Reviewer's report

Title: Chromosomal aberrations and aneuploidy in oral potentially malignant lesions: distinctive features for tongue

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Reviewer: Edward W Odell

Reviewer's report:

This is an interesting paper on oral premalignant lesions that has been undertaken using appropriate methods, apparently correctly performed. The aims are clear. Data is could be better presented, there is data missing relevant to the authors conclusions and presentation is not always clear.

This referee feels that a number of points should be addressed before the paper could be acceptable for publication:

In several places the text describes the concept that the thin mucosa is more sensitive to carcinogens that thick mucosa. There are several problems with this. The mucosal depth is not defined in the mouth because there is no muscularis mucosa. It is usual to divide oral mucosa into masticatory and lining types. The authors presumably mean thickness of epithelium. However there is no evidence to suggest that thickness is of any relevance. Much experimental data shows that permeability does not depend on thickness and that keratin relates only to physical resistance. Thickness does not correlate with turnover either. As the authors note, pooling of carcinogens is likely to be the important factor for floor of mouth carcinogenesis.

I am unclear whether the aneuploid enrichment was performed for the samples used for CGH, it is not explicit.

I am unclear how dysplasia was assessed according to WHO criteria in such small samples because in the WHO system the architecture is very important. This would not be seen in the small samples.

There appears to be no enrichment for epithelial cells in the CGH samples. Thus other cell types would be present? The authors should state this.

There is no explanation of the Totgain index. It is not defined at first use or in the methods section.

There is insufficient data to single out the tongue lesions as different because there is considerable variation in the results from the other sites, which have all been pooled together, The authors need to separate all sites in order to show that tongue is different.

I feel the data should be shown for the segmental aberrations as well and there should be more data on which chromosome sites are commonly affected to
compare with other published data. This would add supporting evidence that the data is correct.

Sample preparation detail for CGH is not sufficient.

The gain scores make no distinction between huge changes of chromosomal arms and small gains and deletions. This seems to not make sense? The score used is not a ‘total’ score, only a count of abnormalities irrespective of size. Which correlates with chromosomal instability, many small or a few large changes? The authors need to justify this methods of analysing their results with references or explanation.

Figure 1 has no confidence intervals or measures of variation

Figure 2. Data is presented as bar charts but there is so much difference between samples that scatter diagrams with confidence intervals other measure or variation would be more appropriate. In part A ‘all other subsites’ column, why are two data points shown outside the bar. Is the bar range or a measure of variation? This is not defined.

Figure 2 gives no indication of the relative numbers of samples in each group. The right hand half of figure 2B is only based on 8 samples but there is no indication of the split between the two columns.

In the discussion the authors state that the data supports more aggressive treatment of tongue lesions but this is not so, there is no evidence here or published to suggest that any of these findings merit more aggressive treatment and this statement should be removed.

Minor points

The authors are also correct in the discussion to say that some suggest that degree of dysplasia is not a statistically significant marker for transformation, but other workers have confirmed this. As it is currently suggested to be the best or reference test in wide clinical use, it would be more accurate to say that the predictive value of dysplasia remains in dispute.

There are many minor errors in English and the authors would be advised to have the manuscript ready by a scientist whose first language is English because in some cases the meaning is not clear.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests