

AIRE gene

autoimmune regulator

Normal Function

The *AIRE* gene provides instructions for making a protein called the autoimmune regulator. This protein is active primarily in the thymus, which is an organ located behind the breastbone that plays an important role in immune system function. The thymus prepares immune cells called T cells for their role in fighting infection; this process is called thymic education.

For a person to remain healthy, immune system cells such as T cells must be able to identify and destroy potentially harmful invaders (such as bacteria, fungi, and viruses) while sparing the body's normal tissues. The autoimmune regulator protein plays an important role in this process by helping T cells distinguish the body's own proteins from those of foreign invaders. When this system malfunctions, the immune system's ability to distinguish between the body's proteins and foreign invaders is impaired, and it may attack the body's own tissues and organs. This abnormal reaction is called autoimmunity. In the thymus, the autoimmune regulator protein destroys T cells that otherwise would cause autoimmune damage.

Health Conditions Related to Genetic Changes

Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy

More than 90 mutations in the *AIRE* gene have been identified in people with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED). APECED is an inherited condition that affects many of the body's organs. A major feature of this disorder is chronic mucocutaneous candidiasis (CMC), which is a tendency to develop infections of the skin, the nails, and the moist lining of body cavities (mucous membranes) caused by a type of fungus called *Candida*. Other common signs and symptoms of APECED involve dysfunction of the body's network of hormone-producing glands (the endocrine system), as well as other organs and tissues.

The *AIRE* gene mutations that cause APECED lead to the production of an abnormally short, nonfunctional version of the autoimmune regulator protein or change single protein building blocks (amino acids) in critical regions of the protein. These mutations reduce or eliminate the function of the autoimmune regulator protein. Without enough of this protein function, the immune system's ability to distinguish between the body's

proteins and foreign invaders is impaired, and immune cells may attack the body's own organs, resulting in autoimmunity. This abnormal reaction leads to inflammation and can damage otherwise healthy cells and tissues. Autoimmune damage to the adrenal glands, parathyroid glands, and other organs underlies many of the major features of APECED.

Studies suggest that *AIRE* gene mutations also result in immune substances (antibodies) mistakenly attacking proteins involved in an immune process called the IL-17 pathway, which is important in the body's defense against *Candida*. This pathway, which depends on specialized proteins called IL-17 cytokines for signaling, creates inflammation, sending additional cytokines and white blood cells to fight foreign invaders and promote tissue repair. In addition, the IL-17 pathway promotes the production of certain antimicrobial protein segments (peptides) that control growth of *Candida* on the surface of mucous membranes. By damaging IL-17 cytokines, *AIRE* gene mutations are thought to impair the IL-17 pathway's function, resulting in CMC in people with APECED.

Alopecia areata

MedlinePlus Genetics provides information about Alopecia areata

Other Names for This Gene

- AIRE1
- AIRE_HUMAN
- APECED
- APS1
- APSI
- Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy protein
- PGA1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of AIRE ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=326\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=326[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28AIRE%5BTIAB%5D%29+OR+%28autoimmune+regulator%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>)

Catalog of Genes and Diseases from OMIM

- AUTOIMMUNE REGULATOR; AIRE (<https://omim.org/entry/607358>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/326>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=AIRE\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=AIRE[gene]))

References

- Anderson MS, Su MA. AIRE expands: new roles in immune tolerance and beyond. *Nat Rev Immunol.* 2016 Apr;16(4):247-58. doi: 10.1038/nri.2016.9. Epub 2016 Mar14. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/26972725>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4831132/>)
- De Martino L, Capalbo D, Improda N, D'Elia F, Di Mase R, D'Assante R, D'Acunzol, Pignata C, Salerno M. APECED: A Paradigm of Complex Interactions between Genetic Background and Susceptibility Factors. *Front Immunol.* 2013 Oct 23;4:331. doi: 10.3389/fimmu.2013.00331. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24167503>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3805967/>)
- De Martino L, Capalbo D, Improda N, Lorello P, Ungaro C, Di Mase R, Cirillo E, Pignata C, Salerno M. Novel Findings into AIRE Genetics and Functioning: Clinical Implications. *Front Pediatr.* 2016 Aug 22;4:86. doi: 10.3389/fped.2016.00086. eCollection 2016. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/27597936>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4992815/>)
- Ferre EM, Rose SR, Rosenzweig SD, Burbelo PD, Romito KR, Niemela JE, Rosen LB, Break TJ, Gu W, Hunsberger S, Browne SK, Hsu AP, Rampertaap S, Swamydas M, Collar AL, Kong HH, Lee CR, Chascsa D, Simcox T, Pham A, Bondici A, Natarajan M, Monsale J, Kleiner DE, Quezado M, Alevizos I, Moutsopoulos NM, Yockey L, Frein C, Soldatos A, Calvo KR, Adjemian J, Similuk MN, Lang DM, Stone KD, Uzel G, Kopp JB, Bishop RJ, Holland SM, Olivier KN, Fleisher TA, Heller T, Winer KK, Lionakis MS. Redefined clinical features and diagnostic criteria in autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy. *JCI Insight.* 2016 Aug18;1(13):e88782. doi: 10.1172/jci.insight.88782. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/27588307>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5004733/>)
- Gallo V, Giardino G, Capalbo D, Palamaro L, Romano R, Santamaria F, Maio F, Salerno M, Vajro P, Pignata C. Alterations of the autoimmune regulator transcription factor and failure of central tolerance: APECED as a model. *Expert Rev Clin Immunol.* 2013 Jan;9(1):43-51. doi: 10.1586/eci.12.88. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23256763>)
- Kisand K, Boe Wolff AS, Podkrajsek KT, Tserel L, Link M, Kisand KV, Ersvaer E,

Perheentupa J, Erichsen MM, Bratanic N, Meloni A, Cetani F, Perniola R, Ergun-Longmire B, Maclaren N, Krohn KJ, Pura M, Schalke B, Strobel P, Leite MI, Battelino T, Husebye ES, Peterson P, Willcox N, Meager A. Chronic mucocutaneous candidiasis in APECED or thymoma patients correlates with autoimmunity to Th17-associated cytokines. *J Exp Med*. 2010 Feb 15;207(2):299-308. doi:10.1084/jem.20091669. Epub 2010 Feb 1. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20123959>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2822605/>)

- Kisand K, Peterson P. Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy. *J Clin Immunol*. 2015 Jul;35(5):463-78. doi: 10.1007/s10875-015-0176-y. Epub 2015 Jul 5. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/26141571>)
- Laan M, Peterson P. The many faces of Aire in central tolerance. *Front Immunol*. 2013 Oct 11;4:326. doi: 10.3389/fimmu.2013.00326. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24130560>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3795325/>)
- Puel A, Doffinger R, Natividad A, Chrabieh M, Barcenas-Morales G, Picard C, Cobat A, Ouachee-Chardin M, Toulon A, Bustamante J, Al-Muhsen S, Al-Owain M, Arkwright PD, Costigan C, McConnell V, Cant AJ, Abinun M, Polak M, Bougneres PF, Kumararatne D, Marodi L, Nahum A, Roifman C, Blanche S, Fischer A, Bodemer C, Abel L, Lilic D, Casanova JL. Autoantibodies against IL-17A, IL-17F, and IL-22 in patients with chronic mucocutaneous candidiasis and autoimmune polyendocrine syndrome type I. *J Exp Med*. 2010 Feb 15;207(2):291-7. doi: 10.1084/jem.20091983. Epub 2010 Feb 1. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20123958>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2822614/>)

Genomic Location

The *AIRE* gene is found on chromosome 21 (<https://medlineplus.gov/genetics/chromosome/21/>).

Last updated October 1, 2016