PMS2 gene
PMS1 homolog 2, mismatch repair system component

Normal Function

The PMS2 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 PMS2 protein joins with another protein called MLH1 (produced from the MLH1 gene) to form a protein complex. This complex coordinates the activities of other proteins that repair errors made during DNA replication. Repairs are made by removing the section of DNA that contains errors and replacing it with a corrected DNA sequence. The PMS2 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 PMS2 gene have been reported in about 2 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. PMS2 gene mutations involved in this condition lead to the production of an abnormally short or inactive PMS2 protein that cannot efficiently repair errors made during DNA replication. 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.

Some mutations in the PMS2 gene can cause a variant of Lynch syndrome called Turcot syndrome. In addition to colorectal cancer, people with Turcot syndrome tend to develop a particular type of brain tumor called a glioblastoma.

Alopecia areata

Ovarian cancer

Other cancers

While Lynch syndrome is associated with a mutation in one copy of the PMS2 gene, very rarely, individuals in affected families inherit two PMS2 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 *PMS2* gene mutation have a syndrome distinct from Lynch syndrome. In addition to colorectal cancer, these individuals 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: 7p22.1, which is the short (p) arm of chromosome 7 at position 22.1

Molecular Location: base pairs 5,970,925 to 6,009,106 on chromosome 7 (Homo sapiens Updated Annotation Release 109.20191205, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

**Other Names for This Gene**

- DNA mismatch repair gene homologue
- HNPCC4
- MLH4
- PMS2-C terminal -like
- PMS2 postmeiotic segregation increased 2 (S. cerevisiae)
- PMS2_HUMAN
- PMS2CL
- PMSL2
- postmeiotic segregation increased (S. cerevisiae) 2
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=%28PMS2%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days+%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

• MISMATCH REPAIR CANCER SYNDROME
  http://omim.org/entry/276300

• NEUROFIBROMATOSIS, TYPE I
  http://omim.org/entry/162200

• PMS1 HOMOLOG 2, MISMATCH REPAIR SYSTEM COMPONENT
  http://omim.org/entry/600259

Research Resources

• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_PMS2.html

• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PMS2%5Bgene%5D

• HGNC Gene Symbol Report

• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:5395
• NCBI Gene  

• UniProt  
  https://www.uniprot.org/uniprot/P54278  

Sources for This Summary  

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  http://omim.org/entry/600259  

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