Reviewer's report

Title: Quantitative methylation profiling in tumour and matched morphologically normal tissues from breast cancer patients

Version: 1 Date: 29 August 2009

Reviewer: Edward Sauter

Reviewer’s report:

Auwera et al. analyzed DNA methylation status of 6 genes (DAPK, TWIST, HIN-1, RASSF1A, RAR#2 and APC) in paired cancerous and adjacent normal tissue samples by comparing them with breast tissue from patients without cancer using quantitative real-time MS-PCR method.

The authors reported that hypermethylation in histologically normal breast tissue adjacent to malignant breast tissue was frequently observed in multiple genes. The findings from this study are consistent with previously published results. A total of 56 paired breast tumor samples were analyzed in this study, which is larger in sample size than some and smaller than similar prior reports.

Major compulsory revisions:

1. This study once again supports the observation that hypermethylation is an event that occurs in an individual's histologically normal breast as well as in malignant breast tissue.

Please expand your discussion of other reports on the subject.

2. This study does not directly address if hypermethylation is early event in the development of breast cancer, for it does not assess the frequency of hypermethylation in precancers of the breast.

Please discuss other reports that did assess hypermethylation of the breast in precancers, both those analyzing tissue and those analyzing intraductal samples. Please incorporate these findings into your discussion.

3. The authors’ observations could be considered a) a field defect or b) due to environmental exposure in the individuals rather than c) an early marker of cancer. Please address why the findings are the latter and not either a) or b).

Minor Essential Revisions

1. This reviewer did not identify a clear description in the abstract of the hypermethylation differences between true normal breast tissue and the paired tumor and the adjacent normal breast tissue samples.

2. There is no need to include Table 2.

3. Table 5 can be deleted, and rather present the findings that are significant in the text.
4. Since there is no difference identified, Table 6 can be omitted as well. The trends observed are already mentioned in text.

5. A more detailed legend should be provided for Figure 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, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests