**Reviewer’s report**

**Title:** Comparative Effects of Alpha- and Gamma-Tocopherol on Proliferation and Apoptosis in Human Colon Cancer Cell Lines

**Version:** 1  **Date:** 22 September 2005

**Reviewer:** Qing Jiang

**Reviewer’s report:**

General
The manuscript has shown that treatment of colon cancer cells with pharmaceutical doses of gamma-tocopherol but not alpha-tocopherol caused cell death or inhibited growth, while the similar treatment did not affect normal healthy cells. The overall study is interesting which is also in line with several recent publications regarding the potentially superior beneficial effects of gamma-tocopherol to alpha-tocopherol against cancer.

-------------------------------------------------------------------------------

**Major Compulsory Revisions** (that the author must respond to before a decision on publication can be reached)

The study is largely observational. Although based on the publications by the others, the authors mentioned several possible mechanisms that may be involved in gamma-tocopherol induced effect, none of the mechanisms were examined in the current study.

-------------------------------------------------------------------------------

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

1. Please clarify the amount of serum present when cells were treated with tocopherols.
2. ref 18 indicated gamma-tocopheryl quinone but not CEHC is a potent inducer of apoptosis.
3. Gysin et al did not find apoptosis induced by gamma-tocopherol in colon cancer cells, which is different from the results in the current study. Please discuss the reasons for the discrepancy.
4. The discussion of Jiang et al study is not correct as in their study, dihydroceramide but not ceramide was found to increase.
5. Relatively high concentrations of gamma-tocopherol have been used in order to induce cell death, which raises a question regarding the physiological significance of the study. Although the authors mentioned that the intracellular levels of gamma-tocopherol was 15-20 fmoles/cell, it is not clear if this level can be achieved in vivo by gamma-tocopherol supplementation. This issue should be further discussed.

-------------------------------------------------------------------------------

**Discretionary Revisions** (which the author can choose to ignore)

What next?: Accept after minor essential revisions

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

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**
we have also done some studies in my lab regarding the effect of vitamin E forms on colon cancer cell growth and cell death. however, this fact does not affect my unbiasedly reviewing this manuscript as our study focused on different aspects.