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Evaluation of the autoimmune regulator (AIRE) gene mutations in a cohort of Italian patients with autoimmune-polyendocrinopathy-candidiasis-ectodermal-dystrophy (APECED) and in their relatives.

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Source

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Abstract

OBJECTIVE: Autoimmune-polyendocrinopathy-candidiasis-ectodermal-dystrophy (APECED) is a rare syndrome characterized by chronic candidiasis, chronic hypoparathyroidism and Addison's disease. APECED has been associated with mutations in autoimmune regulator (AIRE) gene. Our aim is to perform a genetic analysis of the AIRE gene in Italian APECED patients and in their relatives. Design AIRE mutations were determined by DNA sequencing in all subjects. Patients were tested for clinical autoimmune or non-autoimmune diseases, or for organ and non-organ specific autoantibodies.

PATIENTS: A total of 24 Italian patients with APECED (15 from the Venetian region, 2 from Southern-Tyrol, 4 from Apulia, 3 from Sicily), 25 relatives and 116 controls were studied.

RESULTS: Ten out of the 15 Venetian patients (66%) were homozygous for R257X or compound heterozygous with 1094-1106del13. One patient was homozygous for 1094-1106del13 and another for R139X. A novel mutation (1032-1033delGT) in combination with 1094-1106del13 was identified in one patient. No mutations were found in two cases. Two patients from Southern Tyrol were homozygous for R257X and for 1094-1106del13bp. All patients from Apulia were homozygous or heterozygous for W78R combined with Q358X. The patients from Sicily were homozygous for R203X or compound heterozygous with R257X. The analysis of the genotype-phenotype revealed that patients carrying 1094-1106del13 at the onset of Addison's disease were significantly older than those carrying other mutations. The genetic study of 25 relatives identified 20 heterozygous subjects. They suffered from various autoimmune and non-autoimmune diseases but no major disease of APECED was found.

CONCLUSION: These data demonstrate the great genetic heterogeneity for the AIRE mutations in Italian APECED patients, and that the heterozygosity for AIRE mutations do not produce APECED.

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