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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 82809

Title: Modernising autism spectrum disorder model engineering and treatment via CRISPR-Cas9: A gene reprogramming approach

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00503182
Position: Editorial Board
Academic degree: MBChB, MD, PhD
Professional title: Full Professor, Professor, Statistician
Reviewer's Country/Territory: Egypt
Author's Country/Territory: India

Manuscript submission date: 2022-12-28

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-01-10 08:32

Reviewer performed review: 2023-01-10 10:16

Review time: 1 Hour

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

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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) [Y] Accept (General priority) [ ] 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

I have minor edits in the article (see attached)

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Title: Modernising autism spectrum disorder model engineering and treatment via CRISPR-Cas9: A gene reprogramming approach

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00573592
Position: Peer Reviewer
Academic degree: PhD

Professional title: Senior Scientist

Reviewer's Country/Territory: Italy

Author's Country/Territory: India

Manuscript submission date: 2022-12-28

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-01-12 11:48

Reviewer performed review: 2023-01-16 10:32

Review time: 3 Days and 22 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] 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
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[Y] Grade A: Excellent [ ] 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) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Very interesting and informative review manuscript on an emerging topic in ASD research. The manuscript is well, concisely, and coherently organized and presented. Figures help in understanding the text. - In the paragraph "CRISPR-Cas9 engineered organoids of ASD", authors could better address the lack of suitable ASD models. - In the Conclusions, more limitations on the use of CRISPR technology in clinical trials could be added. - Check acronymus frist time used. - Check English spelling.

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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 82809

Title: Modernising autism spectrum disorder model engineering and treatment via CRISPR-Cas9: A gene reprogramming approach

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03664074
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: India

Manuscript submission date: 2022-12-28

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-01-10 05:22

Reviewer performed review: 2023-01-20 04:00

Review time: 9 Days and 22 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 [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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

SPECIFIC COMMENTS TO AUTHORS

This manuscript has reviewed the establishment and treatment of autism spectrum disorder (ASD) model by CRISPR-Cas9 system. The major problem is that these two subject presentation in the title is not proper, and author should show their inner connections in this manuscript. Maybe author can demonstrate the activation and inhibition functions of CRISPR-Cas9 system for the same object via different aspects. In addition, author need provide the similar genes including SHANK, CHD8, MECP2, et al between the establishment and treatment fields of ASD. The other problems are listed as following: 1 The structure of this manuscript seems difficult to read. The introduction is too short to hard achieve the content of full manuscript. But the descriptions of Genetic architecture of ASD as well as structure and function of CRISPR-Cas9 are too long to mislead the theme of this manuscript. 2 The related genes of figure 1 should be simplified because they are repeated in table1. And CRISPR-Cas9-based therapeutic strategies and potential targets genes should be added in the other table. 3 The grammar of this manuscript should be corrected, especially in the presentation of singular and plural, use of conjunctions.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 82809

Title: Modernising autism spectrum disorder model engineering and treatment via CRISPR-Cas9: A gene reprogramming approach

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03664074
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: India

Manuscript submission date: 2022-12-28

Reviewer chosen by: Li Li

Reviewer accepted review: 2023-02-24 13:41

Reviewer performed review: 2023-02-26 02:45

Review time: 1 Day and 13 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The revision manuscript of title "Modernising autism spectrum disorder model engineering and treatment via CRISPR-Cas9: A gene reprogramming approach" has been progressed better than previous manuscript. But the main problem of two subject presentation in the title always exists. The best solution is suggested to change the title into "Modernising autism spectrum disorder model with engineered applications via CRISPR-Cas9: A gene reprogramming approach" of this revised manuscript. Some sentences must be corrected as followings: 1 Plethora of studies is being conducted worldwide using several targets in cultured cells or in animal models, however, their extrapolation to the patients is yet to achieve.(page 15) 2 Among these gnomic editing tools, CRISPR-Cas9 is being considered the most extensive and effective, with the advantages of low mutation rate, high target efficiency and moreover, the cost of its development is very low. (page 16) 3 CRISP has enabled the creation of models that reproduce exactly the same causal mutations identified in patients, which has made it possible to determine an appropriate and disease-specific drug therapy. (page 16) 4 Thus, creating a reliable model, establishing a causal factor and representing all the characteristics of the disease is difficult. (page 16)