Correspondence regarding Ballana et al., “Mitochondrial 12S rRNA gene mutations affect RNA secondary structure and lead to variable penetrance in hearing impairment”


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Abstract

Ballana et al. [1] analyzed the mtDNA 12S rRNA gene in a cohort of 443 families with hearing impairment and detected the T1291C mutation in all maternally related individuals of a Cuban pedigree. They concluded that the mitochondrial mutation T1291C was probably pathogenic, causing hearing loss, based on segregation analysis in the Cuban family, RNA conformation prediction, and the absence of this mutation in a control group of 95 Spanish subjects. We screened a sample of 203 deaf subjects and 300 hearing controls (110 “European-Brazilians” and 190 “African-Brazilians”) for the mitochondrial mutations A1555G and T1291C. Five deaf subjects had the T1291C substitution. Three were isolated cases of deafness. In one familial case, the A1555G mutation was found to segregate with deafness. In the other family, the propositus' father, and paternal grandmother and great-grandmother presented deafness. Therefore, familial data do not support T1291C as the cause of deafness in these patients. Among the 300 unrelated hearing controls, this mutation was found in two individuals of the “African-Brazilian” group. The T1291C mutation was in homoplasmy in all carriers.

The Brazilian population represents a complex admixture of ethnic groups. South American Indians, Portuguese...
settlers, and African slaves contributed to its gene pool, and during the last hundred years the country received other immigrants [4]. Mitochondrial haplogroup analysis showed that all five deaf subjects and one of the two hearing controls with the T1291C mutation belong to the macrohaplogroup L1/L2, indicating an African origin of their mtDNA.

The frequency of 1.05% (2/190) of T1291C in the “African-Brazilian” control samples indicates that it is most likely polymorphic in the African population. The Cuban family reported by Ballana et al. might also have some African genetic background since Cuba has received an important African migration. According to Klein [5], “On the eve of the Haitian rebellion of 1791, Cuba was already well on its way to emerging as the major slave island in the Caribbean”. May be a Spanish control sample was not suitable in this case.

Alignment analysis shows that the 1291 position of the mitochondrial genome is not conserved between species (Fig. 1). In addition, the C is present in the wild-type sequence of the apes Gorilla gorilla (GI 51127246) and Pongo pygmaeus (GI 51122739), supporting the hypothesis that the T1291C substitution might be a non-pathogenic polymorphism.

Therefore, our data point to T1291C substitution as most probably an African non-pathogenic polymorphism.

References