Reviewer's report

Title: No significant role for beta tubulin mutations and mismatch repair defects in ovarian cancer resistance to paclitaxel/cisplatin

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Reviewer: Michael Kelley

Reviewer's report:

General

Mesquita et al. Examined 38 ovarian tumors in archival samples for mutation of TUBB exon 4 and MSI with two STR markers. Results were correlated with clinical response to paclitaxel and cisplatin combination chemotherapy. They found no TUBB mutations and no tumors with MSI.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The lack of detection of TUBB mutations is not surprising as it has been shown that TUBB is wild type in patients with tumors resistant to paclitaxel, including ovarian cancer. If the authors can address the technical question (below), the results add somewhat to the number of human tumor samples examined, and thus increase the certainty of the negative finding. In contrast, the analysis for MSI is insufficient. Only 2 STR markers were examined. Without analysis of at least 5 markers, comparison with results from other studies in ovarian and other tumor types is not possible and statements about absence of MSI must be qualified.

The authors show only a single trace for each STR marker. Did they compare tumor and normal from the same patient? If so, what was the source of the normal DNA? If not, what criteria did they use to call MSI without a comparison trace from normal tissue?

As this is an incomplete study of MSI and there are concerns about the technical aspects of how the MSI assay was performed, the report would be stronger if this was deleted from the manuscript.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Methods, Page 4, last sentence. The authors should include a description of the microdissection technique. Was this by laser capture or some other method? What was the minimum percent of tumor cells in the microdissected samples? Samples with less than 50% sequence have a low probability of detection of mutations by sequence analysis.

Methods, page 5, Sequencing paragraph. The authors used two rounds of PCR with nested primers. At least some of the second round primers appear to be within exon sequence and would be expected to amplify the pseudogenes. Did the authors determine if there were PCR products after the first round of PCR to assure that this did not happen to a significant extent?

Methods, page 5, Sequencing paragraph. The authors compared their TUBB sequences to GenBank accession number J00314. This sequence is known to have errors compared to the genomic sequence published by the Human Genome Project so it is surprising that the authors did not find
any sequence variants compared to J00314.

Discretionary Revisions (which the author can choose to ignore)

Figure 1 adds nothing to the manuscript and can be deleted.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article of limited interest

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

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.