Author’s response to reviews

Title: Development of a computational promoter with highly efficient expression in tumors

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Author’s response to reviews:

Dear editor:

Thank you to inform us that manuscript BCAN-D-17-02214R3, entitled “Development of computational promoter with highly efficient expression in tumors.” is potentially acceptable for publication in BMC Cancer. We have made the modification for the manuscript as editor’s suggestions, and point-by-point responses to the comments.

Thank you for your consideration.
Yours sincerely,

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Responses to editor

1. We thank editor’s suggestion. HPDE is human papillomavirus-E6 and -E7 gene-immortalized pancreatic ductal epithelial cells (Liu et al., 1998). It was established and published in 1998. Later, it was used and published in more than 150 articles. In these articles, all of authors only describe the origin of cell line but not provide any ethical approval, even the current publication. We recheck and there is no license for this cell line. Therefore, the ethical approval was not required for HPDE cell line.


2. In this study, we followed the protocol to scarify the mice by CO2 asphyxiation as suggestion by “AVMA Guidelines for the Euthanasia of Animals: 2013 Edition”. The method was approved by the Institutional Animal Care and Use Committee at National Chiao Tung University (NCTU-IACUC-104034). The statements were incorporated into the revised manuscript (Ethics approval and consent to participate section, line 7-11, page 32).
3. We used eight databases (GEO, TRANSFEC, Gene Ontology, DAVID, PubMed, GENEMANIA, UniPort, The human protein Atlas) in this study. All databases are open and free (except of TRANSFEC), all databases do not need the administrative permission. The statements were incorporated into the revised manuscript (Ethics approval and consent to participate section, line 12, page 32).

4. We thank editor’s suggestion. There were two embedded methods in figure 6 for different experiments. In figure 6A, when the tumors grew to 50 mm³, 100 mm³, 250 mm³, 500 mm³ or 1000 mm³, the tumors were harvested and embedded in paraffin, and the sections (7 μm) were stained with IHC to observe the expression levels of HIF-1α, NF-κB or CREB. In this experiment, the correlation of specific transcriptional factors and tumor sizes were monitored. In Figure 6B and C, the mice were treated by injections in tumors or muscles with LPPC/pD5-hrGFP or LPPC/pCMV-hrGFP complexes. At 7 days after treatments, the mice were sacrificed and the tumors or muscles were harvested and embedded in OCT reagents to monitor the fluorescent expressions of hrGFP. We will further provide the statements for material and method about OCT-embedded. In addition, we also descrip more clearly in “in vivo transfection” and incorporated into the revised manuscript (Materials and Methods section, line 14-17, page 14; line 1-4 and 9-11, page 15).

5. As editor’s suggestion, “Additional files” section was added in the revised manuscript (page 39-41).

6. Thanks for the editor’s reminder. We re-check the additional files in the main manuscript to sure all additional files have been cited in this manuscript.

7. We added the scale bars in all histological pictures (Figure 6, Figure 7A, Figure 8B and Additional file 9).
8. We thank editor’s suggestion, and follow one of the forms. “The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request”, the statement was added and incorporated into the revised manuscript (Availability of data and material section, line 1-2, page 33).

9. We add the statement, “the funding body had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript” into the “Funding” section (Funding section, line 9-10, page 33).

10. The author names in “Authors contributions” were corrected as editor’s suggestion.

11. All authors have approved the final manuscript. The statement was incorporated into the revised manuscript (Authors’ contributions section, line 15, page 33).

12. Thanks for the editor’s reminder. In “Authors contributions” section, CHC1 corresponding to Chen-Han Chung and CHC2 corresponding to Cheng-Hsun Chuang.

13. Thanks for the editor’s reminder. Figure 2 have been separated into two files (figure 2 and figure 3).

14. The figure titles have been removed from all figures.