Reviewer's report

Title: A biomarker based detection and characterization of carcinomas exploiting two fundamental biophysical mechanisms in mammalian cells

Version: 2 Date: 8 October 2013

Reviewer: Tsung-Lin Yang

Reviewer's report:

This paper aims to investigate the roles of two biomarkers, Apo10 and TKTL1 in oral squamous cell carcinomas (OSCC) and other types of carcinomas. Apo10 marks tumor cells with abnormal apoptosis and proliferation, while TKTL1 represents the enzymatic basis for an anaerobic glucose metabolism. The author concluded that these two factors are independent factors, and can be used to diagnose neoplasia and tumor recurrence.

1. What is the reason to combine these two markers together? Is it better? Some strong reasons are required to strengthen the hypothesis.

2. For the survival analysis, the results of combing two factors are not better than using each factor. The attempt to combine two factors aims to successfully separate the survival of Apo10+/TLK1- and Apo10-/TLK1+. However, it had not been achieved in this study. The chart is suggested to be put in the supplementary data.

3. Apo10+ seems to have no effects on the cervical lymph node metastasis, whereas TKTL1 significantly correlates with the conditions of cervical metastasis. However, in the survival analysis, the survival curve of Apo10+/TLK1- seems to be worse than that of Apo10-/TLK1+, any explanation?

4. The photos of Apo10 and TLK1 co-localization is not pertinent to the current investigation, and are suggested to be omitted.

5. Many important confounding factors of oral cancer such as margin status or extracapsular spreading of lymph nodes are not included for analysis. It may result in the bias of survival analysis. These factors should be included and the univariate and multivariate analysis should be recalculated.

6. Similarly, no address was made on the treatment modalities and relevant adjuvant therapies. They also affect the result of survival analysis. The treatments should be compared and counted into the statistical analysis.

7. What is the reason to choose 62 as the age for stratification?

8. The locoregional recurrence rate is around 27.3%. It seems to be a little higher than other studies. Any explanation? Besides, how long is the follow-up?

9. Fig3 c,d,e,f should be put in the supplementary data

10. The data gathering from cell lines, and those gathered from other cancers are suggested to be included in the additional files.
11. English should be edited, some typos are noted such as “cell typs” in page 17

**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:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests