Reviewer's report

Title: Abalone visceral extracts inhibit tumor growth and metastasis by modulating Cox-2 levels and CD8+ T cell activity

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Reviewer: Bernd L Fiebich

Reviewer's report:

In their manuscript "Abalone visceral extracts inhibit tumor growth and metastasis by modulating Cox-2 levels and CD8+ T cell activity" Lee et al., investigated the effects of an extract of the sea snail abalone on tumor growth, COX-2 and tumor growth related parameters.

They showed that by oral administration, the abalone visceral extract reduced tumor growth (tumor volume and weight) and showed reduced metastasis as confirmed by decreased level of splenomegaly (spleen size and weight) and histological analysis of the lung metastasis (gross analysis and histological staining). The authors found reduced expression of Cox-2 (mRNA and protein) from primary tumor and metastasized lung and increased anti-tumor activities of CD8+ T cells by increasing the proliferation capacity and their cytolytic activity.

The authors conclude that the abalone visceral extract has anti-tumor effects by suppressing tumor growth and lung metastasis through decreasing Cox-2 expression level as well as promoting proliferation and cytolytic function of CD8+ T cells.

Although the manuscript provides new and interesting data addressing the effects of abalone extracts on tumour growth, there are some major concerns about the conclusion drawn by the authors, which need to be addressed.

1) Major Compulsory Revisions

One of the key conclusion by the authors is, that due to the decrease of COX-2 by abalone, tumor growth and metastasis is reduced as well as down-stream parameters from COX-2 such as VEGF etc.

However, the authors did not show any data to prove this conclusion.

a) A COX-2 inhibitors needs to be included in the tumor growth experiments to demonstrated, that COX-2 and prostaglandins are involved in tumor growth and metastasis.

b) The read out parameter of COX-2 are prostaglandins. Thus, if COX-2 plays any crucial role in tumor growth, this will be mediated by prostaglandins and their respective receptors EP1-4. The authors show some reduction of COX-2 protein, which does not necessarily has to correspond with reduced prostaglandin release, since there is COX-1 present in most cells and there is also still enough...
COX-2 protein to produce prostaglandins. The important control experiment is missing showing the effect of abalone extract on prostaglandin levels. Moreover, COX-1 should be involved in the Western blot.

c) The authors claim that VEGF, FGF and MMP-13 are COX-2 associated molecules and down-stream factors from COX-2. This is questionable and should be removed. These molecules might be regulated by prostaglandins but not by COX-2 itself!!

d) Related to point c), the authors do not show any evidence, that VEGF, FGF and MMP-13 are dependent on prostaglandin synthesis and release and therefore indirectly on levels of COX-2. The authors have to include an experiment showing the effects of COX-2 inhibitors on those factors before drawing such a conclusion. It is more likely, that abalone interferes with signal transduction cascades common in the expression of COX-2 and VEGF, FGF and MMP-13 and are most likely not linked to each other.

2) Minor Essential Revisions

The title and in most part of the manuscript, the authors state that they have tested the effects of abalone extracts. Looking on the data, it seems like that there was only one type extract used in all experiments and not biochemical different ones.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests!