NBN gene

nibrin

Normal Function

The *NBN* gene provides instructions for making a protein called nibrin. This protein is involved in several critical cellular functions, including the repair of damaged DNA.

Nibrin interacts with two other proteins, produced from the *MRE11A* and *RAD50* genes, as part of a larger protein complex. Nibrin regulates the activity of this complex by carrying the MRE11A and RAD50 proteins into the cell's nucleus and guiding them to sites of DNA damage. The proteins work together to mend broken strands of DNA. DNA can be damaged by agents such as toxic chemicals or radiation, and breaks in DNA strands also occur naturally when chromosomes exchange genetic material in preparation for cell division. Repairing DNA prevents cells from accumulating genetic damage that may cause them to die or to divide uncontrollably.

The MRE11A/RAD50/NBN complex interacts with the protein produced from the *ATM* gene, which plays an essential role in recognizing broken strands of DNA and coordinating their repair. The MRE11A/RAD50/NBN complex helps maintain the stability of a cell's genetic information through its roles in repairing damaged DNA and regulating cell division. Because these functions are critical for preventing the formation of cancerous tumors, nibrin is described as a tumor suppressor.

Health Conditions Related to Genetic Changes

Nijmegen breakage syndrome

At least 10 mutations in the *NBN* gene have been found to cause Nijmegen breakage syndrome, a condition characterized by slow growth, recurrent infections, and an increased risk of developing cancer. The *NBN* gene mutations that cause Nijmegen breakage syndrome typically lead to the production of an abnormally short version of the nibrin protein. The mutation found in most affected individuals, particularly in Slavic populations of Eastern Europe, deletes five DNA building blocks (nucleotides) from the *NBN* gene (written as 657_661del5). This mutation leads to the production of a shortened version of the nibrin protein called p70-nibrin. This shortened protein is not as effective as normal nibrin in responding to DNA damage, but p70-nibrin does appear to have some residual function.

When breaks in DNA are not repaired properly, genetic damage can accumulate. A buildup of errors in DNA can trigger cells to grow and divide abnormally, increasing the risk of cancer in people with Nijmegen breakage syndrome. Nibrin's role in regulating cell division and cell growth (proliferation) is thought to lead to the problems with the immune system that are seen in affected individuals. A lack of functional nibrin results in less immune cell proliferation. A decrease in the amount of immune cells that are produced leads to a malfunctioning immune system. It is unclear how mutations in the *NBN* gene cause the other features of Nijmegen breakage syndrome.

Breast cancer

Inherited mutations in the *NBN* gene, including the c.657_661del5 mutation described above, have also been associated with several other types of cancer. Studies in Eastern European populations reported that people with mutations in one copy of the *NBN* gene in each cell may be more likely to develop breast cancer than people who do not carry *NBN* mutations. Cells with a mutation in one copy of the *NBN* gene do not repair DNA as effectively as cells without these mutations. It is thought that DNA damage accumulates over time, which can trigger cells to grow and divide uncontrollably and increase the risk of developing cancer.

Ovarian cancer

Inherited mutations in the *NBN* gene, including the c.657_661del5 mutation described above, have also been associated with several other types of cancer. Studies in Eastern European populations reported that people with mutations in one copy of the *NBN* gene in each cell may be more likely to develop ovarian cancer than people who do not carry *NBN* mutations. Cells with a mutation in one copy of the *NBN* gene do not repair DNA as effectively as cells without these mutations. It is thought that DNA damage accumulates over time, which can trigger cells to grow and divide uncontrollably and increase the risk of developing cancer.

Prostate cancer

Inherited mutations in the *NBN* gene, including the c.657_661del5 mutation described above, have also been associated with several other types of cancer. Studies in Eastern European populations reported that people with mutations in one copy of the *NBN* gene in each cell may be more likely to develop prostate cancer than people who do not carry *NBN* mutations. Cells with a mutation in one copy of the *NBN* gene do not repair DNA as effectively as cells without these mutations. It is thought that DNA damage accumulates over time, which can trigger cells to grow and divide uncontrollably and increase the risk of developing cancer.

Other cancers

Inherited mutations in the *NBN* gene, including the c.657_661del5 mutation described above, have also been associated with several other types of cancer. Studies in Eastern European populations reported that people with mutations in one copy of the *NBN* gene in each cell may be more likely to develop an aggressive form of skin cancer (

melanoma) or cancer of blood-forming cells (leukemia) than people who do not carry *NBN* mutations. Cells with a mutation in one copy of the *NBN* gene do not repair DNA as effectively as cells without these mutations. It is thought that DNA damage accumulates over time, which can trigger cells to grow and divide uncontrollably and increase the risk of developing cancer.

Other Names for This Gene

- AT-V1
- AT-V2
- ATV
- Cell cycle regulatory protein p95
- NBN_HUMAN
- NBS
- NBS1
- Nijmegen breakage syndrome 1
- p95 protein of the MRE11/RAD50 complex

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of NBN (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4683[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28NBN%5BTIAB%5D%29+OR+%28nibrin%5BTIAB%5D%29+OR+%28NBS1%5BTIAB%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+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- NIBRIN; NBN (https://omim.org/entry/602667)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4683)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=NBN[gene])

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Genomic Location

The *NBN* gene is found on chromosome 8 (https://medlineplus.gov/genetics/chromosome/8/).

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