



MSH6 gene

mutS homolog 6

Normal Function

The *MSH6* gene provides instructions for making a protein that plays an essential role in repairing DNA. This protein helps fix errors that are made when DNA is copied (DNA replication) in preparation for cell division. The MSH6 protein joins with another protein called MSH2 (produced from the *MSH2* gene) to form a protein complex. This complex identifies locations on the DNA where errors have been made during DNA replication. Another group of proteins, the MLH1-PMS2 protein complex, then repairs the errors. The *MSH6* gene is a member of a set of genes known as the mismatch repair (MMR) genes.

Health Conditions Related to Genetic Changes

Lynch syndrome

Mutations in the *MSH6* gene have been reported in about 10 percent of families with Lynch syndrome that have an identified gene mutation. Lynch syndrome increases the risk of many types of cancer, particularly cancers of the colon (large intestine) and rectum, which are collectively referred to as colorectal cancer. People with Lynch syndrome also have an increased risk of cancers of the endometrium (lining of the uterus), ovaries, stomach, small intestine, liver, gallbladder duct, upper urinary tract, and brain. Endometrial cancer is especially common in women with Lynch syndrome caused by *MSH6* gene mutations.

MSH6 gene mutations involved in this condition lead to the production of an abnormally short, nonfunctional MSH6 protein or a partially active version of the protein. When the MSH6 protein is absent or nonfunctional, the number of errors that are left unrepaired during cell division increases substantially. The errors accumulate as the cells continue to divide, which may cause the cells to function abnormally, increasing the risk of tumor formation in the colon or another part of the body.

In a small number of people, mutations in the *MSH6* gene cause a variant of Lynch syndrome called Muir-Torre syndrome. In addition to colorectal cancer, people with this condition have an increased risk of developing several uncommon skin tumors. These rare skin tumors include sebaceous adenomas and carcinomas, which occur in glands that produce an oily substance called sebum (sebaceous glands). Multiple rapidly growing tumors called keratoacanthomas may also occur, usually on sun-exposed areas of skin.

Ovarian cancer

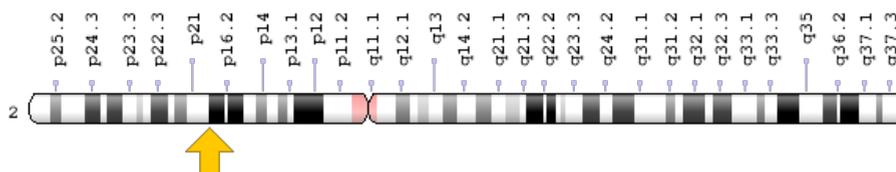
Other cancers

While Lynch syndrome is associated with a mutation in one copy of the *MSH6* gene, very rarely, individuals in affected families inherit two *MSH6* gene mutations, one from each parent. Most often in these cases, the same mutation occurs in both copies of the gene (a homozygous mutation). People with a homozygous *MSH6* gene mutation have a syndrome distinct from Lynch syndrome. In addition to colorectal cancer, they may develop cancers of the blood (leukemia or lymphoma). Some of these individuals will also develop characteristic features of a condition known as neurofibromatosis, including noncancerous tumors that grow along nerves (neurofibromas) and light brown patches of skin called café-au-lait spots. The onset of colon cancer in these individuals is extremely early, often occurring during childhood. This syndrome involving colon cancer, leukemia or lymphoma, and neurofibromatosis is sometimes called CoLoN.

Chromosomal Location

Cytogenetic Location: 2p16.3, which is the short (p) arm of chromosome 2 at position 16.3

Molecular Location: base pairs 47,783,082 to 47,806,954 on chromosome 2 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- DNA Mismatch Repair Protein MSH6
- G/T mismatch-binding protein
- GTBP
- GTMBP
- HNPCC5
- MSH6_HUMAN
- mutS (E. coli) homolog 6
- MutS-alpha 160 kDa subunit
- mutS homolog 6 (E. coli)

Additional Information & Resources

Educational Resources

- Cancer Medicine (sixth edition, 2003): DNA Mismatch Repair Gene Defects and HNPCC
<https://www.ncbi.nlm.nih.gov/books/NBK12469/#A1595>
- Molecular Biology of the Cell (fourth edition, 2002): Defects in DNA Mismatch Repair Provide an Alternative Route to Colorectal Cancer
<https://www.ncbi.nlm.nih.gov/books/NBK26902/#A4345>

Clinical Information from GeneReviews

- Lynch Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1211>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MSH6%5BTIAB%5D%29+OR+%28mutS+homolog+6%5BTIAB%5D%29%29+AND+%28g-t+mismatch-binding+protein%5BNM%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- MUIR-TORRE SYNDROME
<http://omim.org/entry/158320>
- MutS HOMOLOG 6
<http://omim.org/entry/600678>
- NEUROFIBROMATOSIS, TYPE I
<http://omim.org/entry/162200>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
<http://atlasgeneticsoncology.org/Genes/MSH6ID344ch2p16.html>
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=MSH6%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:7329
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:2956>

- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/2956>
- UniProt
<https://www.uniprot.org/uniprot/P52701>

Sources for This Summary

- Bandipalliam P. Syndrome of early onset colon cancers, hematologic malignancies & features of neurofibromatosis in HNPCC families with homozygous mismatch repair gene mutations. *Fam Cancer*. 2005;4(4):323-33. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16341812>
- Cederquist K, Emanuelsson M, Göransson I, Holinski-Feder E, Müller-Koch Y, Golovleva I, Grönberg H. Mutation analysis of the MLH1, MSH2 and MSH6 genes in patients with double primary cancers of the colorectum and the endometrium: a population-based study in northern Sweden. *Int J Cancer*. 2004 Apr 10;109(3):370-6. Erratum in: *Int J Cancer*. 2005 Jul 20;115(6):1011.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14961575>
- Chhibber V, Dresser K, Mahalingam M. MSH-6: extending the reliability of immunohistochemistry as a screening tool in Muir-Torre syndrome. *Mod Pathol*. 2008 Feb;21(2):159-64. Epub 2007 Dec 7.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18065960>
- Cohen MM Jr. Molecular dimensions of gastrointestinal tumors: some thoughts for digestion. *Am J Med Genet A*. 2003 Nov 1;122A(4):303-14. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14518068>
- Edelbrock MA, Kaliyaperumal S, Williams KJ. Structural, molecular and cellular functions of MSH2 and MSH6 during DNA mismatch repair, damage signaling and other noncanonical activities. *Mutat Res*. 2013 Mar-Apr;743-744:53-66. doi: 10.1016/j.mrfmmm.2012.12.008. Epub 2013 Feb 4. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23391514>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3659183/>
- Kohlmann W, Gruber SB. Lynch Syndrome. 2004 Feb 5 [updated 2014 May 22]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1211/>
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20301390>
- Lynch HT, de la Chapelle A. Hereditary colorectal cancer. *N Engl J Med*. 2003 Mar 6;348(10):919-32. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12621137>
- OMIM: MutS HOMOLOG 6
<http://omim.org/entry/600678>
- Pande M, Wei C, Chen J, Amos CI, Lynch PM, Lu KH, Lucio LA, Boyd-Rogers SG, Bannon SA, Mork ME, Frazier ML. Cancer spectrum in DNA mismatch repair gene mutation carriers: results from a hospital based Lynch syndrome registry. *Fam Cancer*. 2012 Sep;11(3):441-7. doi: 10.1007/s10689-012-9534-6.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/22714864>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3475767/>
- Peltomäki P. Lynch syndrome genes. *Fam Cancer*. 2005;4(3):227-32. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16136382>

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