Reviewer's report

Title: An integrated analysis of genes and pathways exhibiting metabolic differences between estrogen receptor positive breast cancer cells

Version: 4 Date: 13 June 2007

Reviewer: Chin-Yo Lin

Reviewer's report:

General
The authors' efforts to address previous comments are appreciated but still does not address previous concerns regarding the validity of the SAGE results and correlation with clinical parameters. First, there was no attempt to experimentally verify that the genes involved in the key pathways or ontology groups that the authors used extensively to define and explain the differences between the two cell lines are indeed differentially expressed between the two cell lines. Confirmation by Northern analysis or quantitative PCR are two possible approaches for accomplishing this, even if it is for only one of the ontology groups. Second, when the authors introduced GSEA data from clinical samples representing luminal A and B and basal epithelial cell tumors to demonstrate similarities or differences in gene set enrichment, there is no clear indication in the figure or the results section how these similarities or differences are measured and statistically supported. It is also not clear whether the tumor data represent three tumor samples or three groups of tumors. Wouldn't a more direct comparison be using gene expression profiles to hierarchically cluster the cell lines with the tumor samples to show similarities and differences, as it has been done previously (Perou et al, Nature 2000 and many other subsequent papers) rather than “eyeing” gene ontology results and trying to discern trends? As it is, the results comparing cell lines with tumors are not convincing and do not support the authors' contention that there is prognostic value in the results. Finally, if it is the authors’ aim to show that their approach represent a significant advance in identifying prognostic genes or gene sets, then they should complete the study by taking expression data from patient samples with corresponding clinical and follow-up data (a number of studies have been published and the data should be publicly available) and show that their gene sets can distinguish the different tumor types and are associated with disease outcome (Kaplan-Meier survival analysis?).

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Reject because scientifically unsound

Level of interest: An article of limited interest

Quality of written English: Acceptable

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

Declaration of competing interests:
I declare that I have no competing interests.