Reviewer's report

Title: SNAI1 Expression: A Rare Event In Oral Squamous Cell Carcinoma Associated With Features Of Poor Prognosis

Version: 1 Date: 20 October 2009

Reviewer: Petra Richter

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Purpose

The purpose of this study by Schwock et al. was to investigate the tumour progressive role of the EMT inducer SNAI1, known to repress E-cadherin, in oral squamous cell carcinoma (OSCC) by means of immunohistochemistry using paraffin material of 46 patients suffering from OSCC. Moreover, an immuno- histochemical analysis of focal adhesion kinase (FAK), E-Cadherin, vimentin, cytokeratin and p63 was added to identify epithelial versus mesenchymal cell phenotypes differentially occurring during the process of EMT.

General comments

Against the background that EMT induced by SNAI1 has been reported to play a special role for tumour invasion and metastasis formation in several carcinomas, the hypothesis of the study that SNAI1 is of tumour developmental importance also in OSCC is of interest for a better understanding of OSCC tumour biology with possible therapeutic consequences for OSCC patients having a poor prognosis even today. Nevertheless, there are reports available in the literature already demonstrating that SNAI1 expression is a rare phenomenon in OSCC occurring in the stromal compartment in association to the myofibroblastic cell phenotype and not contributing to the predict of metastasis occurrence or patient survival.

Schwock and co-workers present an immunohistochemical study on paraffin sections of OSCC and corresponding lymph node metastases from 46 patients. Selectivity testing based selection of SNAI1 antibodies has been performed very well including xenografts of OSCC cell lines showing different cell phenotypes.

Nevertheless there are several concerns.

Major Compulsory Revisions:

1.) The introduction is short but does not sufficiently reflect the level of knowledge concerning SNAI1 and OSCC as available from the literature. Authors should clearly explain why they additionally investigate FAK and p63 and what the known functional linkage within the EMT process is.

2.) In the methods section, the first chapter concerning patients and material should be clarified. Either all characteristics should be given in a table or in the text. The one patient with the reported one-time history of OSCC 25 years prior
to inclusion should be excluded in my eyes. The semi quantitative scoring system applied by the authors is a little bit too complex. How has the category of staining intensity been assessed? It is indispensable to improve presentation of the scoring system i.e. in form of a nice table. Statistical analysis is well performed.

3.) Results section is explicitly too long and unstructured. Authors should concentrate on the main findings and extensively reduce results section in length. Currently there are more than 5 pages! The antibody testing including animal models should be – although performed very well – shortened. The chapter “SNAI1 is a Potential Mediator of OSCC Aggressive Behaviour” should be shortened because there are actually no significances for SNAI1 as the main marker aimed to investigate in the study. The two cases presented at the end of the results do not contribute to the message of the study since these are exceptions and the study was aimed to get a general impression. May be these two interesting cases can be separately presented as case reports.

4.) Discussion / Conclusions: Conclusions made by the authors are not completely supported by the data presented in this study. To conclude that SNAI1 contributes to tumour progression in OSCC from 2 cases exhibiting a sarcomatoid phenotype is a little speculative. The statement that its “presence in a significant portion...is associated with ...poor prognosis” bases on a minimal number of cases (4 of 46) not allowing such a conclusion in a study where the majority of cases exhibited rare SNAI1 expression levels. Again, this might be a justified conclusion from a case report.

Minor Essential Revisions:

1.) The aims section at the end of the introduction is uncommon. Results and conclusions of the study are partially presented here. Is this what the journal structure requires?

2.) In general, there are clearly too many figures and tables in the study even if planned to publish as online supplements. Please reduce them to the main findings making it possible to the reader to visually fathom the results adequately.

Discretionary Revisions:

These revisions have been included in the statements above.

Taken together, the study represents only a limited contribution to the knowledge in the field although it contains some interesting data. Authors should restructure the manuscript strictly focusing on the main new results.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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.