Reviewer’s report

Title: miRNAs associated with chemo-sensitivity in cell lines and in advanced bladder cancer

Version: 1 Date: 5 June 2012

Reviewer: Emily J Noonan

Reviewer’s report:

Major Compulsory Revisions:

1. The discussion contains a lot of tangential information. It is advised the authors review the discussion in full and determine relevance to urothelial cancers, especially when describing miRNAs and their targets or putative targets in the described cancer.

2. The authors need to address the baseline miRNA expression patterns in the cell lines used within and whether these were accounted for when interpreting results from knockdown or knock-in experiments (i.e. if a highly expressed miRNA varied between cell lines, and knock-in proved no results in the highly expressed cell line). At minimal there should be a declaration of no substantial differences.

3. Have the authors considered the idea of multiple comparisons when analyzing array data? Is the significance adjusted to reflect this? Did the authors use a p-value of 0.05?

Minor Essential Revisions

1. In the abstract, first sentence is missing the word “such” when describing cellular processes- proliferation, carcinogenesis etc.

2. In the abstract, methods section, last sentence, the parenthetical reference to transfections can be removed.

3. The introduction contains a lot of background information on miRNAs that the reader can assume most readers are familiar with at this point. Particularly at the bottom of the first page and top of the second page (in the background section).

4. The authors should separate the background into distinct paragraphs

5. At the end of the introduction when describing the effect of miRNAs on cell viability, the authors should clarify their terminology “generally reduced” vs. “reduced the viability of more than half of”. What exactly does generally reduced mean?

6. In the methods “Patient samples” section, the authors should consider adding a reference of supplementary methods section for information regarding the clinical trial; specifically a description of each of the phases so readers can have a clear understanding of the trial groups.

7. The cell culture section was exemplary of good experimental technique and
reporting.

8. In the transient transfection control section of the methods, did the authors use a transfection control? Either a fluorescently labeled small ncRNA or detection by real-time PCR after transfection?

9. Same section: can the authors define the pre-miRNA? Is this a hairpin or short double stranded sequence?

10. In the “Isolation of RNA” section, can the authors indicate what the specific FFPE kit (miRNeasy) does in comparison to the traditional miRNeasy kit?

11. In the “miRNA profiling...” section, can the authors indicate what version of miRBase content the Taqman microRNA panel and any other high-throughput experiments, were using? (version 18 is current)

12. In the results, in Figure S1, what was the baseline set to for relativity? The authors should indicate within the legend.

13. In the section “Cisplatin sensitivity of bladder cancer cell lines” Can the authors indicate which cell lines are more or less sensitive so readers can have a deeper understanding when interpreting the data as the authors indicate this has been described in reference 20.

14. In the following section describing miRNA knock-down, the ordering of information at the end of the first sentence is confusing- “using LNA anti-miRs, followed by viability analysis after cisplating incubation”

15. In the discussion, in reference to citations 26, 27 the authors describe that miRNA-27a functions as an oncogene, but knocking down miR-27a (anti-miR) inhibits the expression of a tumor suppressor gene- this is confusing. Is the terminology “anti-miR-27a” correct?

Discretionary Revisions

1. The first paragraph of the introduction describes bladder cancer specifically, and then the author transitions into a description of treatment and survival in urothelial cancers.

2. In the introduction, the authors also need to more clearly describe why they choose to examine miRNA dysregulation. There is an abrupt change to this topic with no paragraph indentation or transition sentence.

3. In the introduction line 7, “disease stage” sounds awkward- is prognostic indication a more appropriate term?

4. In the introduction line 8, there are two “.” After the phrase “disease dissemination..”

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

I declare that I have no competing interests.