Reviewer's report

Title: High-level inducible Smad4-reexpression is associated with gene expression profiles that predict a preferential role of Smad4 in extracellular matrix composition

Version: 2 Date: 29 August 2007

Reviewer: Gertjan Fleuren

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The authors do not address the question they pose in the abstract: “Are loss of growth inhibition by TGF-# and loss of Smad4 independent events in carcinogenesis”.

This question implies that (in this paper) growth inhibition by TGF-# and loss of Smad4 expression are investigated during the development from normal (squamous epithelial cells) via CIN I, CIN II, CIN III to cancer. I have suggested to rephrase the aim of the study to an aim that covers the experiments that have been performed in this study e.g. “What is the mRNA expression profile of Smad4 deficient C4-II after (inducible) re-expression of Smad4”.

2. No experimental attempt has been made to address our second suggestion. I am well aware of the previous work of the authors, therefore it did not seem impossible to generate additional cervical cell lines with the inducible Smad4 system to demonstrate the general validity of their concept (Baldus et al., 2005). In contrast to pancreas and colorectal cancer in cervical cancer HPV E7 can bind to Smad4 (Lee DK et al. 2002 and Habig M et al., 2006). This phenomenon may influence the expression level of Smad4. Therefore cervical cancer may behave in a different manner as far as the relation between TGF-# and Smad4 is concerned. For this reason it is important to verify the results by using (at least) another cervical cell line.

If thee authors are unable of unwilling to perform the suggested experiments I would suggest that they should change the title of their manuscript into “High-level inducible Smad4-reexpression in the cervical cancer cell line C4-II is associated with a gene expression profile that suggests a preferential role of Smad4 in extracellular matrix composition”.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of
a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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: