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

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Reviewer: Jutta Kirfel

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Minor Essential Revisions

Reversible lysine acetylation and methylation regulate the function of a wide variety of proteins, including histones. Previous studies demonstrated that lysine-specific demethylase 1 (LSD1) and histone deacetylases (HDACs) closely interact in controlling growth of breast cancer cells. Several lines of evidence indicate that Sirt1, a class III histone deacetylase (HDAC) is implicated in the initiation and progression of malignancies and thus gained also attraction as druggable target.

Derr et al. analyzed SIRT1/HDAC2 and LSD1 expression by immunohistochemistry in a large cohort of breast cancer patients and correlated with clinicopathological and survival data. The authors show that combined expression levels of histone-modifying enzymes LSD1, HDAC2 and SIRT1 correlate with tumor differentiation and cell proliferation.

The study by Derr et al. has been carefully performed with an accurate survey of the literature, replacing LSD1, HDAC2 and SIRT1 in the context of breast cancers and their potential usefulness as new combined epigenetic biomarkers and therapeutic targets. The only weakness is the lack of a cell system to validate the clinical impression. Functional effects on the growth of cancer cell lines can be generated by treating breast cancer cells with small interfering RNAs (siRNAs) against histone-modifying enzymes and/or inhibitors against the enzymes and investigation of cell viability.

Level of interest: An article of outstanding merit and interest 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