



## PEER-REVIEW REPORT

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

**Manuscript NO:** 85026

**Title:** Bile acids and their receptors: Potential therapeutic targets in inflammatory bowel disease

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 02446498

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-04-08

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-04-26 07:23

**Reviewer performed review:** 2023-05-04 10:13

**Review time:** 8 Days and 2 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<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
<b>Creativity or innovation of this manuscript</b>	<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



<b>Scientific significance of the conclusion in this manuscript</b>	<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
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

In this review manuscript, the authors summarize the recent findings about bile acids and their receptors in IBD. This is a well-written review paper. I have only minor comments.

1. There is no figure citation in the main text, although there are only citations for Table 2. Please indicate citations for figures and Table 1 in the main text.
2. The section "2.2 Bile acid metabolism in the intestine", 1st paragraph. "Changes in the intestinal epithelium of individuals with IBD decrease the reabsorption of bile acids by ASBT and increase the number of bile acids discharged in teh feces." Is this phenotype related to changed nuclear recdceptor function(s)?
3. The section "2.2 Bile acid metabolism in the intestine", 3rd paragraph. "This alteration reduces depolymerization and 7 $\alpha$ -dehydroxylation, strongly decreasing the conversion capacity of the microbiota, resulting in a decrease in SBAs (DCA, LCA) and an elevation in primary and conjugated bile acids (CA, CDCA, TCA, GCA)." How does this phenotype influence receptor functions?
4. The section "3.2 ROR $\gamma$ t" "Interestingly, similar to isolithocholic acid (isoLCA), isoLCA can also de-suppress Th17 cells differentiation by inhibiting ROR $\gamma$ t." This sentence does not make sense. Is "similar to isoLCA" correct? Is "de-suppress"



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correct? IsoLCA suppresses Th17 cells differentiation, doesn't it? 5. The section "4.3 UDCA". Please discuss what receptors are involved in the UDCA activity.



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**Reviewer's code:** 02620104

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Spain

**Author's Country/Territory:** China

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<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
<b>Creativity or innovation of this manuscript</b>	<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



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

**SPECIFIC COMMENTS TO AUTHORS**

This review on the latest advances concerning the role of bile acids and their receptors as potential therapeutic targets in inflammatory bowel disease. The manuscript is well written and coherently organized. While I recommend this review to be published, there are issues that need to be addressed:

1. Table 1 is not referred in the body of the text.
2. The text does not refer to the Figures. The authors must insert references to the Figures in the appropriate place in the text.
3. “inflammatory bowel disease” is not contracted to its abbreviation IBD on several occasions.
4. Rewrite following sentences:
  - .-Sentence in “2.1. Bile acid in the liver” when introducing HSD37.
  - .-First sentence in “2.2 Bile acid metabolism in the intestine” when mentioning “micellar micelles”.
  - .-“Interestingly, similar to isolithocholic acid (isoLCA), isoLCA can also...”
  - .-“The absence of Pak2 in Th17 cells Genetic deletion of Pak2 in Th17 cells decreases...”
  - .-“ ILC3 in intestinal draining lymph nodes expressed numerous significant class II histocompatibility complexes, according to a recent study (MHCIIIs).”
  - .-“Akagbosu” et al. -Akkermansia muciniphila.
  - .-“PXR and CAR have the typical modular nuclear receptor structure, which consists of a hinge, a DNA-binding



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domain (DBD), a ligand-binding domain, activation function 1 (AF-1), and activation function 2 (AF-2) (LBD).” 5. Suppress following sentences: .-“ROR $\gamma$ t is a main transcription factor for Th17 cells.” Before “In paradox,...” .-“Paneth cells, which are positioned at the base of small intestinal crypts, release -defensins and play a crucial role in regulating intestinal flora and preserving intestinal homeostasis” is repeated.