MC1R gene

melanocortin 1 receptor

Normal Function

The *MC1R* gene provides instructions for making a protein called the melanocortin 1 receptor. This receptor plays an important role in normal pigmentation. The receptor is primarily located on the surface of melanocytes, which are specialized cells that produce a pigment called melanin. Melanin is the substance that gives skin, hair, and eyes their color. Melanin is also found in the light-sensitive tissue at the back of the eye (the retina), where it plays a role in normal vision.

Melanocytes make two forms of melanin, eumelanin and pheomelanin. The relative amounts of these two pigments help determine the color of a person's hair and skin. People who produce mostly eumelanin tend to have brown or black hair and dark skin that tans easily. Eumelanin also protects skin from damage caused by ultraviolet (UV) radiation in sunlight. People who produce mostly pheomelanin tend to have red or blond hair, freckles, and light-colored skin that tans poorly. Because pheomelanin does not protect skin from UV radiation, people with more pheomelanin have an increased risk of skin damage caused by sun exposure.

The melanocortin 1 receptor controls which type of melanin is produced by melanocytes. When the receptor is activated, it triggers a series of chemical reactions inside melanocytes that stimulate these cells to make eumelanin. If the receptor is not activated or is blocked, melanocytes make pheomelanin instead of eumelanin.

Common variations (polymorphisms) in the *MC1R* gene are associated with normal differences in skin and hair color. Certain genetic variations are most common in people with red hair, fair skin, freckles, and an increased sensitivity to sun exposure. These *MC1R* polymorphisms reduce the ability of the melanocortin 1 receptor to stimulate eumelanin production, causing melanocytes to make mostly pheomelanin. Although *MC1R* is a key gene in normal human pigmentation, researchers believe that the effects of other genes also contribute to a person's hair and skin coloring.

The melanocortin 1 receptor is also active in cells other than melanocytes, including cells involved in the body's immune and inflammatory responses. The receptor's function in these cells is unknown.

Health Conditions Related to Genetic Changes

Oculocutaneous albinism

Certain genetic changes in the *MC1R* gene modify the appearance of people with oculocutaneous albinism type 2. This form of albinism, which is caused by mutations

in the *OCA2* gene, is characterized by fair hair, light-colored eyes, creamy white skin, and vision problems. People with genetic changes in both the *OCA2* and *MC1R* genes have many of the usual features of oculocutaneous albinism type 2; however, they typically have red hair instead of the usual yellow, blond, or light brown hair seen with this condition.

Cancers

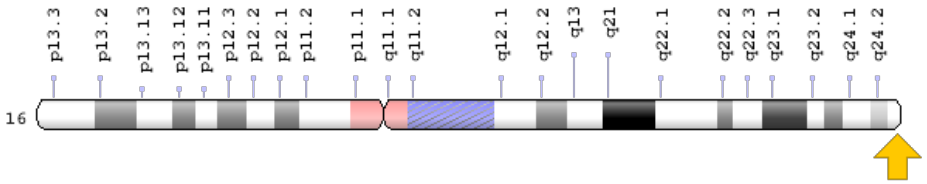
Many genetic changes in the *MC1R* gene increase the risk of developing skin cancer, including a common, serious form of skin cancer that begins in melanocytes (melanoma). Alterations in the *MC1R* gene disrupt the ability of the melanocortin 1 receptor to trigger eumelanin production in melanocytes. Because eumelanin normally protects skin from the harmful effects of UV radiation, a lack of this pigment leaves fair skin more vulnerable to damage from sun exposure. Skin damage caused by UV radiation from the sun is a major risk factor for developing melanoma and other forms of skin cancer.

Studies suggest that variations in the *MC1R* gene may also increase the risk of developing melanoma in the absence of UV radiation-related skin damage. In these cases, melanomas can occur in people of dark or light skin coloring. These cancers are often associated with mutations in additional genes related to melanoma risk, such as the *BRAF* and *CDKN2A* genes. Researchers are working to explain the complex relationship among *MC1R* variations, other genetic and environmental factors, and melanoma risk.

Chromosomal Location

Cytogenetic Location: 16q24.3, which is the long (q) arm of chromosome 16 at position 24.3

Molecular Location: base pairs 89,917,879 to 89,920,977 on chromosome 16 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- MC1-R
- Melanocortin-1 receptor

- melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor)
- melanocyte stimulating hormone receptor
- melanotropin receptor
- MSH-R
- MSHR_HUMAN

Additional Information & Resources

Educational Resources

- National Cancer Institute
  https://www.cancer.gov/types/skin

GeneReviews

- Oculocutaneous Albinism Type 2
  https://www.ncbi.nlm.nih.gov/books/NBK1232

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MC1R%5BTIAB%5D%29+OR+%28melanocortin+1+receptor%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+1080+days%22%5Bdp%5D

OMIM

- MELANOCORTIN 1 RECEPTOR
  http://omim.org/entry/155555
- MELANOMA, CUTANEOUS MALIGNANT, SUSCEPTIBILITY TO, 1
  http://omim.org/entry/155600
- SKIN/HAIR/EYE PIGMENTATION, VARIATION IN, 2
  http://omim.org/entry/266300

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_MC1R.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MC1R%5Bgene%5D
- HGNC Gene Family: Melanocortin receptors
  https://www.genenames.org/cgi-bin/genefamilies/set/236

- HGNC Gene Symbol Report
  https://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=6929
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4157
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Reviewed: March 2007
Published: April 17, 2018

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