Reviewer’s report

Title: Anaphase-promoting complex/cyclosome protein Cdc27 is a target for curcumin-induced cell cycle arrest and apoptosis

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Reviewer: sophie barille-nion

Reviewer’s report:

The manuscript entitled « APC/C protein cdc27 is a target for curcumin-induced cell cycle arrest and apoptosis » identifies a new molecular mechanism involved in curcumin-induced cell cycle arrest in G2/M and cell death in vitro in cancer cells. Indeed, this report provides evidence that curcumin treatment directly induced the dimerization of the APC/C component cdc27 mainly in its phosphorylated form, blockade of mitosis onset and cell death. In addition, curcumin efficiency to induce cell death correlated to phospho-cdc20 levels in a series of cancer cell lines. The manuscript is well-written, easy to read and includes convincing results.

Some following points could be however clarified to improve the manuscript.

Minor essential revisions:
1- Curcumin-treatment clearly triggered a G2/M cell-cycle block and apoptotic cell death. Do the authors check that apoptosis occurred during curcumin-induced mitotic arrest?
2- Could the cdc27 depletion mimic curcumin treatment in DAOY cells? This experiment would directly link impact of curcumin on cell death to its capacity to crosslink cdc27.
3- The authors could not evidence high MW cdc27 complexes in smo/smo transgenic medulloblastoma mouse model. However cdc27 protein levels were lower in curcumin-treated tumors compared to untreated tumors. Are these complexes detectable in DAOY xenografts models (also used in previous publications by the authors) treated with curcumin compared to control? The curcumin concentrations used in in vitro experiments showing high MW cdc27 complexes culminated in 20-40microM: could these concentrations be detected in mice sera?
4- A comment should be made about thymidine block on DAOY cells that only partially triggered a cell cycle block used in fig 1A.
5- In fig 2B, are cells synchronized?
6- In fig 3A, are cells treated before pull-down with curcumin-coated beads? A faint band appeared in control lane: did control sepharose beads pull down cdc27 (not phosphorylated)?
7- Regarding, cdc27 phosphorylation, 2 references could be included in the
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.