Reviewer's report

Title: Flavones inhibit breast cancer proliferation through the Akt/FOXO3a signaling pathway

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Reviewer: Le Meng

Reviewer's report:

The authors demonstrated that flavone, apigenin and luteolin suppressed cell viability in three breast cancer cell lines. They also suggested that these compounds executed these effects by suppressing Akt activity. After careful review of this manuscript, I raised several concerns:

1. The first paragraph in Background is too superficial for readers in cancer field.

2. The second paragraph in Background introduced the signaling pathway of AKT/FOXO3a but at the end suddenly jumped to their hypothesis of flavone, apigenin and luteolin may increase the expression of FOXO3a. I just do not follow the logic reasoning here.

3. The colony formation experiment lasted for 21 days. I was wondering how stable the compounds are?

4. In Fig 2F, both total PARP and cleaved PARP should be shown. Also, positive control (eg. puromycin treatment) should be added. A major flaw is that even MCF-7 bear WT p53 loci, Hs578 and MDA-231 cells have mutant p53. In other words, high level of p53 in these two cell lines does not mean p53 is activated. The authors should show that p53 is truely activated if they argue that the apoptosis is induced via p53.

5. Another question is: Did these compounds show specific toxicity only in breast cancer cells? In other words, if the authors believe these compounds are potent drug candidates, they should show that these compounds are much less toxic in normal cells eg MCF-10A or HMEC.

6. I was also wondering if the authors know whether these compounds suppress Akt activity via direct binding or indirectly eg via PTEN or PI3K. Also, the authors should show more stringent experiment that these compounds specifically target Akt/FOXO3a.

Level of interest: An article of limited interest

Quality of written English: Acceptable

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

I declare that I have no competing interests.