

## **Responses to Reviewers:**

**Questions of Reviewer 1:** This is an interesting study about the role of hsa\_circRNA\_102610 in EMT. Some sequencing matching between has\_circRNA\_102610 and hsa\_miR-130a-3p may be added to show hsa\_circRNA\_102610 sponges the miR-130a-3p. The differences between B and C in Figure7 is not clear. Specific labeling other than B or C may be more readable. It may also apply to Figure6 A-D.

**1 Some sequencing matching between has\_circRNA\_102610 and hsa\_miR-130a-3p may be added to show hsa\_circRNA\_102610 sponges the miR-130a-3p.**

**Answer to question 1 of Reviewer 1:**

Figure 3C shows the sequence matches between hsa\_circRNA\_102610 and has-miR-130a-3p (in the first row). The predicted interaction was verified by FISH and luciferase reporter assays (Figure 6).

**2 The differences between B and C in Figure7 is not clear.**

**Answer to question 2 of Reviewer 2:**

We performed replicate experiments in HIECs and NCM460 cells to observe morphology following TGF- $\beta$ 1 treatment. We have changed Figures 7B and 7C so that the differences are more obvious.

**3 Specific labeling other than B or C may be more readable. It may also apply to Figure6 A-D.**

**Answer to question 3 of Reviewer 2:**

Specific labels have been added to Figure 7B and 7C. Specific labels have also been added to Figure 6A-D.

**Questions of Reviewer 2:** This is an interesting original article aiming to investigate the role of hsa\_circRNA\_102610 in the pathogenesis of CD. Overall, it is a well-written manuscript offering insight regarding new mechanisms into the pathogenesis of CD. Nevertheless, the correlation of hsa\_circRNA\_102610 with Fcal was demonstrated weak despite positive, questioning its diagnostic role in CD. Moreover, according to the evidence presented in the study, it looks that Hsa\_circRNA\_102610 role in CD progression is assumed rather than proved. Finally, although necessary, the constant use of abbreviations makes the manuscript difficult to read. Please correct this point.

**1 Nevertheless, the correlation of hsa\_circRNA\_102610 with Fcal was demonstrated weak despite positive, questioning its diagnostic role in CD.**

**Answer to question 1 of Reviewer 2:**

In our previously published study (reference 7), 155 upregulated and 229 downregulated circRNAs were identified in CD patients compared with healthy controls (HCs) by microarray analysis. However, among the top 40 upregulated circRNAs identified by microarray analysis, only approximately 10 circRNAs were verified by RT-qPCR to be significantly upregulated in CD patients. Among these circRNAs, hsa\_circRNA\_102610 was determined to be the second best diagnostic indicator of CD by ROC curve analysis. While attempting to study the mechanism of the best diagnostic indicator, hsa\_circRNA\_004662, we have encountered problems with overexpression that we still have not solved.

Fecal calprotectin is a sensitive diagnostic marker for CD [refer to 25, 26]. However, the pathogenesis of CD is complex, and there is a lack of sensitive and specific biomarkers for CD. Though the positive correlation we found between fecal calprotectin and hsa\_circRNA\_102610 was weak ( $r=0.3586$   $P=0.0072$ ), we infer that hsa\_circRNA\_102610 plays a possible role in CD. The results of this study also suggest its role in EMT. EMT is an important pathogenetic mechanism in CD (refer to 17, 30), which we have discussed in

paragraph 5 of the discussion section. As predicted, the results in our study suggest a role for hsa\_circRNA\_102610 in CD pathogenesis.

According to your comment, we have revised the second paragraph of the discussion section as follows:

“Our previous studies have suggested that hsa\_circRNA\_102610 was valuable for the diagnosis of CD exhibiting an AUC of 0.78, a sensitivity of 60.53% and a specificity of 78.85% in ROC curve analysis<sup>[7]</sup>. In this study, our further analysis showed that hsa\_circRNA\_102610 levels were positively correlated with CALP levels. CALP is an increasingly accepted sensitive biomarker for assessment of CD<sup>[25, 26]</sup>. Thus, although the positive correlation between hsa\_circRNA\_102610 and CALP in CD patients is weak ( $r=0.3586$   $p=0.0072$ ), this finding indicates a possible role of hsa\_circRNA\_102610 in CD. However, the exact mechanism of hsa\_circRNA\_102610 in the development of CD is still unclear.”

**2 Moreover, according to the evidence presented in the study, it looks that Hsa\_circRNA\_102610 role in CD progression is assumed rather than proved.**

**Answer to question 2 of Reviewer 2:**

According to the comments, we have changed the title from “Hsa\_circRNA\_102610 promotes proliferation and TGF- $\beta$ 1 induced EMT of intestinal epithelial cells by sponging miR-130a-3p to affect Crohn’s disease progression” to “**Hsa\_circRNA\_102610 upregulation in Crohn’s disease promotes TGF- $\beta$ 1-induced EMT via sponging of hsa-miR-130a-3p**”, which may be more appropriate. It is no more than 12 words, as WJG requires.

Accordingly, the running title has been changed to “Hsa\_circRNA\_102610 promotes EMT by sponging hsa-miR-130a-3p”.

The conclusion has been changed to “Hsa\_circRNA\_102610 upregulation in Crohn’s disease patients could promote the proliferation and EMT of intestinal epithelial cells via sponging of hsa-miR-130a-3p”.

In addition, in the core tip, the corresponding parts have been revised.

**3 Finally, although necessary, the constant use of abbreviations makes the manuscript difficult to read. Please correct this point.**

**Answer to question 3 of Reviewer 2:**

We have reduced the use of abbreviations to terms such as “EMT” and “CD”. Abbreviations were used according to the guidelines and requirements of WJG in this revised edition. Please see the article for details.