

MITF Gene

Subjects: Genetics & Heredity

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melanocyte inducing transcription factor

Keywords: genes

1. Introduction

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.

2. Health Conditions Related to Genetic Changes

2.1. 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.

2.2. 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.

2.3. 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.

3. Other Names for This Gene

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

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