Reviewer's report

Title: SIRT1 (rs3740051) role in pituitary adenoma development

Version: 3 Date: 26 Jun 2019

Reviewer: Reviewer 2

Reviewer's report:

"PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses one or several testable research questions? (Brief or other article types: is there a clear objective?)

Yes - there is a clear objective

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

Yes - the approach is appropriate

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

No - there are minor 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 minor issues

OVERALL MANUSCRIPT POTENTIAL - Has the author addressed your concerns sufficiently for you to now recommend the work as a technically sound contribution? If not, can further revisions be made to make the work technically sound?

Maybe - with major revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: The revised manuscript has been improved and table data and results are more clearly. However, majors issues have not yet been solved. Additional files were not available in the attached file and could not be checked.

REQUESTED REVISIONS:
Majors:

1- The association of recurrence and SIRT1 SNPs should be interpreted with caution. The authors referred recurrence in some (n=30) patients that was classified according to re-surgery. However, the majority of cases are PRLomas whose first line of treatment is the medical and not surgical approach (or, in this series, the majority of PRLomas were surgically treated?). In addition, no mention about follow-up is provided and we know that PA recurrence could occur between 1-5 years after surgery. These points need to be clarified (time of follow-up and the criteria for tumor recurrence in active PA) and discussed in the text.

2- No data about the risk of recurrence and invasiveness by genotype (hazard ratio) was presented. This evaluation should be performed and the results included in Table 3 and 4.

3- What is the size effect of the SNP rs3740051-12778366 haplotype in the occurrence of PA since the rs12778366 alone was previously associated with the PA occurrence? (I mean, is the odds ratio greater?).

Minors:

1- Standardize: always use capital (preferred) or lower letter for P value.

2- P1, Line 41: "6.7 %, 86.7 %, p=0.022)" lack the word respectively "6.7 %, 86.7 %, respectively, P=0.022)".

3- Standardize: use always "G/A" for the heterozygous genotype.

4- P1, Line 75: "Sir2" rather than "SIR2".

5- P5, Line 101. If the difference is no statistically significant, the P is > or = 0.05 and not < was referred.

6- P5 Line 103, the phrase "The detailed methodology about invasiveness evaluation has been described previously (28)." Is not necessary, since a detailed description is provided.

7 - P5 Line 104: Standardize: "MRI" rather than "MR".

8- P8, Line 126. More information about recurrence should be provided. See major concern 1.

9- P11-Line 230: Correct the phrase: "The frequency of genotypes and alleles of rs3740051 in patients with PA and control subjects by PA recurrence", no control subjects was compared in this analysis.

10- P14, Line 293-294. Table 6 is unnecessary. This results could be easily presented in the text.

ADDITIONAL REQUESTS/SUGGESTIONS:

All revisions suggested were listed above."
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

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Please indicate the quality of language in the manuscript:

Acceptable

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