Reviewer's report

Title: SIRT1 (rs3740051) role in pituitary adenoma development

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Reviewer: Giampaolo Trivellin

Reviewer's report:

Liutkeviciene and colleagues studied the possible involvement of SIRT1 genotypes (SNPs rs4746720 and rs3740051) on the development of pituitary adenomas (Pas). The population under study consisted of 142 patients with pituitary tumors and 826 controls matched by age and gender. The authors concentrated their analysis on the rs3740051 SNP since the other SNP showed only the presence of the wt allele in all cases. Concerning rs3740051, the authors did not find an association with the development of pituitary tumors. However, they found an association for the A/A genotype with PA recurrence, and for the G/A genotype with non-invasiveness. No significant association with hormonal activity was observed. Finally, the authors reported that the haplotype C-A at the rs12778366-rs3740051 loci was associated with increased risk for PA development.

I think this is an interesting study that, however, needs to address several important issues to be ready for publication. My comments are the following:

1. The authors mentioned several times throughout the manuscript that some data are reported in the supplementary section. However, I could not find that part in the submission portal. Therefore, I cannot fully judge this manuscript with that part missing.

2. In the abstract and in several other parts of the manuscript, the authors state that rs3740051 is associated with PA development. However, that is not correct, as shown in the first part of the Results. rs3740051 is rather associated with PA recurrence.

3. At the end of the Introduction the authors state that the aim of this work was "to find an association between pituitary adenoma and...". This is not correct, as the authors rather "aimed to investigate whether there was an association between…".

4. In the Methods is not clear whether all the pituitary tumors included in the study are prolactinomas or just the majority. If the first case, then all the conclusions should rather be corrected stating e.g. that the A/A genotype is associated with recurrence of prolactin-secreting tumors rather than PAs in general. If the latter, the authors should then specify how many samples for each functional tumor subtypes were present.

5. In the first paragraph of page 9 the authors performed a statistical analysis for rs3740051 genotypes and alleles in patients and controls stratified by gender. What was the purpose to do this analysis in controls? Was it to test whether a specific genotype/allele was associated with gender? If so, then it should be made clear.

6. Page 9, lines 201-204: the results should be presented in Table 3 in a clearer way. Moreover, the numbers for the control group in the Table 3 and the following are a bit different from those for the same group presented in Table 2 and thus should be corrected!
The legend for Table 3 needs also to be corrected as it reports some text (e.g. Hardy-Weinberg significance level) that is not mentioned in that table.

7. Page 9, line 203 and page 10, line 226: those numbers should be presented in their respective tables rather than in their legends.

8. The Discussion needs to be extensively revised since the results are very briefly discussed. The authors indeed mainly concentrated on the role of SIRT1 in other pathologies or cancers, which is only marginally relevant to this study. That part (all page 13 and half page 14) should therefore be consistently reduced and devoted instead to discuss and interpret the data and what are the possible implications of the findings.

9. How were the HWE p values calculated in Table 2? It seems indeed odd that, although both values are non-significant, the one for the control group is almost significant (0.053) when the % for each genotype were not much dissimilar from those of the patients…

10. Page 12, line 277: perhaps the A/A genotype increases rather than decreases odds of recurrent PA?


Minor grammatical mistakes:

1. Page 3, line 59: "Pas" should be corrected to "PAs".

2. Page 8, lines 182-183: "the genotype distribution did not deviated" should be corrected to "the genotype distribution did not deviate".

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.

Yes

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

No

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