Reviewer's report

Title: Association of postmenopausal endogenous sex hormones with global methylation level of leukocyte DNA among Japanese women

Version: 1 Date: 2 May 2012

Reviewer: Heather Nelson

Reviewer's report:

This is an interesting and well-written manuscript investigating endogenous sex hormones and leukocyte global methylation in postmenopausal Japanese women. This is a very topical research question as there is considerable interest in methylation differences by gender at LINE-1, and consistent observations of cancer risk with leukocyte DNA hypo-methylation. Here, the authors have used an alternative measurement (LUMA), and investigated global methylation in relation to sex hormones among healthy subjects.

Discretionary revisions:

The authors have downplayed their findings. Both bioavailable estradiol and estrone were borderline significantly associated with leukocyte methylation I feel the authors could include these p-values in the abstract, and in the discussion indicate results were "not statistically significant" rather than "not significant".

Minor essential revisions:

1. In table 1 the sample sizes should be included; missing data should be noted, as well as missing data due to limit of detection issues.

Major compulsory revisions:

1. The authors observe a borderline statistically significant association between leukocyte methylation and both estrone and bioavailable estradiol, however these associations were in opposite directions. A discussion of this observation in the discussion section is warranted.

2. It is possible that the borderline significant associations are driven by the tail ends of the methylation distribution. It would be very informative to include a figure that plots the estrogen variables against methylation values to better understand the borderline significant relationships reported in table 2.

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

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare I have no competing interests