Reviewer's report

**Title:** Activation of kappa-opioid receptors by U50,488H improves vascular dysfunction in streptozotocin-induced diabetic rats

**Version:** 3  **Date:** 24 November 2014

**Reviewer:** Fernanda Ortis

**Reviewer's report:**

The manuscript “Activation of k-opioid receptors by U50,488H improves vascular dysfunction in streptozotocin-induced diabetics rats” presents interesting results about the beneficial effects of U50 488H on vascular dysfunction in this animal model, however there are some few points that need to be better addressed.

1) The English need to be revised.
2) Since the model used doesn’t involves obesity (type 2 Diabetes) or autoimmunity (type 1 Diabetes) it should be interesting to mention this in the discussion, which indicate that the beneficial effects of the drug are related to the deleterious effect of the hyperglycemia.
3) In figure 1, what is the negative control? Is there any tissue in this control? For the KOR staining, where is this protein being expressed? Could it be pointed in the picture? Was the expression of KOR tested in the presence of the U50,488H group?
4) In figure 2, 4 and 5, DM + U50 and DM + nor-BNI are statically different from control or only from DM?
5) Again in figure 2, the curve in B is for NE treatment, however in results is described to be for PE, this should be corrected.
6) In figure 5, is this western performed for nuclear proteins, as described in results, and if so, why is actin used as a loading control? If the western is performed for total protein content, as described in MM and also in discussion as increase in protein expression (not migration to the nucleus as in results), then the text also need to be corrected.

**Level of interest:** An article of importance in its field

**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:**

I have no competing interests