Reviewer’s report

Title: SIRT1 (rs3740051) role in pituitary adenoma development

Version: 1 Date: 19 Jan 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

No - there are minor issues

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are major issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

No - there are major issues

Statistics - Is the use of statistics in the manuscript appropriate?

No - there are issues with the statistics in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are major issues

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Maybe - with major revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: In this study, the authors investigated the potential role of two SIRT1 polymorphisms in the development of pituitary adenomas. This study is original but largely descriptive. Also, the manuscript is not clear and there are several points (cohort and statistical analysis) that need to be clarified or corrected.

REQUESTED REVISIONS:
Objective

- The purpose includes two SNPS and does not sound appropriate since one of them, the rs4746720, is monomorphic in this population. In fact, this SNP should be excluded from the study.

Design

- Patients section lack important details. Pituitary adenomas subtypes should be presented in cohort description. No convincing explanation is provided in the text of what was considered a recurrent tumor. Data about patient's treatment should also be considered in this analysis since time for the recurrence may differ between surgical and medical therapy (again, pituitary subtype classification is important). Time of follow-up should also be provided. These point needs to be clarified to an accurate analysis considering recurrence of tumors.

Execution/Genotyping

- The method used for genotyping involved real time PCR, but it is not quantitative as mentioned in the text.

- It’s desirable that a method for ascertaining genotyping quality is included (p.e sequencing of 10% of samples). What’s the MAF of rs476720 in databases? If major or 5% it could be particularly important in this case.

Statistical analysis

- It’s not clear why and when the authors used MW test. Also, in some analysis Fisher exact test should be more appropriated than X2 test. Test statistical power should also be included.

- Overall tables are not properly exhibited. Especially tables with binary logistic regression are so confused. Actually, the term "binary regression logistic" is not a good table title. The tables should focus on presenting the SNP frequency comparison between control and PA or invasive or not invasive PA using a genotype as reference (AA, major allele homozygous). Genetic models' terms in tables are also confusing and may be used only in explanation text (the additive model, is a subclassification of codominant one). The authors could choice and discussed the model that best fits to their hypothesis.

- For haplotype analysis of rs3740051 and previously analyzed rs12778366, LOD should be presented with D’ and r2 values. With this information, it’s possible to know if the two SNP comprised a single block. If it's true, the haplotype analysis is unnecessary.

ADDITIONAL REQUESTS/SUGGESTIONS:

Discussion

- No conclusion about SIRT1 role in pituitary adenomas may be drawn. So, the discussion is very wordy and should be focus on the potential role of this SNPs as a biomarker.

Conclusions
The conclusion sound incorrect and should be rewrite.
Supplementary material
Supplementary materials are missing.

Note: This reviewer report can be downloaded - see attached pdf file.

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

No

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

No

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

No

**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.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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