Reviewer’s report

Title: Anti-cancer effect of dung beetle glycosaminoglycans on melanoma

Version: 1 Date: 04 Sep 2018

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT:

This is an interesting manuscript aiming to understand how GAG imposes anti-cancer effect on melanoma cells by using a B16F10 based rodent melanoma model. The conclusions were drawn based on the solid assay results on both non-malignant (HMVEC) and cancer cell lines and animal models. DNA microarrays were further performed to identified potential affected targets upon treatment of cancer cells. While the data were very clearly presented and seemed to be quite convincing, the manuscript is poorly organized with a strange logic flow that need to be fixed or better streamlined. The quality of some figures (Fig 7 for instance) can be further improved. Overall, after a major revision, this manuscript can be reshaped into a more concise and attractive story with considerable novelty.

REQUESTED REVISIONS:

First of all, the language needs to be polished further. Numerous grammar errors spotted throughout the text!!! Need more rigorous description on statistics for each figure (the sample size, the number of repeated experiments, the statistical method used for calculating the significance level; etc.)

Second, some specific points are appended below:

1. The authors started from in vitro characterization of glycosaminoglycan's anti-tumor effect, and then moved on to test the efficacy in vivo. Next, they identified the most affected pathways/targets by performing gene expression profiling with DNA microarray.
2. The layout of the manuscript needs to be significantly improved. First of all, the figures can be reorganized. For instance, Figure 2-4 can be merged into one figure emphasizing the effects of GAG's anti-tumor effect in vivo. Figures 5-6 can be combined to illustrate genes affected by GAG (or other N-glycan) treatment.

3. Figure 1. the label "melanoma" for the black bar is very misleading. I guess the author referring to "control"? If not, a control agent is needed in this figure. the authors need specific which melanoma cells used in the figure legends. Also, it is best to test them in a panel of melanoma cell lines, and to use non-melanoma (normal skin like melanocyte) as non-malignant control.

4. Figure 3. the labels above the curves makes the figure vey messy. Need clean up or list those numbers in a table/plot as a bar graph. Specify the sample sizes for each curve.

5. Figure 4. change "Melanoma" to the appropriate reagent used in the experiment.

6. Figure 6. no error bars!!! This is unacceptable.

7. Figure 7. the panels are distorted horizontally. Need preset them in a higher resolution. Shouldn't the characterization of chemical components in the tested glycans be presented in the beginning? This reviewer is confused by the logic here.

8. Figure 8. Use less color and need improvements on the graphics.

9. Tables 2/3. The microarray data: best to present in heat map format as routinely done in the field. RNA-Seq is more preferred than microarray.

10. Discussions. Need more emphasis on the novelty of this discovery compared to similar studies done using similar glycans in other cancer models. Discuss more in detail on how the findings derived from melanoma models can be extended to other cancer types.

Finally, the title can be changed to something like "Anti-cancer effect of dung beetle glycosaminoglycan on melanoma". It is very strange to combine the anti-cancer effect and gene expression profiling, two totally different aspects, within the same title.

ADDITIONAL REQUESTS/SUGGESTIONS:

See comments above
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.

No

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

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English  
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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