Reviewer's report

Title: Gene-expression of metastasized versus non-metastasized primary head and neck squamous cell carcinomas: a pathway-based analysis

Version: 1 Date: 21 November 2007

Reviewer: Andrew Yeudall

Reviewer's report:

General

In this manuscript, the authors have carried out a microarray-based study of gene expression in a series of metastasized and non-metastasized squamous cell carcinomas. Using a supervised pathway-based analysis, they were able to identify seven pathways showing significant differential expression, which overlapped with pathways in a previously published reference dataset. These included functional groupings with obvious relevance to tumor metastasis, such as extracellular matrix remodeling, hypoxia-induced invasion, and angiogenesis.

One of the major confounding factors when trying to assimilate data from microarray studies present in the literature is the inability to compare gene expression profiles across a range of platforms. The approach taken by the authors of this paper, namely to compare functional differences, goes a considerable way to overcoming this issue. However, several points should be addressed in a revised version.

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

1. The Results section is quite difficult to follow. There is no reference anywhere in the text to Tables 3, 4, or 5, or to the heatmap (Fig. 1). Inclusion of this would make interpretation of the data clearer.

2. Introduction: The authors state that their samples came from three anatomical locations (p5), yet Table 1 includes oral cavity, palatine tonsil, oropharynx and larynx. Do they consider palatine tonsil as oropharyngeal? This inconsistency should be corrected.

3. Results. The authors mention PECAM (CD31) related to extracellular matrix signaling (p12). However, it does not appear in any of the gene lists presented in the manuscript. Further, this molecule is an endothelial cell marker – is it coming from tumor vasculature, rather than from tumor cells?

4. The use of pathway-based analysis considers gene products in functional groups, rather than individually. However, many of the targets identified are members of kinase cascades and, thus, overexpression alone may be insufficient to activate the pathway as they are generally regulated by
phosphorylation/dephosphorylation events. Some discussion of this should be included.

5. The references cited in the text do not, in many cases, appear to reflect the numbering in the reference list. This should be checked carefully before publication.

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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)

1. Table 2. Delete “There is a tendency…….” From the legend. This is repetitious of the main text.

2. Typographical errors: p14, line 5 (colorectal and cervical); throughout: “MMPs” (not “MMP’s”)

3. Abbreviations: JNK – c-jun N-terminal kinase; JUN – c-jun oncogene

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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 whose findings are important to those with closely related research interests

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:

I declare that I have no competing interests