Author's response to reviews

Title: Cancer Testis Antigens and NY-BR-1 expression in primary breast cancer: Prognostic and therapeutic implications.

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Version: 2 Date: 8 May 2013

Author's response to reviews: see over
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Version: 2 Date: May 7, 2013

Author’s response to reviews: see over
Dear Dr. Kalil Helou,

Please find attached the revised version of our manuscript “Cancer Testis Antigens and NY-BR-1 expression in primary breast cancer: Prognostic and therapeutic implications” by D. Balafoutas et al. We have carefully revised our manuscript according to the very helpful comments of the reviewers. These changes and minor others introduced in order to improve reading and understanding are indicated within the text. In addition, we discussed the reviewers’ comments point-by-point on the following pages.

We very much appreciate that our manuscript is considered for publication in BMC Cancer.

Sincerely,

Dr. Elmar Stickeler MD
Reviewer's report

Title: Cancer Testis Antigens and NY-BR-1 expression in primary breast cancer: Prognostic and therapeutic implications.

Version: 1 Date: 1 April 2013

Reviewer: Holger Moch Moch

Reviewer's report:

This study describes the expression of different CT antigens as well as the breast cancer differentiation antigen NY-BR-1 in a cohort of breast cancer cases arranged in a tissue microarray format. The manuscript is well written, the relevant literature is cited and the figures confirm a good quality of the immunohistochemical stainings. Given the controversial data on the prevalence of CT antigens in the literature, the manuscript is worth to publish and is of potential interest for the readers of BMC Cancer.

Reviewer #1 has no suggested changes for the manuscript.

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.

Declaration of competing interests:

I declare that I have no competing interests.
Reviewer's report

**Title:** Cancer Testis Antigens and NY-BR-1 expression in primary breast cancer: Prognostic and therapeutic implications.

**Version:** 1  **Date:** 2 April 2013

**Reviewer:** Kosei Yasumoto

**Reviewer's report:**

This manuscript entitled “Cancer testis antigens and NY-BR-1 expression in primary breast cancer: Prognosis and therapeutic implications.” describes correlations between expressions of 5 CTAs and breast specific Ag NY-BR-1, and clinicopathological factors affecting prognosis of breast cancer patients. The most significant finding was correlation between MAGE A3 expression and poor prognosis. These data were clearly written, however, with regard to function of CTAs, only the description that MAGE A bind to a repressor of p53:KAP1 and suppress apoptosis in MAGE A expressing cell lines, for MAGE A3 it’s down-regulation results in p53 promoter activation, and GAGE seem to have a similar function. What is the functions of NY-ESO-1? 

Currently there are insufficient data about the biological function of the cancer testis antigens and of the breast differentiation antigen NY-BR-1. These antigens were identified with SEREX (serological analysis of recombinant tumor cDNA expression libraries) with their key characteristic being the tumor-restricted expression profile for the cancer testis antigens and the tissue specific expression for NY-BR-1. We included in our manuscript the available information that there is a probable interaction of NY-ESO-1 with DNA methylation as the reviewer indicated (§5 of “Discussion”). Additionally we mentioned the type of immune response for NY-ESO-1 (same §) and also NY-BR-1?

Similarly to cancer testis antigens, because of the lack of available data about the biological function of NY-BR-1 we included in our manuscript the main hypothesis based solely on bioinformatics analyses (Second sentence of §7 of “Discussion”) as the reviewer indicated.

Because they stressed expression of them is the key in immunological treatment without showing any evidence about immune responses against NY-BR-1.

The reviewer is correct: Indeed we failed to include the important information that the immunogenicity of NY-BR-1 is confirmed, not only because it was initially identified by SEREX, but also with antibody detection in seropositive patients and the identification of the corresponding HLA epitopes. This information is now included (middle of §7 of “Discussion”) as the reviewer indicated.

**Level of interest:** An article whose findings are important to those with closely
related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests below.

In addition to the changes suggested by the reviewers, we included changes concerning the specificity of the monoclonal antibodies M3H67 and 57B. According to the recent literature and because of the cross-reactivity of these monoclonal antibodies (as we already point out in the first version of our manuscript), we believe that in terms of improving accuracy it is better to link our results to the antibodies that were used and not to the specific MAGE family members that are predominantly recognized by the above antibodies. The respective changes were also performed in the figure legends and tables.