Reviewer's report

Title: Protection of p53 wild type cells from taxol by nutlin-3 in the combined lung cancer treatment

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Reviewer: Marzia Pennati

Reviewer's report:

This manuscript describes the effect of different compounds (5-fluorouracil, camptothecin, roscovitine, and Nutlin-3) in combination with taxol in cell lines differing in the TP53 gene status. The basic finding is that exposure to Nutlin-3 protects wild-type p53 cells (A549) from taxol, whereas the same combination treatment induces mitotic arrest and apoptosis in p53-deficient cells (FaDu and H1299).

The manuscript is badly written and the results and discussion are very poor. In my view, the paper adds little to the literature and do not provide significant evidence concerning the effects of Nutlin-3 in combination with taxol. Although the idea of the research is interesting, the paper does not warrant publication in its present form. My recommendation would be to explore further the mechanism responsible for the effects mentioned above before re-submitting the manuscript for consideration.

Specific comments:

1. The authors base their conclusions only on cancer cell lines. It would be important to confirm their hypothesis in normal cell lines.
2. How was defined the treatment schedule to be used for the drug combination? Authors should clarify this point.
3. The effects of the treatment with the different compounds (alone or in combination) on cell proliferation should be reported.
4. The data showing the perturbation of the cell cycle after treatment with the different compounds (alone or in combination) are convincing, but it would be interesting to know the effects of the treatment on the expression/activity of the proteins involved in cell cycle regulation.
5. The authors should verify the mechanism by which Nutlin-3 protects cells from taxol.
6. The apoptotic rate should be better determined using more specific assays for apoptosis (i.e., TUNEL assay, caspase-9 and caspase-3 catalytic activity).
7. On the flow cytometry on DNA context for the different treatments, how many independent replications were performed before to draw the conclusions?
8. The compounds reported in “Methods” section (“Flow cytometry”, pag 4) are different from drugs used in the paper.
9. The readability of the manuscript and interpretation of the authors’ findings would benefit greatly by extensive stylistic and linguistic revision.

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

**Quality of written English:** Not suitable for publication unless extensively edited

**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