Reviewer's report

Title: Kinesin Eg5 inhibition by 3,4-dihydropyrimidin-2(1H)-one (or thione) derivatives impairs multiple tumorigenic properties inducing breast cancer cells to apoptosis

Version: 4  Date: 13 January 2015

Reviewer: anna ivana Scovassi

Reviewer's report:

Major Compulsory Revisions

1. The authors did not explain the rationale of the choice of the breast cancer cell lines. I imagine that the best difference concerns the p53 status, having MDA-MB-231 cells a mutant p53 (Olivier M et al, 2002, Hum Mutat 19: 607–14., whereas MCF7 a wild-type p53 (Lu X et al, 2001, Clin Cancer Res 7: 2114–23). This point has to be addressed.

2. Accordingly, the choice of DHPMs as a class of drugs potentially useful against breast cancer is not clear. Add more literature on monastrol activity.

3. The data illustrated in Figure 1B are interpreted by the authors as a demonstration that the drugs are selectively active on cancer cells. However, for the effect of the 4p compound it is not the case, since the viability of fibroblasts is also affected. Please comment. Also the general notion of a dose-dependent effect only for cancer cells is not completely supported by the data. This is a crucial point, given that the compound 4p has a peculiar effect on microtubule organization (Figure 5).

4. For cell cycle distribution (Figure 6C), there is no evidence of a subG1 cell fraction neither of a >4C cell population. Comment this result. In the M&M section, flow cytometry para, the authors say “Adherent and floating cells were harvested and pelleted...”, but they do not specify if the two fractions are analyzed separately or put together. This is an important issue, given that apoptotic cells tend to detach from the solid support.

5. The conclusions can be improved. I suggest to detail the relevance of data with a list of findings, such as i) DHPM derivatives are potent Eg5 inhibitors; ii) two drugs are more efficient than monastrol, a widely recognized inhibitor of microtubule formation; iii) the cytotoxic effect is accompanied by the induction of apoptosis.............and so on.

Minor Essential Revisions

1. The title is not sharp. Alternative title: “Impact of kinesin Eg5 inhibition by 3,4-dihydropyrimidin-2(1H)-one derivatives on various breast cancer cell features.”

2. The lettering of Tables is not uniform.
3. Avoid the use of “culture mediums”, use “culture media”.
4. The title Cell and cell culture is in fact Cells and cell culture.
5. For round coverslips, specify the diameter.
6. References are not updated (only 2 papers published in 2014).
7. Check for English spelling and grammar.

Discretionary Revisions
None

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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.