

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Cholecystokinin (CCK) was first found in the gastrointestinal tract (GIT), and is named for its function of stimulating gallbladder contraction, of which the expression and functional properties remain unknown in common bile duct. To address this challenge, in this study, the authors aimed at exploring the expression and the underlying mechanism of CCK-A receptors in common bile duct. The authors used experimental animals of Guinea Pig, immunofluorescence determination, contractile detection, and statistical method to organize their manuscript. The results showed that, the contraction of smooth muscle by CCK was dose-dependently, and the responses of CBD smooth muscle to CCK was reduced by ICLC-removal. In addition, CCK may also regulate CBD contraction via binding to CCK-A receptors on ICLCs. The study design is reasonable, and the results reflects the conclusion as well. I recommend its acceptance after the minor revision. The detailed comments are: 1) In fig. 1 & 2, the immunofluorescence only showed the c-kit positive cells and CCK-A receptor positive cells. I wonder, why not staining the cell nucleus to locate all the cells in the sample? 2) Some details in the paper need to be revised. For instance, in section of Objective, "Cajal-like cells (ICLCs)" should be "Interstitial Cajal-like cells (ICLCs)". 3) Since this work used experimental animals, the authors should provide ethical statement in the manuscript.

Reply: Thank you for your generous suggestions, we have revised the manuscript according to each comment:

1. Figure 1 showed the expression of c-kit and CCK-A receptors in tissue sections while figure 2 in cells. We primarily assayed receptor expression, and the receptors that signaling molecules recognize and bind to are usually located in the cytoplasmic membrane or inside the cell.
2. We have revised the details.
3. We have provided the ethical statement in the manuscript. All experimental procedures conformed to the Committee on the Ethics of Animal Experiments of the Central Hospital of Wuhan.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors constructed animal models to and used them to investigate the expression and functions of CCK-A receptors on Interstitial Cajal-like cells (ICLCs) of Guinea Pig common bile duct. After reasonable grouping the animal samples into CBD sections and CBD-cultured cells groups, the authors found that co-expression of both c-kit and CCK-A receptors in the CBD muscularis layer. And the

CBD-isolated cells showed that c-kit was expressed on the surface of ICLCs, while after ICLC removal, CCK's contractility on CBD smooth muscle decreased. In short, the topic of this manuscript is timely and interesting. The authors have organized the manuscript rationally, with good methodology and well-written English. However, some important editing needs to be done before publication: 1. I noticed that in Figure 4 and 5, there are no error bars on the data points. So, how many times did the authors repeat these experiments? 2. In the title, there is a word of "ICC-like Cells" that is not present in the main text. Is this a typo mistake? If not, please add the full name of "ICC-like Cells" in the manuscript. 3. All the abbreviation should be added the full name at the first appearance. For example, the CCK-A in the Objective part.

Reply: Thank you for your generous suggestions, we have revised the manuscript according to each comment:

1. We have redrawn the figure using professional mapping software and the error bars were shown in the figure. The small difference in the values of the repeated experiments for each group resulted in the error bars not being evident in the figures.
2. We have modified the mistake, "ICC-like cells" was supposed to be "Interstitial Cajal-like cells".
3. We have provided the full name of the abbreviations when they first appears.