Reviewer's report

Title: A small molecule exclusively eradicates human cancer cells: Extra-centrosomes de-clustering agent

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Reviewer: Myron K Jacobson

Reviewer's report:

The manuscript of Castiel et al. presents new information of great potential mechanistic and therapeutic significance. The authors have identified a class of molecules long known as having potential as anti-cancer agents and more recently known as poly(ADP-ribose) polymerase (PARP) inhibitors as agents that disrupt chromosome clustering that allows cancer cells with progressive genomic instability including instability of chromosome numbers to avoid cell death associated with mitotic catastrophe.

Major compulsory revisions needed:

(1) A title that more effectively communicates the results of the study should be strongly considered.

(2) The work presented in Figure 5 does not add definitive new information concerning chromosome clustering and even detracts from the information presented in human cells. The involvement of PARP-1 in chromosome clustering is not clear and the focus of manuscript would be improved by omission of these data.

(3) The following statement is made on 12 and 13: “Furthermore, the fact that interference of phenanthrene derivatives acting as PARP inhibitors, (PJ-34, Tiq-A, and Phen) with the bipolar clustering of supranumery centrosomes not shared by other non-phenanthrene potent PARP inhibitors (Figures 2c and 5), rules out an exclusive dependence of extra-chromosomes clustering on PARP activity.” It is the view of this reviewer that such a conclusion is premature. Indeed, the results presented may reflect a selective inhibition of a cellular PARP isoform by phenanthrene derivatives or an effect of phenanthrene derivatives on substrate specificity of an as yet identified PARP.

(4) The following statement is made on page 13: “There was no evidence for the necessity of PARP-1 and other known PARP proteins in extra-centrosomes clustering, except for tankyrase-1 and a putative PARP-16 homolog [16, 21].” This is a puzzling negative statement that indeed presents evidence, albeit not conclusive at present, for involvement of cellular PARPs in centrosome clustering as suggested in point 3 above. This evidence should be presented in a positive manner.

(5) The abstract states: “we identified a phenanthrene derivative, which interferes
with cell death mechanisms in quiescent cells, but exclusively eradicates human cancer cells.....”. It is not clear by what is meant by interference with cell death mechanisms in quiescent cells.

(6) The manuscript needs English editing to improve the effectiveness of the presentation of these data. Some examples: page 3: “Here we disclosed”; page 4: “mechanism has been described before decades”; page 14: “has been first described before several decades”

Minor essential revisions:

Figure 5a: The reference to right and left appears to be reversed.

Level of interest: An article of outstanding merit and interest in its field

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

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.