Reviewer's report

Title: MRPS18CP2 alleles and DEFA3 absence as chromosome 8p23.1 modifiers of hearing loss due to mtDNA mutation A1555G in the 12S rRNA gene

Version: 1 Date: 15 September 2007

Reviewer: Michio Hirano

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General
The A1555G mitochondrial DNA (mtDNA) mutation is fairly common cause of non-syndromic and aminoglycoside-induced deafness. Nuclear DNA (nDNA) modifiers are thought to contribute to the pathogenesis and a major modifying locus has been located on chromosome 8p23.1. Identification of this modifier would be very important to predict risks of hearing loss in patients carrying the A1555G mtDNA mutation and to understand its pathogenesis. In this work, Ballana and colleagues have screened three genomic elements in 8p23.1 as potential nDNA modifiers.

Major Compulsory Revisions
1. In families with the A1555G mtDNA mutation, there was a statically significant association with deafness and a polymorphism in the MRPS18CP2 pseudogene and an “overrepresentation” of DEFA3 gene absence. Nevertheless, it is not possible to conclude that these genetic variants contribute to the disease pathogenesis as implied by the title, which must be modified. Because all of the families were of Spanish origin, the genetic associations with deafness could be due to founder effects.

Minor Essential Revisions
1. In the Conclusions of the Abstract, “Although any of the factors…” should be “Although none of the factors…”
2. In the Results (page 11, text line 5), “expands” should be “spans”.
3. In Table 1, decimal points should be “.” not “,”.

Discretionary Revisions
1. It would be interesting to know the size of the chromosome 8p23.1 modifier locus and the number of genes and pseudogenes in this region.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests.