XPA gene

XPA, DNA damage recognition and repair factor

Normal Function

The *XPA* gene provides instructions for making a protein that is involved in repairing damaged DNA. DNA can be damaged by ultraviolet (UV) rays from sunlight and by toxic chemicals, radiation, and unstable molecules called free radicals.

DNA damage occurs frequently, but normal cells are usually able to fix it before it can cause problems. One of the major mechanisms that cells use to fix DNA is known as nucleotide excision repair (NER). As part of this repair mechanism, the XPA protein helps verify DNA damage and stabilize the DNA as it is repaired. The XPA protein attaches (binds) to areas of damaged DNA, where it interacts with many other proteins as part of a large complex. Proteins in this complex unwind the section of DNA where the damage has occurred, snip out (excise) the abnormal section, and replace the damaged area with the correct DNA.

Health Conditions Related to Genetic Changes

Xeroderma pigmentosum

Many variants (also called mutations) in the *XPA* gene have been found to cause xeroderma pigmentosum. People with this condition have an extreme sensitivity to UV rays from sunlight. As a result, affected individuals have a high risk of sunlight-induced cancer and premature aging.

XPA gene variants are responsible for a very severe form of xeroderma pigmentosum that is more common in the Japanese population than in other populations. Most Japanese people with xeroderma pigmentosum have the same *XPA* gene variant, which is written as IVS3AS, G>C. This variant prevents cells from producing any functional XPA protein. Other *XPA* gene variants, which have been reported in Japan and elsewhere, result in the production of a nonfunctional version of the XPA protein or greatly reduce the amount of this protein that is made in cells.

A partial or total loss of the XPA protein prevents cells from repairing DNA damage normally. As damage builds up in DNA, cells malfunction and eventually become cancerous or die. These problems with DNA repair cause people with xeroderma pigmentosum to be extremely sensitive to UV rays. When UV rays damage genes that

control cell growth and division, cells can grow too fast and in an uncontrolled way. This uncontrolled cell growth can lead to cancer. In people with xeroderma pigmentosum, these cancers occur most frequently in areas of the body that are exposed to the sun, such as the skin and eyes.

When xeroderma pigmentosum is caused by *XPA* gene variants, it is often associated with progressive neurological abnormalities. These nervous system problems include hearing loss, poor coordination, difficulty walking, movement problems, loss of intellectual function, difficulty swallowing and talking, and seizures. The neurological abnormalities are thought to result from a buildup of DNA damage, although the brain is not exposed to UV rays. Researchers suspect that other factors damage DNA in nerve cells. It is unclear why some people with xeroderma pigmentosum develop neurological abnormalities and others do not.

Other Names for This Gene

- xeroderma pigmentosum, complementation group A
- XP1
- XPA_HUMAN
- XPAC

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of XPA (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7507[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28XPA%5BTIAB%5D%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

- XPA, DNA DAMAGE RECOGNITION AND REPAIR FACTOR; XPA (https://omim.org/entry/611153)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7507)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=XPA[gene])

References

- Camenisch U, Nageli H. XPA gene, its product and biological roles. Adv Exp MedBiol. 2008;637:28-38. doi: 10.1007/978-0-387-09599-8_4. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19181108)
- Cleaver JE, States JC. The DNA damage-recognition problem in human and othereukaryotic cells: the XPA damage binding protein. Biochem J. 1997 Nov 15;328 (Pt1)(Pt 1):1-12. doi: 10.1042/bj3280001. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/9359827) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1218880/)
- Cleaver JE, Thompson LH, Richardson AS, States JC. A summary of mutations inthe UV-sensitive disorders: xeroderma pigmentosum, Cockayne syndrome, andtrichothiodystrophy. Hum Mutat. 1999;14(1):9-22. doi:10.1002/(SICI)1098-1004(1999)14:13.0.CO;2-6. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10447254)
- Hirai Y, Kodama Y, Moriwaki S, Noda A, Cullings HM, Macphee DG, Kodama K, Mabuchi K, Kraemer KH, Land CE, Nakamura N. Heterozygous individuals bearing afounder mutation in the XPA DNA repair gene comprise nearly 1% of the Japanesepopulation. Mutat Res. 2006 Oct 10;601(1-2):171-8. doi:10.1016/j.mrfmmm.2006.06.010. Epub 2006 Aug 14. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16905156)
- Jones CJ, Wood RD. Preferential binding of the xeroderma pigmentosum group Acomplementing protein to damaged DNA. Biochemistry. 1993 Nov 16;32(45):12096-104.doi: 10.1021/bi00096a021. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/8218288)
- Satokata I, Iwai K, Matsuda T, Okada Y, Tanaka K. Genomic characterization ofthe human DNA excision repair-controlling gene XPAC. Gene. 1993 Dec22;136(1-2):345-8. doi: 10.1016/0378-1119(93)90493-m. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/8294029)

Genomic Location

The *XPA* gene is found on chromosome 9 (https://medlineplus.gov/genetics/chromosome/9/).

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