Reviewer’s report

Title: Carboplatin-induced gene expression changes in vitro are prognostic of survival in epithelial ovarian cancer

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Reviewer: Ulrich US Steidl

Reviewer’s report:

The authors performed a time-course genome-wide expression analysis to delineate transcriptional changes upon Carboplatin treatment. Using the ovarian cancer cell line 36M2 they identified two dynamic transcriptional signatures, one at a single gene level, and a second one based on affected pathways. Each of them was significant alone but they also complemented each other with regards to involved target genes / pathways. Both signatures seem to reflect a general mechanism of action of platinum-based cytotoxic agents as they were confirmed in independently generated data sets in a second ovarian cancer cell line (A2780) as well as a non-small cell lung cancer cell line (A549). The authors went on to assess the prognostic value of the newly defined signatures and demonstrated that both dynamic signatures separate patients into two groups with favorable and unfavorable disease free and overall survival.

The here demonstrated approach of identifying and utilizing dynamic transcriptional signatures upon cytotoxic treatment for prognostication might be helpful for risk stratification in ovarian cancer in the future, and might also be applicable to other types of cancer.

Minor essential revisions:

1. In the survival analysis, it is not entirely clear if the prognostic relevance of identified the signatures was tested in a multivariate analysis together with standard clinical parameters. A multivariate model is mentioned with regard to the expression levels of individual genes, but has the prognostic value of the signatures also been tested against clinical parameters ? The authors mention that clinical features were similarly distributed in the 2 groups. It should be clarified if a formal multivariate analysis with those parameters has been performed.

2. It is interesting that some of the dynamically regulated genes were also affected when baseline expression levels were checked. Did the authors check if a combination of those baseline expression levels was also sufficient for prognostic separation ? If this is not the case (which is likely) this would further strengthen the value of the approach of assessing dynamic expression signatures that the authors propose.

Discretionary revisions:
3. Some functional in vitro evidence would be nice to show exemplarily that some of the newly identified genes are indeed functionally relevant for chemoresistance.

4. In Figure 1, error bars are missing.

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

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests.