Reviewer's report

Title: Resistance to growth inhibition by TGF-beta is associated with a partial loss of Smad signaling in the absence of alterations of Smad protein levels during in vitro progression of HPV16-immortalized human keratinocytes

Version: 1 Date: 16 April 2013

Reviewer: Masao Saitoh

Reviewer's report:

The authors show that Papillomavirus type-16 developed resistance to antiproliferative effect of TGF-b in HKc/DR cells. This underlying mechanism was examined in detail, and they found that nuclear localization of Smad3 in HKc/DR cells was slightly delayed upon TGF-b stimulation, compared to that in control cells. However, this delayed response in HKc/DR cells (Fig. 4A-3) is marginal or too small. I do not think that this minor effect contributes to resistance to antiproliferative effect of TGF-b in the cells. In addition, growth inhibition by TGF-b is evaluated by SBE-Luc (Fig. 7), but the authors should examine p21-luc or c-myc expression, because SBE elements were identified in the TGF-b-responsive elements in the promoter regions of ECM proteins. Thus, the data from this luciferase assay would not support the authors’ conclusion, regarding to growth inhibition by TGF-b.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

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