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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology
ESPS manuscript NO: 26262
Title: Cholesterol metabolism in the setting of cholestatic liver disease and liver transplantation: From molecular mechanisms to clinical implications
Reviewer's code: 00188499
Reviewer's country: Taiwan
Science editor: Jing Yu
Date sent for review: 2016-04-06 16:45
Date reviewed: 2016-04-10 14:33

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[Y] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This manuscript described that the liver plays a key role in cholesterol metabolism. Cholestatic liver disease induces alterations in cholesterol metabolism (e.g. lipoprotein X), which may interfere with cardiovascular risk assessment; apoprotein B-100 measurement may be of help. Cholesterol precursor sterols, diet-derived plant sterols, and liver-synthesized derivate of cholesterol, cholestanol, may provide a better picture of cholesterol metabolism in cholestasis. Some concerns: 1. Page 4 line 12: it is not clear description of "to reduce reduced ezetimibe effect" I can not see that in the text? 2. Page 4 line 16: …"and low cholesterol levels".. seems not correct? 3. Page 6 lines 5-8 is not easy to read? What is the (OMIM #607330)? It should be described more clearly of the "cholesterol". Is it the cause or result of the congenital anomalies. 4. Page 8 lines 11-12: the description can not be clearly seen in the Figure 1. Such as the "oxidizes the precursor squalene to lanosterol" "inhibited by statins"… where should be the "squalene to lanosterol" and "statin" role? 5. Page 9 line 1 and Figure 2: SREBP-2 in on the ER not in the Golgi? The flow from ER to Golgi should be clearer for readers' reading. 6. Page 9 lines 11-15: "cholesterol esters" is not found in the Figure 1? VLDL to IDL to LDL is not clear

in the Figure 1. "the enzymes lipoprotein lipase" not clear in Figure 1. 7. Page 13 lines 19-20 is not clear in Figure 4; …." to serum total"? 8. Page 14 line 18: "associated with reduced post-LT survival" needs revision. Is this for graft or patient survival? Is this contrast to the description in page 11 lines 5-6 "serum cholesterol and lipoprotein measurements do not mirror changes in cholesterol metabolism"? 9. Some references are needed, such as in page 15 line 16, line 25? 10. Page 16 line 10: it needs the more detail description of the apo B-100 in diabetes and insulin resistance. How many risks of what? Insulin sensitive and insulin resistance? 11. The abbreviation word should have a full description when appeared at first time even in text or figures such as ABCG5/G8 etc. 12. If the middle rectangle, in Figure 3, can be expressed as a liver exterior will be better for reading.

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ESPS PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
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		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This review summarizes changes in cholesterol homeostasis and metabolism in the context of liver transplantation. The review also highlights the difficulties associated with the determination of LDL and cholesterol levels in the serum of patients with cholestatic liver disease. Comments 1. I suggest that the authors modify figure 1 such, that it give an overview on the pathways of cholesterol and of cholesterol synthesis. In an additional figure, e.g. Fig. 1B the authors might consider giving an enterocyte and a hepatocyte with the relevant systems involved in uptake and export of cholesterol. I think that such a distinction this might be of help for the non-experts in the field. 2. With respect to cholesterol in bile I suggest that the authors also deal with cholesterol transport in cholangiocytes and explain the role of MDR3 in canalicular cholesterol export. 3. I suggest that the authors summarize all disease related to cholesterol homeostasis, which are covered here in a table in addition to the mentioning of e.g. OMIM numbers in the text. 4. I miss more explanations on the role of reverse cholesterol transport in the context of liver disease. E.g. the authors might include the following overview: Endocr. Pract. 18: 90-97 (2012).

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ESPS PEER-REVIEW REPORT

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		[ ] Duplicate publication	
		[Y] Plagiarism	
		[ ] No	

COMMENTS TO AUTHORS

This work proposes a professional review on cholesterol metabolism in liver disease from molecular mechanisms to clinical implications. The topic of article is of interest, However, the article was difficult to read because of too many language problems, and several issues below need to be addressed. 1. Please ask someone familiar with English language to help you rewrite this paper, paying particular attention to English grammar, sentence structure and spelling so that the article is clear to readers. 2. In the abstract, the aim of this paper was not well-defined. 3. Considering the knowledge level of readers, common sense should not be included. e.g. "Cholesterol is insoluble in water." 4. There are some wrong expressions in sentences e.g. "The importance of cholesterol to human life and the critical role of the liver in cholesterol metabolism is exemplified by lathosterolosis". 5. The content and logic is confusing due to the misuse of grammer. 6. The focues should be clear and cumuli of relative content should be avoided in this article. 7. The paragraphs with similar content should be combined together. e.g. sections "LIPOPROTEIN X" and "CHOLESTEROL AND LIVER REGENERATION"