Reviewer's report

Title: Breast cancers with high DSS1 expression that potentially maintains BRCA2 stability have poor prognoses in the relapse-free survival

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Reviewer: Nicole Dalla Venezia

Reviewer's report:

The authors investigated how the expression of DSS1, a protein that stabilizes BRCA2, is associated with breast cancers. They found that high-DSS1 patients show a poor prognosis. They further investigated using two breast cancer cell lines, the P53-wild type MCF7 and the P53-mutated MDA-MB-231, the impact of DSS1 over-expression or knockdown on cellular proliferation and DNA damage sensitivity. Even though the mechanisms of DDS1-mediated resistance to DNA-damaging drugs are not clear regarding P53 impact, the authors describe several novel findings. The high DSS1 expression could be a marker for drug resistance in breast cancers. From a therapeutic point of view, DSS1 knockdown could serve in combination with DNA-damaging drugs as an anti-tumor drug.

In general, the paper is well written. Background, experiments and results are well described. However, some criticisms and questions can be raised concerning the illustrations and discussion, according to the following comments:

1/ Major Compulsory Revisions

a/ The discussion is a very extensive text that largely appears like an extra background and poorly relates to the findings reported. It has to be shortened and focused to highlight the impact of the findings.

b/ Authors found in figure 1 that DSS1 high group showed a worse prognosis in comparison with the DSS1 low group in breast cancer cases with high P53 expression. Because of the crucial role of P53, authors further used two cell lines that present the particularity to contain either wild-type P53 or mutated P53. Surprisingly, results obtained with these cell lines are not discussed regarding the P53 status. See as follow:

- In figure 2, DSS1 overexpression renders only MCF7, but not MDA-MB-231, resistant to treatment with CPT, whereas DSS1 overexpression reduces CPT-induced DNA damage in both MCF7 and MDA-MB-231 cells.

- At the end of “results”, authors indicate that DSS1 depletion increases chemosensitivity in cancer cells containing either wild type or mutant P53. Therefore, results obtained with the two cell lines should be discussed regarding the potential role of P53, at least in “discussion”.

c/ Figure S4B is described by authors as showing “a marked reduction in DSS1 protein”. This cannot be concluded from the western blot displayed in the figure.
A more convincing western blot experiment has to be shown.

2/ Minor Essential Revisions

a/ Figures S4C and figure 4A-left show almost the same figures, causing the interpretation to be very confusing. It is clear that Figure S4C used Si-DSS1(b) whereas it is not indicated (only in “methods”) that Figure 4A-left used Si-DSS1(a). This point should be elucidated, otherwise it could be tempting to speculate that the apparent effect on cell growth (MTT test) and cell number is not due to DSS1 knockdown.

b/ The MTT results showed in Figure S4C should be accompanied by a western blot using Si-DDS1(b) transfected cells, for the same reason as above: results obtained with MTT test may not be correlated with DSS1 knockdown.

c/ In “methods”, the sequence of the SiCtrl is missing. This sequence must be described in that part of the manuscript.

Level of interest: An article of importance in its field

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.