



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 116016

Title: Peroxiredoxin 1 as a novel pyroptosis inducer in colorectal cancer: insights and future directions

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05399987

Position: Peer Reviewer

Academic degree and professional title: Academic Fellow, MD, Post Doctoral Researcher

Reviewer’s Country/Territory: United States

Author’s Country/Territory: China

Manuscript submission date: 2025-10-30

Reviewer chosen by: Hong-Xin Jiang

Reviewer accepted review: 2025-11-20 14:01

Reviewer performed review: 2025-11-21 00:21

Review time: 10 Hours

<p>Content to be reviewed</p>	<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>
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Are the Key Words complete? **Yes**

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? **Yes**

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? **Yes**

Are all references related to the topic of the
manuscript? **Yes**

Do authors only cite their own earlier publications? **Yes**

Will the manuscript's content be of interest to readers?
Yes

Is the manuscript's text correct, concise, and clear? **Yes**

Are additional experiments needed for the study? **Yes**



	Does the research scope comply with ethics? Yes
Scientific quality	Grade A (Excellent)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
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	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

1. The role of Prdx1 in the existing literature remains controversial. Some studies suggest that its high expression is associated with advanced CRC stage, lymph node metastasis, and poor prognosis, while others have found that it promotes chemotherapy resistance by scavenging 5-FU-induced ROS. Although this article mentions these conflicting findings, it does not delve into their underlying causes. It is recommended to supplement the discussion by incorporating stratified analysis of Prdx1's pro-pyroptotic



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or pro-survival roles based on tumor stage/metastatic status (e.g., in early-stage CRC, Prdx1 may maintain homeostasis through antioxidant activity, whereas in advanced stages, it may promote drug resistance by clearing chemotherapy-induced ROS). Additionally, proposing a hypothesis that “the dual functions of Prdx1 depend on microenvironmental signals (such as oxidative stress levels and inflammatory cytokine concentrations)” could provide conceptual guidance for future research designs—such as using single-cell sequencing to characterize the molecular features of Prdx1-high-expressing cells.

2. Although the study by He et al. confirmed that rPrdx1 activates the NLRP3/GSDMD pathway, it did not exclude other potential mechanisms. While this article emphasizes the canonical nature of this pathway, it does not discuss the target specificity of rPrdx1. It is recommended to supplement the discussion by proposing the experimental need to “validate either the direct interaction between rPrdx1 and NLRP3 or its indirect activation via the ROS-TXNIP-NLRP3 axis.” The potential involvement of other pyroptosis-executing proteins should also be discussed. Furthermore, it is suggested that subsequent studies employ gene knockout approaches to establish the necessity of this pathway.

3. The proposed “rPrdx1 combination therapy” strategy is logically sound but lacks specific parameter design. For instance, what are the dosage and cycle of anti-PD-1 in synergy with rPrdx1? Does the reduction in the IC50 of chemotherapy drugs occur through a pyroptosis-dependent pathway? It is recommended to supplement the discussion by clarifying “the concentration ranges and treatment durations (e.g., synchronous vs. sequential administration) of combination drugs in vitro,” and in vivo models, including “multiple comparison groups such as anti-PD-1 or chemotherapy alone, rPrdx1 combined with anti-PD-1/chemotherapy, and the triple combination group” to verify the specificity of the synergistic effect. Potential side effects (e.g.,



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whether high doses of rPrdx1 might induce systemic inflammation) should also be discussed, along with optimization strategies such as “targeted delivery of rPrdx1 to the tumor site via nanoparticle carriers.”

As a high-quality Letter, this article meets the high standards of commentary-style publications, particularly excelling in terms of topic selection, literature integration, and translational insights. Addressing the above aspects would further enhance its guiding significance for the field and provide a more systematic theoretical foundation for pyroptosis-targeted therapies in CRC.



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Title: Peroxiredoxin 1 as a novel pyroptosis inducer in colorectal cancer: insights and future directions

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 06514904

Position: Peer Reviewer

Academic degree and professional title: PhD, Research Fellow

Reviewer’s Country/Territory: China

Author’s Country/Territory: China

Manuscript submission date: 2025-10-30

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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?

Not Applicable

Is the description of the experiments clear and complete? **Not Applicable**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable**

Are the experimental data of the Results true and reliable? **Not Applicable**

Are the quality and resolution of the images up to standard? **Not Applicable**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Not Applicable**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Not Applicable**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Not Applicable**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **No**

Do authors omit important references? **Yes**

Are all references related to the topic of the manuscript? **No**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **No**

Will the manuscript's content be of interest to readers?



	Yes 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 C (Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
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?	No
Conclusion	Major 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 letter comments on He et al.'s study (World J Gastroenterol 2025; 31(36): 111557) investigating Peroxiredoxin 1 (Prdx1) in colorectal cancer (CRC). He et al. demonstrated via 60 paired clinical samples, in vitro experiments (RKO, SW480, HCT116 cells), and subcutaneous xenograft models that Prdx1 mRNA/protein is overexpressed in CRC,



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while recombinant Prdx1 (rPrdx1) inhibits CRC malignant behaviors by activating the NLRP3/Caspase-1/GSDMD pathway to induce pyroptosis, thereby suppressing xenograft growth. However, there are still some aspects that can be improved.

1.The original study and your letter indicate Prdx1 is overexpressed in CRC tissues but exerts anti-tumor effects via inducing pyroptosis, which seems contradictory to its reported pro-tumor roles (e.g., mediating 5-FU resistance). Could you elaborate on the potential cell context-dependent mechanisms underlying this dual role of Prdx1 in CRC?

2.He et al. used recombinant Prdx1 (rPrdx1) to induce pyroptosis, but the source and post-translational modifications of rPrdx1 were not specified. Do different sources or modifications of rPrdx1 affect its ability to activate the NLRP3/GSDMD pathway, and how does this align with endogenous Prdx1 functions in CRC cells?

3.The NLRP3/GSDMD pathway is involved in both physiological inflammation and pathological processes. Did the original study or your preliminary data evaluate potential off-target inflammatory risks of rPrdx1 (e.g., systemic inflammation or tissue damage in normal organs)? If not, what strategies would you propose to assess its safety profile?

4.The original study demonstrated rPrdx1 enhances oxaliplatin chemosensitivity, but the underlying mechanism (e.g., crosstalk between pyroptosis and DNA damage repair pathways) was not clarified. Could you elaborate on how rPrdx1 modulates chemotherapeutic drug sensitivity beyond direct pyroptosis induction?

5.Please cite the following reference to further enrich the content and enhance the comprehensiveness of the article.

(1)Leukocyte immunoglobulin-like receptor B4: A keystone in immune modulation and therapeutic target in cancer and beyond. <https://doi.org/10.1002/cai2.153>

(2)Organoid co-culture models of the tumor microenvironment promote precision medicine. <https://doi.org/10.1002/cai2.101>



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(3)3D models, cancer, drug development, translational research, tumor microenvironment elements .<https://doi.org/10.1002/cai2.102>



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 116016

Title: Peroxiredoxin 1 as a novel pyroptosis inducer in colorectal cancer: insights and future directions

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05399987

Position: Peer Reviewer

Academic degree and professional title: Academic Fellow, MD, Post Doctoral Researcher

Reviewer’s Country/Territory: United States

Author’s Country/Territory: China

Manuscript submission date: 2025-10-30

Reviewer chosen by: Ming Fan

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Review time: 1 Hour

<p>Content to be reviewed</p>	<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>
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Are the Key Words complete? **Yes**

Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?

Not Applicable

Is the description of the experiments clear and complete? **Not Applicable**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable**

Are the experimental data of the Results true and reliable? **Not Applicable**

Are the quality and resolution of the images up to standard? **Not Applicable**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Not Applicable**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Not Applicable**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Not Applicable**

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**

Are all references related to the topic of the manuscript? **Yes**

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? Not Applicable
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 A (Excellent)
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
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

No others.



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Name of journal: *World Journal of Gastroenterology*

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Position: Peer Reviewer

Academic degree and professional title: PhD, Research Fellow

Reviewer’s Country/Territory: China

Author’s Country/Territory: China

Manuscript submission date: 2025-10-30

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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? No</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**
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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**
Are all references related to the topic of the
manuscript? **Yes**
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 B (Very good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
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
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

All issues have been addressed.