HAPLOTYPING IN THE ATXN10 GENE PROVIDES FURTHER EVIDENCE FOR A COMMON ANCESTRAL ORIGIN OF THE MUTATION ASSOCIATED TO SCA10

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Spinocerebellar ataxia type 10 (SCA10) is an autosomal dominant neurodegenerative disorder characterized by progressive cerebellar ataxia and epilepsy. The disease is caused by an expansion of a pentanucleotide repeat (ATTCT) in intron 9 of the ATXN10 gene, which is located at locus 22q13.3. SCA10 has shown a geographical distribution throughout America, being described in admixed patients of self-reporting Amerindian ancestry from different countries so far. Currently available data suggests that this expansion might have arisen in Amerindian population and has spread out to the rest of the continent during the peopling of the Americas. The aim of this study was to investigate the hypothesis of a common ancestral origin of a mutation founder effect in the Native American populations. SCA10 patients included were from two Latin American countries, being 16 families from Brazil (29 patients) and 21 families from Peru (27 patients) as well as controls from both populations (51 healthy Brazilian individuals and 49 healthy individuals from Indigenous Quechua population). Subjects were genotyped for four highly polymorphic short tandem repeats (STRs) and four single nucleotide polymorphisms (SNPs) by different approaches. These markers span a region of 5.2 cM harboring the ATTCT expansion and were used to define the haplotypes that were inferred by PHASE v.2.1.1 software. Statistical analysis was performed using WINPEPI software. Our data has shown two frequent haplotypes (19-13-CGGC-14-10 and 19-15-CGGC-14-10) identified in Indigenous Quechua controls, with relative frequencies of 14.3% and 13.3%, respectively. The second most frequent haplotype in Quechus, 19-15-CGGC-14-10, is found in 50.0% of Brazilian and in 64.7% of Peruvian families with SCA10. The present study is the most extensive ever performed addressing the SCA10 ancestral origin and including a large number of SCA10 families. Findings presented here bring valuable evidence that ATTCT expansion may has arisen in a Native American chromosome.