DNA ligase I deficiency

GENERAL INFORMATION

Description:

Defects in LIG1 seem to cause immunodeficiencies and cellular hypersensitivity to DNA-damaging agents. DNA ligase I is required for normal development but is not essential for replication.

Alternative names:

- LIG1
- LIG1 deficiency

Classification:

- DNA breakage associated syndromes and DNA epigenetic modification syndromes
  - DNA ligase deficiency

Inheritance:

Autosomal recessive

OMIM:

- *126391 Ligase I, DNA, ATP-dependent; LIG1

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for LIG4 syndrome

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

The patient had sun sensitivity and stunted growth and died at the age of 19 years with lymphoma. The patient was able to sit at 2 years and did not walk or have normal sphincter control until 3 years. Recurrent middle ear and chest infections led to poor hearing and bronchiectasis. Secondary sexual characteristics did not develop during adolescence. At the age of 17, patches of venous dilatation appeared on her skin, mainly on the limbs. There was also some telangiectasia on the bulbar conjunctivae.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Nijmengen Syndrome, eMedicine

Therapeutic options:

- Nijmengen Syndrome, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies 2001-2004, coord.Edvard Smith.

GENE INFORMATION

Names:

HUGO name: LIG1
Alias(es): ligase I, DNA, ATP-dependent , DNA ligase I, EC 6.5.1.1, Polydeoxyribonucleotide synthase [ATP]

Localization:

Reference sequences:

DNA: M36067 (EMBL) AF527418 (EMBL) , **cDNA:** X58957 (EMBL) , **Protein:** P18858 (SWISSPROT)

Chromosomal Location:

19q13.2-q13.3

Maps:

LIG1 (Map View)

Markers:

SHGC-12449, SHGC-132086

Variations / Mutations:

- LIG1base; Mutation registry for DNA ligase I deficiency

Other gene-based resources:

Ensembl: ENSG00000105486, GENATLAS: LIG1, GeneCard: LIG1, UniGene: 1770, Entrez Gene: 3978, euGenes: 3978, GDB: 127274, HomoloGene: 197

PROTEIN INFORMATION

Description:

Protein function:

This protein seals, during DNA replication, DNA recombination and DNA repair, nicks in double-stranded DNA.

Catalytic activity:

ATP + (deoxyribonucleotide)(n) + (deoxyribonucleotide)(m) = AMP + diphosphate + (deoxyribonucleotide)(n+m).

Subcellular location:

Nuclear

Post-translational modification:

Phosphorylated in vivo.

Similarity:

Belongs to the ATP-dependent DNA ligase family.

Other features:

AMP binding site: 568

Other related resourses:

PIR: A41275, InterPro: IPR000977; DNA_ligase, InterPro: IPR008994; Nucleic_acid_OB, Pfam: PF04679; DNA_ligase_A_C, Pfam: PF01068; DNA_ligase_A_M, Pfam: PF04675; DNA_ligase_A_N, PROSITE: PS00697; DNA_LIGASE_A1, PROSITE: PS00333; DNA_LIGASE_A2, PROSITE: PS50160; DNA_LIGASE_A3

Expression pattern for human:

Tissue	Exp. (%)	Clones
thymus	12.49	1:3074
small_intestine	12.33	4:12454
pooled	6.73	1:5703
muscle	6.34	15:90826
colon	4.67	10:82275
lymph_node	4.38	13:113869
testis	4.28	12:107669
placenta	4.04	15:142648
eye	3.87	13:128990
liver	3.61	11:117118
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Animal models:

Mouse:

MGD: ; Lig1

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- European Society for Immunodeficiencies