

REPEAT EXPANSION (CAG)_n OF THE ATXN2 GENE IN PATIENTS OF MEXICO WITH SPINOCEREBELLAR ATAXIA. EVIDENCE OF MODIFIER GENES

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Introduction: The Spinocerebellar Ataxia Type 2 (SCA2) is caused by an expanded (CAG)_n trinucleotide located in the ATXN2 gene, (12q24.1). Clinically is characterized by progressive cerebellar ataxia, ophthalmoplegia, supranuclear anomalies, nystagmus, dysarthria, dysphagia, slow saccades, olivopontocerebellar atrophy, spinocerebellar tract degeneration, myoclonus, among other features.

The aim of this study is to characterize normal alleles, mutant alleles of the repeat expansion (CAG)_n of the ATXN2 gene in patients with SCA in different regions of Mexico as well as to establish the phenotypical variability of other loci.

Material: Eighteen sporadic cases with SCA from Norwest Mexico, were analyzed, and picked up from January 1988 to June 2010. A complete physical examination and RMN were done.

Methods: The molecular analysis was made by identifying the expansion repeats in tandem by RED assay analyzing the repeats in SCA1, 2, 3, 6, 7, 8, PPP2R2B, SCA17 and DRPLA genes. RED products were identified by Southern Blot and sequencing.

Results: The frequency for the expansion of mutant alleles of the (CAG)_n trinucleotide of the ATXN2 gene was 27% with a range of 37-49 repeats. The frequency for alleles with normal repeats did not differ from the literature. We identify two mutant alleles not previously described in Mexican population with 41 and 49 repeats.

Conclusions: The frequency of normal and mutant trinucleotide (CAG)_n of the ATXN2 gene is not different of those reported in the literature. In the present study we found three genes (ATXN3, PPP2R2B, DRPLA) that modulate the phenotype, which have not been reported previously.