Author’s response to reviews

Title: Molecular epidemiology of DFNB1 deafness in France

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Dear Editor,

You will find enclosed the revised manuscript. Revisions have been made in line with the comments from both reviewers and details have been stated when necessary. The title, abstract and discussion have been modified in order to tone down the non pathogenic status of the M34T variant.

We hope that the revised manuscript will be suitable for publication.

Sincerely yours,

Anne-Francoise Roux

Comments to reviewer 1
To avoid any confusion we have replaced the word "control" by "general population" (pages 9 and 10). Moreover, we have never assumed that the general population was invariably normal but as samples have been anonymised consequently there are no phenotypic data available. We have addressed this issue page 6.

Concerning the validity of the study, we cannot exclude that some of individuals in the general population may suffer from partial hearing loss (page 12) but we still expect alleles that are associated with deafness to be more prevalent in the deaf sample than in the Guthrie cards from the general population.

We have modified the title and discussion of the manuscript to modulate the non pathogenic status of the M34T.

Comments to reviewer 2
The discussion has been revised to modulate the non pathogenic status of the M34T in respect to the suggestions.

Last sentence of the abstract has been modified as requested to tone down the non pathogenic status of the M34T, V37I and R127H sequence variations.

Because samples from general population had to be anonymised for the study, no follow up of the M34T homozygote could be performed.
Minor essential revisions
1) The title has been modified accordingly
2) "dependent" has been corrected
3) The contribution of DFNB1 in diverse population is referenced by Kenneson (2002) as suggested
4) The size of the deletion has been updated accordingly
5) "the 35delG mutation" has been corrected (page 4, paragraph 2)
6) the word "symetrical" had been included in the description of the patients. The distribution of the inheritance patterns has been corrected
7) The number of families with non syndromic deafness is already cited in this paragraph (84). Moderate has been replaced by "mild". Fifty five families had a single deaf child; family history is documented in all these cases (not mentioned in the text)
8) The criteria used for the classification of deafness have been included
9) PSDM acronym has been included
10) "the" has been deleted
11) the sentence containing "entire non coding..." has been modified to clarify this point (page 7, paragraph 2)
12) the number of patients with severe of profound patients has been clarified
13) the number of newborn samples has been corrected
14) the number of sequence variations has been corrected
15) requested corrections have been made
16) the references have been corrected
17) independence has been corrected
18) Table 4 has been corrected

Discretionary revisions
1) detection techniques have been detailed (page 6)
2) GJB2/GJB6 mutations have been replaced by DFNB1 mutations when possible