Author's response to reviews

Title: High frequency of Machado-Joseph disease identified in Southeastern Chinese kindreds with spinocerebellar ataxia

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Author's response to reviews: see over
A point-by-point response to the concerns

In response to the reviewer Alfredo Brusco:

1) For instance, abstract: results: “This frequency was also the highest level globally”, may become “This frequency was one of the highest reported worldwide”; “globally” may be substitute with “worldwide” in other parts of the text. This sentence is repeated almost identical one line below in abstract, conclusions.

We have corrected them according to your suggestion.

2) Results, line 4. Approximate numbers (20.79, 19.00, 56.04)

We have approximated them.

3) Page 8 line 1. “Thus it seems”. I don’t think this statement is correct. There are proofs that other factors besides CAG length can predispose to expansions and can act in cis or in trans (see ref 57). The authors are making a circular argument. I would keep this part of the discussion shorter and softer, suggesting that a higher prevalence of AN may be prone for full expansions.

We have deleted the sentence of “Thus it seems to that the relationship between large ANs and the prevalence of MJD differs in different populations.”

4) Page 9 “Additionally,…” this is really too speculative. I would suggest to erase up to “is not affected”.

Since homozygosity for normal alleles in SCA patients should be carefully confirmed by other techniques to exclude the possibility of false negative results as suggested by Maciel et al (Arch Neurol, 2001, 58:1821-1827), we think it is more suitable to retain the sentences of “Additionally,…is not affected”. But anyway, we much appreciate your concern.

In response to the reviewer Conceição Bettencourt:

Major essential revisions

1. In the Discussion and Conclusion sections, the authors should be more careful in the way they present their conclusions.

Thank you very much for your pertinent advice. We have done some revisions according to your advice in Abstract, Background, Discussion and Conclusion sections and we adopt the sentences of “The high frequency of large ANs associated with such a high relative frequency of MJD suggests that in this population large ANs may constitute a reservoir from which the expanded alleles may be emerging” and “The results support the hypothesis that in this population large ANs may constitute a reservoir from which the expanded alleles may be emerging. Furthermore, LA Taq polymerase was proven to be more efficient than Taq polymerase in the amplification of the expanded alleles, facilitating and improving the molecular diagnosis” in your comments on our study.

2. Although the authors added some text to the Abstract and Background sections to clarify the work hypothesis, the main goals of this study are still not obvious when reading those
Sections.

Thanks for your concern. We have added some contents in the Abstract and Background sections again.

Minor Essential Revisions:

3. The English should be revised.

We have done some corrections based on your and another reviewer’s advice. Actually, we have the American Journal Experts to edit this manuscript before we submit it.

4. In the Abstract section, the authors wrote “…denaturing polyacrylamide gel electrophoresis and DNA sequencing in 150 normal individuals and 138 unrelated probands…” which is not completely correct, since they did not sequence all the samples. The authors should change the sentence in order to clarify this issue.

Since DNA sequencing was not the major method compared to PCR and PAGE, we delete “DNA sequencing” in Abstract section. Therefore, the sentence in Abstract section was changed to “Normal and expanded alleles of ATXN3 were detected via PCR using LA Taq DNA polymerase (better for GC-rich sequences) and denaturing polyacrylamide gel electrophoresis in 150 normal individuals and 138 unrelated probands from autosomal dominant SCA families.”

5. In the Molecular analysis item of Methods, where it is written “The DL2000 … were used as DNA size markers” it should be “The DL2000 … was used as DNA size marker”. Furthermore, in the legend of Figure 5 it is written “…M: D2000 marker”, but shouldn’t it be “…M: DL2000 marker”?

We were sorry for the clerical error, we have corrected them.

6. In the Statistical analysis of Methods, the first sentence should be changed, for example, to “All the statistical analyses were performed using SPSS software version 11.0 (SPSS…”)

We have corrected it.

7. In the Analysis of CAG repeats in normal individuals of Results, where it is written “The difference in the frequency of large ANs between present study and other studies…” it should be “The difference in the frequency of large ANs between the present study and other studies…”.

We have corrected it.

8. In the Discussion section, what do the authors intend to say when they wrote “proble”? Would it be “probable”?

Sorry for clerical error again. It would be “probable” and we have corrected it.