

June 19, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 19612- Revised manuscript.doc).

**Title:** Autophagy in colorectal cancer: an important switch from physiology to pathology

**Author:** Florin Burada, Elena Raluca Nicoli, Marius Eugen Ciurea, Daniel Constantin Uscatu, Mihai Ioana and Dan Ionut Gheonea

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 19612

The manuscript has been improved according to the suggestions of reviewers:

Editor's comments

1. The article was class B for language quality; it has been edited by a professional English language editing company (American Journal Experts, [www.ameditor.com](http://www.ameditor.com)) mentioned in 'The Revision Policies of BPG for Topic Highlight'.
2. We moved Conflict-of-interest statement in the manuscript's title page. A signed copy was sent to the BPG in PDF format.
3. We created an audio file describing our final core tip.
4. We supplied the figure 1 as a decomposable image
5. Format and references were updated
- 6 Revision has been made according to the suggestions of the reviewers and all substantive changes are highlighted in the revised manuscript.

Reviewer 3001893.

We thank the reviewer for the comments

C1. There are some grammatical errors in the text, such as page 8, "Autophagy as a promoting factor at late stages" section, "Tumor cells usually have a high proliferation rate demanding more energy and resources than normal cells"

A1. 1. This current version of the manuscript is now edited by a professional English language editing company (American Journal Experts, [www.ameditor.com](http://www.ameditor.com)) mentioned in 'The Revision Policies of BPG for Topic Highlight'.

C2. Page 11: "AUTOPHAGY GENE SWITCHES TO CRC" section, "The treatment of CRC cell lines with 5-fluorouracil (5-FU) activated autophagic process, increased LC3-II level and reduced apoptotic rate compared with untreated cell lines, an increase in the apoptotic rate was found by adding 3-MA to 5-FU" this must be supported by one reference. 3.

A2. We inserted the reference (70) and rewrite the sentence (initially the reference was added at the end of the next phrase)

C3. Page 13: It would be useful to have a brief explanation about the relationship between Bif-1 and autophagy.

A3. We introduced a brief explanation about the relationship between Bif-1 and autophagy in "AUTOPHAGY GENE SWITCHES TO CRC" section.

C4. Inflammatory bowel disease patients have higher risk of colorectal cancer development. It would be useful to have a review on how autophagy regulates the formation of colitis-associated colon tumors.

A4. Thank you for your comment. In this review we focused mainly on colorectal cancer, but at your suggestion we added a paragraph about autophagy involvement in IBD (IBD susceptibility genes in "AUTOPHAGY GENE SWITCHES TO CRC" section).

Reviewer 2454078

A2. This manuscript is a well-written review. It is informative but needs to be improved. My comments are as follows:

C1. In the "AUTOPHAGY GENE SWITCHES TO CRC," characteristics of each gene and product needs to be explained more and under specific subheading for each gene.

A1. Thank you for your comment. We added more details for each gene under specific subheadings.

C2. In the "AUTOPHAGY DRUGS IN CRC," do the mentioned drugs affect on these gene (comment 1) expression levels? If so, please explain and include the effect as a separate column in the table.

A2. We found only few autophagy genes be affected by drugs in CRC studies and we chose to mention the effects in main text "AUTOPHAGY DRUG IN CRC" section. The autophagy was monitored mainly by L3 conversion and electron microscopy and we have now emphasized the importance of LC3 as autophagy marker in revised manuscript "AUTOPHAGY GENE SWITCHES TO CRC" section, LC3 subheading (ref 69)

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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