Title: Butein inhibit metastatic behavior in mouse melanoma cells through VEGF expression and translation-dependent signaling pathway regulation

Reviewer: Elin Gray

Reviewer's report:

The manuscript by Lay et al, “Butein inhibit metastatic behaviour in mouse melanoma cells through VEGF expression and translation-dependent signalling pathway regulation, describes the anti-tumoral and anti-metastatic effect of butein in melanoma cell B16F10. The results presented provide preliminary evidence of the therapeutic potential of butein.

Major comments;

- Given that B16F10 cell do not resemble the mutation pattern found in human melanomas and poorly resemble the pathway activation found in clinical melanomas, could the authors comment on that?

- The western blot images in figure 4 are not very clear and their profiles, except for FAK, do not clearly depict the data presented in the graph. Moreover, it is important to demonstrate that the level of these protein (independent of phosphorylation) is the same.

- Can the authors elaborate on what is the target molecule or mode of action of butein? How can it affect both MAPK and AKT pathways? Are other pathway also affected by butein.

- What is the effect of butein in normal cells?

- In the conclusion the authors state: “... butein exhibited anti-tumor activity in vivo, including pulmonary metastasis”. I would say that this was shown only, not “including” pulmonary metastasis.

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: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

No competing interests