Reviewer's report

Title: Anti-oncogenic and Pro-differentiation Effects of Inhibition of Monoamine oxidase A on High Grade Prostate Cancer Cells

Version: 2 Date: 23 September 2008

Reviewer: Emma Guns

Reviewer's report:

The article describes an in vitro investigation, in primary cultured prostate cancer cells, of the effects of an MAO-A inhibitor (clorgyline) on prostate cancer cell differentiation and oncogenesis.

Major compulsory revisions: By treating with clorgyline, you cannot definitively say that you are confirming that gene expression changes are due to inhibition of MAO-A, there may be off-target effects of clorgyline which account for these effects, independent of MAO-A. The use of siRNA to MAO-A to specifically knock-down MAO-A would be more convincing that the direct links of this effect of clorgyline are due to MAO-A inhibition. Also, this type of conclusive statement is misplaced in the results section e.g. sentence on p.8, starting on line 11. Also, sentence starting on p.9 ,line 5. The sentence starting on p. 9 line. 21 more accurately reflects the conclusions which can be made, however, again I feel that these conclusive statements are misplaced in the results section. I would recommend that this definitive assignment of the effects of clorgyline being MAO-A inhibition be revised and simply state that clorgyline treatment causes these effects – this recurs and is repetitive throughout the results section.

Once again in the discussion section, the effects observed have been assigned directly to MAO-A inhibition and this is not definitive.

Discretionary comment: The results described are contradictory based on the conclusions made - If you induce AR and PSA production you are likely sensitizing cells to the effects of androgens, thus driving cell proliferation. However, all other effects of clorgyline treatment support a pro-differentiation and anti-oncogenesis as is stated in the conclusions.

Minor essential revisions: Table 1 title typo ‘regulated’

Also, table 1 requires more detailed description regarding the citation source for information validating the oncogenic pathways affecting the genes identified by SAM.

Table 3 title typo ‘clorgyline’

Minor comments: Please include some rationale of choice of treatment concentrations and timepoints selected for clorgyline.

Prostate ‘secretory cells’ would be more appropriately described as ‘epithelial cells’ throughout the manuscript.
In summary my biggest concern with this manuscript is the lack of definitive proof that MAO-A inhibition is causing the observed effects in the primary prostate cancer cell line used (and LNCaP cells) – further work using siRNA to MAO-A is required to validate this conclusion.

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