Reviewer's report

Title: Growth of human gastric cancer cells in nude mice is delayed by a ketogenic diet supplemented with omega-3 fatty acids and medium-chain triglycerides

Version: 2 Date: 24 November 2007

Reviewer: W Elaine Hardman

Reviewer's report:

General
This is a well written, interesting paper. The authors have presented some intriguing data that could lead to a clinically significant adjuvant therapy for cancer and for this reason the results should eventually be published. However, I find some difficulties with interpretation of the data and there are statements made without statistical support. The paper is also much longer than necessary for the results that are available, introduction and discussion could be cut in half and should deal mainly with information applicable to the results in the paper. The number of figures should also be reduced.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
The diet was changed immediately after injecting the tumor cells. The main difference was in the first 20 days. I would interpret this as a difference in tumor cell take rather than a difference in tumor growth. This notion is supported by the data that shows that once the cells did take and begin growing, there was no difference in growth rate. I also have difficulty with discarding the results from half of the tumors. It is likely that if animals have two nearly equally sized tumors the growth rate of the larger was slower than the growth rate of the larger tumor in animals in which one tumor was large and the other either very small or did not take due to total tumor mass in the animal rather than due to any characteristic of the treatment.

1) There is not mention of vitamin or mineral mix in the diets. This is standard in most animal diets. The composition of the last three diets in table 1 is unnecessary. Important differences are addressed in the discussion.

2) Figure 2 is not very helpful – there are no differences between groups in the IHC results and the results are not unexpected. Statements in ‘results’ are adequate.

3) There should be a statistical analysis of the body weights to support (or not) the statements (p.14) made about differences. Given the variance, the beginning and end weight do not look different. Statistical analysis can also determine whether the weight gains were really different or not.
4) Tumor growth – of course the end tumor weights were not different, the end was determined by tumor size. The slopes of the tumor growth can be statistically analyzed and should be if the authors want to make statements about differences. The descriptions of tumor growth analyses on p.15 are strange. It is most unusual to split the groups into subgroups so that one can refer to subgroups that ‘fit a hypothesis’. Statistics can also determine if 8 of 12 is different from 2 of 12 or not. The shift in tumor growth rates indicates that ‘take’ was delayed, not tumor growth slowed. This is also indicated in Fig 6, A. Five tumors did not grow from day 7 to day 20, indicating lack of take. It has to be assumed that after day 20, these began to grow, these probably are most of the ‘long term survivors’ This is not trivial since there could be clinical significance for prevention of metastatic tumor take.

5) Most of table 2 is not needed, the values are stated in the text.

6) Table 3 is not needed, data is shown in survival graph.

7) Survival analyses should be statistically analyzed and there should be a section in the results.

8) Figure 5 for tumor volume is not needed – euthanasia was when the volume was at a set point.

9) Figure 7 is not needed. Perhaps a correlation analyses of #-OHB with survival should be used to support the statement on P.16.

10) Table 4 – are there any differences? Statistical analyses and indication of the differences.

11) Figure 8 – unnecessary. Figure 9 and 10 – one sample would be enough.

12) Figure 11 – C and D not necessary. B may not be necessary.

13) Figure 12 not necessary unless some statistical analyses is done, this would require assessing vessels in multiple tumors. If a firm statement cannot be supported, then a statement (i.e. appears to have had fewer vessels) should not be made.

14) Discussion should be shortened.

About statistics - few statistics were done. The needed statistical analyses needed are not complex. If the authors cannot analyze the data then a statistician should be consulted.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

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What next?: Unable to decide on acceptance or rejection until the authors have
responded to the major compulsory revisions

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

**Quality of written English:** Acceptable

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