Reviewer's report

Title: The involvement of AMPK/GSK3-beta signals in the control of metastasis and proliferation in hepato-carcinoma cells treated with anthocyanins extracted from Korea wild berry Meoru

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Reviewer: Geng Wu

Reviewer's report:

The authors report in this manuscript that anthocyanins extracted from a kind of Korean wild berry were able to regulate phosphorylation levels of AMPK and GSK3beta, thus affecting the protein level of beta-catenin, and contributes to the control of cell metastasis and proliferation.

However, there are several unclear issues that the authors need to address before further decision of acceptance or rejection of this manuscript.

1. In the background part, the authors did not provide any introduction on AMPK, and its relation to GSKbeta and beta-catenin. They just jumped to AMPK in the second paragraph of the background part.

2. In the background part, the authors did not give a satisfactory description on anthocyanin. Is it a single chemical compound, or a mixture of many different compounds? If it is a mixture of compounds, could the authors make some effort on providing any surmise on which compound/compounds may be the active components in anthocyanin against hepato-carcinoma?

3. It is generally believed that in Wnt/beta-catenin signaling, the activity of GSK3beta is not regulated by its phosphorylation. Its activity is mainly regulated by its complex formation with Axin and APC, which is not investigated by the authors. Instead, the authors found that the phosphorylation of GSK3beta is inhibited by the anthocyanin treatment. How would the authors resolve this discrepancy?

4. The authors declare that anthocyanin activates AMPK through inhibition of GSK3beta. Yes, I understand that promotion of phosphorylation is the most clear-cut result from anthocyanin treatment, but why does it have anything to do with GSK3beta and beta-catenin? Could it be that anthocyanin regulates AMPK and GSK3beta/beta-catenin separately, in two different unrelated pathways? Although the legend of Figure 4 states that “anthocyanins inhibit GSK3beta and beta-catenin in an AMPK-dependent manner”, I still have difficulty understanding the reasoning behind this statement.

Level of interest: An article whose findings are important to those with closely related research interests
**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 that I have no competing interests.