CIITA, MHCII transactivating protein deficiency

GENERAL INFORMATION

Description:

Defects in MHC2TA are a cause of hereditary MHC class II deficiency (also known as Bare lymphocyte syndrome (BLS) or HLA class II-deficient combined immunodeficiency); a form of severe combined immunodeficiency disease (SCID). MHC2TA is linked with BLS complementation group A. Bare lymphocyte syndromes (BLS) resemble selective T-cell immunodeficiencies but, in some patients, are indistinguishable from that of SCID. MHC class II molecules are expressed at less than 5% of normal intensity on hematopoietic cells from affected patients. The syndrome is caused not only by mutations in the MHC genes, but also by mutations in one of several genes encoding gene-regulatory proteins that are requiered for the transcriptional activation of MHC class II promoters. Four complementing gene defects (known as A, B, C ,D) have been defined in patients who fail to express MHC class II molecules. The gene mutated in group A is MHC class II transactivator, or CIITA, the genes mutated in Groups B, C, and D are named RFXANK, RFX5, and RFXAP. Less than 100 cases have been reported worldwide.

Alternative names:

- Bare Lymphocyte Syndrome Type II
- MHC class II gene transcription complex, CIITA (complementation group A)

Classification:

- Combined B and T cell immunodeficiencies
  - Major histocompatibility complex class II deficiency

Inheritance:

Autosomal recessive

OMIM:

- #209920 Bare lymphocyte syndrome, type II
- *600005 Major histocompatibility complex class II transactivator; MHC2TA

Cross references:

Incidence:

Incidence is not known yet.

CLINICAL INFORMATION

Description:

Presentation similar to SCID. The children have extreme susceptibility to bacterial, viral, and fungal infections in the first year of life and usually results in death by age of four. Type 2 BLS is a rare form of AR T+B +SCID that principally affects children born to cosanguineous families of nothern African or Mediterranean origin. In MHC class II-deficient patients, liver disease associated with chronic Cryptosporidium infection often develops. Recurrent bronchopulmonary infections have been observed in all patients. The infectious agents include viruses (CMV, respiratory syncytial virus, enterovirus), bacteria (Steptococcus, Haemophilus, Proteus, Pseudomonas), Pneumocystis carinii, and Candida albicans. Neurological manifestation due to viral infections have been diagnosed in a number of patients. Hematologic manifestations are characterized by neutropenia and severe autoimmune cytopenia.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Defective expression of HLA class 2, ORPHANET

Genetic:

- MHC2TA, IDdiagnostics

Therapeutic options:

- Treatment of infections with antibacterials, antifungals, and antivirals. Bone marrow transplantation. Other recommendations include: intravenous gamma-globulin infusion, irradiation of all blood products.
- Bone marrow transplantation for Severe Combined Immunodeficiency Disease, University of California

Research programs, clinical trials:

- Pilot Study of Allogeneic Bone Marrow Transplantation Plus Cyclosporine and Mycophenolate Mofetil to Induce Mixed Hematopoietic Chimerism in Patients With Primary T-Cell Immunodeficiency Disorders, ClinicalTrial.gov
- European Initiative for Primary Immunodeficiencies
- Presentation of Self and Foreign Antigens by MHC Class II Molecules, Beckman Research Institute, Division of Immunology
- Molecular basis of immune regulation, Leiden University Medical Center, Department of Immunohaematology and Blood Transfusion
- Immunogenetics of Bare lymphocyte syndrome(BLS), ORPHANET

GENE INFORMATION

Names:

HUGO name: CIITA
Alias(es): C2TA, MHC2TA, MHC class II transactivator, MHC class II transactivator CIITA

Localization:

Reference sequences:

DNA: X87344 (EMBL) , **cDNA:** U18259 (EMBL) , **Protein:** P33076 (SWISSPROT)

Chromosomal Location:

16p13

Maps:

MHC2TA (Map View), SHGC-60649, STS-U18288, RH79123

Variations / Mutations:

- MHC2TAbase; MHC2TAbase: Mutation registry for MHCII transactivating protein deficiency

Other gene-based resources:

Ensembl: ENSG00000179583, GENATLAS: MHC2TA, GeneCard: MHC2TA, UniGene: 126714, Entrez Gene: 4261, euGenes: 4261, GDB: 6268475

PROTEIN INFORMATION

Description:

Protein function:

Essential for transcriptional activity of the HLA class II promoter; activation is via the proximal promoter. No DNA binding of in vitro translated CIITA was detected. May act in a coactivator-like fashion through protein-protein interactions by contacting factors binding to the proximal MHC class II promoter, to elements of the transcription machinery, or both. Alternatively it may activate HLA class II transcription by modifying proteins that bind to the MHC class II promoter.

Domains:

Nacht domain: 414-724

Asp/glu-rich (acidic) domain: 52-137

Other features:

ATP nucleotide phosphate-binding region: 420-427

Other related resourses:

InterPro: IPR001611; LRR, Pfam: PF00560; LRR, SMART: SM00370; LRR, PROSITE: PS50837; NACHT

Expression pattern for human:

Tissue	Exp. (%)	Clones
leukopheresis	26.94	3:4557
tonsil, enriched for germinal center B-cells	22.41	20:36522
lymph	14.62	23:64395
blood	6.47	2:12646
lung metatastic chondrosarcoma	6.35	1:6448
pool, lung+testis+B-cell	5.88	8:55714
leukocyte	4.56	1:8982
pancreas, exocrine	3.82	2:21418
testis	2.36	5:86533
breast	1.94	2:42231

Animal models:

Mouse:

MGD: ; C2ta

Fly:

euGenes: ; CG5871

C. elegans:

euGenes: ; T20B5.3

OTHER RESOURCES

Societies:

General:

- European Society for Immunodeficiencies
- IPOPI, International Patient Organization for Primary Immunodeficiencies
- The Jeffrey Modell Foundation
- Immune Deficiency Foundation
- NIH/National Institute of Allergy and Infectious Diseases
- National Center for Biotechnology Information