Reviewer's report

Title: Lack of efficacy of blueberry in nutritional prevention of azoxymethane-initiated cancers of rat small intestine and colon

Version: 1 Date: 19 May 2009

Reviewer: Bernadene A Magnuson

Reviewer's report:

Overall, this is a well done study. Additional information in the manuscript is recommended as follows:

Major Compulsory Revisions

1. Background/Purpose of study: provide more details about relevance of C-peptide; although it is indicated that its relevance to fruit consumption and colorectal cancer development is not clear, the purpose of the study does not clearly indicate why C-peptide was measured.

2. Background: last statement, “Results do not provide strong…” – clarify, results of what?

3. Methods: clearly explain rationale for using rats exposed to BB throughout gestation and lactation vs. using weanling rats.

4. Methods: clearly state what became of the dams

5. Methods: clearly state that offspring were administered AOM

6. Methods: clearly indicate the number of animals/sex/group. It was indicated that there were 22 dams/group and litters were culled to 5 rats/sex. By my calculation, 22 dams x 1 litter/dam x 10 offspring/litter = 220 offspring/group (110 males and 110 females). 15 rats/sex/group were killed at 6 weeks, which would leave 95 rats/sex/group on the diets until the end of the study; however, Table 4 indicates that there were 73 to 74 rats/sex/group that were evaluated. What happened to the missing rats?

7. Results: tumor incidences in stomach and cecum were reported to be measured in the Methods section, but were not reported in Results section.

8. Results: p. 9, last paragraph; statement indicating that colon tumor incidence was lower in females vs. males – add statement that this occurred regardless of diet

9. Results: p. 10, first line; clarify that tumor incidence in female rat colon and small intestine was unaffected by BB

10. Discussion: p. 10, first paragraph; how would decreased dietary concentration of BB have a more protective effect in the previous study?

11. Discussion: There is a lot of speculation about the reason for the gender differences in tumor incidence regardless of diet. Clarify as to whether there are
any historical data for the following:

a. Differences in AOM-induced colon tumors in F344 vs. Sprague-Dawley rats
b. Sex differences in AOM-induced colon tumors in Sprague-Dawley rats
c. Sex differences in number of AOM-induced ACF vs. colon tumors in this strain
d. Sex differences in progression of adenomas to adenocarcinomas in this strain

12. Discussion addressed ACF formation and overall tumor incidence, but did not clearly discuss differences in tumor pathology, i.e., sex differences in incidence of adenocarcinomas and effect of BB on reduction of adenocarcinomas in females

Minor Essential Revisions

13. Define BB, AOM and PBS at first instance within body of report (Background section)

14. Tables 3 and 4, heading: indicate time points at which measurements were taken, i.e., at 6 and 17 weeks post-second AOM treatment, respectively (similar to that in heading of Table 2)

15. Figure 3 Legend: indicate # animals/sex/group

Discretionary Revisions

In table 4, also add number of animals with tumors for each to clarify that the incidence is # animals with at least one tumor, not number of tumors. Also, I find the data in Figure 3 to be misleading. Would rather see actual number of animals in each group with single and multiple tumors. What is the rationale for expressing as %?

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.