Reviewer’s report

Title: Oct4 upregulates osteopontin via Egr1 and is associated with poor outcome in human lung cancer

Version: 0 Date: 12 Apr 2019

Reviewer: Huei - Lee

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The authors provided evidence that Oct4 up-regulated Egr1 expression at transcriptional level and overexpression of Oct4 may promote invasive potential in cell and animal models. Unfortunately, the data seemed to be not fully support their hypothesis because the data of two lung cancer cells H1299 and A549 cannot support the conclusion of the Oct4-upregulating Egr and OPN. No site-directed mutagenesis was performed in the putative binding site of Oct4 at the Egr1 promoter to direct evidence the hypothesis. No positive controls were included in their experiments. For example, Egr1 induces VEGF-A expression in lung cancer cells (Am J Pathol 2010; 77:70-83); Egr1 enhances MMP9 transcription (Mol Cancer Res 2010; 8:507-519); and mutant p53 initiates a feedback loop to induce Egr1/EGFR/ERK cascades (Oncogene 2010; 29:2628-2637. These observations should be used to verify whether Oct-regulating Egr1 could induce VEGF-A and MMP9 expression and the different effects of Oct4 over-expression observed between p53 null H1299 and p53 wild-type A549 cells could be caused by p53 status. The data of patients should be calculated to explore whether Oct4 expression in tumor tissues could be associated with Erg1 and OPN expression and these may support the findings of cell and animal models. The data of animal model should be separated from the cell model and showed the tumor nodules directly, not used the transformed data. The immunostaining results of animal models should add the immunostaining results of OPN and positive controls. How many mice were used in the animal experiments? Figure 1: the immunostaining results are not clear and should be amplified.

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