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:** 17 December 2007

**Reviewer:** Robert Gillies

**Reviewer's report:**

Review of Otto et al.

This manuscript details the effects of a ketogenic diet with medium chain triglycerides on the growth of a tumor. While the data are comprehensively analyzed, they are available for only a single type of tumor growing heterotopically in a single experiment. Thus, the results are very limited in scope.

**Major Concerns**

1. The major concern is that the experiment describes results from only 24 mice (12 control and 12 experimental). While this likely has enough power for some of the endpoints, it is extremely limited. It is certainly underpowered if animals are split into long- and short-term survivors and statistics on these groups should be discounted. The overall experiment should have been reproduced at least once.

2. Similarly, this only used a single tumor type (gastric adenocarcinomas). In the Methods, these were described as containing the TKTL1 gene product. Is the claim being implied that this gene product required for the observed responses? If so, a matched tumor without TKTL1 should have been used for comparison.

3. The reduction in tumor growth for the KD group was attributed mainly to an increased lag period. Would the same be true if the cells were pre-acclimated to a low/glucose ketogenic media prior to injection? Isn’t it possible that the lag occurred simply because the metabolic landscape changed?

**Minor Concerns**

4. It is also a concern that these tumors were grown heterotopically. While orthotopic models of gastric cancers may not be available, they are available for other types of cancer, including prostate, breast, brain, liver and pancreatic.

5. Personal experience has show us that the NBDG assay does not work as advertised. It is certainly not transported by GLUT-1. Hence, if it is to be reported a full characterization should be provided (quantiatation of intracellular levels at different time points by fluorescence). FACS is not quantitative enough to ascribe a 65-fold difference. Also, why were PBMC used as controls?

**What next?:** Reject because too small an advance to publish
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
Yes- I have received antibodies from Dr. Coy, a co-author on the paper other than that, I have no competing interests