Adenosine deaminase deficiency

GENERAL INFORMATION

Description:

Adenosine deaminase (ADA) deficiency accounts for about half of the autosomal recessive forms of SCIDs. ADA follows PNP in purine nucleoside catabolism, but deficiency in this enzyme causes even more severe symptoms than PNP deficiency, which is a T cell deficiency. ADA degrades toxic adenosine and deoxyadenosine, which accumulate in the cells of patients. Immature lymphoid cells are particularly sensitive to these nucleotides. In addition to immunological defect, most patients with ADA deficiency also have skeletal abnormalities.

Alternative names:

- Adenosine aminohydrolase, Severe combined immunodeficiency due to adenosine deaminase deficiency
- SCID Due to ADA deficiency
- ADA-SCID

Classification:

- Combined B and T cell immunodeficiencies
  - Deficiencies of purine metabolism

Inheritance:

Autosomal recessive

OMIM:

- #202500 Severe combined immunodeficiency 1, SCID1
- +102700 Adenosine deaminase; ADA

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for PNP deficiency

Incidence:

1/2 x 100 to 1 x 100 births.

CLINICAL INFORMATION

Description:

Affected infants present: recurrent chronic viral, fungal, protozoal, and bacterial infections and frequently present with persistent diarrhoea, failure to thrive and candidiasis. Severely affected cases present neonatally with no detectable lymphocytes in peripheral blood or bone marrow and both cell-mediated and humoral immunity is defective. Some patients have had associated bony and hair growth abnormalities and occasionally non-specific neurological disorders, attributed to malnutrition or viral infection.There are two forms of ADA deficiency, complete ADA deficiency with associating immunodeficiency (B-T cell CD4-lympho and thrombopenia), skeletal dysplasia, recurrent respiratory infections and asthma, hepatosplenomegaly and partial ADA deficiency with slow progressive or late onset.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Purine nucleoside phosphorylase deficiency, eMedicine

Genetic:

- ADA, GeneTest

Therapeutic options:

- Treatment of infections with antibacterials, antifungals, and antivirals. Bone marrow transplantation and gene therapy. Other recommendations include: intravenous gamma-globulin infusion, irradiation of all blood products and early isolation.
- Gene therapy in peripheral blood lymphocytes and bone marrow for ADA- immunodeficient patients
- Gene therapy for adenosine deaminase deficiency

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

GENE INFORMATION

Names:

HUGO name: ADA
Alias(es): Adenosine deaminase, Adenosine aminohydrolase

Localization:

Reference sequences:

DNA: M13792 (EMBL) , **cDNA:** X02994 (EMBL) , **Protein:** P00813 (SWISSPROT) Other Sequences

Chromosomal Location:

20q13.2-q13.11

Maps:

ADA (Map View)

Variations / Mutations:

- ADAbase; Mutation registry for autosomal recessive ADA deficiency

Other gene-based resources:

Ensembl: ENSG00000196839, GENATLAS: ADA, GeneCard: ADA, UniGene: 407135, Entrez Gene: 100, euGenes: 100, GDB: 119649

PROTEIN INFORMATION

Description:

Catalytic activity:

Adenosine + h(2)o = inosine + nh(3)

Polymorphism:

There is a common allele, ADA*2, also known as the ADA 2 allozyme

Other features:

Other related resourses:

PIR: DUHUA, InterPro: IPR001365; A/AMP_deaminase, Pfam: PF00962; A_deaminase, PROSITE: PS00485; A_DEAMINASE

Expression pattern for human:

Tissue	Exp. (%)	Clones
T cells from T cell leukemia	41.02	12:2397
nasopharynx	12.68	1:646
blood, white cells	9.00	1:910
brain, hippocampus	6.46	1:1269
lymph, T-cell	4.82	5:8503
umbilical cord, endothelium	4.41	2:3718
ovary (pool of 3)	3.74	2:4380
thymus, pooled	2.59	1:3169
human optic nerve	1.86	1:4406
testis	1.80	19:86533

Animal models:

Mouse::

MGD: ; Ada

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:

- The Purine Research Society
- European Society for the Study of Purine and Pyrimidine Metabolism in Man
- The SCID Homepage

Other information sources:

- Severe combined immunodeficiency, Patient and Family Handbook, IDF
- Severe combined immunodeficiency (SCID), JMF
- Severe combined immunodeficiency, KidsHealth