Reviewer’s report

Title: An integrated analysis of genes and pathways participating in adaptive survival in estrogen receptor positive breast cancer cells

Version: 1 Date: 19 March 2007

Reviewer: Steven Van Laere

Reviewer’s report:

General

This manuscript deals with the question if differences in adaptive mechanisms favoring survival of ER+ breast cancer cells can influence the breast cancer progression. Therefore, the authors have examined SAGE libraries from MCF-7, ZR75-1 and NBr cells using GO classification software.

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

1. This manuscript provides the reader with an exhaustive list of GO terms related to metabolic pathways. Conclusions written in the body of the text are not always supported by the figures.

2. The study is very descriptive and lacks appropriate statistical tests. For example, Goeman’s Global tests, Gene set enrichment analyses procedures or fisher exact tests on weighted contingency tables can be performed. I’m further worried about the statistical power of this study.

3. The authors should explain their use of the MCF7 and ZR75-1 cells. The study demonstrates that there is a metabolic difference between both cell lines. But it is unclear how this relates to breast cancer progression. Further testing is needed. For example, compare luminal A (high ER) to luminal B (low ER) and basal-like (no ER) tumours with respect to these conclusions. How are their findings translated in human samples. What happens when clustering publically available microarray data using the list of 263 genes.

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

1. The authors should carefully proofread the manuscript, since some of the evidence in the manuscript is not supported by the evidence in the figures. In addition, chromosome 17 also counts 5 common genes and is not listed in the list of important chromosomes. The structure of some sentences is not clear.

2. The dendrogram resulting from the clustering of 263 genes should be provided in figure 3a. This would add some statistical power to the identification of the Cluster Signatures.

3. The authors should, where possible, add statistical tests to their results sections. In most cases fisher's exact test can be used to assess significance of the distribution of the genes.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.