Author's response to reviews

Title: Elevated expression of LSD1 (Lysine-specific demethylase 1) during tumour progression from pre-invasive to invasive ductal carcinoma of the breast

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Elevated expression of LSD1 (Lysine-specific demethylase 1) during tumour progression from pre-invasive to invasive ductal carcinoma of the breast

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Responses to reviewers' comments:

Dear Professor Patel,

We would like to thank the reviewers for their valuable comments which helped us to further improve the manuscript. Please find enclosed our response letter. The revised parts of the text have been marked by underlining in the manuscript text. We included the statistical data (table 1).

Referee 1’s (Elad Katz) comments:

Comment:

Serce et al. present an interesting small study into the differential expression of LSD1 in human breast cancer. The manuscript is well written and presented. However, it is presented as a validation study for Lim et al. (ref 13). In fact, the cohorts and biomarkers used are different. I would suggest presenting these results head to head (if possible) or adding a statistically defined validation set to show the reproducibility of the results in the current manuscript.

Response:

Dear Professor Katz, thank you very much for your valuable comments. Our study was not constructed as a validation study for Lim et al. (ref 13) as they do not analysed pre-invasive lesions as low, intermediate and high grade ductal carcinoma in situ. Our aim was to primarily investigate LSD1 expression during tumour progression from non-invasive to invasive ductal
breast carcinoma. We agree with your comment that our results are preliminary and have to be confirmed in a larger cohort in prospective studies. We will start to collect more samples for a greater cohort and we expect to verify our results as they are statistical significant in this initial study.

**Referee 2’s (Rzymowska Jolanta) comments:**

major compulsory revisions - absence

**Referee 3’s (Hossein Mozdarani) comments:**

**Comment:**

Manuscript entitled "Elevated expression of LSD1 (Lysine-specific demethylase 1) during tumour progression from pre-invasive to invasive ductal carcinoma of the breast" by Nuran Serce et al. is a well written manuscript describing an important candidate biomarker for breast cancer. My main concerns about this manuscript are as follows:

1- The number of tumour tissues studied with G1, G2 and G3 are not comparable. It is difficult to compare results from 2 samples in G1 with 16 in G2.

2- It is expected that authors relate the findings with LSD1 with other clinical and experimental features of the studied samples. e.g. was there a correlation between LSD1 expression with Her2 expression? What was the status of LSD1 expression with triple negative of triple positive samples?

If authors could provide more data correlating expression of LSD1 with other clinical and experimental information their manuscript worth publishing.

I think the data provided is not supporting the title of manuscript because of non uniformity of sample size.

**Response 1:**

We appreciate the reviewer’s comments very much. Our aim was to primarily investigate LSD1 expression during tumour progression from non-invasive to invasive ductal breast carcinoma. We have chosen approximately equal group size considering low grade (n=27), intermediate grade (n=30) and high grade ductal carcinoma in situ (n=31). So the groups are comparable and there is nearly uniformity of sample size. Regarding invasive breast
carcinoma (n=32) the distribution according to the histological grade was: G1 (n=2), G2 (n=16), G3 (n=14) (see also table 1).

**Response 2:**
In invasive breast carcinoma LSD1 expression was correlated with tumour stage, lymph node status, histological grade, oestrogen/progesterone receptor status and with Her2 expression. We included the statistical data (see table 1) and added comments in the “results” and “discussion” part.