

Format for ANSWERING REVIEWERS



Professor Lian-Sheng Ma
President and Company Editor-in-Chief
World Journal of Gastroenterology

Jin-Lei Wang
 Director
 Editorial Office

Budapest, January 25, 2014

Dear Editor-in-Chief,

Dear Director,

Please find enclosed the edited and revised version of our manuscript (ESPS Manuscript No. **6687-Review**).

Title: “The Impact of Proteolytic Enzymes in Colorectal Cancer Development and Progression”

Authors: László Herszényi, Loránd Barabás, István Hritz, Gábor István, Zsolt Tulassay

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript No: **6687-Review**

As suggested by the Reviewers, the manuscript has been improved and the paper has undergone minor revision.

Changes made to the paper:

- **1.** Format has been updated.
- **2.** References and typesetting were corrected.
- **3.** A new author has been added (Gábor István).
- **4.** The abstract has been completed: classes of proteolytic enzymes have been included.
- **5.** Core tip has been added.
- **6.** A section discussing in more detail the molecular mechanism how the proteolytic enzymes regulate carcinogenesis and cancer progression has been added (Page 4. last paragraph)
- **7.** A section discussing the role of proteolytic enzyme in predicting early CRC survival has been added, showing that proteolytic enzymes could constitute useful independent markers additive to TNM staging system for the intermediate groups including stage II and stage III CRC, identifying patients who are more likely to have disease relapse, thus being potential candidates to receive aggressive adjuvant chemotherapy (Section 4., page 9., last paragraph).
- **8.** Section 5 (“Proteolytic enzymes as potential target for cancer therapy”) has been re-written and completed, paying more attention to the review of the potential role of proteolytic enzymes in the treatment of cancer.
- **9.** “Conclusion and future prospects” section has been added.
- **10.** Three tables have been added for making the concepts more easily to be caught by the readers.
- **11.** The Reference list has been completed.
- **12.** The English language has been revised and improved by an English native speaker and certified English-Hungarian medical interpreter.

All changes made to the paper are highlighted with yellow colour in the revised manuscript.

- We enclose five itemized, point-by-point answers for the Reviewers.

All authors have read and approved the revised paper, have met the criteria for authorship.

We hope you will find our revised version of the paper eligible for publication in ***World Journal of Gastroenterology***.

Looking forward to hearing from you soon.

Sincerely yours,



László Herszenyi MD, DSc (corresponding author)

Second Department of Medicine

Semmelweis University Budapest

H-1088 Budapest,

Szentkirályi str. 46.

Hungary

Tel: +36-1-2660926

Fax: +36-1-2660816

e-mail: herszenyi.laszlo@med.semmelweis-univ.hu

Point-by-point answer to Reviewer No. 00058180

- As suggested, Section 5 (“Proteolytic enzymes as potential target for cancer therapy”) has been re-written and completed, paying more attention to the review of the potential role of proteolytic enzymes in the treatment of cancer.
- The Reference list has been completed: nine new references have been added with respect to the potential impact of proteolytic enzymes in the treatment of cancer.
- Please also see the enclosed list of changes made to the paper.

Answer to Reviewer No. 00009760

- Thank you very much that you positively evaluated our manuscript and accepted it for publication.
- Please also see the enclosed list of changes made to the paper.

Point-by-point answer to Reviewer No. 00039963

- As requested, the Reference list has been completed by the paper of Montemuro *et al.* Int Clin Lab Res 1995 (Ref. no. 100).
- Please also see the enclosed list of changes made to the paper.

Point-by-point answer to Reviewer No. 00043117

- As requested by the Reviewer, a section discussing in more detail the molecular mechanism how the proteolytic enzymes regulate carcinogenesis and cancer progression has been added (Section 3., Page 4. last paragraph).
 - The Reference list has been completed with five additional references in this context (References 32-36).
- As suggested, a section discussing the role of proteolytic enzyme in predicting early CRC survival has been added, showing that proteolytic enzymes could constitute useful independent markers additive to TNM staging system for the intermediate groups including stage II and stage III CRC, identifying patients who are more likely to have disease relapse, thus being potential candidates to receive aggressive adjuvant chemotherapy (Section 4., page 9., last paragraph).
 - The Reference list has been completed with four additional references in this context (References 147-150).
- As also requested by the Reviewer, three tables have been added for making the concepts more easily to be caught by the readers.
- “Conclusion and future prospects” section has been added.
- Please also see the enclosed list of changes made to the paper.

Point-by-point answer to Reviewer No. 00041968

- As requested by the Reviewer, the abstract has been completed: classes of proteolytic enzymes have been included.
- “Conclusion and future prospects” section has been added in the manuscript about the potential future role roles of proteolytic enzymes in CRC.
- Three tables have been added for making the concepts more easily to be caught by the readers and to document the general role of proteolytic enzymes in cancers and more specifically, their clinical significance in colorectal cancer
- The Reference format has been updated.
- The English language has been revised and improved by an English native speaker.
- Please also see the enclosed list of changes made to the paper.

List of *changes* made to the paper

- 1. Format has been updated.
- 2. References and typesetting were corrected.
- 3. A new author has been added (Gábor István).
- 4. The abstract has been completed: classes of proteolytic enzymes have been included.
- 5. Core tip has been added.
- 6. A section discussing in more detail the molecular mechanism how the proteolytic enzymes regulate carcinogenesis and cancer progression has been added (Page 4. last paragraph)
- 7. A section discussing the role of proteolytic enzyme in predicting early CRC survival has been added, showing that proteolytic enzymes could constitute useful independent markers additive to TNM staging system for the intermediate groups including stage II and stage III CRC, identifying patients who are more likely to have disease relapse, thus being potential candidates to receive aggressive adjuvant chemotherapy (Section 4., page 9., last paragraph).
- 8. Section 5 (“Proteolytic enzymes as potential target for cancer therapy”) has been re-written and completed, paying more attention to the review of the potential role of proteolytic enzymes in the treatment of cancer.
- 9. “Conclusion and future prospects” section has been added.
- 10. Three tables have been added for making the concepts more easily to be caught by the readers.
- 11. The Reference list has been completed.
- 12. The English language has been revised and improved by an English native speaker and certified English-Hungarian medical interpreter.