Reviewer's report

**Title:** EIF4G1 gene variants are not associated with Parkinson's disease in the ethnic Chinese population

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**Reviewer:** Carles Vilarino-Guell

**Reviewer's report:**

Li et al present a study characterizing eIF4G1 in 29 familial probands of Chinese ethnicity followed by genotyping of three missense variants in ~500 cases and ~500 controls. Overall the study design is appropriate, but there are several errors in the manuscript.

-Major Compulsory Revisions-

The conclusion drawn in the abstract is inaccurate, the authors can conclude that pathogenic mutations in eIF4G1 are not common in Han Chinese as the previously reported mutations were not identified and they did not identify any Chinese specific ones. However they cannot conclude that there are no associated variants as they only genotyped three and two were monomorphic.

The description of the variants identified in eIF4G1 is not accurate. The authors reported variants according to NM_198241.2, as with the original study by Chartier Harlin et al (I think); as there are many transcripts from this gene it is important to describe the transcript used for describing the variants. Regardless, the authors have started counting the exons from the first coding exon, not the real first exon; as a result, their promoter variant is not in the promoter but in intron 2, rs13319149 is in exon 7 not 5, and so on… all the positions need to be changed and the reference transcript used stated.

Statistical analyses of genotypes are performed with two degrees of freedom. This is not accurate as there are only two independent variables and as such the degrees of freedom should be one.

-Minor Essential Revisions –

The introduction states that “to date, the (should not be there) mutations in SNCA, LRRK2, PINK1, ATP13A (is missing a 2), PLA2G6, and VPS35 are known to cause familial PD” This statement is missing PRKN, DJ1 and probably FOBX7 if they include PLA2G6.

The authors don’t state very clearly why they only genotyped two of the variants they identified in their sequencing until the discussion. It would be advantageous to state from the very beginning that two of the variants are missense while the third is silent; and hence no further genotyped.
The authors use the sentence “no mutations” throughout the manuscript to describe previously reported mutations, this doesn’t come across very clearly and they should rewrite those statements. In addition, the variant of interest p.R1205H is consistently called c.3614G>A. I strongly advice the authors to use the protein position (or both) as mutations are most commonly reported from proteins.

The description of the study by Chartier-Harlin et al in the introduction is excessive, it should be cut down significantly. Just stating how it was identified is sufficient, hence the description of the two potential loci, and the fine mapping is overkill. Similarly, the first three paragraphs of the discussion are excessive and they should be combined with this one paragraph in the introduction to describe the function of eIF4G1.

In the genetic analysis section of the methods the authors provide the results of the sequencing analysis. This is out of place and should be removed.

Table 3 and 4 present age at onset and gender specific association, however there is no mention of these analyses in the manuscript. These two tables should be removed. Similarly Figure 1 is unnecessary.

- Discretionary Revisions –

I would recommend the authors cut down the manuscript to a shorter format if suitable to the journal. This is a simple report describing the sequencing of eIF4G1 in 29 probands and genotyping of one previously reported pathogenic mutations, one polymorphic and one monomorphic SNP in 1,000 samples; with negative results.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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