Reviewer's report

Title: Estrogen receptor alpha-coupled Bmi1 regulation pathway in breast cancer and its clinical implications

Version: 2
Date: 6 January 2014
Reviewer: Valerie Speirs

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Major Compulsory Revisions

1) Legend to Fig 1 could misled the non-specialist reader into thinking all ER-negative breast cancers are universally negative for PR, cyclin D1 and pRB, especially the last sentence in the fig legend, and contracts what is presented in Table 3. This needs addressing.

2) There is not …"marked down-regulation of ER# protein by these three siRNAs..." as described on pg 14 with reference to Fig 4. Only siRNA 3 shows this. The text and legend should be modified to reflect this.

3) The results section “ER#-coupled Bm1 regulatory pathway in breast cancer” (pg15) is too long (4+ pages) and contains discussion points as well as the results. This section should contain just results with the discussion points being assimilated into the discussion section of the manuscript.

Minor Essential Revisions

1) Given the heterogeneity of breast cancer, the clinical cohort is relatively modest (n=92). The authors should acknowledge this in the context of the correlative results they describe in Table 1.

2) Fig 2 is quite confusing in its presentation. I recommend the Western images be presented sequentially underneath each other (likewise for the quantification graphs) so that data for each cell line can be more easily compared.

3) Fig 3 legend; best to say empty rather than blank vector

4) The authors use some strong statements e.g. pg14 “…results conclusively demonstrated that ER# can specifically stimulate the functional expression of Bmi1”. While this may prove to be the case it needs validation by others so this statement should be toned done.

Discretionary Revisions

1) In the supplementary table please check SP1 antibody is supplied by Dako. Could you mean ID5 rather than SP1?

Level of interest: An article whose findings are important to those with closely related research interests
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