X-linked hyper-IgM syndrome and hypohydrotic ectodermal dysplasia (Nemo deficiency)

GENERAL INFORMATION

Description:

Defects in IKBKG, a modulator of NF-kB activation, are the cause of anhidrotic (hypohidrotic) ectodermal dysplasia with immunodeficiency (specific antibody deficiency), characterized by absence of sweat glands, sparse scalp hair, rare conical teeth and immunological abnormalities (lack of antibody response to plysaccharides) resulting in severe infectious diseases (mycobacteria and pyogens).

Alternative names:

- EDA-ID, HED-ID
- XHM-ED
- Nemo deficiency
- X-linked anhidrotic ectodermal dysplasia with immunodeficiency

Classification:

- Defects of innate immune system, receptors and signaling components

Inheritance:

X-linked

OMIM:

- #300291 Ectodermal dysplasia, hypohidrotic, with immune deficiency
- *300248 Inhibitor of kappa light polypeptide gene enhancer in B cells, kinase of, gamma; IKBKG

Cross references:

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Nemo defect affects multiple organs and presents with vesiculo-bullous lesions with erythema with linear arrangement on the extremities and lateral aspects of the trunk. These bullous and erythematous lesions evolve into verrucous lessions after weeks to month, and then are followed by atrophy or depigmentation with a slate-brown or blue-gray pigmentation. In adulthood, there are hypopigmented linear macules on the extremities and the trunk with a lack of skin appendages. This disorder is usually prenatally lethal in males and contributes to abnormalities of skin, hair, nails, teeth and central nervous system in carrier females.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Ectodermal dysplasia anhidrotica, ORPHANET
- Combined B-cell and T-cell disorders, eMedicine

Therapeutic options:

- Combined B-cell and T-cell disorders, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies
- Human Pigmentation Disorder Linked to Genetic Defect in Inflammatory Pathway
- Genetic and biochemical analysis of the NF-kB signalling pathway

GENE INFORMATION

Names:

HUGO name: IKBKG
Alias(es): FIP-3, FIP3, Fip3p, IKK-gamma, IP2, NEMO, inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase gamma, NF-kappaB essential modulator, NF-kappaB essential modifier, Inhibitor of nuclear factor kappa-B kinase gamma subunit, IkB kinase gamma subunit, I-kappa-B kinase gamma, IKKG, IkB kinase-associated protein 1, IKKAP1, FIP-3

Localization:

Reference sequences:

DNA: AJ271718 (EMBL) , **cDNA:** AF091453 (EMBL) , **Protein:** Q9Y6K9 (SWISSPROT)

Chromosomal Location:

Xq28

Maps:

IKBKG (Map View)

Variations / Mutations:

- IKBKGbase; Mutation registry for Nemo deficiency

Other gene-based resources:

Ensembl: ENSG00000073009, GENATLAS: IKBKG, GeneCard: IKBKG, UniGene: 43505, Entrez Gene: 8517, euGenes: 8517

PROTEIN INFORMATION

Description:

Protein function:

Regulatory subunit part of the IKK-signalosome complex activation. Also considered to be a mediator for TAX activation of NF-kappa-B. Could be implicated in NF-kappa-B-mediated protection from cytokine toxicity

Subunit:

Interacts preferentially with IKK-beta but also able to interact with IKK-alpha, IKAP, TAX, RIP and MAP3k14/NIK. Binds to T-cell leukemia virus type I TAX oncoprotein.

Subcellular location:

Cytoplasmic and nuclear

Domains:

Coiled coil domain: 49-356

Leucine-zipper domain: 322-343

Other features:

Other related resourses:

InterPro: IPR000822; Znf_C2H2, Pfam: PF00096; zf-C2H2

Expression pattern for human:

Tissue	Exp. (%)	Clones
skin, melanocyte	22.39	1:520
fibrosarcoma	12.47	2:1867
T cells from T cell leukemia	9.71	2:2397
B cells from Burkitt lymphoma	5.43	1:2143
ovary (pool of 3)	5.32	2:4380
leukocyte	5.18	4:8982
esophagus	3.95	1:2949
human optic nerve	2.64	1:4406
leukopheresis	2.55	1:4557
germ cell	2.32	4:20077

Animal models:

Mouse:

MGD: ; Ikbkg

Fly:

euGenes: ; CG10535

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- March of Dimes Birth Defects Foundation
- NIH/National Institute of Allergy and Infectious Diseases
- European Society for Immunodeficiencies

Disease specific:

- Ectodermal Dysplasia Society
- National Foundation for Ectodermal Dysplasia
- The CaF Directory

Other information sources:

- NEMO, Cytokine Encyclopaedia