Reviewer's report

Title: Identification of Fluorescence in Situ Hybridization Assay Markers for Prediction of Disease Progression in Prostate Cancer Patients on Active Surveillance

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Reviewer: Yeung Ho

Reviewer's report:

The manuscript by Pestova K et al. described the use of the fluorescence in situ hybridization (FISH) method to evaluate the combinations of various FISH probes as the biomarkers to predict disease progression in prostate cancer. The authors identified seven best combinations of FISH probes based on receiver operating characteristic (ROC) curve analysis. The authors showed that the combination of clinical parameters with FISH outperformed clinical parameters only. Logistic regression analysis showed that the combinations of the FISH probes could discriminate progressive vs non-progressive cases in lower and intermediate risk groups. Altogether, these results demonstrated the potential use of those FISH panels as predictive biomarkers for evaluating progression in prostate cancer.

This is an interesting study as the results of the paper provided several panels of FISH probes that might be useful for prognostic diagnosis. I have the following comments:

1. The authors included a total of 12 probes for FISH. But there is no AR probe. Alterations in AR pathway is the most commonly found alterations in prostate cancer. The authors may want to include it in the future validation of the FISH panels.

2. In table 2, it is not clear the case numbers for each FISH combination. Are those FISH combinations performed on all 108 patients and their respective controls? If not, the case number in each group of FISH combinations should be shown in the table. The authors mentioned that the combination of clinical parameters with FISH outperformed clinical parameters of FISH alone for all investigated FISH probe combinations. The authors should show the odd ratios of the clinical parameters for each FISH combinations then.

3. In table 3, the authors showed that the clinical parameters and FISH combinations for MYC, PTEN, NMYC and FGFR1. It didn't shown the combinations of both clinical parameters and FISH. Does it outperform that of the clinical parameter? It seems
contradictory to what was stated above. It is not clearly stated that how the authors obtain the odd ratios of clinical parameters only as 3.7.

Minor point:

On page 14, under the title "Performance of FISH with clinical parameters in the logistic regression model", the authors mentioned that "...In the logistic regression analysis, FISH had significant contribution to the prediction of PCa outcome (progression) with the highest odds ratio of 6.635 observed for the combination of 5 probes (4 parameters0, as shown in Table 2. This data was not found in the table 2.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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