Reviewer’s report

Title: Comparative actions of progesterone, medroxyprogesterone acetate, drospirenone and nestorone on breast cancer cell migration and invasion

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Reviewer: Brian Rowan

Reviewer’s report:

This manuscript investigated the effects of progesterone (P), medroxyprogesterone acetate (MPA), drospirenone (DRSP) and nestorone (NES) alone or with estradiol (E2) on T47-D breast cancer cell migration and invasion. The data demonstrate effects of progestin ligands on T47-D cell migration/invasion and modest effect with the addition of E2 to the progestins. This study is a fairly comprehensive assessment of progestin effects in one breast cancer cell line and contributes important new information to the breast cancer field. Some additional experimentation is required including additional breast cancer cell lines and better quantification of some data.

Minor Essential Revisions

1. E2 mediated enhancement of progestin activation of actin rearrangement is overstated and is not borne out on comparing data shown in Figures 1 and 2. For definitive conclusions, data in Figures 1-2 must be quantitated. While Figures 1-2 are impressive representative pictures of morphology changes, a quantitation of the % cells with spatial modifications of actin fibers and cells that form specialized cell membrane structures (longitudinal actin fibers, pseudopodia, ruffles) would permit a more rigorous comparison among treatments with statistical analysis.

2. A panel of three additional representative breast cancer cell lines is needed in Figures 1 and 2 to demonstrate the generality of these morphology changes for breast cancer. These data should be quantitated as described in #1 above and data compared among the cell lines. T47-D is not the best representative model of estrogen receptor positive breast cancer and one needs to know whether these ligands have similar or different effects in other breast cancer cells.

3. The additive effects of E2 and Progestins on moesin phosphorylation are not convincing based on the data presented (Figures 4A-C). Densitometry data of moesin and phosphorylated moesin bands normalized to an internal control with statistical analysis are needed for definitive conclusions to be made.

4. Combination of E2 and Progestins does not appear to significantly alter the cell migration index compared to effects of Progestins alone, although E2 alone significantly increases the invasion index compared to Progestins alone. The Discussion on the combinatorial effects of E2 and Progestins on moesin phosphorylation, cell migration and cell invasion should be modified. Although E2 induces actin rearrangement, cell migration and invasion E2 does not appear to
further enhance Progestin induced actin rearrangement moesin phosphorylation, and cell migration and invasion.

What next?: Accept after minor essential revisions

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