

Peer Review File

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Reviewer A

Authors should address the variable approaches for craniopharyngioma management PMID: 36624954.

In particular, should expand the post-operative ICU algorithm for managing DI.

If the above is addressed and references included, paper could be of interest.

Reply: The question you raise is very relevant, but our current study is on a new biomarker for Adamantinomatous craniopharyngioma and the corresponding targeted drug.

Reviewer B

Congratulations for this interesting study. I suggest adding the topic 'statistical analyses' within 'Methods' and not in 'Results'. I also suggest adding on figures legends p-values that were considered in correlation analyses. In Figure 9, I suggest adding p-value of difference between control and treat groups.

Reply: We have modified our text as advised (see Page8,33, line 263-268, 740) and we have modified our Figure 9 as advised (see figure 9-revised.tif).

Reviewer C

Comment 1: First, the title did not indicate that this is a bioinformatics analysis. The current title is also overstated since, without real-world validation in clinical practice, the findings from bioinformatics analysis are not convincing. The authors need to reconsider a title. Further the title should be specific to ACP, not CP, according to the main text.

Reply 1: We have modified our text as advised (see Page 1, line 2).

Comment 2: Second, the abstract needs further revisions. In the background, the authors did not describe the difficulties in the diagnosis of ACP and treatments and explain why a bioinformatics analysis is suitable to address the two research questions. The methods need to describe the two datasets used as training and validation sets, the method for assessing the diagnostic accuracy, and the method for assessing the treatment sensitivity. The results need to describe the diagnostic accuracy parameters in both the training and validation sets and the biomarkers involved in the diagnostic model. The conclusion needs more detailed comments for the clinical implications of the findings.

Reply 2: We have modified our text as advised (see Page 1-3, line 34-73).

Comment 3: Third, in the introduction of the main text, the authors need to explain why a bioinformatics analysis can help address the difficulties in the diagnosis of ACP and its treatment. Without validation in real-world patients, the evidence provided by this study is very weak. The authors should consider to tone down the statements on the significance of this study.

Reply 3: We have modified our text as advised (see Page 5, line 141-143).

Comment 4: Fourth, in the methodology of the main text, it is very bad that the sample sizes of patients with ACP and controls in both the training and validation databases are very small. In this case, the identified genes used for the diagnosis and the parameters of diagnostic accuracy are very unstable. Please describe the indicator for assessing the diagnostic accuracy such as AUC and its threshold value for a good diagnostic model.

Reply 4: We have modified our text as advised (see Page 8, line 239-241).

Reviewer D

1. Abstract

Please define ROC in the abstract.

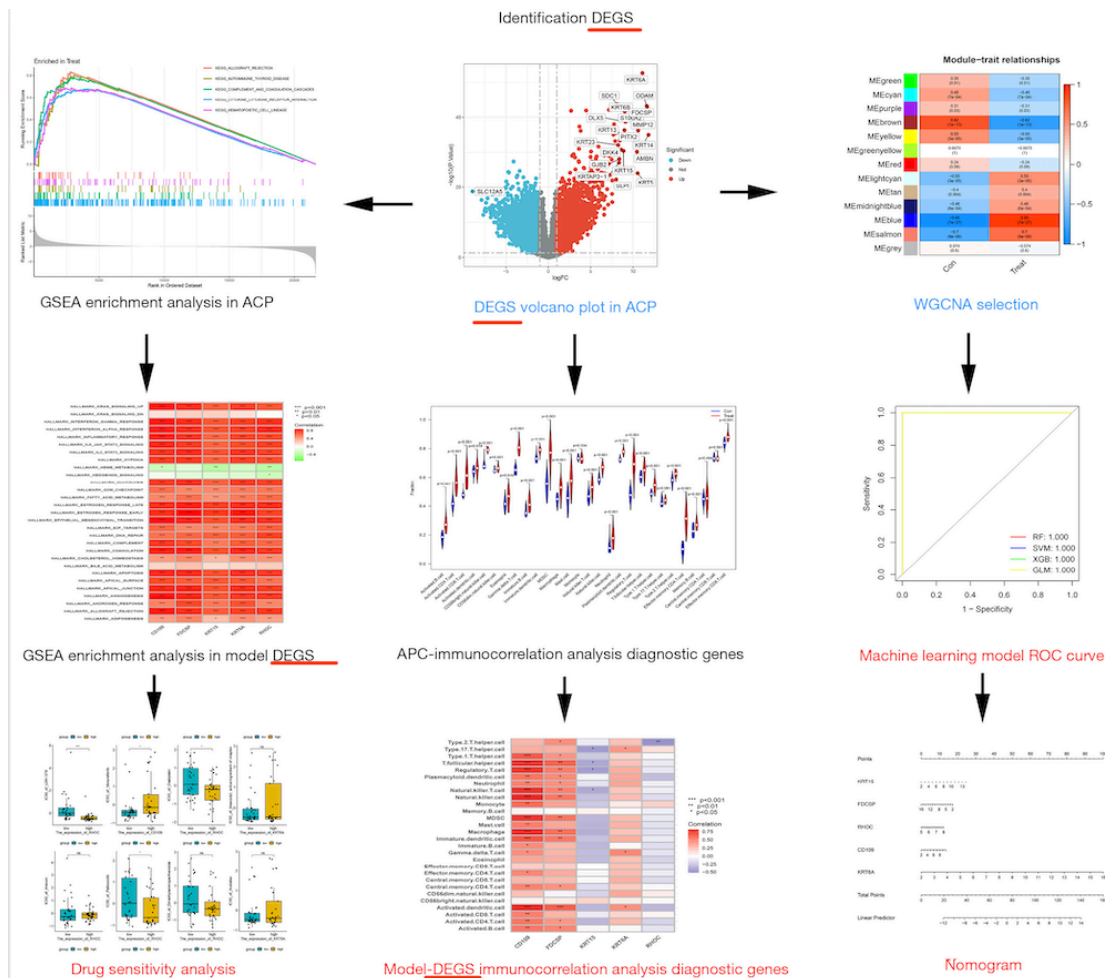
47 [screened using machine learning algorithms to assess diagnostic accuracy using ROC](#)

Reply: we have modified our text as advised (see Page 2, line 46).

Changes in the text: receiver operating characteristic

2. Figure 1

a) Please revise DEGS to DEGs in the figure.



Reply: we have modified our Figure 1 as advised (see figure 1-revised.jpg).

b) Please explain RF, SVM, XGB, and GLM in the legend.

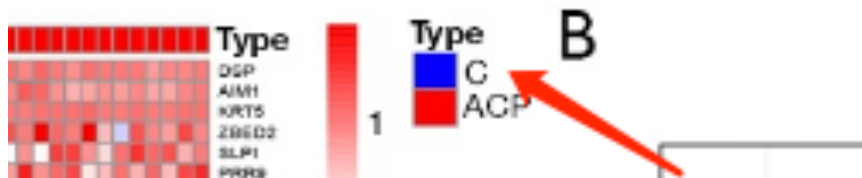
Reply: we have modified our text as advised (see Page 21, line 656-658).

Changes in the text: SVM, support vector machine; GLM, generalized linear model; RF, RF random forest tree; XGB, Tree Ensemble.

3. Figure 2

a) Please explain FC in the legend.

b) Please explain what's C stand for in the legend.



Reply: we have modified our text as advised (see Page 21, line 663).

Changes in the text: FC, fold change; C, control group.

4. Figure 4

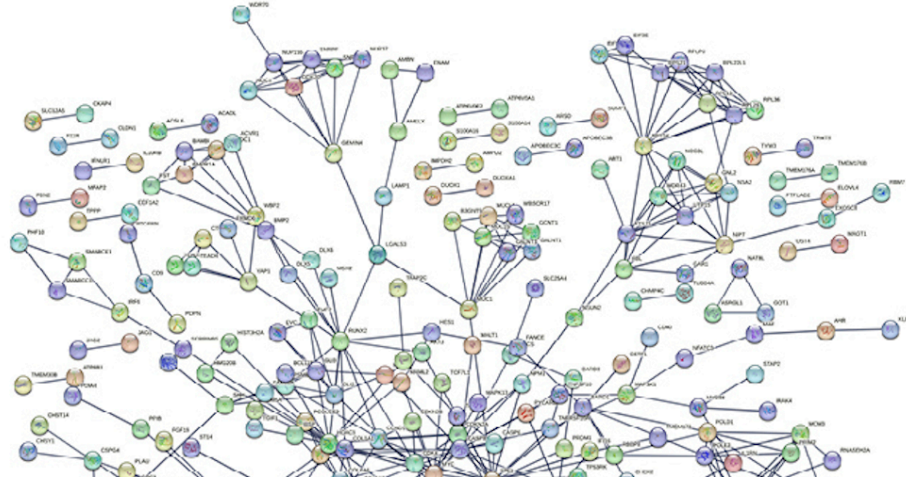
Please explain KEGG in the legend.

Reply: we have modified our text as advised (see Page 22, line 675-676).
Changes in the text: KEGG, Kyoto Encyclopedia of Genes and Genomes.

5. Figure 5

Please provide a clearer version of figure 5, the current one cannot be seen clearly (as you can see the screenshot below).

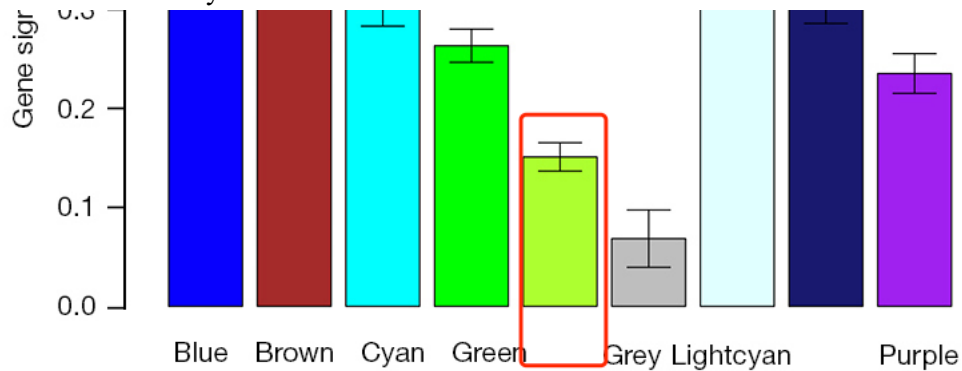
A



Reply: we have modified our Figure 5 as advised (see figure 5-revised.jpg).

6. Figure 6

Please add Greenyellow to the x-axis.

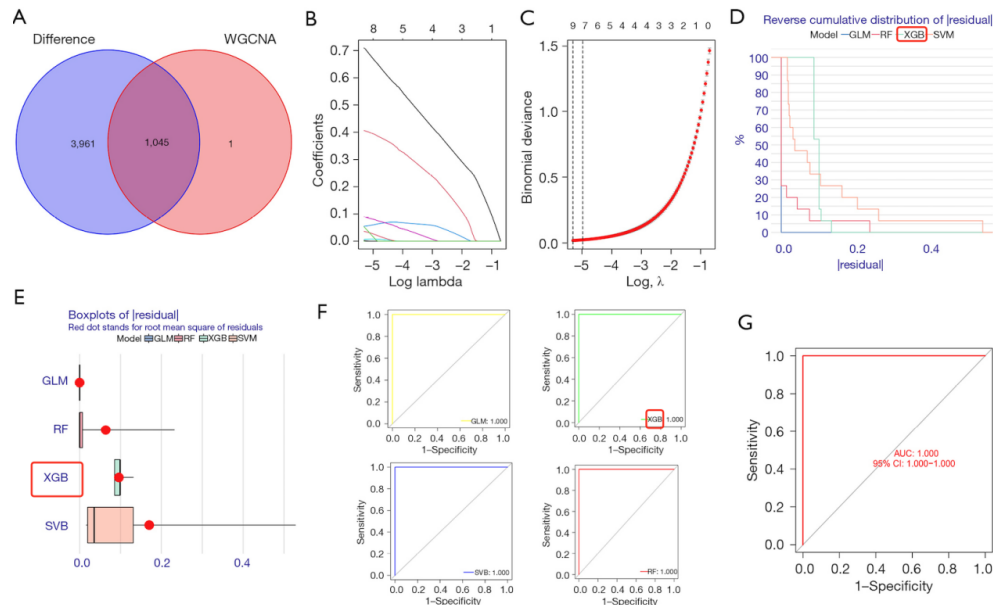


Reply: we have modified our Figure 6 as advised (see figure 6-revised.jpg).

7. Figure 7

a. Please double check and unify the word.

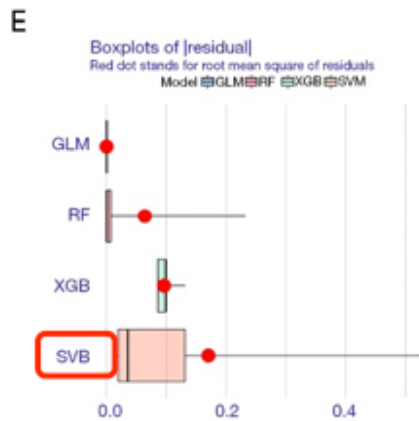
755 the SVM, RF tree, GLM, and **XGBoost** constructed models. (E) Reverse cumulative
756 distribution of the residuals of the SVM, RF tree, GLM, and **XGBoost** constructed
757 models. The Y-axis value represents the percentile of the outliers. (F) ROC analysis of
758 the SVM, RF tree, GLM and **XGBoost** algorithms. (G) ROC analysis of the GLM
759 model in the GSE68015 validation set. WGCNA, weighted gene co-expression
760 network analysis; GLM, generalized linear models; RF, random-forest; **XGBoost**,



Reply: we have modified our text as advised (see Page 24, line 708-710).

b. Legend (7E) does not match the figure 7E. Please check and unify.

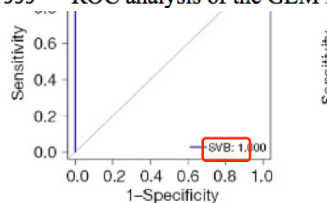
996 the SVM, RF tree, GLM, and XGB. (E) Reverse cumulative distribution of th
 997 residuals of the SVM, RF tree, GLM, and XGB. The Y-axis value represents th
 998 percentile of the outliers. (F) ROC analysis of the SVM, RF tree, GLM and XGB. (C



Reply: we have modified our Figure 7 as advised (see figure 7-revised.tif).

c. Legend (7F) does not match the figure 7F. Please check and unify.

998 percentile of the outliers. (F) ROC analysis of the SVM, RF tree, GLM and XGB. (G)
 999 ROC analysis of the GLM model in the GSE68015 validation set. WGCNA, weighted



Reply: we have modified our Figure 7 as advised (see figure 7-revised.tif).

8. Figure 8

Please double check if a scale is missing.



Reply: we have modified our Figure 8 as advised (see figure 8-revised.tif).

9. Figure 9

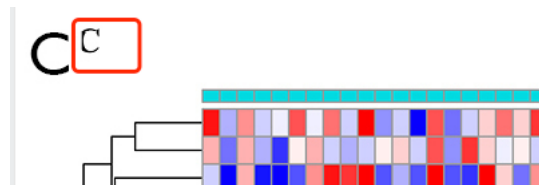
Please provide the meaning of “***” in the legend.

Reply: we have modified our text as advised (see Page 25, line 728).

Changes in the text: ***, $P < 0.001$.

10. Figure 10

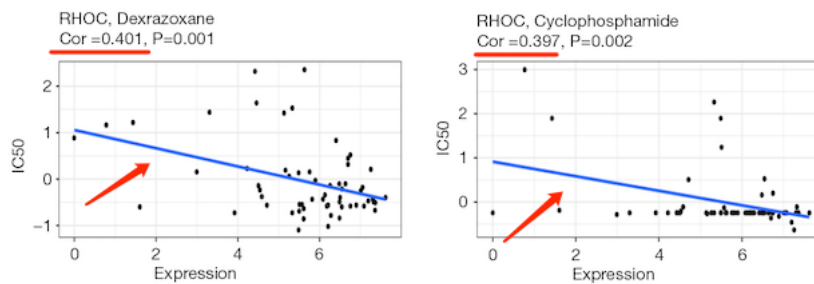
Please remove another C in the figure.



Reply: we have modified our Figure 10 as advised (see figure 10-revised.jpg).

11. Figure 13

a) Please double check if the figure is correct.



Reply: we have modified our Figure 13 as advised (see figure 13-revised.tif).

b) Please provide the meaning *, *** in the legend.

Reply: we have modified our text as advised (see Page 30, line 752-753).

Changes in the text: *, $P < 0.05$; ***, $P < 0.001$.