Reviewer's report

Title: Cancer-testis antigen Cyclin A1 is broadly expressed in ovarian cancer and is associated with prolonged time to tumor progression after platinum-based therapy

Version: 4
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Reviewer: Alexander Brodsky

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Review of Ruza et al.

The authors present evidence to support the use of Cyclin A1 as a marker and potential target for T cell therapy. They present evidence that cyclin A1 is associated with longer survival. The manuscript needs some upgrades to be considered for publication. It appears the authors used online tools but have limited statistical support or experience with expression data analysis.

Major Compulsory Revisions

1. It is not clear which datasets were used for the analysis. Which datasets were used to analyze probe set 205899_at for Figure 1? There are many other tools to evaluate cyclin A1 in ovarian cancer and many datasets. One relatively easy one to use is OVMark. It is not clear that Cyclin A1 has prognostic power in the datasets included in OVMark. This may or may not be meaningful at the RNA level compared to the protein level, but should be considered and presented in the manuscript. The authors should clarify in the datasets used to evaluate Cyclin A1 and evaluate cyclin A1 in as many datasets as possible given the large amount of data publicly available.

2. The y-axis for Figure 2 needs to be clarified. Are the data normalized to Human testis relative to GAPDH?

3. Was residual disease not an independent predictor of OS in the patient cohort used for IHC? It seems based on lines 228-231 that it is not. Why? This differs from most ovarian cancer cohorts and if so, could explain why Cyclin A1 appears to be independent of residual disease in the multivariate analysis. The numbers from the univariate analysis for each parameter, stage, residual disease, etc. should be added to the Supplemental figure to be able to evaluate the cohort. In the discussion, lines 324-325 say that Cyclin A1 predictions were strong than residual disease, but residual disease has not signal in this cohort, so this whole argument is weak as this dataset may have biases not seen in most ovarian cancer datasets.

4. Why is high Cyclin A1 expression associated with longer survival in the presented data, but has high expression in the C1 category, which has short survival? Is this due to the modest to borderline statistical significance of the Cyclin A1 association with survival?
5. Why do the authors think that Cyclin A1 is a good target for immunotherapy if it is associated with better responses? Would these responses be improved further by targeting Cyclin A1? Or is the expression pattern what is really important for T cell therapy? What is the importance between the prognostic impact of Cyclin A1 and its potential use for immunotherapy?

Minor Essential Revisions

1. The manuscript has a number of grammatical errors and couple of typos.

2. Figure 6 A and 6B appear mixed up relative to the Figure legend.

3. The key for Figure 6 is too small and hard to read. Actually, the font size in Figure 6 should be generally increased.

Level of interest: An article whose findings are important to those with closely related research interests

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

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