Reviewer’s report

Title: Synergistic action of N-palmitoylethanolamine and the FAAH inhibitor URB597 on melanoma growth

Version: 1 Date: 17 November 2011

Reviewer: Natsuo Ueda

Reviewer’s report:

The authors show that co-administration of palmitoylethanolamide (PEA) and URB597 (an inhibitor for fatty acid amide hydrolase) significantly reduces growth of B16 melanoma cells. The results are clear, and the methods are solid.

Discretionary Revisions:

1. URB 597 is a FAAH inhibitor. Administration of this compound should increase endogenous levels of not only PEA but also other N-acylethanolamines. Furthermore, the authors showed that antagonists of CB1, TRPV1, PPAR-alpha, PPAR-gamma or GPR55 did not alter the effect of PEA and/or URB597. Therefore, the authors need to discuss possible molecular mechanism(s) mediating the anti-tumor activity of PEA and URB597.

2. (page 4) The endocannabinoid system should also contain cannabinoid receptors CB1 and CB2 in addition to endogenous ligands and enzymes/transporters.

3. (page 4) Biological activity of PEA unrelated to binding to CB1 and CB2 may not be “cannabimimetic”.

4. (page 7) Concerning radioactive substrates used for enzyme assays, there is no information about concentrations. Therefore readers cannot compare activities among different enzymes.

5. (Fig. 5C) Why does not the administration of PEA increase the endogenous level of PEA?

Level of interest: An article whose findings are important to those with closely related research interests

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.