Reviewer's report

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

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Reviewer: B.R Achyut

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

Manuscript focuses on expression of mir145 in human urothelial carcinoma cell lines that decreased cell proliferation and induced cell senescence. Authors found Syndecan-1 expression was diminished and stem cell markers (SOX2, NANOG, OCT4, and E2F3) were increased. miR-145 up-regulated markers of differentiation into squamous (p63, TP63, and CK5), glandular (MUC-1, MUC-2, and MUC-5AC), and neuroendocrine cells (NSE and UCHL-1). Expression of miR-145 was down-regulated in high-grade urothelial carcinomas, but not in low-grade tumors. Please consider following points to improve the quality of manuscript.

Major Compulsory Revisions

1. Authors did not mention any previous report or experiment in present manuscript that validate the down expression of mir145 in human urothelial carcinoma and cell lines (T24, KU7). Further, rationale of overexpressing or using precursor mir145 in experiments in human urothelial carcinoma is needed in the manuscript.

2. As reported in other cancers, authors failed to show if top targets of mir145 such as EGFR, FSCN1, N-cadherin, and IGF are decreased following adding precursor mir145 in cell lines.

3. Interestingly, authors noticed that miR-145 induces expression of stem cell markers such as SOX2, OCT4, NANOG, and E2F3. However, expression of stem cell markers favors invasiveness due to epithelial to mesenchymal transition. In addition, expression of E-cadherin was increased. Authors should evaluate the expression of N-cadherin to see if invasiveness has decreased following mir145 expression.

Minor Essential Revision

There is inconsistency of statement of mir145 expression in low grade vs high grade carcinoma in last paragraph of introduction and results. Introduction (lines 82-83) reflects mir145 is up-regulated in high-grade urothelial carcinoma, but not in low grade tumors. However, result showed opposite (lines 183-184).
Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: no competing interests