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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 39689

**Title:** Daikenchuto (Da-Jian-Zhong-Tang) ameliorates intestinal fibrosis by activating myofibroblast TRP Y channel

**Reviewer's code:** 04213385

**Reviewer's country:** Spain

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2018-05-21

**Date reviewed:** 2018-05-25

**Review time:** 3 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

The manuscript titled Daikenchuto (Da-Jian-Zhong-Tang) ameliorates intestinal fibrosis by activating myofibroblast TRPA1 channel described the properties of DKK in colonic fibrosis through TRPA1. The title reflect the main subject of the manuscript. The abstract



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summarize the work described but the conclusion is generic and has to be more concise. The key words reflect the focus of the manuscript. The background describe in a simple way the postoperative use of DKK. The Methods are adequate. However the authors have to explain how they measure the optical density of the blue-stained (with image J?). That item is not explained in the reference 18. The Results and experiments are well designed and improve knowledge. WB from Fig 2A WT can be improved. The authors interpret the findings adequately and the findings have relevance and the manuscript discuss the applicability. However, failed to explain what the pattern of treatment with DKK is. The illustrations and biostatistics are well, I haven't seen any errors. However, the genes of animals are named in italics and lowercase.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- The same title
- Duplicate publication
- Plagiarism
- No

##### ***BPG Search:***

- The same title
- Duplicate publication
- Plagiarism
- No



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 39689

**Title:** Daikenchuto (Da-Jian-Zhong-Tang) ameliorates intestinal fibrosis by activating myofibroblast TRP Y channel

**Reviewer's code:** 03538272

**Reviewer's country:** Australia

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2018-05-23

**Date reviewed:** 2018-05-28

**Review time:** 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

Hiraishi et al present a series of experiments in which they demonstrate that topical DKT treatment induced calcium influx in intestinal myofibroblasts, which appeared to be related to TRPA1 channel activation and upregulation. It was also shown that TRPA1 is



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increased in segments of stenosed bowel in specimens from patients with Crohn's disease and in the presence of collagen, suggesting a potential role in negative feedback for collagen production. The paper is well written with appropriate conclusions, and it is certainly an area of interest given the lack of anti-fibrotic therapies. I have a few suggestions: 1. You have not discussed any potential limitations of the techniques used in your discussion. These should be identified and discussed. Minor comments: - Figure 9 is not referenced in the text - it could be referenced in the introduction to improve understanding of the pathways that are being evaluated - For the statistics section "p" value should be in lower case. - For the results section "Chronic TNBS fibrosis model of TRPA1-KO mice", the first paragraph can be moved to the TNBS model section in methods. - consider changing the wording of cold sensation to cold sensitivity in the discussion - Do you believe the fact that all patients with resection specimens were on anti-TNF therapy impacted your findings?

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

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- No

##### ***BPG Search:***

- The same title
- Duplicate publication
- Plagiarism
- No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 39689

**Title:** Daikenchuto (Da-Jian-Zhong-Tang) ameliorates intestinal fibrosis by activating myofibroblast TRP Y channel

**Reviewer's code:** 03316915

**Reviewer's country:** United States

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2018-05-23

**Date reviewed:** 2018-06-04

**Review time:** 12 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This reviewer is very impressed with the study design, performance of the experiments and the way the data were collected, analyzed and presented. The effects of the well known Chinese medicine DKT on the expression and activation of the TRPA1 channel is



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well investigated in this study. The data clearly demonstrates DKT suppresses intestinal fibrosis which should be a step forward toward reducing intestinal inflammation. The technical design for running PCR, and collecting histopathology data were adequate. The manuscript is written concisely and nicely. The discussion is a bit long but it seems it was necessary to address all the data. Fig 9 (the Diagram) illustrates the proposed mechanism and it is well done. I have no reservations about this manuscript. I did not invest time on typos and minor issues.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

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- Plagiarism
- No

##### ***BPG Search:***

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- Duplicate publication
- Plagiarism
- No