IKBKG gene

inhibitor of nuclear factor kappa B kinase regulatory 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 the protein complex is in the resting state (inactive), nuclear factor-kappa-B and the IKK complex are attached (bound) together. In response to certain chemical signals, the IKK complex releases nuclear factor-kappa-B.

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 releases nuclear factor-kappa-B. The loose nuclear factor-kappa-B 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

Variants (also called 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 abnormal development of ectodermal tissues. In addition, immune system function is reduced in people with EDA-ID, resulting in recurrent infections.

The *IKBKG* gene variants 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.This impairs the immune system and disrupts the development of ectodermal tissues.

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 typically associated with milder disease.

Some people with EDA-ID have unusually dense bones (osteopetrosis) and swelling (lymphedema). This is sometimes referred to as OL-EDA-ID; the acronym is derived from each of the major features of the disorder. It is unclear how variants in the *IKBKG* gene contribute to osteopetrosis and lymphedema in EDA-ID.

Incontinentia pigmenti

Variants in the *IKBKG* gene have been identified in people with incontinentia pigmenti, a condition characterized by skin, tooth, and nail abnormalities as well as increased risks of stroke and vision loss.

The most common *IKBKG* gene change is a complex rearrangement that deletes some genetic material from the *IKBKG* gene. This change accounts for more than 60 to 80 percent of all cases of the condition. This common change probably leads to the production of an abnormally small, nonfunctional version of the IKBKG protein.

Other *IKBKG* gene variants that cause incontinentia pigmenti prevent the production of any IKBKG 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.

Other disorders

IKBKG gene variants may 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 *IKBKG* gene variants associated with X-linked susceptibility to mycobacterial disease alter the structure of the IKBKG protein. The defective protein disrupts certain signaling pathways within immune cells, which prevents the immune system from defending the body effectively against mycobacterial infection.

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

Tests Listed in the Genetic Testing Registry

- Tests of IKBKG (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=8517[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?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; IMD33 (https://omim.org/entry/300636)
- INHIBITOR OF NUCLEAR FACTOR KAPPA-B KINASE, REGULATORY SUBUNIT GAMMA; IKBKG (https://omim.org/entry/300248)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/8517)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=IKBKG[gene])

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Genomic Location

The *IKBKG* gene is found on the X chromosome (https://medlineplus.gov/genetics/chromosome/x/).

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