Reviewer's report

Title: Integrity of the LXXLL motif in Stat6 is Required for the Inhibition of Breast Cancer Cell Growth and Enhancement of Differentiation in the Context of Progesterone

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Reviewer: Itamar Barash

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Integrity of the LXXLL motif in Stat6 is Required for the Inhibition of Breast Cancer Cell Growth and Enhancement of Differentiation in the Context of Progesterone by Wei et al.

The interaction between Stat6 and PR were studied in the PR-positive mammary carcinoma T47D cell line, as well as their effect p21 and p27 gene promoters activation, cell cycle and cell proliferation. The data are of interest, but for publication, the manuscript needs additional scientific and grammar editing. Importantly, there are inconsistencies between the data and their description, some of which are described below.

Minor revisions.

1. Please add page numbers.

Materials and Methods:
"Chromatin immunoprecipitation assays were performed as described elsewhere [28] using 4µg of anti-Stat6 (Abcam)". Please elaborate.

Major revisions.

Results:

2. General: The study was performed with single cell line. Major findings should be supported and generalized with an additional PR-positive cell line (see. Neve et al. CANCER CELL 10, 515–527, 2006).

3. Fig. 1 - " As previously reported, the mutation of the Sp1-3 and Sp1-1 sites diminished the basal activity and abolished the responses of the p21 and p27 promoters to Stat6 or progesterone alone" - I do not see evidence.

4. Fig. 3A " Low levels of endogenous PR were found in the complex immunoprecipitated with the anti-Stat6 antibody in untreated T47D cells. However, the amount of PR co-immunoprecipitated with Stat6 was drastically increased in cells treated with progesterone alone. This is not shown in the figure.
5. Fig. 4. "This effect was attenuated by co-treatment with RU486 (supplementary figure 4). Supplementary Fig. 4 and Fig 3A do not seem to correspond.

6. As reported, progesterone induced the early gene expression of desmoplakin and Na+/K+-ATPase #1, which are markers for epithelial differentiation and glandular development, respectively [46, 47] (Fig. 7A). This is not shown in Fig. 7A.

Discussion

6. The discussion is written as a review. It is much too long and should focus on the results. The description of the supplemented figures should appear in the Results section. Not in Discussion.

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

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