Reviewer’s report

Title: Polysaccharopeptide enhanced the anti-cancer effect of gamma-tocotrienol through activation of AMPK.

Version: 2 Date: 16 July 2014

Reviewer: Nitin Telang

Reviewer’s report:

General Comments: This study has provided reasonably convincing evidence that supports a synergistic interaction of PSP and #-trocotrienol (#-T3) leading to growth inhibition of prostate cancer cells in vitro and tumors in vivo. However, the manuscript contains some areas that lack sufficient clarity and therefore, foster confusion.

Major Compulsory Revisions:

1) Introduction:

The authors refer to the published studies, including their own, on the prostate cancer stem cells. There is ample evidence to suggest that the cancer stem cells represent the therapy resistant subpopulation that is responsible for disease progression. In the light of these aspects, it is important to state a clear, scientifically robust rationale for the present study conducted on PC3 cells that may contain a mixed population of non-stem cell and stem cell phenotypes.

2) Material and Methods:

The specific concentrations of #-T3 and PSP used should be clarified as derived from the dose response experiments. The concentration of PSP is stated as 30 mg/mL in this section, while in the result section the PSP concentration used is stated as 30µg/mL. This aspect needs to be clarified.

3) Results:

Colony Formation Assay: Since the cells were seeded on PolyHEMA coated wells, it is important to clarify whether the colonies were formed under non-adherent or adherent conditions. In addition, the data for the number of colonies formed should be included together with the normalized percentage values.

Fig.1: Vit. E should be changed to #-T3

Fig. 2: The data for quantitative signal intensity as evidenced by arbitrary scanning units (ASU) should be included.

4) Discussion:

This section should include a comparison of the current data with that obtained from the cancer stem cell study that is published by the authors. This
comparison, in the light of the documented association of the AMPK pathway in the cancer stem cells, should enhance the scientific impact of the present study.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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"