Reviewer’s report

Title: Gene signatures ESC, MYC and ERG-fusion are early markers of a potentially dangerous subtype of prostate cancer

Version: 2 Date: 8 April 2014

Reviewer: Chunde Li

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Major Comments to 1495784736125909_manuscript

This work in a way validated the previous defined ESC signature but not the clinical importance because the lack of clinical follow-up data in the present cohort. There are two interesting findings. First, the molecular similarity between tumors with different Gleason scores in the same patient (prostate) is stronger than between tumors with the same Gleason score in different patients (prostates). Second, tumors with low Gleason score but rich in ESC, ERG-fusion and MYC+ signatures seem to have poor prognosis.

In fact, this study was a validation of previously described signatures but not a validation of clinical importance of the signature. The clinical importance analysis was not validated by clinical follow up data in the present cohort, instead was dependent of previous studies. This weak point should be addressed already in the introduction and method sections.

Despite the above major weakness, the study is presented with sound analyses and interesting data and may meet the standard to be published after minor revisions.

Major questions

1. The sample assignment or classification is not only influenced by sample composition but also by different selections of genes or gene sets. Can selections of gene sets lead to the phenomenon of the finding that the molecular similarity between tumors with different Gleason scores in the same patient (prostate) is stronger than between tumors with the same Gleason score in different patients (prostates)? Is this phenomenon observed when the all samples are analyzed by the original microarray dataset with all genes?

2. Peng Z et al (Prostate Cancer and Prostatic Disease (2014) 17, 81–90) recently described an ESCGP signature. What are the similarities and differences between this ESCGP and the ESC signature?

Minor Comments:

The PRC signature is misspelled to PCR signature in several places.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I am a inventor of two patent applications.

1. Embryonic stem cell markers for cancer diagnosis and prognosis
   WO 2008013492 A1

2. Marker genes for prostate cancer classification
   WO 2013060739 A1

The above has not influenced my objective reviewing of this article.