Dear editor and reviewers,

Thank you very much for your letter and the comments from the reviewers about our paper submitted to “World Journal of Gastroenterology” (Manuscript NO: 79865). We very much appreciate the careful reading of our manuscript and valuable suggestions of the reviewers. We have carefully checked the manuscript and revised it according to the comments. We also responded point by point to each reviewer's comments as listed below, along with a clear indication of the location of the revision. If you have any questions about this paper, please don’t hesitate to let me know.

Sincerely yours,

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Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Dear authors, very interesting and informative review. It will be desirable to have your criteria for literature search.

Response: Very thanks for your positive comments. Here are some of our literature retrieval strategies and fliting criteria:

First, we searched articles with the key terms “Colorectal Cancer”, “Oxaliplatin”, “Chemotherapy Resistance”, “Non-coding RNA”, “Exosomes” and “Liquid Biopsy” since 2017 using PubMed, Web of Science, Google Scholar, and ScienceDirect databases. Second, the articles are filtered and classified by taking microRNAs, lncRNAs, and circRNAs as the research objects. Meantime, we searched these key terms by cross-matching and discovered that several non-coding RNAs may play a

significant role in CRC oxaliplatin resistance. Finally, we separately integrated and discussed the potential of exosomal ncRNAs as emerging biomarkers for fluid biopsy.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This is a well-summarized comprehensive review about roles of non-coding RNAs (ncRNAs) in oxaliplatin resistance of colorectal cancer. This manuscript would be useful for readers interested in the relevant field. I have some comments to improve the manuscript. 1. Paragraphs of "MiRNAs as regulators of CRC oxaliplatin resistance," "LncRNAs as regulators of CRC oxaliplatin resistance," and "CircRNAs as regulators of CRC oxaliplatin resistance" are too long and boring to read. I recommend subdividing those paragraphs, for example, in upregulated ncRNAs and downregulated ones. 2. In page 10, a term "sponge" appears. Please specify the meaning of the word. 3. Cancer-associated fibroblasts (CAFs) is defined twice in pages 10 and 17. 4. In page 13, lines 12, 13, and 19, has_circ_0040809 must be hsa_circ_0040809. 5. In page 14, line 1, miR-59-5p/CDK6/PRA3 must be miR-597-5p/CDK6/PRA3. 6. In page 14, line 28, CCDC66 must be circular CCDC66. 7. In page 17, line 14, miR-766-5P/TRIM67 must be miR-766-5p/TRIM67. 8. In page18, line 15, EVs are not defined. Please explain. 9. In Figure 2, labels of a right lower cell (e.g., oxaliplatin-resistant CRC cell) and a left upper cell had better be added. Apoptosis and Autophagy had better be accompanied by either activated (↑) or repressed (↓). 10. In page 6, line 27, "assession" may be "assessment." 11. In page 12, line 20, "to in parental" may be "to parental." 12. In page 16, line 6, "amongst" may be "and.".

Response: We feel great thanks for your professional and careful review work. I apologize for some mistakes. The following is a point-to-point response according to your nice suggestions.

Response 1: According to your suggestions, we have subdivided those paragraphs and

added the corresponding subtitles.

Response 2: Thank you for reminding us that we have explained “sponge” on page 10, line 38.

Abundant studies have demonstrated that some endogenous transcripts (such as endogenous pseudogenes, lncRNAs, and circRNAs) can complement miRNAs in sequences and inhibit their expression, resulting in the upregulation of target gene expression. This phenomenon is called the miRNA “sponge” effect.

Response 3: We have corrected the second definition of cancer-associated fibers (CAFs) to CAFs on page 16, line 34.

Response 4: In page 13, lines 1, has_circ_0040809 has been revised to hsa_circ_0040809.

Response 5: In page 13, line 31, miR-59-5p/CDK6/PRA3 has been revised to miR-597-5p/CDK6/PRA3.

Response 6: In page 14, line 23, CCDC66 has been revised to circular CCDC66;

Response 7: In page 17, line 2, miR-766-5P/TRIM67 has been revised to miR-766-5p/TRIM67.

Response 8: We have added a definition for EVs on page 15, line 26.

Extracellular vesicles (EVs) are defined as a class of membranous vesicles that are released by cells to the extracellular matrix and play a key role in various physiological and pathological processes. According to the difference in their origin, size, content, and biological function, EVs can be roughly divided into three main subtypes—microbubbles, exosomes, and apoptotic bodies.

Response 9: Thank you for your nice advice. We have added the labels of oxaliplatin-resistant CRC cells and donor/receptor cells in the lower right and upper left cells in figure2, respectively. Meantime, we highlight the activated (↑) or repressed (⊥) of ncRNAs on apoptosis and autophagy with red labels.

Response 10 - 12: According to your nice suggestions, “assession” was revised to “evaluation.” on page 6, line 36; “to in parental” was revised to “to parental.” on page 12, line 19; “amongst” was revised to “and.” on page 15, line 43.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This review well summarizes the role of ncRNAs in oxaliplatin resistance on CRC. The only issue, it is strongly suggested that the analysis of ncRNA using liquid biopsy consists of a separate paragraph. Please refer to the following paper (Int J Mol Sci. 2020 Feb; 21(4): 1398).

Response: Thank you for your positive comments and valuable suggestions to improve the quality of our manuscript. According to your nice suggestions, we have added a separate paragraph about exosomal ncRNAs as potential liquid biopsy biomarkers and cited the paper (Int J Mol Sci. 2020 Feb; 21(4): 1398).