Reviewer’s report

Title: Targeted next-generation sequencing identifies novel variants in candidate genes for Parkinson’s disease in Black South African and Nigerian patients

Version: 1 Date: 10 Oct 2019

Reviewer: Pyotr A. Slominsky

Reviewer's report:

1. Line 109-110. It is very interesting that in your sample there are two patients with a purely mendelian inheritance of the disease. But for these patients, another analysis option must be applied - a direct analysis of cosegregation of the mutation and disease. You must at least exclude this patients from Table 1 and discuss this patients separately.

2. Table 2. You use Meta Score to evaluate mutations in two ways - LR and SVM. First, you must indicate that in both cases, a pred score is used. The critical levels of these score must be mentioned (https://softgenetics.com/PDF/GeneticistAssistant-Variant-Reference-Fields.pdf). But not all variants described in Table 1 correspond to these score - thus, all variants in the PINK1 and PRKN genes do not pass the Meta score value. As a result, the number of potentially significant mutations will change dramatically.

   Also in some cases a mutation frequency in patients is very close to GnomAD MAF. It is necessary to discuss.

3. Table 3. The problem of multiple mutations in one patient remains not sufficiently discussed. It is necessary to prioritize mutations taking into account both the Meta score, allele frequency and the biological function of the corresponding proteins. Nevertheless, choose a priority missense variant for each patient, taking into account all factors.

4. Given all the factors, modeling makes sense only for one protein, ATP13A2. In this regard, this piece of work needs to be reduced.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

Acceptable

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