Reviewer’s report

Title: Common genetic polymorphisms of microRNA biogenesis pathway genes and breast cancer survival

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Reviewer: Song Yao

Reviewer’s report:

In the submitted manuscript, Sung and colleagues reported findings of associations between SNPs in microRNA processing genes and breast cancer survival in 488 patients in Korea. The study was well designed and performed, and the manuscript was clearly written and presented. Although similar studies have been reported for other cancers, this is the first on breast cancer. The results are novel and interesting. Pending on further validation, the findings, particularly the cumulative risk genotypes, may be clinical significant for breast cancer prognosis. The findings also provide evidence that microRNAs play an important role in breast cancer progress. I have concerns on some minor methodological issues that would warrant clarification.

Minor essential revisions:

1. In the methods, it was stated a total of 3,497 of breast cancer cases were recruited between 2001 and 2007. This number is much higher than the total when adding up those with history of cancer, history of hysterectomy or oophorectomy, no or insufficient DNA samples, and those genotyped (total n=1,469). Please clarify this discrepancy.

2. In the methods, “patients were followed from October 2009 to March 2010”. This is confusing since the follow-up should start after the surgery until the events occurred or patients censored. Is October 2009 to March 2010 referred to the period when the chart review was done? This is not the follow-up time. Please clarify. Also in Table 1, the follow-up time for overall survival is longer for disease-free survival. Why is this? Should the two outcomes identified through the same length of follow-up? Please clarify.

3. In the methods, “Indicator variables were used for patients with missing covariate data…”. Please explain what indicator variables mean here.

4. Since 41 SNPs were tested without a priori hypothesis of their functions in breast cancer survival, it would make sense to make adjustment for multiple comparisons, such as FDR or permutation. Although some of the results significant at 0.05 level may become non-significant after the correction, the highly significant p-values of the cumulative risk genotypes should justify.

5. This patient population is relative young, with an average age of 46.6 years and about two thirds were premenopausal. Some explanation of this young population would help better understanding the generalizability of the findings to the overall breast cancer patients in Korea.
6. Page 11 second paragraph, “HIWI rs4759659 variant allele (A) had associated…” should be “was associated”.

7. Page 15, first line, it seems the first author’s name of this reference is not “No”. Please double check.

Discretionary revisions:

8. Since the SNPs were chosen as tags, it would make sense to perform haplotype analysis for SNPs in LD blocks.

Hope the authors find the above comments helpful.

**Level of interest:** An article of outstanding merit and interest 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.