Reviewer’s report

Title: Adenosine A2b Receptor Promotes Progression of Human Oral Cancer

Version: 2
Date: 18 March 2015

Reviewer: Keith Hunter

Reviewer’s report:

This is an interesting paper which investigates the role of ADORA2B in oral SCC. There is background literature in other conditions and other cancers, but not in OSCC, which does give some novelty to what is presented. On the whole, the paper is well written and the data clearly presented. Below are a few comments.

Major compulsory revisions

In the methods section, the method chosen to assess cell growth is cell counting. This has obvious disadvantages as it does not separate the possible mechanisms of changes in cells number – this may be by increased proliferation or by reduction in cell death (by whatever method). Thus it would be preferable to have a direct assessment of proliferation (e.g. EDU incorporation) and of apoptosis. Given that the stably transfected cells are available, this should be achievable.

In order to complete the presented links between HIF1a and ADORA2b and number of other experiments would be very useful and would add to the paper:

1. Repeat the data presented in Figure 6 under hypoxic conditions. If the hypothesis presented is correct, the increase in ADORA2b and HIF1a under hypoxia should be abrogated/markedly reduced in the ADORA2a knockdown cells. Again, as the stably transfected cells are available, this could be easily done.

2. Correlate the expression of ADORA2b in the tissues with HIF1a expression by IHC in the same samples.

Minor essential revisions/clarifications

P8 L15: are these cells spontaneously immortal or have they been artificially immortalised?

P15 L1: please state the level of agreement between the 2 pathologists

Figure 1: some comment on the mismatch of RNA and protein expression should be made, especially for Ho1-N-1 and KOSC2 cells. Is there an explanation for this?

Figure 2: in the version I had for review, the immunohistochemistry figures are of poor quality. These should be improved and a high and low power for each presented to allow assessment of localisation of expression.

Table 1. If clinical outcome data is available, this would also add to the paper. Is it would lend weight to the possible usefulness of ADORA2b in OSCC
Level of interest: An article of importance in its field

Quality of written English: Acceptable

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