



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 113524

Title: Exosomal miR-191 promotes colorectal cancer progression by inducing M2 macrophage polarization and inhibiting ferroptosis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 02909329

Position: Peer Reviewer

Academic degree and professional title: PhD

Reviewer’s Country/Territory: China

Author’s Country/Territory: China

Manuscript submission date: 2025-08-27

Reviewer chosen by: AI Editor

Reviewer accepted review: 2025-08-29 12:48

Reviewer performed review: 2025-08-31 13:55

Review time: 2 Days and 1 Hour

Content to be reviewed	<p>Does the manuscript’s content fall within the scope of the journal? Yes</p> <p>Is there any Key Word that is not included in the manuscript title? Yes</p> <p>Do authors’ affiliations correspond to the content of the manuscript? Yes</p> <p>Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes</p> <p>Are the Key Words complete? Yes</p>
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Is the content of the Introduction adequate? **Yes**
Is the content of the Materials and Methods complete?
Yes
Is the description of the experiments clear and
complete? **Yes**
Are the experimental data presented in the
manuscript's biostatistics content reliable? **Yes**
Are the experimental data of the Results true and
reliable? **Yes**
Are the quality and resolution of the images up to
standard? **Yes**
Do the selection and design of the figures and tables
follow the principles of necessity and clarity? **Yes**
Is there any duplication between various parts of the
manuscript and between the main text and the content
presented in the figures and tables? **No**
Are the figures and tables numbered consecutively in
the order in which they appear in the manuscript? **Yes**
Is the content of the Discussion reasonable? **Yes**
Is the Conclusion reasonable? **Yes**
Are all references necessary and reasonable? **Yes**
Do authors omit important references? **No**
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Do authors only cite their own earlier publications? **No**
Is the manuscript's text correct, concise, and clear? **Yes**
Will the manuscript's content be of interest to readers?
Yes
Are additional experiments needed for the study? **No**
Does the research scope comply with ethics? **Yes**



Scientific quality	Grade A (Excellent)
Novelty of this manuscript	Grade A (Excellent)
Creativity or innovation of this manuscript	Grade A (Excellent)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Accept
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

Manuscript Review

Title: Inhibition of exosomal miR-191 inhibits M2 polarization of macrophages, accelerates ferroptosis and apoptosis of colorectal cancer cells by inducing ferroptosis in macrophages

Authors: Qingyun Zhao, Shoujiang Wei

General Comments:

This manuscript presents a well-structured and comprehensive study investigating the



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role of exosomal miR-191 in colorectal cancer (CRC) through modulation of macrophage polarization and ferroptosis. The topic is timely and relevant, with potential implications for CRC immunotherapy. The experiments are logically designed and support the conclusions. However, several issues need to be resolved.

Minor Comments:

1.The title is descriptive but overly long and slightly repetitive. Consider simplifying to:
“Exosomal miR-191 promotes colorectal cancer progression by inducing M2 macrophage polarization and inhibiting ferroptosis”

Or:“Inhibition of exosomal miR-191 suppresses CRC growth via macrophage ferroptosis and M2 polarization”*

2.The abstract should briefly mention the methods used for in vivo experiments (e.g., nude mouse model, Erastin treatment).

3.The conclusion could be strengthened by explicitly stating the novelty: e.g., *“This study reveals a novel mechanism by which exosomal miR-191 modulates the tumor microenvironment...”*

4.The introduction is well-written and provides sufficient background. However, it would benefit from a clearer statement of the research gap and hypothesis at the end.

5.Include scale bars in H&E images

6.The discussion is thorough but could be more focused on the novelty of the findings – specifically, the dual role of exosomal miR-191 in regulating both macrophage polarization and ferroptosis.

7.The Western blot results require quantitative statistical analysis.

8.Some sentences are awkwardly phrased. Consider professional editing for fluency.

Example: “We succeeded in obtaining exosomes derived from CRC cells” → “We successfully isolated exosomes from CRC cells”

9.Use either “miR-191” or “microRNA-191” consistently throughout.



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This study provides valuable insights into the role of exosomal miR-191 in CRC progression via macrophage modulation and ferroptosis. The findings are novel and supported by robust in vitro and in vivo data. With minor revisions, particularly in methodological details and language polishing, this manuscript will be suitable for publication in a good oncology journal.



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Peer-review model: Single blind

Reviewer’s code: 08578713

Position: Peer Reviewer

Academic degree and professional title: Assistant Professor

Reviewer’s Country/Territory: China

Author’s Country/Territory: China

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Will the manuscript's content be of interest to readers?
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Are additional experiments needed for the study? **Yes**
Does the research scope comply with ethics? **Yes**



Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade A (Excellent)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

Dear editors and authors:

I have carefully reviewed the manuscript entitled "Inhibition of exosomal miR-191 inhibits M2 polarization of macrophages, accelerates ferroptosis and apoptosis of colorectal cancer cells by inducing ferroptosis in macrophages". This study uncovers the mechanism by which exosomal miR-191 from colorectal cancer promotes tumor progression by inducing M2 polarization of macrophages, offering a novel therapeutic target and experimental basis for immunotherapy in colorectal cancer.



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However, several aspects of the manuscript require clarification, and revision to strengthen the conclusions and enhance the overall clarity and impact. Here are my detailed comments and suggestions for improvement.

1. It is widely recognized that microRNAs (miRNAs) direct the RNA-induced silencing complex (RISC) to target mRNAs through imperfect base-pairing between their seed region (nucleotides 2-8 at the 5' end) and complementary sequences in the 3' untranslated region (3' UTR), thereby repressing translation or accelerating mRNA degradation and ultimately reducing protein output. Multiple studies have demonstrated oncogenic up-regulation of miR-191 in various malignancies, including colorectal cancer (CRC); nevertheless, its biological roles and molecular mechanisms within CRC-derived exosomes remain elusive. Consequently, the authors selected miR-191 as the focus of the present investigation. However, no systematic target prediction or functional validation of miR-191 regulated mRNAs was performed. The authors are requested to provide the specific rationale for omitting these analyses.

2. In the animal experiments, the authors administered exosomal miR-191 together with Erastin to mice, yet they did not employ miR-191-loss of function approaches (e.g., knock-down) or the ferroptosis inhibitor ferrostatin-1 for validation. We recommend establishing an miR-191 knock-down model to further clarify the functional role of miR-191 in vivo.

3. The flow-cytometry plot shown in Figure 3B is not readily matched to the corresponding bar graph. Please revise it to the same format used in Figure 4A and Figure 5B, or add the grouping and treatment labels to the flow cytometry result graph.



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Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

This manuscript investigates the role of exosomal miR-191 in CRC, focusing on its ability to promote M2 macrophage polarization and its subsequent effects on ferroptosis, apoptosis, and tumor growth. The study is well-structured, with a clear rationale, comprehensive experimental design, and both in vitro and in vivo validation. The findings suggest that targeting exosomal miR-191 could be a promising therapeutic strategy for CRC by modulating macrophage polarization and ferroptosis. The manuscript is generally well-written, though some revisions are recommended to



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strengthen clarity, statistical reporting, and methodological details.

-The methods section is detailed but could benefit from better organization. However, some key details are missing. Please specify the exact concentrations and durations for exosome treatment in co-culture experiments. Also, provide catalog numbers for key reagents (antibodies, ELISA kits) to enhance reproducibility.

-In the discussion section, limitations of the study are necessary. The study lacks validation in patient-derived samples or clinical data, which is acceptable for a mechanistic study but could be noted as a limitation.

-Some pictures lack scale bar, such as Figure 3D, Figure 5D, Figure 6A and Figure 6D. It is suggested that they be improved.

-The results of Western blotting should be quantitatively statistically analyzed; otherwise, it will be difficult to accurately explain the results of this experiment.