

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 59404

Title: A molecular overview of Progressive Familial Intrahepatic Cholestasis

Reviewer's code: 00742373

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2020-09-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-09-16 00:55

Reviewer performed review: 2020-09-16 12:29

Review time: 11 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 Grade E: Do not publish
Language quality	<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
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input 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 manuscript “A molecular overview of progressive familial intrahepatic cholestasis” reviewed ATP8B1、ABCB11、MDR3 genes causing progressive familial intrahepatic cholestasis (PFIC) type 1, type 2 and type 3, which are autosomal recessive disease. The authors also discussed the alterations in the NR1H4, TJP2, and MYO5B genes which have been reported linked with new phenotypes of PFIC type 4, type 5. It provided a brief overview of the molecular mechanism and clinical features associated with each type of PFIC. PFIC is a genetic disease affecting the bile secretion process of the hepatocytes due to alteration protein metabolism. It is necessary to understand the molecular alterations in this disease to elucidate new targets and pathways that could be focus of the new management in the future. This article reviewed the genes and their variations associated with PFIC. As well, while describing the clinical conditions, it reviewed the development of cholestasis condition and its pathways and mechanisms of the related genes. It will help readers updates the knowledge of molecular and mechanism of the disease and maybe help in the development of new models which could be potentially be used in the treatment method in the future. Suggestions for improvement:

- As a review, it is suggested to demonstrate which sources and the duration of years of literatures was researched.
- In the section of HOW TO STUDY PFIC, the authors mentioned pluripotent stem cell as a potential method in the treatment of PFIC. We only see a few sentences describing the possibility. Reviewer would like to suggest collect more studies involved in the cholestasis management, in animal models or human being. If there are more studies in this field, reviewer suggest describe as a separate section of pluripotent stem cell as a potential method in the treatment of PFIC.
- Figure 1 placed in the wrong place.
- Figure 1 and 2 seems too simple to demonstrate the PFIC diseases and their related genes, or the mechanism of bile acid production.
- Grammar improvement: capital spellings in the main text might need to



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correct pending on the journal requirements, such as: “Progressive Familial Intrahepatic Cholestasis.....” in abstract, core tip, last paragraph in page 5, second paragraph in page 8, conclusion.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 59404

Title: A molecular overview of Progressive Familial Intrahepatic Cholestasis

Reviewer's code: 03766000

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Assistant Professor, Research Assistant Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2020-09-11

Reviewer chosen by: Yue Yang (Quit in 2020)

Reviewer accepted review: 2020-09-16 00:09

Reviewer performed review: 2020-09-22 06:17

Review time: 6 Days and 6 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
Language quality	<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
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 checked="" type="checkbox"/> Yes <input 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

In this manuscript intitlled "A molecular overview of Progressive Familial Intrahepatic Cholestasis", Sriram Amirneni et al introduced and summarized the recent progress in the molecular characteristics of the five types of Progressive Familial Intrahepatic Cholestasis (PFIC1, PFIC2, PFIC3, PFIC4, and PFIC5). I have two relatively minor concerns: (1) A table is wanted to summarize the clinical features, clinical outcomes, gene mutation information, diagnosis of different types of PFIC. (2) A molecular mechanism figure is also wanted to illustrate the molecular characteristic of PFIC.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 59404

Title: A molecular overview of Progressive Familial Intrahepatic Cholestasis

Reviewer's code: 00742373

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2020-09-11

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2020-11-09 10:49

Reviewer performed review: 2020-11-09 11:07

Review time: 1 Hour

Scientific quality	<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
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
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 author revised the whole article carefully according to the reviewers' suggestions.



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All the questions from reviewers were carefully answered and an improvement have been made or explained. The answer and improvement are logical and meaningful. Reviewer agree the changes in the manuscript.