Reviewer’s report

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

Version: 1 Date: 29 March 2012

Reviewer: Unhee Lim

Reviewer’s report:

Minor revision recommended.

Comments to Authors:

1. It is not clear to me why so many covariates were adjusted for in the model. Were the associations confounded by any of them – if any, how did they differ from age-adjusted estimates? Most of the covariates have been associated with global DNA methylation in leukocytes but not all consistently. Also, over-adjustment is of concern if any covariate associations are mediated by sex hormone levels.

2. The interpretation would be limited to postmenopausal women, not premenopausal women. Were women with recent or current use of HRT excluded? – if included, an adjustment or stratification would be appropriate depending on the sex hormone levels among users.

3. The authors present good to acceptable quality control data for the measurements. Were these from blind QCs, especially for hormone measurements that were obtained from commercial labs?

4. Did folate intake include folic acid supplement? In table 3, it would be helpful to see the median values of alcohol or folate intake.

5. Typo: in Laboratory analysis, 48.1% should have a concentration unit for estradiol.

6. Some demographic description (e.g., distribution of age and age at menopause) would be helpful, maybe as a supplemental material.

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 do not have any conflict of interest.