

NPM1 gene

nucleophosmin 1

Normal Function

The *NPM1* gene provides instructions for making a protein called nucleophosmin, which is found in a small region inside the nucleus of the cell called the nucleolus. Nucleophosmin shuttles back and forth between the nucleus and the fluid surrounding it (the cytoplasm). It is thought to play a part in many cellular functions, including processes involved in protein formation, DNA replication, and the progression of the cell through the step-by-step process it takes to replicate itself (called the cell cycle). In the nucleolus, nucleophosmin attaches to another protein called ARF, keeping it in the proper location and protecting it from being broken down. The ARF protein is considered a tumor suppressor because it is involved in pathways that prevent cells from growing and dividing in an uncontrolled way.

Health Conditions Related to Genetic Changes

Acute promyelocytic leukemia

MedlinePlus Genetics provides information about Acute promyelocytic leukemia

Cytogenetically normal acute myeloid leukemia

Mutations in the *NPM1* gene are involved in a form of blood cell cancer known as cytogenetically normal acute myeloid leukemia (CN-AML). While large chromosomal abnormalities can be involved in the development of acute myeloid leukemia, about half of cases do not have these abnormalities; these are classified as CN-AML. Approximately 64 percent of people with CN-AML have a mutation in the *NPM1* gene.

The *NPM1* gene mutations involved in CN-AML are called somatic mutations; they are found only in cells that become cancerous and are not inherited. These mutations occur in a region of the gene designated exon 12. They change the blueprint used to make the nucleophosmin protein, leading to production of a protein with an altered sequence of protein building blocks (amino acids). The alterations change the amino acid tryptophan at protein position 290 and often the tryptophan at position 288. These two tryptophans are important for localization of the protein in the nucleolus. The new sequence also provides a signal (called the nuclear export signal) for the protein to be moved out of the nucleus. As a result, the nucleophosmin protein is found in the

cytoplasm rather than the nucleolus.

It is not clear how abnormal localization of the nucleophosmin protein leads to acute myeloid leukemia. Research suggests that it affects the function of the ARF protein. Because of its interaction with the altered nucleophosmin, the ARF protein is also found in the cytoplasm in cells with these genetic changes. In addition, the altered nucleophosmin protein is unable to protect ARF from being broken down. A reduction of the tumor suppressor function of the ARF protein is believed to lead to the uncontrolled production of abnormal white blood cells that occurs in acute myeloid leukemia. Other effects of *NPM1* gene mutations may also be involved in the development of leukemia.

Other cancers

A genetic rearrangement (translocation) involving the *NPM1* gene is found in another blood cell cancer known as anaplastic large cell lymphoma (ALCL). In ALCL, white blood cells known as T cells grow and divide uncontrollably and often form tumors in the lymph nodes. The translocation involved in this cancer, known as t(2;5), fuses part of the *NPM1* gene on chromosome 5 with part of another gene called *ALK* on chromosome 2. This rearrangement is a somatic mutation.

The protein produced from the fusion gene is called NPM-ALK. Like the normal activated ALK protein, NPM-ALK turns on signaling pathways that stimulate cell growth and division (proliferation) and maturation (differentiation). Unlike ALK, the NPM-ALK protein is active all the time, which causes uncontrolled cell proliferation and leads to ALCL.

Other Names for This Gene

- B23
- NPM
- NPM_HUMAN
- nucleolar protein NO38
- nucleophosmin
- nucleophosmin (nucleolar phosphoprotein B23, numatrin)
- nucleophosmin/nucleoplasmin family, member 1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of NPM1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4869\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4869[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28NPM1%5BTI%5D%29+>

OR+%28nucleophosmin%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+360+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- NUCLEOPHOSMIN/NUCLEOPLASMIN FAMILY, MEMBER 1; NPM1 (<https://omim.org/entry/164040>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/4869>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=NPM1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=NPM1[gene]))

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Genomic Location

The *NPM1* gene is found on chromosome 5 (<https://medlineplus.gov/genetics/chromosome/5/>).

Last updated January 1, 2014