

X-LINKED ADRENOLEUKODYSTROPHY IN SOUTH AMERICAN PATIENTS: IDENTIFICATION OF 23 MUTATIONS IN THE ABCD1 GENE IN 24 INDEX CASES AND 83 RELATIVES

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Abstract X-linked adrenoleukodystrophy is caused by a defect in the gene for the adenosine triphosphate (ATP)-binding cassette ABCD1. This gene codes for ALD protein (ALDP), a peroxisomal membrane protein that belongs to the ATP-binding cassette superfamily of membrane transport proteins. In this study, we analyzed the ABCD1 gene in X-ALD patients and relatives from 34 unrelated families. Methods: Male ALD patients from Brazil and Uruguay have been previously diagnosed by VLCFA analysis. Families were then invited to participate in molecular studies to improve genetic counseling. After consent, blood was collected and DNA was extracted. All samples were screened by SSCP analysis of PCR fragments, followed by automated DNA sequencing to establish the specific mutation in each family. Results: We identified twenty-three different mutations, of which 12 were novel. This population had an important allelic heterogeneity, as only p.Arg518Gln was found in two families, all other mutations being private. Intra-familial phenotype variability was observed in all families. Twenty one families were sufficiently studied in order to define mother carrier status and two de novo mutations were found (2/21, or 10%). Conclusions: This study extends the spectrum of mutations in X-ALD and confirmed the usual rate of *de novo* mutations. Financial Support: FIPE/HCPA, CAPES.