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RE: Submission of <u>REVISED</u> 'Review paper' (Manuscript NO.: 64615)

Dear Editor

Please find enclosed our REVISED Review entitled **"The role of autophagy in cholangiocarcinoma. An autophagy-based treatment strategy"** to be considered for publication. We would like to thank you and the reviewers for your thoughtful evaluation of our manuscript and your most welcome comments/suggestions. Accordingly, we have now revised our manuscript thoroughly to reflect these comments.

Please find below a point-by-point **response** to <u>ALL</u> the issues raised by the Reviewers:

Reviewer #1:

Specific Comments to Authors: - Based on the abbreviations provided by the authors, CC should be replaced into CCA. - Authors should summarize the preclinical studies with autophagy modulators in CCAs.

AUTHOR RESPONSE: We thank the reviewer. We have made the appropriate editing and the abbreviation for Cholangiocarcinoma CC has been replaced into CCA. Moreover, in part 3, we added a concluded paragraph where we summarized the controversial role of autophagy in CCA.

Page 9: "Autophagy modulators in combination...its clinical value for patients with CCA."

Reviewer #2:

Specific Comments to Authors: There were some significance in this review, and author summarized researches in this field. I suggest author should delete unnecessary introduction in Part 1 and 2.

AUTHOR RESPONSE: We thank the reviewer. We have made the appropriate editing and we deleted unnecessary introduction in Part 1 and 2.

EDITORIAL OFFICE'S COMMENTS

Issues raised: (1) The "Author Contributions" section is missing. Please provide the author contributions; (2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (3) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

AUTHOR RESPONSE: We thank the editor. We have made the appropriate editing.

- (1) A new statement was added. *Page 30: "All the authors made substantial contributions to the conception and design of the study, analysis and interpretation of data. Also, drafted the article, made critical revisions and gave the final approval of the version of the article to be published."*
- (2) We submitted the PowerPoint file with the original figure.
- (3) We provided the PMID, DOI and the full list of authors for all references.

Trusting that we have adequately **addressed** the reviewers' concerns, we would like to thank you for your help in improving our work significantly.

Kind regards, Koustas Evangelos, MD, PhD Corresponding author