Reviewer's report

Title: Autocrine Regulation of Cell Proliferation by Estrogen Receptor-alpha in Estrogen Receptor-alpha-positive Breast Cancer Cell Lines

Version: 2 Date: 16 October 2008

Reviewer: Benita S Katzenellenbogen

Reviewer's report:

In this paper Han et al show ERalpha and Ki67 colocalization in three different breast cancer cell lines. ER alpha was always highly expressed throughout the cell cycle. Antiestrogen ICI treatment decreased ER alpha protein expression and kept the cells at the G1 phase of the cell cycle. E2 treatment promoted ER alpha and Ki67 expression and colocalization and cell cycle progression through S and G2/M phases. These effects were not abrogated by EGFR inhibitor which supports the autocrine action of ER alpha in cell cycle progression and Ki67 expression in MCF-7 cells. Overall, the paper addresses interesting questions in the field.

There are minor points that the authors should address:

1. Figure 1:
   We already know that ERalpha is required for cell cycle progression in MCF-7 cells but it might be worthwhile to check Ki67 expression in cells where ERalpha protein levels are reduced with siRNA, since it has been shown that ERalpha induces other transcription factors that drive the cell cycle (such as E2F family members).

2. Figure 2A:
   It is not clear from the Methods section or legend which staining is what. They labelled all the red stained images as Ki67 and I don't know how they colocalized Cyclins with ERalpha. Did they use a third dye for Cyclins or is Ki67 a mislabel for each panel and they did not do Ki67 staining in this section?

3. Figure 6:
   It would be worthwhile to use an IGFR inhibitor in addition to EGFR inhibitor. Also it is not clear from the Methods or legend of the figure if they kept Gefinitib in the media during E2 treatment.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests