Author’s response to reviews

Title: Screening key genes for abdominal aortic aneurysm based on Gene Expression Omnibus dataset

Authors:

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Author’s response to reviews:

Dear Barry Palmer,

We are submitting the revised manuscript with the ID BCAR-D-17-00607R3, entitled "Screening key genes for abdominal aortic aneurysm based on Gene Expression Omnibus dataset" for publication in BMC Cardiovascular Disorders. According to the comments, we have already revised the manuscript. All revisions have been marked in red in the revised manuscript. The following are our reply to the comments, item by item.

Once again, thank you for your kind reconsideration.

Yours sincerely,

Jingyong Huang

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Technical Comments:

Editor Comments:

My sincere apologies, it appears the document of my comments on typographical and grammatical errors and suggested wording changes to improve clarity, did not attach to my previous decision.

Please address the issues I have copied below. Individually they are generally minor, but cumulatively they are likely to make the article confusing for readers. In a number of cases I have indicated the meaning of sentences is unclear and require rewording. Please seek appropriate advice on clearer wording if necessary. Also some of my suggestions for rewording may not convey your intended meaning, if so please revise with appropriate alternatives.

Page 2/Line 32

diagnosis value  -> diagnostic value

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Abstract” section (line 32, page 2) of the revised manuscript. Thanks again!

Page 2/Line 37

Top…  -> The top …

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Abstract” section (line 37-38, page 2) of the revised manuscript. Thanks again!

Page 2/Line 39

network  -> networks

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Abstract” section (line 39, page 2) of the revised manuscript. Thanks again!
Page 2/Line 40

IHC -> IHC staining

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Abstract” section (line 40-41, page 2) of the revised manuscript. Thanks again!

Line 50

that characterized -> that is characterized

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Background” section (line 50, page 3) of the revised manuscript. Thanks again!

Line 53

it -> AAA

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Background” section (line 53, page 3) of the revised manuscript. Thanks again!

Line 61

...are critical -> ...are the critical

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Background” section (line 61, page 3) of the revised manuscript. Thanks again!

Line 65

However, the morbidity and mortality after operation …->

However, morbidity and mortality after surgery…
Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Background” section (line 65, page 3) of the revised manuscript. Thanks again!

Lines 67-68

of pathogenesis mechanism and signal pathway in AAA and discovery of potential biomarker and drug target …-> of pathogenic mechanism(s) and signal pathway(s) in AAA and the discovery of potential biomarkers and drug targets…

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Background” section (line 67-68, page 4) of the revised manuscript. Thanks again!

Line 77

Our study was helpful... -> Our study may be helpful...

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Background” section (line 77, page 4) of the revised manuscript. Thanks again!

Line 87

was -> were

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Datasets” section (line 87, page 4) of the revised manuscript. Thanks again!

Line 94

meta MA -> metaMA

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Analysis of DEGs” section (line 91, page 5) of the revised manuscript. Thanks again!
Line 101
by studying -> to study

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “PPI network construction” section (line 101, page 5) of the revised manuscript. Thanks again!

Line 105
Then, PPI network … -> The PPI network generated…

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “PPI network construction” section (line 105, page 5) of the revised manuscript. Thanks again!

Line 121
IHC staining area … -> The IHC staining area …

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Immunohistochemical (IHC) staining for CCR7 and PDGFA” section (line 121, page 6) of the revised manuscript. Thanks again!

Lines 123-126
Intensity score of negative-, positive+, positive++, positive+++ in slides was respectively assigned 0, 1, 2 and 3; positive rate score of negative, 1-25%, 26-50%, 51-75% and 76-100% in slides was assigned 0, 1, 2, 3 and 4. ->

Intensity scores of negative-, positive+, positive++, positive+++ in slides were respectively assigned 0, 1, 2 and 3; a positive rate score of negative, 1-25%, 26-50%, 51-75% or 76-100% in slides was assigned 0, 1, 2, 3 or 4.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the
“Immunohistochemical (IHC) staining for CCR7 and PDGFA” section (line 123-126, page 6) of the revised manuscript. Thanks again!

Lines 126-127

was defined -> were categorised

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Immunohistochemical (IHC) staining for CCR7 and PDGFA” section (line 127, page 6) of the revised manuscript. Thanks again!

Line 133

using pROC package … -> using the pROC package …

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Receiver operating characteristic analyses” section (line 134, page 7) of the revised manuscript. Thanks again!

Lines 137-138

of GEO database. Total of 1199 DEGs…

-> of GEO the database. A total of 1199 DEGs…

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “DEGs analysis” section (line 138-139, page 7) of the revised manuscript. Thanks again!

Line 138

identified as the threshold -> identified at the threshold ?

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “DEGs analysis” section (line 139, page 7) of the revised manuscript. Thanks again!
Top 10 up- and down-regulated DEGs were listed in Table 2. The heat map of top 50 DEGs was shown in Figure 1.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “DEGs analysis” section (line 140-141, page 7) of the revised manuscript. Thanks again!

…most remark enrichment … -> …most notable enrichment … ???

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Functional and pathway enrichment analyses of DEGs” section (line 148, page 7) of the revised manuscript.

Thanks again!

The top 10 GO terms of DEGs were shown in Table 3. The KEGG enrichment signal pathways of DEGs were shown in Table 4. Among which, vascular smooth muscle contraction and pathways in cancer were significantly related to AAA, which was showed in Figure 5 and Figure 6, respectively.
Line 155

to obtain TFs regulating top ten up-regulated or down-regulated DEGs. ->

to identify TFs regulating the top ten up-regulated or down-regulated DEGs.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Establishment of TFs-target genes regulatory network” section (line 156, page 8) of the revised manuscript. Thanks again!

Line 156

comprising of -> comprised of

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Establishment of TFs-target genes regulatory network” section (line 157, page 8) of the revised manuscript. Thanks again!

Line 164-165

PPI networks of top 10 up-regulated and top 10 down-regulated DEGs were presented in Figure 8. As Figure 8 shown…

->

PPI networks of the top 10 up-regulated and the top 10 down-regulated DEGs were presented in Figure 8. As Figure 8 shows …

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “PPI network” section (line 165-166, page 8) of the revised manuscript. Thanks again!

Line 166

And the red and green diamond presented the up- and down-regulated genes in AAA, respectively. ->

The red and green diamonds indicate the up- and down-regulated genes in AAA, respectively.
Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “PPI network” section (line 167-168, page 8) of the revised manuscript. Thanks again!

Line 167

The blue ellipse presented the proteins that interacted with those proteins encoded by DEGs. ->

The blue ellipses represent the proteins that interacted with those proteins encoded by DEGs.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “PPI network” section (line 168-169, page 8) of the revised manuscript. Thanks again!

Line 185-186

In spite of improvement of surgical techniques has been made in AAA treatment, the morbidity and mortality after operation are still common, ->

In spite of improvement to surgical techniques that have been made in AAA treatment, morbidity and mortality after operations are still common,

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Discussion” section (line 186-187, page 9) of the revised manuscript. Thanks again!

Line 188

carcinogenesis -> pathogenesis?

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Discussion” section (line 189, page 9) of the revised manuscript. Thanks again!

Line 187-189 –the meaning of this sentence is unclear.

Therefore, it is urgent to elucidate AAA carcinogenesis mechanism for developing novel diagnose and therapeutic target that will be highly specific to malignant cells, with minimal or no risk of adverse effect.
Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have rewritten the sentence and marked in red in the “Discussion” section (line 188-189, page 9) of the revised manuscript. Thanks again!

Line 190

TFs were key regulatory factors in gene expression. The construction of regulatory network…

TFs are key regulatory factors in gene expression. The construction of regulatory networks …

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Discussion” section (line 190, page 9) of the revised manuscript. Thanks again!

Line 194-196

NELL2 is a neural tissue-enriched protein in mammal. And it is the receptor for vascular endothelial growth factor-A, which plays an important role in angiogenesis. ->

NELL2 is a neural tissue-enriched protein in mammal and it is a receptor for vascular endothelial growth factor-A, which plays an important role in angiogenesis.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Discussion” section (line 194-196, page 9) of the revised manuscript. Thanks again!

Line 122

cancer cell -> cancer cells

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Discussion” section (line 211, page 10) of the revised manuscript. Thanks again!
In addition, PDGFA was one of the top ten

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Discussion” section (line 218, page 10) of the revised manuscript. Thanks again!

Moreover, an in situ …

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Discussion” section (line 223, page 11) of the revised manuscript. Thanks again!

Apart from the cancer signal pathway, vascular smooth muscle contraction was another signal pathway identified that associated with AAA.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have deleted the sentence. Thanks again!

Caldesmon 1 (CALD1) is the protein coding smooth muscle contractile.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have deleted the sentence. Thanks again!
had a diagnosis value in the development of AAA. -> may have value in diagnosis of the development of AAA.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Discussion” section (line 264-265, page 12) of the revised manuscript. Thanks again!

Thirdly, the sample size of normal individuals in selected dataset... ->
Thirdly, the sample size of normal individuals in the selected dataset ...

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Conclusions” section (line 276-277, page 13) of the revised manuscript. Thanks again!

Table 5
Target neges -> Target genes

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in Table 5. Thanks again!

Diagram presents the result of a two-way hierarchical clustering of top 50 DEGs and samples. ->
The diagram presents the result of a two-way hierarchical clustering of the top 50 DEGs and samples.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Figure legends” section (line 509-510, page 24) of the revised manuscript. Thanks again!

Significant enrichment… -> Significantly enriched …
Legends for Figures 2, 3 & 4 – explain the meaning of the different colours of the bars in the legend of each of these figures.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Figure legends” section (line 514, 517, 520, 523 and 525 page 24) of the revised manuscript. In addition, the x-coordinate axis in the Figures 2, 3 and 4 presents the FDR value. FDR value is more highly, the colour of the bar is more deeply. We have added the interpretation and marked in red in the “Figure legends” section (line 515-516, 518-519 and 521-522, page 24) of the revised manuscript. Thanks again!

Line 522, 525 & 526
…top 20 DEGs… -> …the top 20 DEGs…

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Figure legends” section (line 527, page 24, line 530-531, page 25) of the revised manuscript. Thanks again!

Line 539
…health controls -> …healthy controls

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have corrected and marked in red in the “Figure legends” section (line 545, page 25) of the revised manuscript. Thanks again!

Reviewer reports:

If improvements to the English language within your manuscript have been requested, you should have your manuscript reviewed by someone who is fluent in English. If you would like professional help in revising this manuscript, you can use any reputable English language editing service. We can recommend our affiliates Nature Research Editing Service (http://bit.ly/NRES_BS) and American Journal Experts (http://bit.ly/AJE_BS) for help with English usage. Please note that use of an editing service is neither a requirement nor a guarantee of publication. Free assistance is available from our English language tutorial (https://www.springer.com/gb/authors-editors/authorandreviewertutorials/writinginenglish) and
our Writing resources (http://www.biomedcentral.com/getpublished/writing-resources). These cover common mistakes that occur when writing in English.

Answer: We thank the Reviewer for his/her kind evaluation of our work. We are sorry for our poor English writing. As suggested, we have checked and corrected the spelling and grammar mistakes of the manuscript. All changes have been marked in red in the “” section (line 54, 57, 60, page 3; line 70, page 4; line 102, 109, page 5; line 187-188, page 9; line 220, page 10; line 234, page 11) of the revised manuscript. Thanks again!