Reviewer’s report

Title: Cytotoxicity of amide-linked local anesthetics on melanoma cells via inhibition of Ras and RhoA signaling independent of sodium channel blockade

Version: 0 Date: 20 Sep 2019

Reviewer: Hailin Zhao

Reviewer's report:

The authors carried out a very interesting study to investigate the cytotoxicity of local anesthetics on melanoma cells. The data is robust and the conclusion is quite solid. I have some comments here.

1) What is the clinical significance of this study? Would the data help the clinicians to select the best anesthetics for cancer patients? Please discuss more.

2) The molecular mechanisms still remain unclear to me. It would be nicer that the authors draw a diagram showing the complicated molecular pathways involved in this study.

3) Could the authors discuss why bupivacaine behaves differently from ropivacaine and lidocaine? The authors could discuss more with other previous studies. E.g. Xuan W et al 2016, doi: 10.1038/srep26277.

4) It would be better to see some raw data presented in the results section.

5) This study focused very heavily on in vitro work. The in vivo animal model would be more convincing and supportive. Could authors discuss this further?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

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

Yes
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.

I am able to assess the statistics

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

Needs some language corrections before being published

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