

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 87228

Title: Thioridazine reverses trastuzumab resistance in HER-2-positive gastric cancer by inhibiting Skp2-mediated aerobic glycolysis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03731081

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Russia

Author's Country/Territory: China

Manuscript submission date: 2023-09-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-09-17 21:30

Reviewer performed review: 2023-09-20 14:11

Review time: 2 Days and 16 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors presented an interesting manuscript on the topic of increasing the effectiveness of drug therapy for resistant gastric cancer. They described in detail the molecular genetic mechanisms of the development of resistance of gastric cancer cells as a result of exposure to trastuzumab. The level of Skp2 has a strong direct correlation with the level of resistance. As shown thioridazine significantly inhibited cell viability and restored the sensitivity of trastuzumab to gastric cancer cells. Their data demonstrate that thioridazine enhances the anti-tumor activities of trastuzumab in vitro as well as in vivo. I believe that it is now necessary to begin clinical trials of thioridazine in oncological practice. The manuscript is recommended for publication in the World Journal of Gastroenterology.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03769068

Position: Editorial Board

Academic degree: PhD

Professional title: Adjunct Professor, Professor

Reviewer's Country/Territory: Brazil

Author's Country/Territory: China

Manuscript submission date: 2023-09-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-10-03 11:27

Reviewer performed review: 2023-10-07 19:10

Review time: 4 Days and 7 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
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Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I have now reviewed your paper and recognize the importance of your research question. Manuscript NO. 87228 aimed to identify a clinical drug capable of inhibiting Skp2 and reversing trastuzumab resistance in HER-2-positive gastric cancer.

ABSTRACT: [The "BACKGROUND" subsection is well-written.] [The "AIM" subsection should be more concise and appealing to the reader.] [Consider expanding upon the "METHODS" subsection to provide a more detailed account of the procedures used to evaluate the impact of thioridazine, trastuzumab, and lapatinib on resistant cells. This could involve specifying the dosages administered, the duration of treatments, and the specific outcome measures that were assessed. Additionally, it's important to ensure that the METHODS subsection remains distinct from the RESULTS subsection to maintain clarity in the manuscript.] [The "CONCLUSION" subsection requires improvement to emphasize the significance of the results within the framework of a thorough critical analysis, with a specific focus on the clinical relevance of the findings and a discussion of the study's inherent limitations.] INTRODUCTION: [The "INTRODUCTION" section effectively provides context for the reader and serves as a strong point of the manuscript.]



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METHODS: The "MATERIALS AND METHODS" section provides a comprehensive description that effectively supports the results and conclusions presented in the preceding sections. **RESULTS:** The "RESULTS" section furnishes ample experimental evidence, enabling the formulation of intriguing and promising scientific conclusions regarding the role of Thioridazine in mitigating trastuzumab resistance in HER-2 positive gastric cancer. **DISCUSSION:** In the "DISCUSSION" section, it is essential that the findings are expounded upon through a systematic theoretical analysis of the results. Additionally, I recommend that the authors delve into future prospects for their research, expanding on potential avenues for continued investigation.