Reviewer's report

Title: Neural protein gamma-synuclein interacting with androgen receptor promotes human prostate cancer progression

Version: 2 Date: 30 April 2012

Reviewer: Sharon Glynn

Reviewer's report:

Review of BMC Cancer

The authors present an interesting study on the role of SNCG in prostate cancer progression. They present evidence for the potential role of SNCG in prostate cancer metastasis.

Major Points

1. In the introduction the authors mention that there are three types of SNCG proteins. After this point, there is no mention in the manuscript which SNCG protein they are investigating. The authors need to clarify this in the manuscript, and if they are only investigating one of the proteins, describe why they have focused on this particular one. Looking at the primers it suggests that they are researching the gamma version, please clarify.

2. One major worry is the sole focus of the in vitro work on the LnCap cell line as the only AR dependent cell line, and the focus on only one siRNA (166). It would be preferable to see an additional AR dependent cell line e.g. CWR22 or use of the other siRNAs to see a dose response effect of SNCG inhibition.

3. The invasion/migration assays demonstrate a modest inhibition of invasion and migration, considering the level of SNCG knockdown, what is the mechanism for this inhibition? It is unlikely to be proliferation inhibition as migrating/invading cells are usually not proliferating at the same time. This is very interesting but requires further investigation. Is there an inhibition of MMP expression or Rho-GTPases for example?

4. Regarding Table 1 clinical information. The authors were only able to look at 5 cases of androgen independent disease versus 122 of androgen dependent disease. 5 is too low a number to have sufficient power to draw any conclusions of statistical significance. Again this is the same for comparison in normal tissue or prostatitis. These results are indeed intriguing, but it needs to be clarified in the manuscript that solid conclusions can not be made at this time. Instead a larger cohort will need to be examined in the future.

Minor points

4. The authors looked at the effects of SNCG inhibition and increased expression in LnCap cells. Inhibition of SNCG resulted in decreased proliferation and accumulation in the G1 phase. Vice versa increased SNCG caused increased
proliferation, however the authors do not present corresponding information on Cell cycle progression. Did they not collect this information?

5. In the results section under the heading “SNCG protein interacts with AR in human prostate cells”, the authors describe how they investigated SNCG mRNA expression in LnCAP and LnCAP-AI cells. This section however doesn’t contain any experimental work on the LnCAP-AI cells, which are in the following section. Please delete LnCAP-AI cells and leave until the following section for greater clarity.

6. How do the AR levels compare between LnCAPs and LnCAPs-AI? Can the authors show this?

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

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare I have no competing interests.