Reviewer’s report

Title: Selective Inhibition of Fatty Acid Synthase by (-)-Epigallocatechin-3-gallate Against Lung Cancer Xenografts

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Reviewer: William Coleman

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“Selective inhibition of fatty acid synthase by (-)-Epigallocatechin-3-gallate against lung cancer xenografts”

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In this manuscript, the authors have investigated the anti-cancer effects of fatty acid synthase inhibitors C75 and (-)-epigallocatechin-3-gallate (ECGC) in a lung cancer model using A549 lung adenocarcinoma cells and xenografts. The authors found that C75 and ECGC blocks fatty acid synthase activity, induces apoptosis, and affects EGFR-signaling in cells in culture. In lung cancer xenografts, both C75 and ECGC blocked tumor growth, but C75 had other adverse affects on the host animal. The authors conclude that inhibition of fatty acid synthase can be achieved through effects of ECGC on EGFR signaling and that ECGC may be a good candidate for future pre-clinical drug development.

This is a well written manuscript that describes an interesting study. The results clearly demonstrate a positive effect of fatty acid synthase inhibitors C75 and ECGC on lung adenocarcinoma cell line growth in vitro and in vivo, and dissects some of the pathways that may be involved. The authors have utilized excellent methods and the results are clearly presented in the text and figures. This study will be of interest to investigators in the field, and advances our knowledge of how lung adenocarcinoma might be therapeutically addressed. The major issue with this study is that it involves one lung adenocarcinoma cell line (A549) and derived xenografts. Hence, it is impossible to know if this is a generalizable effect, or if this effect is specific to this particular cell line.

Specific Comments:

1. Abstract, page 2 – The abstract summarizes the studies and results with both C75 and ECGC, but the conclusions are restricted to ECGC and the title of the manuscript does not mention C75.

2. Figure 1 is presented in a diffuse fashion. These results could be displayed on a single bar graph (rather than an A and B).

3. Figure 2 is not mentioned in order in the text of the results.

4. Results – The authors should insert P values for all references to statistically significant results (such as the significant induction of CPT by C75 on page 7).
5. The in vivo xenograft studies suggest that ECGC or C75 treatment may impair xenograft growth (resulting in a smaller tumor at the end of the experimental period). Nevertheless, the tumors do increase in size from 150-250 mm³ at time zero to nearly 900% that size by day 33. Will these compounds also result in tumor shrinkage under different conditions?

6. No histological images of the xenografts are included. Was the growth fraction different between control versus C75 or ECGC treated animals? Was there observable/measurable apoptosis in the tumor masses?

**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:**

I declare I have no competing interests