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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 84682

Title: 18β-glycyrrhetinic acid promotes gastric cancer cell autophagy and inhibits proliferation by regulating miR-328-3p/signal transducer and activator of transcription-3

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03270609
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Professor
Reviewer's Country/Territory: Russia
Author's Country/Territory: China

Manuscript submission date: 2023-03-28

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-04-17 14:12

Reviewer performed review: 2023-04-25 19:44

Review time: 8 Days and 5 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty

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Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation
Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Review of manuscript 84682 "18β-glycyrrhetinic acid promotes gastric cancer cell autophagy and inhibits proliferation by regulating miR-328-3p/signal transducer and activator of transcription-3" Gastric cancer remains a serious medical and social problem, which is associated with the diagnosis of gastric cancer in the late stages, poor treatment results and high mortality. In this regard, the search for new drugs that improve the results of gastric cancer treatment remains relevant. The authors demonstrate that 18β-glycyrrhetinic acid, which is an important bioactive component of glycyrrhiza liquorice, has a number of properties that allow it to be considered as a new promising drug in the prevention and treatment of gastric cancer. Despite the relevance of the study, a number of remarks should be noted: Abstract 1. It seems that this part of the manuscript can be shortened by removing excessively detailed information. For example, in the "METHODS" section, simply list the databases that were used for

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bioinformatics analysis. In the "RESULTS" section, it seems redundant to indicate the methods, since they are already given in the corresponding section. 2. It is necessary to correct the sentence “The effect of flow cytometry on cell cycle and apoptosis was detected”, since flow cytometry cannot influence the cell cycle and apoptosis. 3. In the "Results" section, it is not clear which groups are in question (NC and Vector groups). Explain this in the METHODS section or reformulate the text. It is also necessary to give a transcript of the abbreviation "NC" INTRODUCTION 1. The statement “5-year survival rate is low due to serious toxic and side effects (hair loss, bone marrow transplantation, gastrointestinal reactions, etc.) is incorrect. The low 5-year survival rate is due to late diagnosis and not to the toxic effects of chemotherapy. 2. The last paragraph of this section seems out of place in INTRODUCTION. It is more logical to formulate the purpose of this study here. MATERIALS AND METHODS 1. More logical to present cell culture data first 2. It seems that when presenting the "Methods" the authors sometimes used the texts of the instructions not quite successfully, without changing them according to the style of presenting the information. 3. Not entirely correct description of the sections "Hematoxylin-Eosin (HE) staining" and "Immunohistochemical staining". For example, the sections are first cut and then fixed and dehydrated. It is unclear why, with this coloring, "bake the slices at 65℃ for 4.5 h" (is this a mistake?). For IHC staining, the duration of incubation with primary antibodies is not clear, the names of antibodies and their manufacturers, as well as dilutions are not given. It is not clear which imaging system was used. DISCUSSION 1. According to the results of the study, 18β-GRA causes an increase in miR-328-3p expression, and overexpression of miR-328-3p reduces the survival of gastric cancer cells, colony formation, stops the cell cycle and promotes apoptosis of tumor cells. However, according to the Kaplan-Meier Plotter online database and the data Zhe et al. an increase in miR-328-3p expression is associated with the progression of gastric cancer and a

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decrease in patient survival. How can the authors explain this contradiction? 2. The DISCUSSION section, on the one hand, contains a lot of information duplicating the RESULTS section, and on the other hand, a lot of information without references to the relevant literature. 3. It seems that some of the information given in the "INTRODUCTION" is more logical to transfer to the "DISCUSSION" General remarks 1. The text of the manuscript contains a number of stylistic inaccuracies and incorrect expressions.

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Academic degree: FRCS (Ed), MD, MS
Professional title: Professor
Reviewer's Country/Territory: India
Author's Country/Territory: China

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Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The study conducted by Yang et al on the topic "18β-glycyrrhetinic acid promotes gastric cancer cell autophagy and inhibits proliferation by regulating miR-328-3p/signal transducer and activator of transcription-3" to study the active ingredient of licorice, 18β-glycyrrhetinic acid (18β-GRA) as a variety of pharmacological effects for clinical prevention and treatment of GC. It is a well thought of study and various techniques like Whole Transcriptomic, flow cytometry, mouse transplanted tumor model, hematoxylin-eosin staining, immunohistochemistry, etc. Have been used to prove the hypothesis. It has been concluded that the 18β-GRA promotes the synthesis of auto phagosomes and inhibits GC cell proliferation by regulating the miR-328-3p/STAT3 signalling pathway. The study has been conducted in a well-designed manner and all the techniques involved have been standardised well. The study is accepted for publication, However, there are a few of the queries which need to be addressed by the

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authors which are mentioned below. 1. The main focus of this study is to target miR-328-3p/STAT3 pathway to inhibit cell proliferation, arrest cell cycle and promote cell apoptosis. What are the possibilities that other pathways would still lead to tumor progression? 2. Though 18B GRA resulted in over expression of miR-328-3p and resulted in inhibition of cell proliferation, what is the probability that other MiRs were not involved in the inhibition process? 3. Could there be a role of some pro-inflammatory cytokines especially (TNF alpha/IL1B/IL6 getting down regulated also and causing shrinking of tumors.