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Original article

Haplotypes *Eco*47 III–*Nsp* I sites frequencies on the *IDUA* gene in Mexican native population

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Abstract

Background. **–** The frequency of haplotypes of *Nsp* I–*Eco*47 III sites, at the IDUA (α-L iduronidase) gene, in Huichol, Tarahumara and Mestizo Mexican population is reported.

Methods. **–** *Eco*47 III and *Nsp* I intragenic polymorphisms in IDUA gene are studied in three (Mestizo, Huichol and Tarahumara populations) Mexican groups. Data from normal Australian [Hum. Genet. 90 (1992) 327] individuals were considered for comparative analyses.

Results. **–** The genotypes for IDUA *Eco*47 III and *Nsp* I sites in Mexicans were in agreement with Hardy–Weinberg equilibrium. Allele frequency distributions for individual sites differed ($P < 0.05$) except at site B_1 in the Huichol group. Haplotype *Eco*47 III–*Nsp* I frequency distributions were different in the three Mexican normal groups, and it was also observed when to compared with the normal Australians.

Conclusions. **–** This characteristic makes the two IDUA polymorphic sites useful for identification purposes, and these polymorphisms could be included in a PCR based battery of DNA markers.

Keywords: IDUA; *Eco*47 III; *Nsp* I; Mexican population; Gene frequencies

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1. Introduction

The IDUA (α-L iduronidase) gene maps to human chromosome 4p16.3, it spans approximately 19 kilobases (kb), containing 14 exons. It is approximately 1.1 megabases (Mb) apart from the telomere, and 1 Mb from the Huntington's disease locus [1]. IDUA deficiency cause mucopolysaccharidosis type I (MPS I). In 1991, *Nsp* I and *Eco*47 III intragenic IDUA polymorphisms were identified by the presence or absence of corresponding restriction sites, they were analyzed in Australian normal population [2], and suggested as diagnostic markers in families with IDUA deficiency (MPS-I) and Huntington's disease [3]. In this report, we present the results of the polymorphisms typing in Mestizo, Huichol and Tarahumara populations, to estimates the genetic polymorphisms in the Mexican population.

2. Material and methods

The control group 262 (524 chromosomes) blood samples analyzed from mestizo group were individuals healthy unrelated adults, living in Guadalajara City and surroundings, 110 of students at a local university; the 152 samples were from blood bank donors. The both Huichol and Tarahumara groups were 50 (100 chromosomes) blood samples from each these native populations are living at the North-Western of Mexico. All individuals signed a letter of informed consent.

Genomic DNA was extracted according to standard protocols [3]. The primers ID-58 and ID-65 5′ were used to amplify a 245 base pair (bp) fragment of the human IDUA gene, which includes exon I. This product contains a polymorphic *Eco*47 III site, caused by a silent C to A change in the last base of the Ala_8 codon, which in the IDUA gene, and digestion produces fragments of 132 and 113 bp after digestion. The 245 bp, PCR product also contains a polymorphic *Nsp* I site, caused by a G to T substitution, switching Gln_{33} to His in the IDUA protein, and which produces DNA fragments of 187 and 58 bp after restriction enzyme [2].

Allele frequencies were calculated by the gene counting method [4]. Hardy–Weinberg equilibrium (HWE) was analyzed by the likelihood ratio [5], exact [6], and χ^2 tests for total heterozygosity. The levels of significance for each test statistic ($P < 0.05$) were determined by a permutation program, as used by Chakraborty et al. [7]. Total heterozygosity was calculated as $H_T = 1 - \Sigma p_i^2$, where p_i represents the frequency of every allele in the sample.

Haplotypes were counted from homozygous individuals, for at least one polymorphism, and calculated by the estimation-maximization haplotype frequency (EM) computer program, by Excoffier and Slatkin [8]. Expected haplotype represents the average number of the different possible genotypes that could be present at the analyzed individuals, and them were calculated from the original *Eco*47 III and *Nsp* I data. Comparison between observed and expected values was made using a χ^2 test, with Yate's correction when necessary. Pairwise comparison of allele and haplotype counts was done between both groups using a contingency table (exact test) [9].