Author's response to reviews

Title: The first report of RPSA polymorphisms, also called 37/67 kDa LRP/LR gene, in sporadic Creutzfeldt-Jakob disease (CJD)

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Author's response to reviews: see over
Dear Prof. Thomas Klopstock

Thank you very much for forwarding the review of our manuscript entitled “The first report of RPSA polymorphisms, also called 37/67 kDa LRP/LR gene, in sporadic Creutzfeldt-Jakob disease (CJD)”. We have revised the manuscript in accordance with the suggestions made by the editor and two reviewers and are therefore submitting the revised manuscript.

In relation to the comments of the editor and two reviewers, our corrections and revisions are as follows:

**Referee 1 (Dr. Maurizio Pocchiari)**

Q) In the Methods section (page 6, Subjects, 1st paragraph) the Authors should add some statistics to prove that sporadic CJD patients and controls share same distribution in gender and age at onset.

Response: According to the reviewer’s suggestion, we had added statistical method about age at onset in the Methods section and statistics for gender and age at onset had added in Table 1 [page 7, lines 3-4 and Table 1].

Q) Moreover, the Authors should also clarify what ‘age at onset’ means for controls.

Response: As you know, ‘age at onset’ is generally used for patient. From this point of view, we used ‘age at disease onset’ for sporadic CJD patients and ‘age at blood collection’ for healthy control [page 5, lines 3-5].

Q) In the following paragraph, the Authors should correct the definition for probable CJD cases (for example, duration of less than 2 years is not required unless the classification of probable CJD is made by upgrading the classification of possible CJD with a positive 14-3-3- test). A better and more updated reference should be provided.

Response: As suggested by the reviewer, we had corrected the definition for
probable CJD patients according to the WHO diagnostic criteria for
definite or probable CJD and had updated references [page 5, lines 7, 8,
10-13 and Reference (27)].

Referee 2 (Dr. Pierluigi Gambetti)

Q) The genetic study that is central part of the manuscript appears to be carefully
executed and, therefore, the conclusions appear to be firm. The size of the patient
population is also adequate for this study. However, the authors fail to provide
sufficient information as for the characteristics of this population. How many
patients had a definitive and how many a probable diagnosis of sCJD?
Response: According to the reviewer’s suggestion, we had added information of
definite sCJD and probable sCJD cases [page 6, lines 14, 15].

Q) How was the distribution of the 129 polymorphism, i.e. how many patients were
129MM and how many 129MV (as likely there were no VV subjects)? The authors
should provide this information.
Response: As suggested by the reviewer, we had analyzed genotype and allele
frequencies of RPSA 5′-UTR -8T>C polymorphism according to the
PRNP codon 129 or 219 status from our previous results. For this
analysis, we had added in the Table 6 and some data were corrected for
some mistakes on statistical analysis [page 9, lines 7-9, page 12, lines 12-
16 and Table 6].

Other editorial requirements:

Q) Structure: Please check the instructions for authors on the journal website to ensure
that your manuscript follows the correct structure for this journal and article type.
http://www.biomedcentral.com/bmcmedgenet/ifora/
Response: As suggested by the editor, our manuscript was correctly structured by
the journal style.

Q) NOTE: Keywords are not required for BMC-series journals.
Response: We have deleted the Keywords from the manuscript.
In conclusion, we have addressed all of the comments raised by the editor and two reviewers. We believe that the changes suggested by the reviewers have improved the manuscript, and we hope that it is now acceptable for publication in “BMC Medical Genetics”.

Very sincerely yours,

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