that functions as a transcription factor. The other region, known as the basic motif, binds to specific areas of DNA, allowing the dimer to control gene activity.

Health Conditions Related to Genetic Changes

Tietz syndrome

At least two *MITF* gene mutations have been identified in people with Tietz syndrome, which is characterized by profound hearing loss from birth, fair skin, and light-colored hair. Researchers suggest that Tietz syndrome may be a severe form of Waardenburg syndrome (described below).

The *MITF* gene mutations that cause Tietz syndrome either delete or change a single protein building block (amino acid) in the basic motif region of the melanocyte inducing transcription factor structure. Dimers incorporating the abnormal melanocyte inducing transcription factor cannot be transported into the cell nucleus to bind with DNA. As a result, most of the dimers are unavailable to bind to DNA, which

affects the development of melanocytes and the production of melanin. The resulting reduction or absence of melanocytes in the inner ear leads to hearing loss. Decreased melanin production (hypopigmentation) accounts for the light skin and hair color that are characteristic of Tietz syndrome.

Waardenburg syndrome

More than 35 mutations in the *MITF* gene have been identified in people with Waardenburg syndrome type II, a disorder that can cause hearing loss and changes in coloring (pigmentation) of the hair, skin, and eyes. Some *MITF* gene mutations change the amino acids used to make melanocyte inducing transcription factor, which alters the helix-loop-helix or leucine-zipper motif. Other mutations result in an abnormally small version of the protein. Researchers believe that both types of mutations disrupt the formation of dimers. Although some dimers are produced, the amount is insufficient for full development of melanocytes. As a result, there is a shortage of melanocytes in certain areas of the skin, hair, eyes, and inner ear. This shortage leads to hearing loss and the patchy loss of pigmentation associated with Waardenburg syndrome.

Melanoma

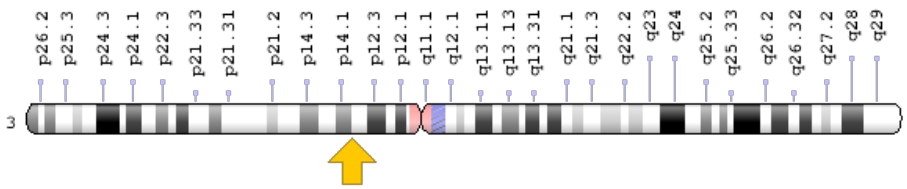
Cancers

MITF gene mutations have also been found in people with an aggressive form of skin cancer called melanoma. Most of these mutations are somatic, meaning that they occur during a person's lifetime and are present only in certain cells, in this case cells that give rise to the melanoma. Occasionally the mutation is inherited and is found in every cell of the body (known as a germline mutation). Some of the *MITF* gene mutations associated with melanoma increase cell growth and division (proliferation) directly. Other mutations have an indirect effect, increasing the activity (expression) of other genes involved in proliferation and resulting in the abnormal cell growth that occurs in melanoma.

Chromosomal Location

Cytogenetic Location: 3p13, which is the short (p) arm of chromosome 3 at position 13

Molecular Location: base pairs 69,739,464 to 69,968,337 on chromosome 3 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- homolog of mouse microphthalmia
- melanogenesis associated transcription factor
- microphthalmia-associated transcription factor
- MITF_HUMAN
- WS2A

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database: The Genetic Regulation of Pigment Cell Development
  https://www.ncbi.nlm.nih.gov/books/NBK6603/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MITF%5BTIAB%5D%29+OR+%28microphthalmia-associated+transcription+factor%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+360+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- MELANOMA, CUTANEOUS MALIGNANT, SUSCEPTIBILITY TO, 8
  http://omim.org/entry/614456
- MICROPHTHALMIA-ASSOCIATED TRANSCRIPTION FACTOR
  http://omim.org/entry/156845

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/MITFID44193ch3p13.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MITF%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:7105
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4286
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4286
- UniProt
  https://www.uniprot.org/uniprot/O75030

Sources for This Summary

- Amiel J, Watkin PM, Tassabehji M, Read AP, Winter RM. Mutation of the MITF gene in albinism-deafness syndrome (Tietz syndrome). Clin Dysmorphol. 1998 Jan;7(1):17-20.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9546825
- Bondurand N, Pingault V, Goerich DE, Lemort N, Sock E, Le Caignec C, Wegner M, Goossens M. Interaction among SOX10, PAX3 and MITF, three genes altered in Waardenburg syndrome. Hum Mol Genet. 2000 Aug 12;9(13):1907-17.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10942418
- Grill C, Bergsteinsdóttir K, Ogmundsdóttir MH, Pogenberg V, Schepsky A, Wilmanns M, Pingault V, Steingrímsson E. MITF mutations associated with pigment deficiency syndromes and melanoma have different effects on protein function. Hum Mol Genet. 2013 Nov 1;22(21):4357-67. doi: 10.1093/hmg/ddt285. Epub 2013 Jun 20.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23787126
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3888191/
- Izumi K, Kohta T, Kimura Y, Ishida S, Takahashi T, Ishiko A, Kosaki K. Tietz syndrome: unique phenotype specific to mutations of MITF nuclear localization signal. Clin Genet. 2008 Jul;74(1):93-5. doi: 10.1111/j.1399-0004.2008.01010.x. Epub 2008 May 28.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18510545

- Léger S, Balguerie X, Goldenberg A, Drouin-Garraud V, Cabot A, Amstutz-Montadert I, Young P, Joly P, Bodereau V, Holder-Espinasse M, Jamieson RV, Krause A, Chen H, Baumann C, Nunes L, Dollfus H, Goossens M, Pingault V. Novel and recurrent non-truncating mutations of the MITF basic domain: genotypic and phenotypic variations in Waardenburg and Tietz syndromes. Eur J Hum Genet. 2012 May;20(5):584-7. doi: 10.1038/ejhg.2011.234. Epub 2012 Jan 18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22258527
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3330215/
- OMIM: MICROPHTHALMIA-ASSOCIATED TRANSCRIPTION FACTOR
  http://omim.org/entry/156845
- Murakami H, Arnheiter H. Sumoylation modulates transcriptional activity of MITF in a promoter-specific manner. Pigment Cell Res. 2005 Aug;18(4):265-77.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16029420
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1351050/
- Potterf SB, Furumura M, Dunn KJ, Arnheiter H, Pavan WJ. Transcription factor hierarchy in Waardenburg syndrome: regulation of MITF expression by SOX10 and PAX3. Hum Genet. 2000 Jul;107(1):1-6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10982026
- Read AP. Waardenburg syndrome. Adv Otorhinolaryngol. 2000;56:32-8. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10868211
- Smith SD, Kelley PM, Kenyon JB, Hoover D. Tietz syndrome (hypopigmentation/deafness) caused by mutation of MITF. J Med Genet. 2000 Jun;37(6):446-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10851256
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1734605/
- Tachibana M. Cochlear melanocytes and MITF signaling. J Investig Dermatol Symp Proc. 2001 Nov;6(1):95-8. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11764294
- Tachibana M. MITF: a stream flowing for pigment cells. Pigment Cell Res. 2000 Aug;13(4):230-40. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10952390
- Widlund HR, Fisher DE. Microphthalamia-associated transcription factor: a critical regulator of pigment cell development and survival. Oncogene. 2003 May 19;22(20):3035-41. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12789278

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

Reviewed: August 2016
Published: September 10, 2019

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