Reviewer's report

**Title:** Low expression of the X-linked ribosomal protein S4 in human serous epithelial ovarian cancer is associated with a poor prognosis

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**Reviewer:** Harriet Feilotter

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The manuscript “Low expression of the X-linked ribosomal protein S4 in human serous epithelial ovarian cancer is associated with a poor prognosis” by Tsofack et al is a study on a series of primary ovarian carcinomas and two ovarian cell lines aimed at examining correlation of expression of RBS4X with clinical parameters. Overall, the manuscript is well written and the goals and outcomes of the work are clearly presented. However, there are a few points that make review of this manuscript difficult because of the confusion that they generate (see major revisions).

**Major compulsory revisions:**

1) Table 1 shows the summary of the characteristics of the tumours used. The tumours are divided into Grade 2 and Grade 3. The mean disease free interval and the mean overall survivals are substantially shorter for the Grade 2 group than for the Grade 3 group. Is this expected? It seems counterintuitive. Given that these clinical parameters are important factors in the subsequent univariate and multivariate analyses, this should be explained.

2) In Table 2, the expression of RPS4X is positively associated with grade and mitotic index, and negatively associated with death and recurrence. This is confusing- does this mean that low levels of RPS4X expression are associated with higher rates of death, higher rates of recurrence, lower grade and lower mitotic index? It is not clear from this presentation of the data exactly what the correlations are.

**Minor essential revisions:**

1) In M&M, the description of the tumours used should include the fact that these tumours were chemo naïve. This fact is mentioned in the discussion, and can be inferred from the description in the methods, but should be specified.

2) The TMA data for YP-1 and RBS4X are reported as 1 through 5, representing no through high levels of staining. In the analyses, the tumours are grouped into low versus high expression. Low is defined as categories 1-3, and high is categories 4 and 5. How is this division of categories justified?

3) In the results, there is a statement that Kaplan-Meier plots for RPS4X showed that the overall survival of patients with low or no RPSX expression was
significantly worse than those with high expression. There were, apparently, no cases with no expression, so this statement is not accurate and should be amended.

4) There is a statement in the results that Figure 3B shows that RPS4X and YP-1 do not regulate each other at either the transcriptional or translational level. Since Figure 3 is entirely based on protein-based assays, there is no data in this manuscript about possible effects at the transcriptional level.

Discretionary revisions:

1) The experiments were aimed at examining both the expression patterns of YB-1 as well as RBS4X. YB-1 is discussed in the context of its direct interaction with RBS4X, and indeed previous studies showed that expression of this protein is correlated with prognosis. In this study, YB-1 does not correlate with outcome parameters, and the authors suggest that either the high-grade nature of this cohort, or, alternatively, the particular antibody used, may account for this difference. The fact that the use of a different antibody might radically change the interpretation of how protein levels might correlate with outcome would seem to be important for the discussions in this paper. This could be examined relatively easily in this same cohort and would further explore the true relationship of the expression of these proteins to clinical outcomes.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.