Reviewer's report

Title: Breast Tumor Copy Number Aberration Phenotypes and Genomic Instability

Version: Date: 17 March 2006

Reviewer: Petra Marleen Nederlof

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General
Title: Breast Tumor Copy Number Aberration Phenotypes and Genomic Instability

Jane Fridlyand et al

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

1. Is the question posed by the authors new and well defined?

The authors applied array-CGH to a series of breast tumors and could distinguish three subtypes on basis of their genomic aberrations. The subtypes were correlated with p53 status, ER status and expression analysis of a selected set of genes known to be involved in maintenance of genome integrity. Although other studies have tried to sub-classify (sporadic) breast carcinomas by e.g. expression array analysis, this publication adds new data regarding the chromosomal aberrations.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?

The technology applied is well documented and since all raw data is available as supplementary data results can be checked easily. However, the paper describes results obtained on two independent data sets. One data set is well described, including patient characteristics; the other is referred to as Chin et al (submitted). This patient material is however not just used as reference (stating that ‘the same three clusters were observed in an independent set of tumors’), but also used as material for the gene expression analysis and correlation to array-CGH data. Because the tumor set has such an important role in the paper, more information on e.g. the patient characteristics is desirable.

3. Are the data sound and well controlled?

The array-CGH results shown are of high quality. The correlation of the telomere length with the extent of amplification events in the genome is not convincing. In figure 3 one can see that the telomere length shows large variation between the tumors, and the correlation with amplification is not clear, although the spearman correlation gives a p value of 0.2.
It is observed that ‘expression of genes in the functional class …. ‘DNA damage/repair’ were associated with greater numbers of copy number transition’ One would expect that reduced expression of DNA repair genes would correlate with more aberrations, however it is not clear from the results if the authors mean increased of decreased expression.
4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

Yes

5. Are the discussion and conclusions well balanced and adequately supported by the data?

In the discussion it is mentioned that copy number loss on 17q includes the BRCA1 locus, however the data does not support this, only few tumors show loss at this locus. The discussion, on the chromosomal instability and involvement of various genes involved in genome stability related genes, is interesting and supported by the findings. Only the telomere length involvement is not convincing.

6. Do the title and abstract accurately convey what has been found?

yes

7. Is the writing acceptable?

yes

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

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Discretionary Revisions (which the author can choose to ignore)

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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 importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

'I declare that I have no competing interests'