Reviewer's report

Title: NF-kappa B genes have a major role in Inflammatory Breast Cancer

Version: 1  Date: 31 July 2007

Reviewer: Nathalie Cervera

Reviewer's report:

General

In this manuscript, the authors have compared the mRNA expression levels of 60 NF-kB-related genes in a series of 35 IBC with 22 non-IBC, by using real-time quantitative RT-PCR.

They, first, identified a gene signature included six “master genes” discriminating IBC from non-IBC.

And then, they detected two genes, VEGF and IL8, with lower expression in IBC patients with relapse. Hierarchical analysis of the 35 IBC based on this two genes with three they had previously identified, subdivided the IBC patients in two subgroups with high and low relapse rates.

The paper could be improved by paying attention to the following issues:

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

- the authors identified two signatures, one that correctly classified IBC and the second that matched patient outcome. However, they employed no tumor set of validation. Many sets of breast cancer data expression are now available in the bibliography. It is therefore necessary to test these two signatures on expression data of independent sets of IBC to assess the accuracy, sensitivity and specificity of the discriminator gene list.

- figure 1 presents 6 groups of upregulated genes with the 6 “master genes”. But the CCND3 gene, master gene of the group including NFkBIB/ IkBkG/RELA could also be associated with the group including CXCL2/ NFkB1/MCL1L/GADD45B/CCND2/TNC if rotating the branch: how can the authors explain their choice ?

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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)

- Cell cycle genes GADD45, CCND2, and CCND3, and angiogenesis-associated VEGF, can hardly be defined as NFkB pathway genes ! A little rewriting would be appropriate.

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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 importance in its field

**Quality of written English**: Acceptable

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