

ANSWERING REVIEWERS



July, 19th, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11304-Revised). We appreciate the helpful comments and modified the manuscript according to the reviewer's and your suggestions. Modifications in the text are marked by applying the track-changes option of Microsoft Word.

Title: Reactivity against microsatellite instability-induced frameshift mutations in patients with inflammatory bowel disease

Authors: Florian Kuehn, Ernst Klar, Anja Bliemeister, Michael Linnebacher

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 11304

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

Response to reviewer 1:

1. The reviewer remarked that a number of un-introduced and unnecessary abbreviations have been used in the text of the manuscript. We are very grateful for this precious tip and changed everything as requested.
2. He or she remarked that ““Significant T cell reactivities against MSI-induced FSPs were observed in 59 of 75 IBD patients (78.7%) compared to healthy controls (p=0.001)” is confusing and that the conclusion “these findings have potential implications for...and additionally of MSI+ cancer patients” was out of the population of this group of patients.” We agree that the first sentence was confusing and changed it to “Significant T cell reactivities against MSI-induced FSPs were observed in 59 of 75 IBD patients (78.7%). This was significantly more as we could observe compared in 20 healthy controls (p=0.001).” In the second sentence, the referral to MSI+ cancer patients, which we did indeed not analyze in this study, was removed.
3. Similarly, the reviewer asks for removal of referrals to MSI+ cancer patients in the core tip and in the main part of the article. Both have been removed as wished.
4. Next, he or she wanted the results to be optimized in order to be more clear-cut. We did this accordingly.
5. Furthermore, the reviewer asked for a stronger focus in the discussion. We did this and especially condensed two aspects in the discussion (MSI in pancreatitis and MLH1 germ-line alterations). However, we have to admit that the following two points raised by the reviewer lengthened the discussion again slightly.
6. Besides, we were asked to discuss limitations of our study. We added one aspect accordingly: “However, our findings have to be verified by other research groups and by direct approaches to validate FSP expression in IBD. The presence of T cells reacting against FSPs is of course only an indirect proof of the antigens’ presence.” Of course there

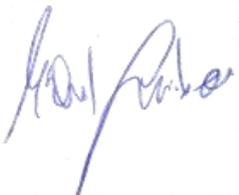
are other aspects which may limit some of the conclusions of the present work. However, in our discussion we already pointed to the fact that further studies are urgently needed to shed more light into this interesting aspect of IBD.

6. Finally, the reviewer wanted Figure 3 additionally explained. We totally agree with his or her opinion, that Figure 3 contains indeed a very important piece of information and very happily added the following to the discussion part of the revised manuscript: "Exemplarily, we could further confirm these data by repetitive analysis four cases. As can be depicted from Figure 3, the overall FSP recognition seems to increase with the duration of the disease also on an individual patient level."

We are very confident that the enhanced version now matches the requirements for publication in the *World Journal of Gastroenterology*.

In the name of all authors,

Sincerely yours,



Michael Linnebacher