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: 5 January 2009

Reviewer: audrey player

Reviewer's report:

Reviewer for Manuscript "Anti-oncogenic and Pro-differentiation Effects of Inhibition of Monoamine oxidase A on High Grade Prostate Cancer Cells"

The authors make an interesting observation. I understand the point being made and agree that the data suggest anti-oncogenic effect of the MAO-A inhibitor. However, I have made a few suggests (including experimental validation and some re-phasing for the sake of clarity).

Major
Title- "Anti-ongenic....."
Reviewer: I feel the study demonstrates " Examination of a MAO-A inhibitor on transcriptional control of high grade epithelial PC-A cells and possible anti-oncogenic implications".

Results Section:
Reviewer suggestion 1: The data appears to be generated using 1 patient sample? Should these data be generated using other (ie, at least 1 other for validation)?
Reviewer suggestion 2: experimental suggestion...
Study lends itself very nicely to a cell-culture-model for validation of the authors theory that "inhibiting MAO-A can effect differentiation and reverse the tumorgenic behavior of the cancer cells.
Reviewer suggestion 3:
The top 10 genes were selected for validation of the microarray. Might the authors consider validation of select (a) genes suspected as important in a particular pathway as done with APC?

Minor
Reviewer suggestion 4 page 6): 37,340 clones. Were these clones or the result of hybridization signal intensities on microarray?
Previous data (by authors) show that morphological changes occur under these conditions. one step further would be the exp suggested above.
Reviewer suggestion 5:
Can the authors address the proliferative capacity of the chlorgyline-treated cells used for RNA extraction (as all 'SAM-genes' were upregulated).

Reviewer suggestion 5: Statement "In fact, expression of many.... this statement was unclear. How many is "many".

Minor

Section beginning-"Inhibition of MAO-A induces...":

Reviewer suggestion 6:

First paragraph of this section was difficult to follow. Table 1= clear, but derivation of Table 2 was not clear. How were the genes (1839, etc...) derived? from Creighton study or this study?

Reviewer suggestion 7: Consider Table 1 as supplemental material?

Reviewer suggestion 8: Paragraph beginning "Genes downregulated by beta-catenin....." is unclear. I understand derivation of the '156genes', but others are somewhat unclear (ie, 1839,etc...).

Minor

Section beginning "Chorgyline induces differentiation-related...."

Reviewer suggestion 9:

Consider validation of the differentiation associated genes, not all, but a few.

Reviewer suggestion 10:

EZH2 expression appears to be transient, but associated Polycomb signatures appear enriched. The authors might consider Q-PCR validation of a few of these?

13 of 87 appear consistent across 6-24hr time points. this considered enrichment?

Minor

Materials and Methods:

Reviewer suggestion 11:

All PCR primers included (ie, APC?)

Minor

Figure legends:

Reviewer suggestion 12 (Figure 2):

(B) is unclear- difference averaged across 6, 24, 96hr, SAM then, PCR?

Reviewer suggestion 13 (Figure 3):

(D) and (E) are somewhat confusing. red and green designate up and downregulation, respectively. What does "below the "0" designate, even though red and green? Same question for Figure 4
Reviewer suggestion 14 (Table 1):
There are 126 genes listed representing the 156??
Reviewer suggestion 15 (Additional data file 2):
Are all of the genes listed here upregulated?
Reviewer suggestion 16 (Figure 5): "(A)" noted twice in legend

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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