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ESPS PEER-REVIEW REPORT

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

COMMENTS TO AUTHORS

Comment: Liver cirrhosis is the late stage of different liver diseases and the impaired liver function is closely associated with therapeutic options for patients. MELD and Child-Pugh are established global scores for estimation of liver function but these scores have limitations in the efficacy and validity. Sequence of enzymatic steps during metabolism in the liver is as follows: compounds enter into the hepatocyte from the portal blood; compounds are oxygenated in hepatocyte; solubilization of metabolites is done by glucuronidation or sulfation; metabolites secret to the caval blood or the bile. This review summarizes the regulatory and functional changes in all steps mentioned above. Changes of transport proteins and lipid and glucose metabolism in cirrhotic patients were also reviewed in the manuscipt. The data summarized in this review show down-regulation of important CYP 450 isoforms and basolateral import transporters. Phase II enzymes (UGT, SULT) are mostly preserved in their expression but data from animal in vivo experiments point to reduction of enzymatic function. Lipid or glucose metabolism is individually altered as a result of cytokine regulation, differential enzyme expression and basic metabolic status, but in general is characterized

by hyperinsulinemia, insulin resistance and catabolism. These data show the complexity of metabolic processes and their regulation in cirrhosis. Possible non-invasive tests, especially breath tests, for components of liver metabolism are discussed. Breath tests are non-invasive, readily available and can be applied in vivo in the intact metabolic sequence. However, until now there is no reliable breath tests in estimating liver function because liver function is extremely complex and encompasses diverse functions. The authors suggest combined breath tests with different test substances and different rate limiting metabolic steps in order to examine different aspects of liver function in a test panel. The authors also points out that many of these studies are conducted in animal models whose transferability is unclear. Various animal models have been developed in rodents that closely reflect relevant human disease entities and their unique differences but human studies are scarce and mostly small. Since human studies providing data on molecular changes in hepatic metabolism and transport in cirrhosis are very scarce, data from animal models of cirrhosis have been incorporated into this work as far as these models adequately reflect human disease counterparts. This review comprehensively described the all steps in hepatocyte that occurred during compound metabolism. Studies on the changes of relevant molecules in recent years were reviewed and potential value of these molecules in assessing liver function was discussed. In general, this review provided useful information for further research. A more concise version may be preferable due to the length of this manuscript.