Response letter

Dear Mr. Wang,

Thank you very much for considering our manuscript for publication. We are very pleased to the comments of the reviewers. We have considered each suggestion and will comment these below step-by-step. We believe that we can comment to each criticism and hope that you and the reviewers will consider our manuscript for publication that has been changed according to the reviewers' suggestion.

(First reviewer)

1. The paragraph about colon and rectal cancer has been abridged, as the first author suggested. We deleted aspects that are not essential for understanding the approaches of the cited studies.

2. The results of the paragraph CORRELATION OF MIRNA EXPRESSION TO CLINICAL PARAMETERS are summarized in table 1, also the main results of the paragraph ALTERATION DUE TO THERAPY AND PREDICTING THERAPY RESPONSE are summarized in figure 2. Summarizing the paragraph DIFFERENTIAL EXPRESSION OF MIRNA IN RECTAL CANCER is challenging, because so many different miRNAs were found, but we found a way to bring more clarity into the manuscript by creating figure 1.

3. The third comment of the first reviewer says, "The review is not included into a systematic review", if there is something specific missing, let us know, because this comment is very vague, so we don't know what to change. In the paragraph "Methods" we explained the systematic literature search, we hope that helps.

(Second reviewer)

4. The first comment of the second reviewer says, "…according to my opinion it is impossible to gain useful information from the current literature […] As stated by the authors, a clear identification of miRNAs useful for prognostic purposes still failed". This comment we take as a general information or opinion, since we cannot change anything about the current studies.

5. We re-wrote some passages and hope the content is clear now.

6. In figure 1 (which is now figure 2 in the revised manuscript) there are microRNAs shown out of pretreatment biopsies (on the LEFT side), which (according to the mentioned studies) can predict a good response if upregulated (miR-21-5p, miR125a-3p, miR-188-5p, miR-233, miR-483-5p, miR-622, miR-671, miR-630, miR-765, miR-1183, miR-1224-5p, miR-1471,

miR1909) or downregulated (miR-720 and miR-1274). For miR-200c a downregulation of its expression predicts non-response.

On the RIGHT side, there are miRNAs out of post-treatment biopsies of tumors, who did not respond well to the chemoradiotherapy. There are no studies who looked for specific miRNAs in post-therapeutic biopsies of tumors, who responded well. One reason is that in case of complete response there is no tumor left to win biopsies from.

7. The manuscript has now been read and corrected by a native speaker, so the language should not be an issue anymore.