CDKN2A gene

cyclin dependent kinase inhibitor 2A

Normal Function

The *CDKN2A* gene provides instructions for making several proteins. The most well-studied are the p16(INK4a) and the p14(ARF) proteins. Both function as tumor suppressors, which means they keep cells from growing and dividing too rapidly or in an uncontrolled way.

The p16(INK4a) protein attaches (binds) to two other proteins called CDK4 and CDK6. These proteins help regulate the cell cycle, which is the cell's way of replicating itself in an organized, step-by-step fashion. CDK4 and CDK6 normally stimulate the cell to continue through the cycle and divide. However, binding of p16(INK4a) blocks CDK4's or CDK6's ability to stimulate cell cycle progression. In this way, p16(INK4a) controls cell growth and division.

The p14(ARF) protein protects a different protein called p53 from being broken down. The p53 protein is an important tumor suppressor that is essential for regulating cell division and self-destruction (apoptosis). By protecting p53, p14(ARF) also helps prevent tumor formation.

Health Conditions Related to Genetic Changes

head and neck squamous cell carcinoma

Mutations in the *CDKN2A* gene are found in up to one-quarter of head and neck squamous cell carcinomas (HNSCC). This type of cancerous tumor occurs in the moist lining of the mouth, nose, and throat. *CDKN2A* gene mutations associated with this condition are acquired during a person's lifetime and are found only in tumor cells; these changes are known as somatic mutations. Most of these mutations lead to production of little or no functional p16(INK4a) protein. Without p16(INK4a) to regulate cell growth and division, cells can continue to grow and divide without control, which can lead to tumor formation.

A different type of alteration involving the *CDKN2A* gene can result in reduced amounts of the p16(INK4a) or p14(ARF) protein. This alteration, known as promoter hypermethylation, turns off the production of p16(INK4a) or p14(ARF). Without one of these tumor suppressors, cells can grow and divide unchecked, leading to the development of cancer.

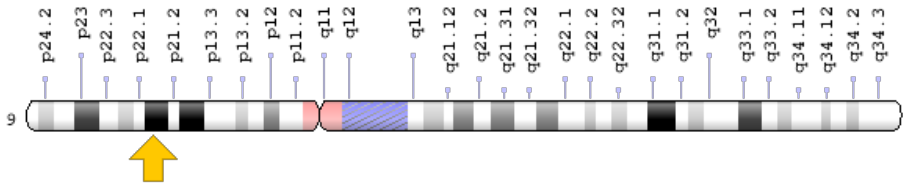
other cancers

Mutations affecting the *CDKN2A* gene are associated with other cancers, including a type of skin cancer called melanoma, breast cancer, lung cancer, and pancreatic cancer. The mutations associated with these cancers are typically inherited (called germline mutations) and are found in all cells in the body. In some families, *CDKN2A* gene mutations are associated with development of only one type of cancer. In other families, mutations can lead to a cancer predisposition syndrome, which increases the risk of developing multiple types of cancer. *CDKN2A* gene mutations involved in cancer impair production of functional p16(INK4a) or, less commonly, p14(ARF), which can result in uncontrolled cell growth and tumor formation.

Chromosomal Location

Cytogenetic Location: 9p21.3, which is the short (p) arm of chromosome 9 at position 21.3

Molecular Location: base pairs 21,967,752 to 21,995,043 on chromosome 9 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ARF
- CDK4 inhibitor p16-INK4
- CDK4I
- CDKN2
- cell cycle negative regulator beta
- CMM2
- cyclin-dependent kinase 4 inhibitor A
- cyclin-dependent kinase inhibitor 2A
- cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4)
- cyclin-dependent kinase inhibitor 2A isoform p12

- cyclin-dependent kinase inhibitor 2A isoform p14ARF
- cyclin-dependent kinase inhibitor 2A isoform p16gamma
- cyclin-dependent kinase inhibitor 2A isoform p16INK4a
- INK4
- INK4A
- MLM
- MTS-1
- MTS1
- multiple tumor suppressor 1
- P14
- P14ARF
- P16
- P16-INK4A
- P16INK4
- P16INK4A
- P19
- P19ARF
- TP16

Additional Information & Resources

Educational Resources

- Molecular Cell Biology (fourth edition, 2000): Loss-of-Function Mutations in Tumor-Suppressor Genes Are Oncogenic
  https://www.ncbi.nlm.nih.gov/books/NBK21662/#_A7100_

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CDKN2A%5BTI%5D%29+OR+%28cyclin-dependent+kinase+inhibitor+2A%5BTI%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+720+days%22%5Bdp%5D

OMIM

- CYCLIN-DEPENDENT KINASE INHIBITOR 2A
  http://omim.org/entry/600160
- MELANOMA-ASTROCYTOMA SYNDROME
  http://omim.org/entry/155755
- MELANOMA-PANCREATIC CANCER SYNDROME
  http://omim.org/entry/606719
- MELANOMA, CUTANEOUS MALIGNANT, SUSCEPTIBILITY TO, 2
  http://omim.org/entry/155601
- PANCREATIC CANCER
  http://omim.org/entry/260350

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/CDKN2aID146.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=CDKN2A%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=1787
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/1029
- UniProt: ARF_HUMAN
  http://www.uniprot.org/uniprot/Q8N726
- UniProt: CDN2A_HUMAN
  http://www.uniprot.org/uniprot/P42771

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