Author's response to reviews

Title: Analysis of EIF4G1 in ethnic Chinese

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Version: 4 Date: 5 January 2013

Author's response to reviews: see over
Author's response to editors

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Thank you for consideration of our manuscript for publication in your journal. We have reviewed the above manuscript according to your editor’s comments.

Reviewer's report:

1. The authors have addressed most of the concerns and it is much improved. In reference to the analysis with one or two degrees of freedom, the authors should understand that the three genotypes are not independent values, as they are dependent on allele frequencies; in a way the first genotype is p-squared, the second is 2pq and the third is q-squared; therefore only two variables p and q are present, and hence only on degree of freedom is the appropriate analysis. Please correct the values on the table to represent a one degree of freedom analysis.

   • Thank for your comments. We have changed our p-value from 0.413 to 0.184 in table 2 and our revised manuscript by using one degree of freedom analysis.

- Minor Essential Revisions –
1. In several instances, the authors refer to previously reported pathogenic mutations as “mutations”, this is not very clear and doesn’t read right. These should be corrected probably to “previously reported pathogenic mutations” or “reported mutations” or something similar, and these are found in page 2 line 11; page 5 line 2 from the bottom and page 6 line 5 from the bottom. In page 4 the authors write “The translation initiation complex is a large family, including eukaryotic translation initiation factor 4E, eukaryotic translation initiation factor 3e (eIF3e) and so on.” I believe this sentence would read better as “The translation initiation complex is a large family, including eukaryotic translation initiation factor 4E and eukaryotic translation initiation factor 3e (eIF3e)”.

The authors state in two places that “the eight intronic variants are in introns” this is rhetoric and unnecessary, and should be removed. Also in page 6 line 3; it would be better to describe the “two exonic variants” as “two nonsynonymous exonic variants”.

- Thank you for your comment. We have changed “mutations” to “reported mutations” in our revised manuscript.

We have rewritten sentences mentioned above in the paper as follows:

“ The translation initiation complex is a large family, including eukaryotic translation initiation factor 4E and eukaryotic translation initiation factor 3e (eIF3e)”. 
“The synonymous coding variant rs2230571 in exon 27 and the eight intronic variants were not used for further sequencing, but the specific mutation c.3614G>A (p.R1205H) and the two nonsynonymous variants (rs13319149 and rs2178403) were chosen for further analysis in a case-control study.”

2. In several instances the authors report exon numbers without a space from the exon (ie exon27); a space should be added between the exon and the number. A few similar errors with spacing can be found throughout the manuscript. The new title is not grammatically correct… it read as if EIF4G1 has Parkinson’s disease… I would suggest “Analysis of EIF4G1 in ethnic Chinese Parkinson’s disease patients” or “Analysis of EIF4G1 in ethnic Chinese”. Although the grammar has significantly improved, a final double checked would be welcomed.

- Necessary spaces have been added between the exon and the number and similar places. We have changed the title to “Analysis of EIF4G1 in ethnic Chinese”. Also, we have the language in our manuscript edited by a native-English speaker with scientific expertise in Edanz.

-Additional comments from the Associate Editor-

1. More academic language is needed. I would suggest the authors to check carefully the language.

   One example is below, but please check the manuscript carefully.
- As rs2230571 in exon27 is synonymous coding, and the eight intronic variants are in introns; we didn’t get them for further sequencing.

This sentence will sound better as follows:

“As rs2230571 in exon27 is a synonymous coding variation and the remaining eight variants were intronic, they were not subject to further sequencing.”

- We have checked our language carefully. Also, we have the language in our manuscript edited by a native-English speaker with scientific expertise in Edanz.

2. Spaces are needed after some periods in the discussion.

- Done.

3. After period, please start with a capital letter.

- Done.

4. Regarding the PD genes listed in the introduction, please note that some articles cited in this section are associated with sporadic PD and not inherited PD. Please cite more appropriate references. Also although the role of GIGYF2 in PD is controversial, there are in the literature several GIGYF2 mutations associated with PD not yet identified in control population; however, all previously reported PD-associated HTRA2 mutations were later identified in control population. For this reason, if you cite this gene please add a comment regarding these follow up studies nullifying its pathogenicity. Authors
can also add that some GIGYF2 mutations previously reported as pathogenic were identified in control population. Proper references should be cited.

- We have changed some articles cited in this section associated with sporadic PD to more appropriate references associated with familial PD. Considering that the role of GIGYF2 and HTRA2 in PD is controversial, we have deleted GYGIF2 and HTRA2 from list of genes implicated in PD in our introduction in our revised manuscript.