



IKBKG gene

inhibitor of nuclear factor kappa B kinase subunit gamma

Normal Function

The *IKBKG* gene provides instructions for producing one piece (subunit) of the IKK protein complex, which is a group of related proteins that regulates the activity of nuclear factor-kappa-B. Nuclear factor-kappa-B is a protein complex that binds to DNA and controls the activity of other genes. When it is turned off (inactive), nuclear factor-kappa-B is attached (bound) to the IKK complex. In response to certain signals, the IKK complex turns on (activates) nuclear factor-kappa-B and releases it.

The IKBKG protein plays a regulatory role in the IKK complex. Once the IKBKG protein is turned on (activated), it activates the other proteins in the complex, which in turn activates and releases nuclear factor-kappa-B. The activated factor then moves into the nucleus and binds to DNA. Nuclear factor-kappa-B regulates the activity of multiple genes, including genes that control the body's immune responses and inflammatory reactions. Nuclear factor-kappa-B also appears to play a role in the signaling pathway that is critical for the formation of ectodermal tissues including the skin, hair, teeth, and sweat glands. In addition, it protects the cell from certain signals that would otherwise cause it to self-destruct (undergo apoptosis).

Health Conditions Related to Genetic Changes

Anhidrotic ectodermal dysplasia with immune deficiency

More than 20 mutations in the *IKBKG* gene have been found to cause anhidrotic ectodermal dysplasia with immune deficiency (EDA-ID). EDA-ID is a condition characterized by reduced function of the immune system, resulting in recurrent infections, and abnormal development of ectodermal tissues. The *IKBKG* gene mutations that cause EDA-ID impair the function of the IKBKG protein but do not completely eliminate its ability to regulate nuclear factor-kappa-B. These changes disrupt certain signaling pathways within immune cells and cells that form ectodermal tissues, resulting in immune deficiency and incomplete development of tissues of the ectoderm. The severity of the signs and symptoms of EDA-ID depends on the amount of protein function remaining; a greater level of protein function is associated with milder disease.

Incontinentia pigmenti

More than 30 mutations in the *IKBKG* gene have been identified in people with incontinentia pigmenti, a condition characterized by skin, teeth, and nail abnormalities as well as vision loss and hair loss. The most common mutation, a complex rearrangement that deletes some genetic material from the *IKBKG* gene, accounts

for more than 80 percent of all cases of the condition. This mutation probably leads to the production of an abnormally small, nonfunctional version of the *IKBK*G protein. Other people with incontinentia pigmenti have mutations that prevent the production of any *IKBK*G protein. Without this protein, nuclear factor-kappa-B cannot be activated. Cells without active nuclear factor-kappa-B are more sensitive to signals that trigger them to self-destruct. The resulting abnormal cell death likely leads to the signs and symptoms of incontinentia pigmenti.

Osteopetrosis

Several mutations in the *IKBK*G gene have been found to cause a rare form of osteopetrosis with an X-linked pattern of inheritance. Researchers often refer to this condition as OL-EDA-ID, an acronym derived from each of the major features of the disorder. In addition to the abnormally dense bones characteristic of osteopetrosis, OL-EDA-ID is associated with abnormal swelling caused by a buildup of fluid (lymphedema) and anhidrotic ectodermal dysplasia, which affects the skin, hair, teeth, and sweat glands. Affected individuals also have immune deficiency, which allows severe, recurrent infections to develop.

The mutations responsible for OL-EDA-ID impair the normal function of the *IKBK*G protein, which reduces activation of nuclear factor-kappa-B. These changes disrupt certain signaling pathways within immune cells and cells that form ectodermal tissues, resulting in immunodeficiency and incomplete development of tissues of the ectoderm. It is unclear how *IKBK*G mutations lead to the other features of OL-EDA-ID, although the signs and symptoms are likely caused by abnormal nuclear factor-kappa-B signaling in other types of cells, including bone forming cells.

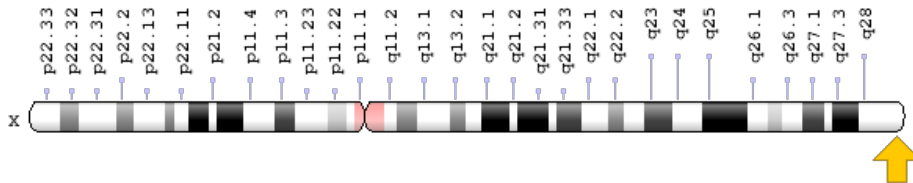
Other disorders

*IKBK*G gene mutations also account for some cases of a condition known as X-linked susceptibility to mycobacterial disease. People with this condition have an increased risk of infection with forms of bacteria called mycobacteria. Some of these foreign invaders are described as "opportunistic" organisms because they do not cause illness in people with a normal immune system. Another type of mycobacterium causes tuberculosis, a respiratory disease that can be serious or life-threatening. The *IKBK*G gene mutations responsible for X-linked susceptibility to mycobacterial disease alter the structure of the *IKBK*G protein. The defective protein disrupts certain signaling pathways within immune cells, which prevents the immune system from defending the body effectively against mycobacterial infection.

Chromosomal Location

Cytogenetic Location: Xq28, which is the long (q) arm of the X chromosome at position 28

Molecular Location: base pairs 154,542,212 to 154,565,046 on the X chromosome (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- FIP-3
- FIP3
- Fip3p
- IKK-gamma
- inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase gamma
- IP2
- NEMO
- NEMO_HUMAN
- NF-kappa-B essential modulator
- ZC2HC9

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): Multiple Stressful and Proinflammatory Stimuli Act Through an NF- κ B-Dependent Signaling Pathway
<https://www.ncbi.nlm.nih.gov/books/NBK26918/#A2894>

Clinical Information from GeneReviews

- Incontinentia Pigmenti
<https://www.ncbi.nlm.nih.gov/books/NBK1472>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28IKBKG%5BTIAB%5D%29+OR+%28%28IKK-gamma%5BTIAB%5D%29+OR+%28NEMO%5BTIAB%5D%29+OR+%28NF-kappa-B+essential+modulator%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+720+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- IMMUNODEFICIENCY 33
<http://omim.org/entry/300636>
- INHIBITOR OF KAPPA LIGHT POLYPEPTIDE GENE ENHANCER IN B CELLS, KINASE OF, GAMMA
<http://omim.org/entry/300248>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_IKBKG.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=IKBKG%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report#!/hgnc_id/HGNC:5961
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:8517>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/8517>
- UniProt
<https://www.uniprot.org/uniprot/Q9Y6K9>

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Reprinted from Genetics Home Reference:
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Reviewed: August 2013
Published: November 12, 2019

Lister Hill National Center for Biomedical Communications
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