Reviewer's report

Title: Significant Random Signatures Reveals New Biomarker for Breast Cancer

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Reviewer: Zhi-Ping Liu

Reviewer's report:

In this paper, the authors proposed a study of identifying the gene signature of breast cancer by a permutation test. This paper is interested to me. The following lists some comments.

1. The motivation. It is good to question a published paper (ref. 18). In this paper, the authors found the randomly selected genes also contain the distinguishing power of classifying control and disease samples. Here, the authors reported there are differences between the signatures and the randomly selected genes. In fact, this is very complicated to interpret the effectiveness of random genes in classifying samples. Many kinds of possibility should be checked before we set up a general finding about why these randomly selected genes contain the differential information in controls and diseases. In my understanding, the generic causal disease genes are very important for discovering the true signatures. Thus, I suggest to include this issue in the background section.

2. The methods. In the method section, the empirical p-value is identified by permutations. There are some alternatives of identifying the p-values, such as the label permutation and the gene random selection. The reference of obtaining the p-values need be mentioned. And p-values need be corrected for multiple testing issue. And the definitions of pathway score need be introduced in more details. And the score need be normalized for the number of genes contained in the pathway.

3. The results. The table 4 is rather hard to understand because there is no valuable information. I suggest to do some statistics and replace it by a figure about the percentage with the features in these patients. And the table also need also be correlated with the subject of this paper, the randomly selected genes contain biomarker information. Moreover, the results are based on two datasets of breast cancer in GEO. I suggest do the experiments in more data sets for obtaining a consistent result.
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.

Unable to assess

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

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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