Reviewer’s report

Title: Novel secrortome-transcriptome integrated or secreto-transcriptomic approach to reveal liquid biopsy biomarkers for predicting individualized prognosis of breast cancer patients

Version: 0 Date: 05 Mar 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are major issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

Yes - experiments and analyses were performed appropriately

Statistics - Is the use of statistics in the manuscript appropriate?

Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

Yes - the author's interpretation is reasonable
OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Probably - with minor revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: The premise of the article is interesting. There is a clear need to better stratify breast cancer patients. Therefore, this manuscript is an effort in the right direction. However, I do have some concerns about the methodology. Here are some of my concerns -

The Introduction is a little too long. Can it be shortened to be more focused? The information deleted from here can be moved to Discussion.

Here is my biggest concern - authors begin by showing a displeasure towards the 50-gene expression model and by detailing how this does not adequately represent all the different BC subtypes. Then they take just 5 cell lines - 4 cancer cell lines representing TNBC and luminal subtypes (just two subtypes) and one normal. How do these 5 cell lines represent all the major BC subtypes?

In continuation of my above concern, why did not the authors consider HER2 overexpressing cell lines as a necessary model to be included here?

Given the inherent differences between cell lines, even the 2 cell lines representing same BC subtype can be very different. Obviously, this is reflective of the variations observed in the patient populations. But my concern is how can similarly expressed / secreted proteins only represent the relevant proteins secreted by a given BC subtype tumor. In this era of personalized therapy, this is a very dangerous approach.

The statement in the Abstract 'There is a pressing need for inexpensive and minimally invasive biomarker tests to easily and accurately predict individuals' clinical outcomes, stage disease progression, and monitor response to treatments' is a little too far reaching and clearly not supported well by the results. Need to tone it down.

The Results section is too elaborated but no efforts have been made to draft a compelling Discussion. Its just too short. This section needs much more writing.

REQUESTED REVISIONS:

Please see my detailed comments above
Note: This reviewer report can be downloaded - see attached pdf file.

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

No

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

No

**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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