

## 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

### Melanoma

Certain variations in the *MC1R* gene increase the risk of developing melanoma, a type of skin cancer that begins in melanocytes. These variations reduce the ability of the melanocortin 1 receptor to stimulate eumelanin production in melanocytes, resulting in fair skin. Because eumelanin normally protects skin from the harmful effects of UV radiation, a lack of this pigment leaves 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.

Studies suggest that other 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.

### 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.

### **Other Names for This Gene**

- MC1-R
- melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor)
- Melanocortin-1 receptor
- melanocyte stimulating hormone receptor
- melanotropin receptor
- MSH-R
- MSHR\_HUMAN

### **Additional Information & Resources**

#### Tests Listed in the Genetic Testing Registry

- Tests of MC1R ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4157\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4157[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?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>)

### Catalog of Genes and Diseases from OMIM

- MELANOCORTIN 1 RECEPTOR (<https://omim.org/entry/155555>)
- SKIN/HAIR/EYE PIGMENTATION, VARIATION IN, 2 (<https://omim.org/entry/266300>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/4157>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=MC1R\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=MC1R[gene]))

### **References**

- Duffy DL, Box NF, Chen W, Palmer JS, Montgomery GW, James MR, Hayward NK, Martin NG, Sturm RA. Interactive effects of MC1R and OCA2 on melanoma risk phenotypes. *Hum Mol Genet.* 2004 Feb 15;13(4):447-61. doi: 10.1093/hmg/ddh043. Epub 2004 Jan 6. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/14709592>)
- Garcia-Borrón JC, Sanchez-Laorden BL, Jimenez-Cervantes C. Melanocortin-1 receptor structure and functional regulation. *Pigment Cell Res.* 2005 Dec;18(6):393-410. doi: 10.1111/j.1600-0749.2005.00278.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16280005>)
- Ha T, Naysmith L, Waterston K, Oh C, Weller R, Rees JL. Defining the quantitative contribution of the melanocortin 1 receptor (MC1R) to variation in pigimentary phenotype. *Ann N Y Acad Sci.* 2003 Jun;994:339-47. doi:10.1111/j.1749-6632.2003.tb03198.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12851334>)
- Healy E. Melanocortin 1 receptor variants, pigmentation, and skin cancer susceptibility. *Photodermatol Photoimmunol Photomed.* 2004 Dec;20(6):283-8. doi:10.1111/j.1600-0781.2004.00132.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15533235>)
- Kanetsky PA, Rebbeck TR, Hummer AJ, Panossian S, Armstrong BK, Krickler A, Marrett LD, Millikan RC, Gruber SB, Culver HA, Zanetti R, Gallagher RP, Dwyer T, Busam K, From L, Mujumdar U, Wilcox H, Begg CB, Berwick M. Population-based study of natural variation in the melanocortin-1 receptor gene and melanoma.

CancerRes. 2006 Sep 15;66(18):9330-7. doi: 10.1158/0008-5472.CAN-06-1634. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16982779>)

- King RA, Willaert RK, Schmidt RM, Pietsch J, Savage S, Brott MJ, Fryer JP, Summers CG, Oetting WS. MC1R mutations modify the classic phenotype of oculocutaneous albinism type 2 (OCA2). Am J Hum Genet. 2003 Sep;73(3):638-45. doi: 10.1086/377569. Epub 2003 Jul 22. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12876664>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180688/>)
- Landi MT, Bauer J, Pfeiffer RM, Elder DE, Hulley B, Minghetti P, Calista D, Kanetsky PA, Pinkel D, Bastian BC. MC1R germline variants confer risk for BRAF-mutant melanoma. Science. 2006 Jul 28;313(5786):521-2. doi:10.1126/science.1127515. Epub 2006 Jun 29. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16809487>)
- Mumm CD, Draznin M. Melanocortin-1 receptor: loss of function mutations and skin cancer. Dermatol Online J. 2006 Sep 8;12(5):13. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16962028>)
- Rees JL. Genetics of hair and skin color. Annu Rev Genet. 2003;37:67-90. doi:10.1146/annurev.genet.37.110801.143233. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/14616056>)
- Rees JL. The genetics of sun sensitivity in humans. Am J Hum Genet. 2004 Nov;75(5):739-51. doi: 10.1086/425285. Epub 2004 Sep 15. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15372380>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1182105/>)
- Rouzaud F, Kadekaro AL, Abdel-Malek ZA, Hearing VJ. MC1R and the response of melanocytes to ultraviolet radiation. Mutat Res. 2005 Apr 1;571(1-2):133-52. doi: 10.1016/j.mrfmmm.2004.09.014. Epub 2005 Jan 26. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15748644>)
- Sturm RA. Skin colour and skin cancer - MC1R, the genetic link. Melanoma Res. 2002 Oct;12(5):405-16. doi: 10.1097/00008390-200209000-00001. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12394181>)

## Genomic Location

The *MC1R* gene is found on chromosome 16 (<https://medlineplus.gov/genetics/chromosome/16/>).

**Last updated August 1, 2018**