

### **Response to Reviewer #1:**

I am sorry to state having serious problems in finding addressable points in the review from this reviewer. Obviously, he or she was not a suited peer for the topic of our manuscript.

He or she states correctly "... if it is to define a new "model" or methodology for the study of rectal tumors, I guess a molecular biologist should better review this paper ...". Indeed, this is the purpose of this description and characterization of three rectal cancer models.

We totally agree with the reviewer that three cases would not be sufficient for a clinical study type of manuscript or the like. We also agree that especially the heterogeneity of the three cases would make any generalization very difficult – even scientifically incorrect. However, we feel that the opposite is the case when describing three cell (and PDX) models from rectal cancer – they represent a greater proportion of the subtypes present in rectal cancer and are especially when analyzed together side-by-side a very useful tool for gaining knowledge in rectal cancer research.

To sum this up and with all necessary respect, we ask to neglect the negative conclusion of this reviewer since it simply based largely on the wrong assumption that our manuscript deals with biomarker analysis, rectal tumor testing pattern, behavior etc. with a clinical purpose.

### **Response to Reviewer #2:**

Contrary to Reviewer #1, this reviewer clearly recognized the novelty of this model description. According to his or her suggestions, we added a clear description of the overall strengths and also limitations of the study. This has been included into the last paragraph of the discussion.

In addition, he or she suggested "to include more references on the topic". We carefully checked the suggested references and after some internal discussion added two of the three suggested references as novel references 24 and 25 into the manuscript. Moreover, we carefully revised all references and citations in the text of the manuscript.

Christina Mullins, an American native speaker, revised the manuscript thoroughly.

Overall, we are now very confident that the slightly improved manuscript now matches the requirements for publication in the prestigious "*World Journal of Gastroenterology*".

We would be very pleased if you and the reviewers find our improved manuscript suitable for publication.

In the name of all authors,  
yours sincerely,

Michael Linnebacher, PhD