Reviewer’s report

Title: Gene expression variation to predict 10-year survival in lymph-node-negative breast cancer

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Reviewer: Johanna Smeds

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Gene expression variation to predict 10-year survival in lymph-node negative breast cancer

Karlsson et al. present a study dealing with gene expression profiling in lymph node negative breast cancer. They have identified a 51 gene signature that could predict clinical outcome. Although the sample set is small, the study provides data on a new gene expression signature, which could predict outcome with high accuracy in the studied breast cancer patients. Overall, the article is very interesting and well written.

Suggested revisions:

The 51 gene signature showed good predictive value when tested on another publicly available data set published by van’t Veer at al., containing lymph node negative breast cancer patients, whereas the predictive value was poor when tested on the Wang data set. The 70-gene signature identified by van’t Veer et al. was later validated in a larger tumour set including both lymph node negative and node positive breast cancer patients. Did the authors also attempt to evaluate the signature in any other data set, where also lymph node positive patients were included? Perhaps the authors want to discuss the limitations of using this type of selected material for analysis of gene expression profiles.

On page 5, in the materials and methods section, it is stated that the authors accepted RNA specimens with 28S/18S ratio >1.0 and RIN>6.7. On what basis were these thresholds accepted? I believe it is more common to use higher threshold values in the order of 28S/18S ratio >2.0 and RIN>8. Perhaps sub-optimal quality of RNA could explain the failure to verify the microarray findings for 4 out of the 14 genes analysed by RT-PCR? Please correct the typo 28S/16S.

The authors did not find any overlapping genes with the van’t Veer and Wang signatures, respectively. Some of the genes of these signatures, however, appear to be involved in similar biological pathways, which perhaps could be mentioned. This has been found in other publications, where a low degree of overlap with other gene expression signatures was reported.

The discussion section is slightly over-detailed and could probably be modified and shortened; for example some sentences repeating facts provided in the
results section could be removed.
It is not clear if the present microarray data will be made publicly available.

1. Is the question posed by the authors well defined? Yes.
2. Are the methods appropriate and well described? Yes.
3. Are the data sound? Yes.
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? GEO access? Policy of BMC cancer?
5. Are the discussion and conclusions well balanced and adequately supported by the data? Yes.
6. Are limitations of the work clearly stated? Yes.
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes.
8. Do the title and abstract accurately convey what has been found? Yes.
9. Is the writing acceptable? Yes.

Level of interest
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- An article whose findings are important to those with closely related research interests

Quality of written English
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- Acceptable

Statistical review
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Is it essential that this manuscript be seen by an expert statistician?
If you feel that the manuscript needs to be seen by a statistician, but are unable to assess it yourself then please could you suggest alternative experts in your confidential comments to the editors.
- Yes, but I do not feel adequately qualified to assess the statistics.

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