Reviewer’s report

Title: Differential Proteomic Comparison of Breast Cancer Secretome Using a Quantitative Paired Analysis Workflow

Version: 0 Date: 21 Aug 2018

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT: The work presented is another computational pipeline approach to examine differences in NAF between matched tumor-bearing and non-tumor-bearing breasts in patients. The samples collected offer a unique way to look at how NAF changes in breast cancer patients. The use of NAF to study breast health and breast cancer has been studied since the 90's and has yet to be developed into a routine clinical diagnostic. Doing so would have a significant impact in the field. Whether this approach will lead to a robust diagnostic for detection of early presence of biomarkers is unclear. Given that previous studies have robustly shown signatures such as uPA + PAI-1 + TF have a near 100% accuracy in separating pre-cancerous and cancerous tissues in the challenging setting of patient heterogeneity, the impact of this work may be limited. Furthermore, whilst new potential markers were identified computationally in this manuscript, no follow-up orthogonal validation has been undertaken to confirm the reliability of the computational approach.

REQUESTED REVISIONS:

Modification searches in the proteomic pipeline only include carbamidomethylation of cysteine and oxidation of methionine. Given the majority of the factors in NAF are secreted, they should include other common extracellular modifications such as glycosylation, and hydroxylation of prolines, etc. to increase coverage. Whilst the authors contextualise some of the more novel components they find in the text, additional orthogonal validation of their presence is required to validate the accuracy of the approach.
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.

No

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.

Not relevant to this manuscript

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

Acceptable

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