Reviewer's report

Title: microRNA-145 promotes differentiation in human urothelial carcinoma through down-regulation of syndecan-1

Version: 2 Date: 16 July 2015

Reviewer: DN Rao

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Comments to the Author:

In this manuscript Fujii et al., explained the role of miR-145 as a diagnostic/prognostic marker as well as its potential in up-regulation of stem cells factors and induction of senescence and differentiation in urothelial carcinoma via suppressing the Syndecan-1. Syndecan-1(CD138) is well known to be associated with cell proliferation, adhesion, and migration in several malignancies including urothelial carcinoma. In this present study, authors used multiple approaches successfully try to understand the role of miR-145. The interesting fact in this study is that miR-145 endorses differentiation via up-regulating the stem cell markers. miR-145 also causes senescence and down-regulate the Syndecan-1 expression. Outcomes of these data might be contribute to further understand the role if this newly discovered miR-145 microRNA role in urothelial carcinoma.

Major Points

1) Briefly describe the cell culture condition or provide the references (Line-86).
2) Table-2 is not provided (Line-121)
3) Provide scale as well as magnification power on the Figure-1B
4) The study published in Oncogene (2010) 29, 1073-1084 (Ostenfeld MS), suggested that “miR145 induces caspase-dependent and independent cell death” but author has seen senescence instead of cell death even in both study used same cell (T24) lines. Author should comments on that.
5) In Figure-2B, Y-Axis legend make self explanatory, mentioned the name of base line housekeeping gene against that author has calculated the “Fold Changes” in mRNA expression.
6) Why “Standard Error” is very high in cytokeratin 5 mRNA expressions?
7) Order of Figure No-3 is not correctly display/explained in text. Revised the text from line-162 to 177.
8) In Figure-S1-B, add the name CD44 in the legend
9) Figure S1-D result is contradictory the as the statement used by author in legend as well as in text. (Figure has shown high Syndecan 1 expression after miR145 transfection): Line-430
10) Author has shown the experiment when cells are transfected with miR-145, Syndecan-1 mRNA expression is down regulated. Could author have conducted the vice-versa experiment i.e. What is the effect on miR-145 expression after inhibiting the Syndecan-1 expression.

Minor points
1. There are many typographical errors (-) in manuscript e.g. Syndecan-1. Corrected: Syndecan-1. In Figure 3B: mIR-145 pre
2. Word “that” is repeated in line no-77.
3. Provide full IUPAC name of ‘MTS’ (Line-108)