STAT3 deficiency

GENERAL INFORMATION

Description:

Hyper IgE syndrome is a rare complex disorder characterised by markedly elevated serum IgE levels (>2000IU/ml), chronic dermatitis and serious recurrent infections, pneumonia with pneumatocele formation, recurring staphylococcal skin abcesses. There may be IgG subclass and specific antibody deficiencies, with poor/absent immunization responses. Also have been reported variable abnormalities of neutrophil function, affecting chemotaxis, phagocytosis, and microbicidal activity. There is an imbalance of cytokine production due to Th2 predominance (IL-4, IL-5). Most cases are sporadic, but both autosomal recessive forms (AR-HIES) and autosomal dominant forms of HIES (AD-HIES) have been described. AR-HIES forms are characterized by severe recurrent viral infections, extreme eosinophilia, neurological complications, but without skeletal or dental abnormalities. AD-HIES are associated with skeletal symptoms such as hyperextensibility of joints, scoliosis, osteoporosis, and retained primary teeth.

Alternative names:

- AD-HIES, Job syndrome
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Classification:

- Other well-defined immunodeficiency syndromes

Inheritance:

Autosomal dominant, many de novo mutations

OMIM:

- *102582 Signal transducer and activator of transcription 3; STAT3
- %147060 Hyper-IgE syndrome
- 243700 Job syndrome

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Hyper-IgE recurrent infection syndrome
- IDR factfile for TYK2 deficiency

Incidence:

1:1000000

CLINICAL INFORMATION

Description:

Patients with STAT3 deficiency have skeletal/ dental abnormalities, skin abcesses, cyst-forming pneumonia and highly elevated serum IgE.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Job syndrome, ORPHANET
- Job Syndrome, eMedicine
- Hyperimmunoglobulinemia E, eMedicine

Genetic:

- STAT3, IDdiagnostics

Therapeutic options:

- Intravenous immunoglobulins should be used for the antibody deficiency. Antibiotic therapy (10-14 days) together with physiotherapy and postural drainage in case of lung damage. Ciprofloxacin is a valuable antibiotic but is not licensed for small children. Oral poliovaccine should not be given because there is risk of paralytic disease.
- Hyperimmunoglobulinemia E (Job) Syndrome, eMedicine
- Job Syndrome, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies.

GENE INFORMATION

Names:

HUGO name: STAT3

Localization:

Reference sequences:

DNA: D0128 (IDRefSeq) , **cDNA:** L29277 (EMBL) , **Protein:** P40763 (SWISSPROT) Other Sequences

Chromosomal Location:

17q21

Maps:

STAT3 (Map View)

Variations / Mutations:

- STAT3base; Mutation registry for STAT3 deficiency

Other gene-based resources:

Ensembl: ENSG00000168610, GENATLAS: STAT3, GeneCard: STAT3, UniGene: 463059 , Entrez Gene: 6774, euGenes: 463059, GDB: 358950, HomoloGene: 6774

PROTEIN INFORMATION

Description:

Protein function:

Transcription factor that binds to the interleukin-6 (IL-6)-responsive elements identified in the promoters of various acute-phase protein genes. Activated by il31 through il31ra

Subunit:

Forms a homodimer or a heterodimer with a related family member (at least STAT1). Interacts with NCOAL, PELP1, SOCS7 and STATIP1. Interacts with HCV core protein. Interacts with IL23r in presence of IL23. Interacts with IL31ra

Subcellular location:

Cytoplasm. Nucleus. Note=translocated into the nucleus in response to phosphorylation

Post-translational modification:

Tyrosine phosphorylated in response to IL-6, IL-11, CNTF, LIF, CSF-1, EGF, PDGF, IFN-alpha and OSM. Phosphorylated on serine upon DNA damage, probably by ATM or ATR. Serine phosphorylation is important for the formation of stable DNA-binding STAT3 homodimers and maximal transcriptional activity

Protein function:

Event=alternative splicing; named isoforms=2; name=1; isoid=p40763-1; sequence=displayed; name=del-701; isoid=p40763-2; sequence=vsp_010474;

Miscellaneous:

Involved in the GP130-mediated signaling pathway

Tissue specificity:

Heart, brain, placenta, lung, liver, skeletal muscle, kidney and pancreas

Similarity:

Belongs to the transcription factor STAT family

Domains:

SH2 domain: 580-670

Other features:

Signal transducer and activator of transcription 3: 1-770

Other related resourses:

PIR: A54444, InterPro: IPR011992; EF-Hand_type, InterPro: IPR000980; SH2, InterPro: IPR001217; STAT, InterPro: IPR013800; STAT_alpha, InterPro: IPR013801; STAT_DNA_bd, InterPro: IPR012345; STAT_DNA_bd_sub, InterPro: IPR013799; STAT_protein_interaction, Pfam: PF00017; SH2, Pfam: PF01017; STAT_alpha, Pfam: PF02864; STAT_bind, Pfam: PF02865; STAT_int, SMART: SM00252; SH2, PROSITE: PS50001; SH2

Expression pattern for human:

Tissue	Exp. (%)	Clones
mouth	12.35	49:42918
trachea	7.21	34:51029
dorsal_root_ganglion	6.43	5:8404
spleen	5.97	27:48893
nerve	4.15	6:15651
thymus	3.84	27:76036
rectum	3.65	2:5929
salivary_gland	3.38	6:19187
thyroid	3.37	3:9629
tonsil	3.06	5:17653

Animal models:

Mouse:

MGD: ; Stat3

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies (IPOPI)
- Immune Deficiency Foundation
- European Society for Immunodeficiencies
- NIH/National Institute of Allergy and Infectious Diseases

Other information sources:

- Immunodeficiencies+STAT3 deficiency