Autosomal dominant anhidrotic ectodermal dysplasia and T-cell immunodeficiency

GENERAL INFORMATION

Description:

X-linked anhidrotic ectodermal dysplasia with immunodeficiency is caused by mutations in NEMO/IKKgamma, the regulatory subunit of the IkB kinase complex. Autosomal-dominant form of EDA-ID is associated with a mutation in NFKBIA. The disease is characterised by severe bacterial infections and a severe and unique T -cell deficiency. There is a marked lymphocytosis, no detectable memory T cells in vivo, and naive T cells do not respond to CD3-TCR activation in vitro.

Alternative names:

- ED3
- Anhidrotic ectodermal dysplasia with T cell deficiency

Classification:

- Defects of innate immune system, receptors and signaling components

Inheritance:

Autosomal dominant

OMIM:

- #129490 Ectodermal dysplasia 3, anhidrotic; ED3
- *164008 Nuclear factor of kappa light chain gene enhancer in B cells inhibitor, alpha; NFKBIA
- #300291 Ectodermal dysplasia, hypohidrotic, with immune deficiency

Cross references:

Phenotype related immunodeficiencies:

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

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients present impaired development of skin appendices, resulting in sparse hair, conical teeth, and anhidrosis/hypohidrosis. Host defense is also impaired and the patients can have multiple and severe bacterial disease.

Diagnosis:

Therapeutic options:

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

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies, coord. Edvart Smith
- Human Pigmentation Disorder Linked to Genetic Defect in Inflammatory Pathway, National Institute of Environmental Health Sciences, USA
- Genetic and biochemical analysis of the NF-kB signalling pathway, Courtois G. et al, France

GENE INFORMATION

Names:

HUGO name: NFKBIA
Alias(es): IKBA, MAD-3, MAD3, NFKBI, Nuclear factor of kappa light chain gene enhancer in B-cells, Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha, NF-kappaB inhibitor alpha , Major histocompatibility complex enhancer- binding protein MAD3 , I-kappa-B-alpha, IkappaBalpha, IKB-alpha

Localization:

Reference sequences:

DNA: M69043 (EMBL) AJ249294 (EMBL) AY033600 (EMBL) BC002601 (EMBL) BC004983 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** P25963 (SWISSPROT) Other Sequences

Chromosomal Location:

14q13

Maps:

NFKBIA (Map View)

Markers:

D14S1326, RH69167, G44344, GDB:366518

Variations / Mutations:

- NFKBIAbase; Mutation registry for Autosomal dominant anhidrotic ectodermal dysplasia and T-cell immunodeficiency

Other gene-based resources:

Ensembl: ENSG00000100906, GENATLAS: NFKBIA, GeneCard: NFKBIA, UniGene: 81328, Entrez Gene: 4792, euGenes: 4792, GDB: 131399, HomoloGene: 7863

PROTEIN INFORMATION

Description:

Protein function:

Inhibits NF-kappa-B by complexing with and trapping it in the cytoplasm. May be involved in regulation of transcriptional responses to NF-kappa-B, including cell adhesion, immune and proinflammatory responses, apoptosis, differentiation and growth. Controlled by sequential serine-phosphorylation, ubiquitination and degradation. Tyrosine-phosphorylation could only lead to dissociation from NF-kappa-B.

Subunit:

Interacts with p65.

Subcellular location:

Cytoplasmic

Post-translational modification:

Phosphorylated; disables inhibition of NF-kappa-B DNA-binding activity.

Induction:

Induced in adherent monocytes.

Similarity:

Belongs to the NF-kappa-B inhibitor family.

Other features:

Ubiquitin binding site: 21

Ubiquitin binding site: 22

Other related resourses:

PIR: A39935, InterPro: IPR002110; ANK, Pfam: PF00023; ank, SMART: SM00248; ANK, PROSITE: PS50088; ANK_REPEAT, PROSITE: PS50297; ANK_REP_REGION

Expression pattern for human:

Tissue	Exp. (%)	Clones
Fetal pancreas (4 Pooled Donors, 18 - 20 weeks, Stratagene #738023)	92.14	1:2
larynx	0.48	2:771
eye	0.40	1:463
lymph node	0.22	9:7498
two pooled squamous cell carcinomas	0.22	4:3340
Placenta cot 25-normalized	0.21	28:24002
lung tumor	0.21	2:1790
glioblastoma without EGFR amplification	0.20	1:929
placenta	0.19	6:5763
cord blood	0.19	7:6733
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Animal models:

Mouse:

MGD: ; Nfkbia, NCBI Gene: ; 18035 (91.72 % aminoacid similarity to human)

Rat:

NCBI Gene: ; 25493 (91.72 % aminoacid similarity to human)

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- European Society for Immunodeficiencies

Disease specific:

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