

Referee 00722166: “This is an interesting manuscript on the regulation of food intake through a mechanism that implies gastric production and release of Nucleob2/Nesfatin-1. Well written, no major suggestions”.

Thank you very much the referee for its very kindly comments.

Referee 02536349: Congratulations for this comprehensive work.

- I would suggest the addition of numbers of rats in two groups instead of a group of rats.

Thank you very much for your interesting suggestions. As the referee suggests the numbers of rats were now added to each group in the figure legends.

- Also correction of three typographic errors (substrate, Although therapeutical (therapeutic)) is recommended..

All these typos have been corrected in the new version of the manuscript.

-As mentioned Gastric X/A like cells share also Ghrelin production which the levels are not assessed.

The ghrelin production in X/A cells by cannabinoid system were previously measured and published by our group (Senin LL et al. “The gastric CB1 receptor modulates ghrelin production through the mTOR pathway to regulate food intake”; Plos One 2013 Nov 26;8(11).) From the data obtained in the mentioned work we found that the blockade of the cannabinoid receptor CB1 decreases ghrelin expression in the stomach, and this effect was mediated by activation of the mTOR/pS6k1 pathway.

-Also the preparation of stomach for tissue extraction localisation of stomach should be uniform and this should be written in manuscript.

The sample from tissue extraction used in the western blot studied was obtained after euthanasia of the animal models by excision of the gastric fundus. This sample was homogenized in a TissueLyser II (Qiagen, Tokyo, Japan) as described in the methods section in this new version of the manuscript.

Referee 03001969: The study at hand deals with an important finding that of an association between cannabinoid system and Nucleob2/nefastatin-1 regulated through mtor signaling pathway. I would only recommend inserting a figure pertaining to pathways of ghrelin and nucleob2/nefastatin-1 and association with cannabinoid system and mtor pathway. It would greatly improve the work at hand.

I would like to thank the referee for its constructive comments. In this new version of the manuscript a graphical abstract is now included (Figure 5) where ghrelin and nucb2 pathways are included and the interactions with the cannabinoid system and mTOR pathway to regulate food intake represented.

We would like to thank once again you and the Reviewers for the constructive comments of the manuscript. We believe that we have been able to meet all of the reviewer's requirements in full and hope that the revised study will be acceptable for publication.