

The Molecular Basis and Its Novel Factors in Polyendocrinopathy-Candidiasis Ectodermal Dystrophy

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DESCRIPTION

Autoimmune Regulator (AIRE) is a transcription factor that is expressed in Medullary Thymic Epithelial Cells (mTECs). Its role in the regulation of immune tolerance is critical, as it is involved in the expression of self-antigens in the thymus. AIRE mutations have been associated with Autoimmune Polyendocrinopathy Candidiasis Ectodermal Dystrophy (APECED), a rare autoimmune disorder characterized by the presence of multiple endocrine and non-endocrine autoimmune manifestations [1].

AIRE was first identified in 1997 by Finnish researchers who were studying the genetic basis of APECED. The gene encoding AIRE was found to be located on chromosomes, and mutations in this gene were subsequently found to be associated with APECED.

AIRE is a transcription factor that belongs to the nuclear receptor superfamily. It contains a conserved DNA-binding domain, a nuclear localization signal, and two Plant Homeodomain (PHD) fingers. The PHD fingers of AIRE are thought to be involved in chromatin remodeling, and AIRE has been shown to interact with the transcriptional coactivator CBP/p300.

The primary function of AIRE is the induction of immune tolerance to self-antigens. This is achieved by the expression of Tissue Restricted Antigens (TRAs) in mTECs. TRAs are antigens that are normally expressed only in specific tissues or cell types, and their expression in the thymus is critical for the education of T cells. In the absence of AIRE, mTECs fail to express a complete repertoire of TRAs, resulting in the production of autoreactive T cells that can cause autoimmune disease [2].

Mechanism of AIRE

The mechanism by which AIRE induces the expression of TRAs is complex and not fully understood. It is thought that AIRE binds to chromatin and induces the recruitment of transcriptional coactivators such as CBP/p300. This results in the activation of genes encoding TRAs, which are subsequently

expressed in mTECs. The expression of TRAs in mTECs is thought to be necessary for the deletion of autoreactive T cells and the induction of immune tolerance.

Mutations of AIRE

AIRE mutations have been associated with APECED, a rare autoimmune disorder that is characterized by the presence of multiple endocrine and non-endocrine autoimmune manifestations. The most common endocrine manifestations of APECED are hypoparathyroidism and adrenal insufficiency, but other endocrine disorders such as type 1 diabetes and hypothyroidism can also occur. Non-endocrine autoimmune manifestations of APECED include autoimmune hepatitis, pernicious anemia, and vitiligo [3].

The exact mechanism by which AIRE mutations lead to the development of autoimmune disease is not fully understood. It is thought that the lack of expression of TRAs in mTECs leads to the production of autoreactive T cells, which can target multiple organs and tissues. This results in the development of autoimmune disease.

The diagnosis of APECED is based on clinical features, laboratory findings, and genetic testing. The presence of two or more of the characteristic features of APECED, including endocrine and non-endocrine autoimmune manifestations, along with the presence of anti-interferon omega antibodies, is highly suggestive of APECED. Genetic testing can confirm the diagnosis by identifying mutations in the AIRE gene.

Treatment of APECED is primarily symptomatic and supportive. Replacement therapy for endocrine deficiencies is necessary, and immunosuppressive therapy may be used to treat autoimmune manifestations such as autoimmune hepatitis. Thymectomy has been used in some cases to treat refractory autoimmune manifestations, but its efficacy is uncertain [4].

CONCLUSION

Autoimmune Regulator (AIRE) is an important transcription factor that is critical for the induction of immune tolerance to

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self-antigens. Its role in the expression of Tissue-Restricted Antigens (TRAs) in the thymus is essential for the education of T cells and the prevention of autoimmune disease. Mutations in the AIRE gene have been associated with Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED), a rare autoimmune disorder characterized by the presence of multiple endocrine and non-endocrine autoimmune manifestations. The diagnosis of APECED is based on clinical features, laboratory findings, and genetic testing, and treatment is primarily symptomatic and supportive. Further research into the mechanisms underlying AIRE function and its role in the pathogenesis of autoimmune disease may lead to the development of novel therapies for autoimmune disorders.

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