MRAP gene

melanocortin 2 receptor accessory protein

Normal Function

The *MRAP* gene provides instructions for making a protein called melanocortin-2 receptor accessory protein (MRAP). This protein transports another protein, called the melanocortin-2 receptor (or more commonly the adrenocorticotropic hormone [ACTH] receptor), from the interior of the cell to the cell surface. Specifically, the MRAP protein transports the ACTH receptor from a cell structure called the endoplasmic reticulum (ER), which is involved in protein processing and transport, to the cell membrane so that the receptor can function. The MRAP protein is also needed to turn on (activate) the ACTH receptor.

At the cell membrane, the activated ACTH receptor attaches (binds) to ACTH, which triggers the production of a group of hormones called glucocorticoids. These hormones, which include cortisol and corticosterone, aid in immune system function, play a role in maintaining normal blood sugar levels, help trigger nerve cell signaling in the brain, and serve many other purposes in the body.

Health Conditions Related to Genetic Changes

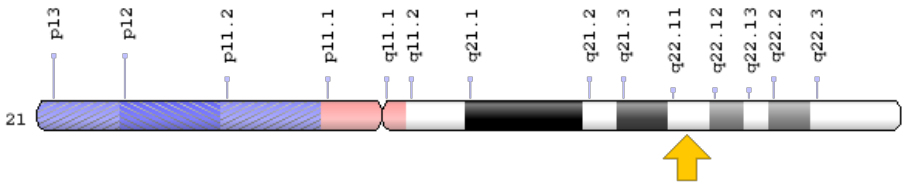
Familial glucocorticoid deficiency

At least 13 mutations in the *MRAP* gene have been found to cause familial glucocorticoid deficiency. This condition is characterized by potentially life-threatening low blood sugar (hypoglycemia), recurrent infections, and skin coloring darker than that of other family members (hyperpigmentation). *MRAP* gene mutations account for approximately 20 percent of cases of this condition. Most of these mutations lead to the production of a protein that cannot interact with the ACTH receptor and so is unable to transport it out of the ER to the cell membrane. As a result, the ACTH receptor is not at the cell surface where it is needed to bind to ACTH. Without the binding of the ACTH receptor to its hormone, there is no signal to trigger the adrenal glands to produce glucocorticoids. A shortage of these hormones impairs blood sugar regulation, immune system function, and other cellular functions, leading to the signs and symptoms of familial glucocorticoid deficiency.

Chromosomal Location

Cytogenetic Location: 21q22.11, which is the long (q) arm of chromosome 21 at position 22.11

Molecular Location: base pairs 32,291,813 to 32,314,784 on chromosome 21 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- B27
- C21orf61
- FALP
- fat cell-specific low molecular weight protein
- fat tissue-specific low MW protein
- GCCD2
- melanocortin-2 receptor accessory protein
- MRAP_HUMAN

Additional Information & Resources

Educational Resources

- Endocrinology: An Integrated Approach (2001): Feedback Control of Glucocorticoids
  https://www.ncbi.nlm.nih.gov/books/NBK26/#A526

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MRAP%5BTIAB%5D%29+OR+%28melanocortin+2+receptor+accessory+protein%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+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- MELANOCORTIN 2 RECEPTOR ACCESSORY PROTEIN
  http://omim.org/entry/609196

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_MRAP.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MRAP%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:1304
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:56246
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/56246
- UniProt
  https://www.uniprot.org/uniprot/Q8TCY5

Sources for This Summary

- Cerdá-Reverter JM, Agulleiro MJ, Cortés R, Sánchez E, Guillot R, Leal E, Fernández-Durán B, Puchol S, Eley M. Involvement of melanocortin receptor accessory proteins (MRAPs) in the function of melanocortin receptors. Gen Comp Endocrinol. 2013 Jul 1;188:133-6. doi: 10.1016/j.ygcen.2013.01.017. Epub 2013 Feb 11. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23410915
- Clark AJ, Chan LF, Chung TT, Metherell LA. The genetics of familial glucocorticoid deficiency. Best Pract Res Clin Endocrinol Metab. 2009 Apr;23(2):159-65. doi: 10.1016/j.beem.2008.09.006. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19500760
- OMIM: MELANOCORTIN 2 RECEPTOR ACCESSORY PROTEIN
  http://omim.org/entry/609196
- Meimaridou E, Hughes CR, Kowalczyk J, Guasti L, Chapple JP, King PJ, Chan LF, Clark AJ, Metherell LA. Familial glucocorticoid deficiency: New genes and mechanisms. Mol Cell Endocrinol. 2013 May 22;371(1-2):195-200. doi: 10.1016/j.mce.2012.12.010. Epub 2012 Dec 29. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23279877
- Metherell LA, Chapple JP, Cooray S, David A, Becker C, Rüschendorf F, Naville D, Begeot M, Khoo B, Nürnberg P, Huebner A, Cheetham ME, Clark AJ. Mutations in MRAP, encoding a new interacting partner of the ACTH receptor, cause familial glucocorticoid deficiency type 2. Nat Genet. 2005 Feb;37(2):166-70. Epub 2005 Jan 16.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15654338
- Novoselova TV, Jackson D, Campbell DC, Clark AJ, Chan LF. Melanocortin receptor accessory proteins in adrenal gland physiology and beyond. J Endocrinol. 2013 Mar 19;217(1):R1-11. doi: 10.1530/JOE-12-0501. Print 2013 Apr. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23418361

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