

Dear Editor,

This manuscript is a resubmission of “World Journal of Gastroenterology; Manuscript NO: 69158” by Lapaquette et al. Please find attached the revised version of our manuscript. We are grateful to the Editor and the reviewers for their constructive remarks which helped improve our manuscript. We have replied point by point to the questions raised by the reviewer 1 and hope to have met her/his requirements. Changes to the text are highlighted in yellow.

**Reviewer #1:**

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The manuscript is interesting and provides us up-to-date and comprehensive information on reciprocal interactions of autophagy with the gut microbiota. I would like to suggest some improvements in the manuscript.

**1. The introduction section must be improved. This section is too poor. I think that the introduction could be improved by a better link between paragraphs.**

→ The « Introduction » section has been substantially modified in order to better present the topic of the review (see modifications on p4-6). We reworked the links between the paragraphs and added new information with the corresponding references.

**2. In the systemic effects of the gut microbiota on host autophagy part, the authors discuss the effects of gut microbiota on the autophagy of nervous tissues, liver, muscle tissues in health and disease conditions, but there is no clear understanding regarding this unique relation. Please insert a table to summarize the studies discussed in this section.**

→ As recommended by the reviewer, a table has been added. This table summarizes data from the literature suggesting or showing a systemic effect of the gut microbiota on autophagy (see new Table 1).

**3. In the shaping of the gut microbiota by autophagy part (lines 291-438). These sections are fundamental for the manuscript, but the three sections including “Mucus layer maintenance”, “Secretion of antimicrobial compounds in the gut lumen” and “Modulation of inflammation” only delineate the interactions of autophagy with the gut. Therefore, these sections should be extended and include more studies regarding this unique relation between autophagy and gut microbiota.**

→ Substantial modifications have been made to the sub-sections « Mucus layer maintenance » (see p13-14), « Secretion of antimicrobial compounds in the gut lumen » (see p15-16) and « Modulation of inflammation » (see p17-18). More detailed information and new studies and references have been added.

**4. Figure 1 is too poor and lacks some clear pathways of the interplay between gut microbiota and autophagy. The figure must be improved.**

→ Figure 1 and its legend (p19) have been enriched with more information. Particular attention has been paid to the figure in order to better present the interaction between the gut microbiota and autophagy. In particular, schemes have been added to allow a better understanding of 1) how the « microbiota message » is transmitted to peripheral organs and 2) how molecules

derived from the gut microbiota are detected by host cells at the gut mucosa and by peripheral organs.

**5. There is no clear idea and should add some discussions on the current challenges and an outlook toward the future interventions.**

→ A paragraph has been added in the "Conclusion" section to explain how far we are yet from understanding the complexity of interactions between the gut microbiota and autophagy, particularly at the systemic level. Due to the plurality of functions exerted by the gut microbiota and autophagy on the host physiology, these gaps must be filled before future interventions can be developed to target this « gut microbiota-autophagy » bidirectionnal axis. See modifications on p18-19.

**Reviewer #2:**

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: The article presented the correlation between the autophagy and gut microbiota. The topic is very interesting. The article was well organized and good in presentation.

→ We thank the reviewer for the time she/he devoted to reviewing our manuscript.