Author's response to reviews

Title: Clinical relevance of breast cancer-related genes as potential biomarkers for oral squamous cell carcinoma

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Dafne Solera, Ph.D., Executive Editor
BMC Cancer
BioMed Central
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Dear Dr. Solera,

Thank you for the review of our revised manuscript (Manuscript MS: 1350618841124049) entitled "Clinical relevance of breast cancer-related genes as potential biomarkers for oral squamous cell carcinoma" by Toshima Z. Parris, Luaay Aziz, Anikó Kovács, Shahin Hajizadeh, Szilárd Nemes, May Semaan, Chang Yan Chen, Per Karlsson, and Khalil Helou. The reviewers’ comments are carefully addressed in this cover letter and in the revised manuscript. We hope that you will find the revised manuscript more suitable for publication.

Reviewer 1 (Hsuan-Ying Huang)
The reviewer had no further comments.

Reviewer 2 (Jenn-Ren MD, PhD Hsiao)
1. This re-submitted manuscript has significantly improved compared to the previous one. The “normal mucous membrane” has been clarified as the “peritumoral normal mucous membrane” (p11. line 9). And the authors provided a plausible speculation regarding why positive expression of S100A8 was independently correlated with OS, while CNTNAP2 was independently correlated with DSS, in the DISCUSSION section. The authors also provided a more detailed definition regarding “peritumor inflammatory infiltrate” (p7, lines 21-23) and histological grading (p7, lines 10-12), and provided the information of cigarette smoking in their OSCC cohort, although the information regarding alcohol usage is still lacking.

Response: Unfortunately, information on alcohol consumption wasn’t available for Cohorts I-II and was only recorded in medical records of 2/43 patients in Cohort III. This clinical parameter was therefore excluded from Table 1.

2. It would be interesting for the authors to perform an additional multivariate analysis by adjusting tumor size, lymph node status and differentiation to demonstrate the prognostic impact of S100A8 on OS of these OSCC patients, since the authors had demonstrated that expression of this protein is significantly associated with tumor differentiation.

Response: The multivariate analysis was originally performed by adjusting for statistically significant parameters for OS in the univariate analysis (tumor size, lymph node status, age,
and S100A8 protein expression). Here, we have included differentiation in the multivariate analysis with and without adjusting for age and S100A8 protein expression:

a. Tumor size, lymph node status, differentiation C-index 0.605
b. Tumor size, lymph node status, differentiation, S100A8 C-index 0.771
c. Tumor size, lymph node status, differentiation, age C-index 0.605
d. Tumor size, lymph node status, differentiation, age, S100A8 C-index 0.833

In models b and d, S100A8 was still statistically significant. Table 5 and Figure 2b have been updated using the results above from bullets c-d to include differentiation. In addition, lines 217-221 on page 12 have been updated to read “Following multivariate analysis adjusting for tumor size, lymph node status, differentiation and age, S100A8 was still statistically significant (P = 0.013 - HR (95% CI) = 0.11 (0.013-0.92; Table 5)). Combining S100A8 in a predictive model for OS with tumor size, lymph node status, differentiation and age improved outcome prediction significantly from 0.605 to 0.833 (Figure 2).”

With the resubmission of this manuscript I would like to undertake that the above mentioned manuscript has not been published, accepted for publication or under editorial review for publication elsewhere.

We await your response and the comments of the reviewers.

Yours sincerely,

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