Reviewer's report

**Title:** High nuclear expression levels of histone-modifying enzymes LSD1, HDAC2, and SIRT1 in tumor cells correlate with decreased survival and increased relapse in breast cancer patients

**Version:** 2  
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**Reviewer:** Bimal Ray

**Reviewer's report:**

In this manuscript, Derr et al. described a finding where three enzymes, LSD1, HDAC2, and SIRT1, were found express at different levels that was correlated with survival and relapse of cancer in breast cancer patients. A cohort of 460 patients was used in this study and immunohistochemical (IHC) analysis has been performed to assess relative levels of the three enzymes in patients with different stages of the cancer and comparisons were also made between normal breast epithelial tissue and breast cancer tissues for the same three enzymes. Based on the IHC analysis, authors have concluded that LSD1 and SIRT1 are present at significantly higher levels in cancer tissues and correlate well with the cancer stages. Furthermore, authors conclude that high expression of LSD1, HDAC2 and SIRT1 show shorter patient survival time and tumor relapse as well as poor tumor differentiation and high level of tumor cell proliferation.

Overall, this is an interesting observation that focused on three nuclear proteins that play very important roles in the regulation of expression of many genes. By analyzing the levels of these proteins using IHC procedure, authors have identified a novel correlation between these proteins and breast cancer. While IHC is a powerful technique for analysis of proteins, the findings presented in this manuscript should be strengthened and verified by another approach such as western immunoblot. Also, there was no IHC analysis for normal breast epithelial tissues in support of data presented in Fig. 2 and must be included.

According to Fig. 3, HDAC2 level seems to increase in stage III cancer tissue, perhaps to the same level as that of LSD1, although the median may be different. Authors need to address this issue.

Figs. 4 and 5 are very difficult to read and must be enlarged.

Total number of patients has been indicated as 460, but the legend of Fig. 3 indicates 465, when three number are added. These numbers should be corrected.

There are minor typographical errors, for example, in the Fig. 3 legend, line 2, the word “en” it should be “and”.

**Level of interest:** An article of importance in its field

**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.