Reviewer’s report

Title: Threonyl-tRNA Synthetase Overexpression Correlates with Angiogenesis and Progression of Human Ovarian Cancer

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Reviewer: Karen Liby

Reviewer’s report:

The manuscript by Wellman et al describes the novel and important observations that expression of TARS increases with the progression of ovarian cancer and, unexpectedly, that TARS expression is inversely correlated with the risk of mortality in advanced disease. The manuscript is well-written and the data clearly presented. As with most initial studies in a new area, the data in this manuscript raise several interesting questions for additional studies, but the answers to these questions are not required for acceptance of this manuscript.

Specific comments - discretionary revisions:

1) What percentage of ovarian tumor tissues contain robust TARS staining in leukocytes and what is the outcome/survival of the patients with this staining? Is the TARS staining in infiltrating leukocytes produced by the immune cells or secreted by ovarian epithelial cells? Additional characterization of the phenotype of these infiltrating cells would be helpful.

2) What effect do hypoxia and TNF-alpha have on mRNA stability in Fig. 4C?

3) Is there a correlation between CA-125 and TARS expression?

4) As shown in Fig 2C, TARS expression is highly variable in ovarian tissue and increases with advanced stages. Even in normal or stage 1-2 samples, however, the TARS staining score is approximately 2. What is the function of TARS in normal ovaries?

Level of interest: An article of importance 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'