Reviewer's report

Title: Novel pharmacogenomic markers associated with paclitaxel response in cancer

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Reviewer: Zhenfeng Duan

Reviewer's report:

In this manuscript, the authors used the NCI 60 cancer cell line panel and different bioinformatics tools to identify SNPs associated with drug response to paclitaxel. This study is straightforward and the manuscript is well written. The manuscript deserve for publication.

Specific comments:

1) The major concern is all the results and data described in this manuscript were collected from bioinformatics tools analysis without further biological experiments validation. For example, mRNA of five genes (DCT, SNTG1, CFTR, GRIK1, and SGCD) showed significantly different expression levels between sensitive and resistant cell lines through computational analysis; any possibilities these genes can be validated by Real-time PCR or Northern blot analysis?

2) It will be interesting if the author could include some SNPs, mRNA gene expression array data from clinical tumor tissue samples in patients with or without paclitaxel treatment.

3) Page 8 and Page 9, only 8 cell lines (14%) were in the resistant group while there were 50 cell lines in sensitive group based on the arbitrary z-scores (1.2). As the NCI 60 cancer cell lines were initially established from patient samples, this distribution does not reflecting the response rates in clinic. As the authors described in the manuscript, the response rates observed from clinical studies of breast cancer patients treated with paclitaxel vary from 21-86%. Similarly in ovarian cancer, the response rate varied from 20-65% and in non-small lung cancer, 30-56%. The distribution of the resistant and sensitive groups can be changes by using a different z-score. In addition, there are several paclitaxel resistant breast and cancer cell lines (with their mRNA gene array data) available and these cell line pairs could be included in this study.

3) The authors mentioned that “In all cases, these genes were found to have significantly increased mRNA expression in sensitive cell lines for all probes available, supporting their predicted effect by FastSNP”. In order to confirm the SNP predict genes such as DCT, SNTG1, CFTR, GRIK1, and SGCD play a role in paclitaxel response, some functional studies of these genes may be necessary. For example, inhibit gene expression in sensitive cell line by siRNA or overexpress gene in resistant cell line by transfection and then evaluated paclitaxel sensitivity.
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'