Reviewer’s report

**Title:** Gamma Tocotrienol Targets Both Tyrosine Phosphatase SHP1 and SHP2 in Mamma-spheres resulting in Cell Death through RAS/ERK pathway

**Version:** 3  **Date:** 10 May 2015

**Reviewer:** Subash C. Gupta

**Reviewer's report:**

In the manuscript “Gamma Tocotrienol Targets Both Tyrosine Phosphatase SHP1 and SHP2 in Mamma-spheres resulting in Cell Death through RAS/ERK pathway” by Gu et al., authors have demonstrated that gamma-tocotrienol (g-T3) can inhibit sphere formation from cancers of breast, colon and cervix. g-T3 was found to target SHP-1 and SHP-2. The experiments are properly designed and data supports the conclusion. However, the writing requires significant improvement. The clinical relevance of g-T3 doses used in the study needs to be discussed. A discussion on prior PK studies that may have been done elsewhere is required. Was the efficacy of this agent against normal stem cells examined? How specifically this agent target to SHP pathway? The model presented in Figure 7 is not experimentally proven and thus requires modifications.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

None