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 two-protein complex called a dimer. 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

Constitutional mismatch repair deficiency syndrome

More than 55 mutations in the PMS2 gene have been associated with a condition called constitutional mismatch repair deficiency (CMMRD) syndrome. PMS2 gene mutations are the most frequent cause of this condition. Individuals with CMMRD syndrome are at increased risk of developing cancers of the colon (large intestine) and rectum (collectively referred to as colorectal cancer), brain, and blood (leukemia or lymphoma). These cancers usually first occur in childhood, with the vast majority of cancers in CMMRD syndrome diagnosed in people under the age of 18. Many people with CMMRD syndrome also develop changes in skin coloring (pigmentation), similar to those that occur in a condition called neurofibromatosis type 1.

Individuals with CMMRD syndrome inherit two PMS2 gene mutations, one from each parent, while people with Lynch syndrome (described below) have a mutation in one copy of the PMS2 gene.

PMS2 gene mutations result in near or complete loss of PMS2 protein production. A shortage of this protein eliminates mismatch repair activity and prevents the proper repair of DNA replication errors. These errors accumulate as the abnormal cells continue to divide. The errors disrupt other genes involved in important cellular processes, such as controlling cell growth and division (proliferation). If cell growth is uncontrolled, it can lead to childhood cancer in people with CMMRD syndrome.

It is thought that the features of neurofibromatosis type 1 in people with CMMRD syndrome are due to genetic changes in the NF1 gene that result from loss of mismatch repair. These changes are present only in certain cells (somatic mutations), whereas NF1 gene mutations that are present in all cells of the body cause neurofibromatosis type 1.
Lynch syndrome

Mutations in the PMS2 gene have been reported in about 6 percent of families with Lynch syndrome that have an identified gene mutation. Lynch syndrome increases the risk of many types of cancer, particularly 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 ducts, upper urinary tract, and brain. By age 75, the risk of developing one of these cancers is 30 percent for women and 25 percent for men with a PMS2 gene mutation. These mutations lead to a form of Lynch syndrome with a lower risk of cancer development compared to other causes of this condition. Additionally, in people with a PMS2 gene mutation, cancer tends to occur at a later age compared to others with Lynch syndrome. The reason for this lower cancer risk is unclear.

PMS2 gene mutations involved in this condition lead to the production of an abnormally short or inactive PMS2 protein from one copy of the gene. The altered protein cannot efficiently repair errors made during DNA replication. The errors accumulate as the cells continue to divide, increasing the risk of tumor formation in the colon or another part of the body.

Because there is some functional PMS2 protein produced from the normal copy of the gene, mismatch repair activity in Lynch syndrome is reduced but not absent, as it is in CMMRD syndrome (described above). This difference in DNA repair activity levels likely explains why cancers in Lynch syndrome generally develop in adulthood while those in CMMRD syndrome often affect children.

Alopecia areata

Ovarian cancer

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 109.20200522, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI
Other Names for This Gene

- PMS2 postmeiotic segregation increased 2 (S. cerevisiae)
- PMS2_HUMAN
- 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

- 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

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16341812


  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4834863/


  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301390
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Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6349460/

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