Clinical features and possible founder mutation of the 8bp duplication mutation in the SLC4A11 gene causing corneal dystrophy and perceptive deafness in three South American families

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Background: Corneal Dystrophy and Perceptive Deafness (CDPD) or Harboyan syndrome is an autosomal recessive rare disorder, characterized by congenital corneal opacities and progressive sensorineural hearing loss, which usually begins after the second decades of life. This study reports the ophthalmic, audiological and genetic features, in five CDPD affected patients from three Chilean families. Materials and Methods: Five individuals affected with CDPD from three unrelated Chilean families were clinically and genetically examined. To evaluate a putative founder mutation 7 SNPs were analyzed in the three families, an Argentinian patient (carrier of the same mutation previously reported) and 87 Chilean controls. Results: The ophthalmic symptoms in the five patients were bilateral and symmetric, starting before one year of age, and visual acuity varied from 0.1 to 0.3. In all cases, hearing loss began over 8 years old. The sequence of the 19 exons of SLC4A11 gene of all the affected patients exhibited homozygous eight nucleotide sequence duplication

(c.2233_2240dup TATGACAC, p.(Ile748Metfs*5)) at the end of exon 16. All the affected patients of the three families were homozygous for a haplotype composed of five SNPs and covering 4,1 Mb. The same haplotype was present in one allele of the heterozygous Argentinean patient and has a frequency of 2.76% in Chilean population. Conclusions: The five CDPD patients were homozygous for the same mutation in the SLC4A11 gene. Haplotype analysis of all the affected, including the case reported from Argentina was in accordance with a founder mutation.