Autoimmune polyendocrinopathy with candidiasis and ectodermal dystrophy

GENERAL INFORMATION

Description:

APECED is due to a monogenic mutation of AIRE (autoimmune regulator) which codes for a transcription factor. Its pathophysiological substrate is related to an anomaly of normal immunological tolerogenesis leading to the formation of autoantibodies directed against specific tissue antigens: surface receptors, intracellular enzymes, secreted proteins (hormones). APECED usually occurs in children before the age of 5, or in early adolescence.

Alternative names:

- APECED
- Autoimmune polyendocrine syndrome, type I; APS1
- Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy
- Autoimmune polyglandular syndrome, type I
- Polyglandular autoimmune syndrome, type I
- PGA I
- Hypoadrenocorticism with hypoparathyroidism and superficial moniliasis
- Polyglandular deficiency syndrome, persian-jewish type
- Autoimmune polyendocrinopathy syndrome, type I, autosomal dominant
- Autoimmune regulator

Classification:

- Other well-defined immunodeficiency syndromes
  - Autoimmune disorders

Inheritance:

Autosomal recessive

OMIM:

- #240300 Autoimmune polyendocrinopathy syndrome, type I
- *607358 Autoimmune regulator; AIRE

Incidence:

1:25000 in Finnish population and 1:9000 in the Iranian jews.

CLINICAL INFORMATION

Description:

Patients with APECED have autoimmune polyendocrinopathies (hypoparathyroidism, adrenocortical failure, IDDM, gonadal failure, hypothyroidism, pernicious anemia, and hepatitis), chronic mucocutaneous candidiasis, ectodermal dystrophies (vitiligo, alopecia, keratopathy, dystrophy of dental enamel, nails and tympanic membranes). Chronic candidiasis is classically the first clinical sign, occurring before the age of 5. It is followed by hypoparathyroidism and the Addison disease. In addition, a high proportion of patients develop squamous cell carcinoma of the oral mucosa.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Autoimmune polyendocrinopathy type 1, ORPHANET
- Poliglandular autoimmune syndrome, type I, eMedicine

Genetic:

- AIRE, IDdiagnostics
- AIRE, GeneTest
- AIRE, EDDNAL

Therapeutic options:

- Candidiasis needs an antimycotic treatment. Hypoparathyroidism can be influenced by calcium and vitamin D therapy. In case of adrenal failure hydrocortisone replacement is needed. Vitamin and mineral replacement can be useful to compliment hormonal replacement.
- Poliglandular autoimmune syndrome, type I, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies.

GENE INFORMATION

Names:

HUGO name: AIRE
Alias(es): APECED, PGA1, autoimmune regulator (APECED protein)

Localization:

Reference sequences:

DNA: AB006684 (EMBL) , **cDNA:** AB006682 (EMBL) , **Protein:** O43918 (SWISSPROT) Other Sequences

Chromosomal Location:

21q22.3

Maps:

AIRE (Map View)

Variations / Mutations:

- AIREbase; Mutation registry for Autoimmune polyendocrinopathy candidiasis-ectodermal dystrophy (APECED)

Other gene-based resources:

Ensembl: ENSG00000160224, GENATLAS: AIRE, GeneCard: AIRE, UniGene: 129829, Entrez Gene: 326, euGenes: 326, GDB: 567198

PROTEIN INFORMATION

Description:

Protein function:

Probable transcriptional regulator protein that binds to DNA as dimer and tetramer, but not as a monomer. Binds to G-doublets in an A/T-rich environment; the preferred motiv is a tandem repeat of ATTGGTTA combined with a TTATTA-box. May be involved in immune regulation.

Subunit:

Homodimer and homotetramer. Interacts with crebbp

Subcellular location:

Nuclear and cytoplasmic; associated with tubular structures and in discrete nuclear dots ressembling ND10 nuclear bodies. May shuttle between nucleus and cytoplasm.

Post-translational modification:

Phosphorylated. Phosphorylation could trigger oligomerization.

Protein function:

At least 3 isoforms; 1/AIRE-1, 2/AIRE-2 and 3/AIRE-3; may be produced by alternative splicing.

Other features:

Other related resourses:

InterPro: IPR000770; SAND_domain, InterPro: IPR004865; Sp100, InterPro: IPR001965; Znf_PHD, Pfam: PF00628; PHD, Pfam: PF01342; SAND, Pfam: PF03172; Sp100, SMART: SM00249; PHD, SMART: SM00258; SAND, PROSITE: PS50864; SAND, PROSITE: PS01359; ZF_PHD_1, PROSITE: PS50016; ZF_PHD_2

Expression pattern for human:

Tissue	Exp. (%)	Clones
germ cell	100.00	1:20077

OTHER RESOURCES

Societies:

General:

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