

# RAG2 deficiency

## GENERAL INFORMATION

### Description:

The functional failure of one of the constituents of the V(D)J recombinase machinery, such as RAG1 or RAG2, results in a severe combined immunodeficiency without B and T cells. The RAG1 and RAG2 deficiency is an autosomal recessive disease.

### Alternative names:

- SCID
- Recombination defect
- Recombinase activating genes 2
- Complete RAG2 deficiency
- SCID with RAG2 deficiency

### Classification:

- Combined B and T cell immunodeficiencies
  - T<sup>+</sup>B<sup>+</sup> Severe combined immunodeficiency (SCID)

### Inheritance:

Autosomal recessive

### OMIM:

- #601457 Severe combined immunodeficiency, B cell-negative
- \*179616 Recombination-activating gene 2; RAG2

### Cross references:

#### Phenotype related immunodeficiencies:

- IDR factfile for RAG1 deficiency
- IDR factfile for Omenn syndrome

### Incidence:

~ 1/100,000 live births.

## CLINICAL INFORMATION

### Description:

The clinical description is relatively uniform. No symptoms are detected during pregnancy, birth and within the first few weeks of life. In the majority of cases, the symptoms start within the second or third month of birth. Infectious complications with a high preponderance of opportunistic infections are the hallmark of the disease. The clinical signs are characterized by chronic respiratory disease, recurrent acute pneumonia, therapy-resistant mucocutaneous candidiasis, eczematous dermatitis and systemic bacterial infections. The recurrent infections in addition to chronic enteritis lead to a therapy-resistant growth failure. Intracellular parasites (*Listeria*, *Legionella*), viruses (EBV) and cytomegaloviruses (CMV) cause lethal complications. All SCID children die within few months if they are not provided with haematopoietic stem cells.

### Diagnosis:

#### Diagnostic laboratories:

#### Clinical:

- Severe combined immunodeficiency, eMedicine

#### Genetic:

- RAG2, 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.
- National Marrow Donor Program
- Severe combined immunodeficiency, eMedicine

## 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
- Lisa A. Steiner at Yale University
- Recombination and expression of antigen receptor genes
- David Schatz at Howard Hughes Medical Institute
- European Initiative for Primary Immunodeficiencies

## GENE INFORMATION

### Names:

**HUGO name:** RAG2

**Alias(es):** recombination activating gene 2, V(D)J recombination activating protein 2 (RAG-2)

## Localization:

### Reference sequences:

**DNA:** M94633 (EMBL) , **cDNA:** M94633 (EMBL) , **Protein:** P55895 (SWISSPROT)

### Chromosomal Location:

11p13

### Maps:

RAG2 (Map View), Rag2

## Variations / Mutations:

- RAG2base; Mutation registry for autosomal recessive RAG2 deficiency

## Other gene-based resources:

Ensembl: ENSG00000175097, GENATLAS: RAG2, GeneCard: RAG2, UniGene: 159376, Entrez Gene: 5897, euGenes: 5897, GDB: 125186

## PROTEIN INFORMATION

### Description:

#### Protein function:

During lymphocyte development, the genes encoding immunoglobulins and T cell receptors are assembled from Variable (V), Diversity (D), and Joining (J) gene segments. This combinatorial process, known as V(D)J recombination, allows the generation of an enormous range of binding specificities from a limited amount of genetic information. The RAG1/RAG2 complex initiates this process by binding to the conserved Recombination Signal Sequences (RSS) and introducing a double-strand break between the RSS and the adjacent coding segment. These breaks are generated in two steps, nicking of one strand (hydrolysis), followed by hairpin formation (transesterification). RAG1/2 has also been shown to function as a transposase in vitro, and to possess RSS-independent endonuclease activity (end processing) and hairpin opening. RAG1 alone can bind to RSS but stable, efficient binding requires RAG2. All known catalytic activities require the presence of both proteins.

#### Subunit:

The RAG complexes appear to contain three to five molecules of RAG2 for each molecule of RAG1

#### Subcellular location:

Nuclear

### Other features:

#### Other related resources:

InterPro: IPR004321; RAG2, Pfam: PF03089; RAG2

### Expression pattern for human:

Tissue	Exp. (%)	Clones
leukopheresis	52.14	2:4557
thymus, pooled	37.49	1:3169
testis	8.24	6:86533
pool, lung+testis+B-cell	2.13	1:55714

### Animal models:

#### Mus musculus (Mouse):

MGD: MGI:97849; Rag2

#### Oryctolagus cuniculus (Rabbit):

#### Gallus gallus (Chicken):

#### Xenopus laevis (African clawed frog):

#### Oncorhynchus mykiss (Rainbow trout)

#### (Salmo gairdneri):

## OTHER RESOURCES

### Societies:

#### General:

- European Society for Immunodeficiencies
- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- March of Dimes Birth Defects Foundation
- NIH/National Institute of Allergy and Infectious Diseases

#### Disease specific:

- The SCID Homepage

### Other information sources:

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