Author’s response to reviews

Title: Oct4 upregulates osteopontin via Egr1 and is associated with poor outcome in human lung cancer

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Point-to-point responses to referees:
Editor Comments:

1 - Please remove any files from the file inventory that you do not wish to see published.
Response: Yes, we have checked it.

2 - If human cell lines are used, authors are strongly encouraged to include the following information in their manuscript:
• The source of the cell line, including when and from where it was obtained
• Whether the cell line has recently been authenticated and by what method
• Whether the cell line has recently been tested for mycoplasma contamination
Further information is available from the International Cell Line Authentication Committee (ICLAC). We recommend that authors check the NCBI database for misidentification and contamination of human cell lines. Please include the sources of all cell lines and their catalogue numbers.
Response: The condition of cell lines has been verified.

3 - Please confirm whether any of the cell lines required ethics approval for their use and include a statement in the Ethics approval and consent to participate section in the Declarations.
Response: No cell line is required for declaration of ethic approval.

4 - For all research involving human subjects, informed consent to participate in the study should be obtained from participants (or their parent or guardian in the case of children under 16) and a statement to this effect should appear in the ‘Ethics approval and consent to participate’ section of the Declarations including whether the consent was written. When reporting on such studies, individual patient data should not be made available unless consent for publication has also been obtained.

If the need for informed consent has been waived by an IRB or is deemed unnecessary according to national regulations, please clearly state this with details, including the name of the Board or a reference to the relevant legislation in the ‘Ethics approval and consent to participate’ section of the Declarations.
Response: The approval of IRB was reported in the section and Declaration (IRB serial No. 10308-002).

5 - In the Funding section of the Declarations please indicate the role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript. If no specific funding was received for this study, please clearly indicate this in the Funding section.

Response: We had reported this issue in the funding section.

6 - If you wish to acknowledge someone by their full name in the Acknowledgements, please ensure you have obtained permission from them to so do.

Response: Yuan Chang and Chung-Han Ho have been informed.

7 - Please include a statement in the Authors' contributions section to the effect that all authors have read and approved the manuscript, and ensure that this is the case.

Response: The Authors’ contribution section was completed.

8 - At this stage, please upload your proofread manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethrough or text in different colours. All relevant tables and figures should also be clean versions. Figures (and additional files) should remain uploaded as separate files. Should you wish to respond to these revision requests, please include the information in the designated input box only.

Response: Understand.

BMC Cancer operates a policy of open peer review, which means that you will be able to see the names of the reviewers who provided the reports via the online peer review system. We encourage you to also view the reports there, via the action links on the left-hand side of the page, to see the names of the reviewers.
Reviewer reports:

Reviewer 2 (Reviewer 2): 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?
Yes - experiments and analyses were performed appropriately

STATISTICS - Is the use of statistics in the manuscript appropriate?
Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
Yes - the author's interpretation is reasonable

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?
Yes - current version is technically sound
GENERAL COMMENTS: The Authors prepared the careful responses to the previously raised questions. All responses are reasonable and call no objections. All my doubts related to the statistical issues were explained and presented appropriately in the new version of the manuscript. Ok, I can agree that there is a chance that ELISA could provide satisfactory quantitative results.

ADDITIONAL REQUESTS/SUGGESTIONS:

I like the paper and consider positively the next research supporting the role of osteopontin as the potential biomarker. The current report supports positively those hypotheses and contributes to the strengthening therapeutic strategies targeting additionally Oct4 and Egr1 along with OPN.

Reviewer 3 (Reviewer 3): "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?

Yes - experiments and analyses were performed appropriately
STATISTICS - Is the use of statistics in the manuscript appropriate?
Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
Yes - the author's interpretation is reasonable

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?
Probably - with minor revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: The revised manuscript that describes analyses and demonstrate that the Egr1/OPN axis is regulated in Oct4-expressing lung cancer includes corrections and modifications as requested by the two prior reviewers. The authors have addressed most of the requested issues.

ADDITIONAL REQUESTS/SUGGESTIONS:
There is one major and a few minor issues to be corrected that are indicated below.

1. Figure 1 immunostaining was said to be improved, but the quality remains low.
2. Page 15, line 15: the euthanasia of these mice……
3. Page 16, line 3: Fischer's not Fish?
4. Page 16, line 5: Kolmogorov-Smirnov (no space)
5. Page 16, line 8: error is correct spelling
6. Page 16, line 15: p-value should be italicized
7. Page 30, line 9: statistical

Response: We corrected them all.