Reviewer’s report

Title: Citrus auraptene suppresses cyclin D1 and significantly delays N-methyl nitrosourea (MNU) induced mammary carcinogenesis in female Sprague-Dawley rats

Version: 2 Date: 5 May 2009

Reviewer: Takuji Tanaka

Reviewer’s report:

1. Is the question posed by the authors well defined?
   Yes.
2. Are the methods appropriate and well described?
   Yes.
3. Are the data sound?
   Yes.
4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes.
5. Are the discussion and conclusions well balanced and adequately supported by the data?
   Yes.
6. Are limitations of the work clearly stated?
   Yes.
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
   Yes.
8. Do the title and abstract accurately convey what has been found?
   Yes.
9. Is the writing acceptable?
   Yes.

This manuscript by Krishnan et al. describes chemopreventive ability of aurapetne in vitro and in vivo experiments of mammary carcinogenesis. The authors demonstrated the effects were due to suppression of cyclin D1 expression. The experimental design was straight forward and the results contain new findings. Overall the manuscript is well-written. However, this reviewer has some minor points listed below.

1. The title: Delete ‘(MNU)’.
2. The rationale for the dose-selection of auraptene (200 and 500 ppm) should be given.

3. Page 8, line 7 from the bottom: ‘immunohistochemical’ must be ‘histopathological’.

4. Page 13, line 5 from the bottom: What is ‘lactating adenoma’? I guess this tumor is rare in rodents that receive chemical carcinogens. The authors are recommended to briefly describe the criteria for diagnosis of experimental mammary tumors in ‘Histopathology’ in Page 8 with citing a reference. In this context, fibroadenomas develop male SD rats given MNU. Did the authors observe this type of tumor?

5. Page 15, line 10: ‘ODC’ must be ‘ornithine decarboxylase (ODC)’.

6. Page 17, line 8 from the bottom: ‘ornithine decarboxylase (ODC)’ must be ‘ODC’.

7. Page 17, line 6 from the bottom: Delete ‘(TMA)’.

8. Too many figures. Some can be combined. Also, representative figures of histology of mammary tumors should be given.