Reviewer’s report

Title: MicroRNA profile in very young women with Breast Cancer

Version: 2

Date: 15 May 2014

Reviewer: Jodie Fleming

Reviewer’s report:

Major Compulsory Revisions:

1. The authors have addressed selected of the concerns through the addition of comments in the discussion, and have added some information on the patient samples. The addition of the ethnic origin and BMI of the tumor samples significantly enhance the overall report. However, the authors need to fully address the limitations of their study in the discussion and throughout. For example, while the miRNAs identified suggest pathways related to cell motility, proliferation and invasion, without testing these functions in vitro in tissue specific context (i.e. breast cancer) the authors should be more conservative with their language in drawing conclusions.

2. A major limitation of the study is the small and undefined sample size of the “normal” breast tissue samples that were used to compare against the tumor samples. It can be argued that the reduction mammoplasty samples were obtained from significantly obese patients (statistically the norm). As the BMI was not accounted for in the normal samples, and that obesity has a strong influence on the tissue microenvironment, estrogen metabolism, and overall physiology of the breast, it should be with caution that the authors draw as strong of conclusions. More healthy patient samples for the analyses would make the data more relevant. Specifically, the normal samples were only obtained from young patients, and a cohort of older normal tissue samples would be beneficial to the study.

3. A collection of H&E images of the normal breast tissue and tumors samples is a strongly suggested improvement and would add valuable information to the manuscript. The epithelial vs stromal content of the normal tissue could be evaluated in comparison to the tumor samples. The adipocyte size and abundance, in addition to overall tissue composition would be helpful. As epithelia vs stromal content is something that must be addressed, and is currently lacking, this would be a valued contribution to the manuscript.

4. Moreover, the authors state that the BMI of the BCVY is normal and the older are overweight. The authors should point out this significance in their Table 1. By not highlighting the obvious significant differences listed in Table 1 it may appear they are withholding observations. The significance should be denoted with a * and they should state the numerical significance level.
5. The authors mention other miRNAs that have been identified as molecular markers for breast cancer and correlate with metastatic and proliferative capacity. It would be beneficial for the authors to discuss why their analysis did not identify any of these previously validated miRNA markers for breast cancer, given they identify similar pathways found with their miRNAs including proliferation and motility and invasion. If the authors are highlighting the unique differences with the BCVY, do the older patients have a correlation with these previously identified miRNAs?

Minor Compulsory Revisions:

The authors that in the discussion that “no distinct therapies are considered for young or very young patients” However, many studies have shown that young women have concerns about fertility that drive their choice of treatment. To this end, doctors are considering alternate or more conservative treatments specifically for young women to retain fertility.


1. Minor typos such as missing spaces between references and words, or spaces between periods and the next sentence should be fixed in the newly added sections.

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