Author's response to reviews

Title: The breast cancer genome - a key for better oncology

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Author's response to reviews: see over
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Dear editors in BMC Cancer.

We hereby resubmit a revised version of our mini-review “Breast Cancer Genomics – a key for better oncology”. We are thankful for the comments made by the reviewer and the revised version is modified according to these comments. Below is a point-by-point response (in blue) to the remarks. We have also made an updated version of Figure 1.

Best regards

Hans Kristian M. Vollan and Carlos Caldas
The review article entitled “The breast cancer genome – a key for better oncology” is a short yet informative work that summarizes the current state of art regarding “Molecular classification of breast cancer”, “The era of sequencing of cancer genomes”, and “Implementation strategies in the clinic”. It has been known that a large number of genetic alterations present in the human tumor cells. However, it is difficult to discriminate between genes that are critical for maintaining the disease state and genes those are merely coincidental. In last decade, the array-based technologies revolutionized the understanding of breast cancer biology and thereby considerably improved therapeutic strategies. Since the information presented in the article is already published in a number of review articles, it would have been most appropriate if authors describe the “clear objective” of this review article.

We thank the reviewer for this comment. We have added a more precise description of the objective of the review in the manuscript abstract.

Specific Comments:

1. This is a well-written article.
We thank the reviewer for this comment.

2. Authors rightly pointed out that examining only the gene copy number (change) is not adequate to answer questions related to the design of the therapy; mutational analysis also play an indispensable role in deciding the treatment strategy.
We strongly agree with this comment.
3. In “Molecular classification of breast cancer”, authors have informed about the diversity of breast cancer and the role of technical advances in the understanding of the extent of molecular heterogeneity of breast cancer. However, the three paragraphs under “Molecular classification of breast cancer” are not seamlessly connected. The section is revised.

4. The gene array literature is polluted with many gene expression signatures that have inadequate validation (see the article of Serge Koscielny, Science Translational Medicine January 2010). In light of the above fact, authors should emphasize on the validation issue.

We genuinely agree that validation is of utmost importance and that signatures need adequate validation not only of the signature as such but also in clinical relevant subgroups of patients. This concept is elaborated on in the revised version of the
5. It has been known that genetically simple isogenic systems can be very powerful in identifying the prime determinants of response to particular therapeutic approach (Farmer H et al Nature 2005 434:917). Authors should discuss about isogenic systems in their review.

We have included a description on synthetic lethality in the section ‘Implementation strategies in the clinic’.

6. Authors mentioned “Fusion genes” but did not mention what is it? It will be easy for the reader to have a short description of “Fusion genes” and what is the relevance of “Fusion genes” in the context of the review.

A definition of fusion genes is added to the section ‘The era of sequencing of cancer genomes’.

7. A reader will also appreciate a “conclusion/future direction” at the end of the review.

Consider for acceptance following the revision.

A conclusion is added to the end of the manuscript.