X-linked SCID(γc-chain deficiency)

GENERAL INFORMATION

Description:

X-linked SCID, accounting for about 50-60% of SCID cases, is caused by IL-2 receptor γ chain mutations, which lead to very low numbers of T cells and NK cells, whereas B cells are present in high numbers. The B cells are immature and defective. IL-2 receptor (IL-2R) γ -chain (CD25) deficiency has also been reported. The γ chain of the receptor forms part of the receptor also for IL-2, -4, -7, -9, and -15, affecting the differentiation and growth of lymphocytes. The γ chain consists of an extracellular domain with WS motif, transmembrane region, as well as intracellular domain with Box1 and Box2 regions. Some 150 different mutations distributed in all the domains have been determined.

Alternative names:

- Scidx; XSCID
- Scid, x-linked
- Cytokine receptor common gamma chain
- Agammaglobulinemia, swiss type
- Thymic epithelial hypoplasia
- Immunodeficiency 4; IMD4

Classification:

- Combined B and T cell immunodeficiencies
  - T⁻B⁺ SCID

Inheritance:

X-linked

OMIM:

- #300400 Severe Combined Immunodeficiency, X-linked; SCIDX1
- *308380 Interleukin 2 Receptor , Gamma; IL2RG

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for JAK3 deficiency

Incidence:

1/200,000 births/year

CLINICAL INFORMATION

Description:

Male infants with XSCID appear normal at birth. Clinical features of XSCID contain failure to thrive, oral trush, candidal diaper rash, absent tonsils, persistence of infection despite conventional treatment. Other features include presence of lymphocytopenia ('alymphocytosis'), earlier age at death, vulnerability to viral and fungal and bacterial infections, lack of delayed hypersensitivity, atrophy of the thymus, and lack of benefit by gamma globulin administration. Patients with X-SCID have extreme susceptibility to infections.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Severe combined immunodeficiency, X-linked, eMedicine

Genetic:

- IL2RG, IDdiagnostics

Therapeutic options:

- Bone marrow transplantation is the only treatment of SCID. Other recommendations include intravenous gamma-globulin infusion, irradiation of all blood products, antibiotherapy. Gene therapy is now succesful for X-linked SCID.
- Gene therapy of human severe combined immunodeficiency (SCID)-X1 disease

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
- Publications related to SCID-X1 gene therapy trial
- European Initiative for Primary Immunodeficiencies

GENE INFORMATION

Names:

HUGO name: IL2RG
Alias(es): CD132, IMD4, SCIDX, SCIDX1, XSCID, interleukin 2 receptor, gamma (severe combined immunodeficiency), Cytokine receptor common gamma chain precursor (Gamma-C) (Interleukin- 2 receptor gamma chain) (IL-2R gamma chain) (P64) (CD132 antigen)

Localization:

Reference sequences:

DNA: L19546 (EMBL) , **cDNA:** D11086 (EMBL) , **Protein:** P31785 (SWISSPROT) Other Sequences

Chromosomal Location:

Xq13.1-q13.3

Maps:

IL2RG (Map View), RH17366, RH11053, SGC35235

Variations / Mutations:

- IL2RGbase; X-linked SCID mutation database (IL2RGbase)

Other gene-based resources:

Ensembl: ENSG00000147168, GENATLAS: IL2RG, GeneCard: IL2RG, UniGene: 84, Entrez Gene: 3561, euGenes: 3561, GDB: 134807

PROTEIN INFORMATION

Description:

Other features:

Other related resourses:

PIR: A42565, InterPro: IPR002996; CR1A, InterPro: IPR003531; Hemtopoptn_S_F1, PROSITE: PS01355; HEMATOPO_REC_S_F1

Expression pattern for human:

Tissue	Exp. (%)	Clones
cord blood	22.05	14:7759
lymph, T-cell	14.37	10:8503
blood, white cells	13.43	1:910
lung with fibrosis	8.26	1:1479
B cells from Burkitt lymphoma	5.70	1:2143
T cells from T cell leukemia	5.10	1:2397
esophagus	4.14	1:2949
blood	3.86	4:12646
human retina	3.03	1:4036
lymph	2.47	13:64395

Animal models:

M. musculus::

MGD: ; IL2RG

FlyBase::

euGenes: ; FlyBase

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 SCID Homepage

Other information sources:

- Severe Combined Immunodeficiency, Patient and Family Handbook
- Severe Combined Immunodeficiency, KidsHealth