

Responses to the reviewers' comments

Reviewer #1

In this manuscript (74878), entitled "ATG16L1, a multifunctional protein involved in autophagy, innate immunity, and Crohn's disease", Okai et al. reviewed the important roles of ATG16L1 in induction of autophagy, regulation of innate immunity, and involvement in Crohn's disease. Generally, the topic is interesting, this manuscript is easy to read, and the references are properly cited. Therefore, I only have several minor concerns which should be properly addressed before accepting for publication.

Reply; We appreciate positive general evaluation of our manuscript.

Minor concerns:

1. The title should be modified, because "autophagy", "innate immunity", and "Crohn's disease" are not parallel.

Reply; We changed the title as suggested by this reviewer. The revised title is Alterations of autophagic and innate immune responses by the T300A mutation in *ATG16L1* associated with Crohn's disease.

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2. The section "MOLECULAR INTERACTION BETWEEN ATG16L1 AND NOD2 OR RIPK2" should be integrated into the section of "ATG16L1 AND INNATE IMMUNITY".

Reply; We reorganized the section in accordance with this suggestion.

3. The current figure summarizes the regulatory mechanisms of ATG16L1. It is better to prepare an additional table highlighting the physiological functions of ATG16L1.

Reply; We added physiological functions of ATG16L1 as Table 1 in the revised manuscript.

Reviewer #2

I have only one remark: 1. In „Core tip” section the last sentence is: „ In this minireview article, we have summarized the immunopathogenesis of Crohn’s disease caused by this ATG16L1 variant.” This sentence may be confusing; the reader may understand that the ATG16L1 variant is the only one that causes the disease. I suggest modifying it.

Reply; We rewrote the sentence as follows; In this minireview article, we have summarized the immunopathogenesis of Crohn’s disease in the presence of the ATG16L1 mutation.