Reviewer's report

Title: The Effects of MicroRNA Transfections on Global Patterns of Gene Expression in Ovarian Cancer Cells are Functionally Coordinated

Version: 1 Date: 25 March 2012

Reviewer: Carlos Moreno

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In the manuscript by Shahab et al, the authors analyze the global changes in gene expression upon transfection with two microRNAs on the HEY ovarian cancer cell line. They identify 754 differentially expressed genes after transfection with miR-7, and 2338 genes after transfection with miR-128. They further go on to analyze the percentage of genes that are likely to be direct targets, and the mechanisms for indirect changes in gene expression. Pathway enrichment analysis is followed by some functional biological assays in cell adhesion and cell cycle progression. In general, this is a well-performed and well-written study. However, there are some items that should be addressed by the authors.

Major Compulsory Revisions

1) The most significant concern with this manuscript is that regarding the ripple effect of hub genes. One of the hubs identified in Supplementary Tables 7 and 8 is centered on EGFR. However, the authors show in Supplementary Table 3 that siRNA knockdown of EGFR only impacts expression of 9 genes. How do they explain this observation and reconcile it with their model of indirect changes via effects on hub genes?

Minor Compulsory Revisions

1) The authors verify changes in EGFR expression in three independent biological replicates, but do not indicate if the microarray analysis was performed on three independent biological replicates. Is this the case? It is implied, but not specifically stated. The authors should indicate this in the Methods section.

2) The statement on page 6 that “the percentage of predicted targets remains, on average, < 20%” is (while technically correct), somewhat misleading, since the authors are averaging three different algorithms (PicTar, MiRanda, and TargetScan). It would be helpful to also indicate the total percentage of predicted targets by indicating the percentage of genes predicted by ANY of the three algorithms.

Discretionary Revisions

1) The sentence on page 5 beginning with “Three of the genes…” is somewhat confusingly written. It might be better to say “while five of nine” instead of “only five of nine” and putting these data into a table might make it clearer to the...
reader, or perhaps revise Supplementary Table 3 to include the effects of miR-7 and miR-128.

**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 declare that I have no competing interests