Reviewer's report

Title: Down-regulation of estrogen receptor-alpha and RET are associated with Withaferin A-induced apoptosis in MCF-7 breast cancer cells

Version: 1 Date: 12 July 2011

Reviewer: Nik Soriani Yaacob

Reviewer's report:

The study approach and methodology data are sound and appropriate. The findings are appropriately sufficiently discussed. However, reference citation for previous work is lacking. This paper is acceptable for publication after minor revisions as stated below:

Minor Essential Revisions

1. Line 41: “un-regulation” should be replaced with “up-regulation”
2. Line 126: “conducted” should be replaced with “visualized”
3. Line 132: please ensure the term “Turkey’s honestly significant difference” is correct
4. Line 142 & Figure 2: to check and clarify how IC50 is between 0.5 to 1 #M
5. Line 172: The sentence “We then examined the protein expression of RET proto-oncogene which plays an essential role in …..” needs to have a reference.
6. Line 176: “supresser” should be spelled “suppressor”
7. Line 179: The sentence “As p21 is a key inhibitor of cell cycle progression in MCF-7 cells ……….” needs to have a reference.
8. Line 190: “addition” should be replaced with “additional”
9. Line 208: remove the word “of”
10. Line 210: The sentence “Recent research revealed that ER##…..” needs to have a reference.
11. Line 224: the sentence “Although whether decreased RET protein levels …” lacks clarity and should be re-phrased
12. Line 237: The sentence “The pattern of p21 correlated well with that of p53, suggesting that p53 may play a role in p21 up-regulation” should be replaced with “The pattern of p21 correlated well with that of p53, suggesting that p53 may play a role in p21 up-regulation by WA” since p21 up-regulation can also occur independent of p53.
13. Line 239: The sentence “Since phospho-p38 has been demonstrated to up-regulate p53 expression, ……” needs to have a reference, if different from the one cited for the next part of the sentence.
14. Need to label the graphs in figure 2 (for eg., as A & B) for clarity. Furthermore, an explanation in the legend should also be provided separately for
each graph

Discretionary Revisions:

1. Line 260: for the argument on 2.5 and 5.0 \#M WA significantly decreasing HSF1 and surviving expression, an explanation on the opposite effect observed with the lower WA concentration should be given or this may be transferred from the Results section (line 186)

2. The authors should include a similar work reported recently by Hahm et al. Withaferin A suppresses estrogen receptor-\# expression in human breast cancer cells. Molecular Carcinogenesis, 2011, in their discussion.

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