

June 12, 2015

Editor-in-chief,  
World Journal of Gastroenterology

**Invited manuscript ID: 00593657, Manuscript #: 18938, entitled  
“Pathophysiological mechanisms of death resistance in colorectal carcinoma”**

Dear Dr. Ya-Juan Ma,

Thank you very much for your letter on June 9, 2015. We have addressed the questions and reconstructed the manuscript as suggested by the referees. The changes are underlined in the revised manuscript. All co-authors accept responsibility for the contents of the amended manuscript. In the following, please find a point-by-point response to all the comments that were raised by the referees. We are grateful for the helpful suggestions, and we thank you for your editorial input.

Sincerely yours,

Linda

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## **Response to reviewers:**

### **Reviewer #00070191**

1. The manuscript was reconstructed and the context in section 4 was shortened.
2. Schematic presentations that summarize mechanisms of cell death and death resistance are included in the manuscript (Figure 1 and 2).
3. The novel necroptotic pathways are described in more details.
4. The paper was sent for language editing.

### **Reviewer #00073640**

1. A short description of autophagy and the reason for not including it in cell death pathways are added in the text.
2. The manuscript was reconstructed and the context in section 4 was shortened. The authors thank the reviewer for clearly pointing out where the red line of the manuscript is broken. This suggestion was helpful in revising the text to highlight the focus (death resistance strategies in cancer) while trying to point out its similarity and disparity to normal anti-death cytoprotective mechanisms.
3. Death resistance pathways in cancers in general are explained in section 5 with reference to many types of tumors. The autocrine, paracrine and exogenous factors for death resistance are focused on colon cancers (section 6).
4. Schematic presentations that summarize mechanisms of cell death and death resistance are included in the manuscript (Figure 1 and 2).