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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 20154
Title: Chemoprevention of obesity-related liver carcinogenesis by using pharmaceutical and nutraceutical agents
Reviewer's code: 00182548
Reviewer's country: Romania
Science editor: Ya-Juan Ma
Date sent for review: 2015-06-02 19:31
Date reviewed: 2015-08-17 23:38

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] 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	[ ] 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 review is very interesting for clinicians and researchers. As the authors write on the etiology and pathogenesis of obesity, they must mention and explain the role of heredity and the microbiome composition. I suggest to make small corrections, as: ?In this review, we demonstrated the possibility…" - In this review, we highlighted the possibility…; at Conclusions chapter the last sentence is again: ?In conclusion…"

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 20154
Title: Chemoprevention of obesity-related liver carcinogenesis by using pharmaceutical and nutraceutical agents
Reviewer's code: 00004157
Reviewer's country: Italy
Science editor: Ya-Juan Ma
Date sent for review: 2015-06-02 19:31
Date reviewed: 2015-08-10 18:55

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] 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

Sakai et al. This is an interesting short-review on the role and mechanism of pharamaceutical/nutraceutical agents in the prevention of hepatic carcinogenesis related to obesity. I have a few comments to further improve the manuscript. 1. Genetic risk factors play also a major role in the predisposition towards hepatic carcinogenesis in NAFLD, and should be highlighted: this has recently been reviewed by Dongiovanni et al. in this journal (WJG, 2014) 2. In particular PNPLA3 I148M variant is a common strong risk factor for HCC in NAFLD and obesity, independently of its effect on predisposition towards progressive fibrosis (reviwed by Dongiovanni, WJG 2013) and cirrhosis. Interestingly, PNPLA3 has retynil-esterase activity in hepatic stellate cells (Pirazzi, Valenti et al. Hum Mol Genet 2014; Mondul, Mancina, Merlo et al, J Nutr 2015), and the 148M risk allele reduces retinol availability. I think this may be relevant to support a role of retinol availability in predisposition towards hepatic carcinogenesis and HCC chemoprevention in NAFLD patients at high risk. 3. It should be cited that retinol reduced HCC incidence in a secondary prevention trial in patients with HCC (although not exclusively developed in NAFLD): the cited paper of Muto and the

original published in NEJM in 1999 should be highlighted. 4. In contrast, there is no experimental demonstration that the other approaches proposed in the manuscript may be effective in humans. This extremely important fact, and the need for larger studies in the field, should be stressed in the manuscript, the abstract, and the conclusions of the manuscript. 5. A very important mechanism linking obesity to hepatic carcinogenesis that has not been addressed by the Authors is senescence of hepatic stellate cells due to obesity-induced gut microbial metabolites, inducing a senescence secretome (Yoshimoto, Nature 2013). This needs to be cited. 6. Minor language editing: e.g. in the core tip inhibition of hepatic carcinogenesis or HCC devopment, not HCC;

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 20154
Title: Chemoprevention of obesity-related liver carcinogenesis by using pharmaceutical and nutraceutical agents
Reviewer's code: 00032933
Reviewer's country: Taiwan
Science editor: Ya-Juan Ma
Date sent for review: 2015-06-02 19:31
Date reviewed: 2015-08-12 23:50

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[Y] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] 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	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Prevalence of obesity and its related metabolic disorders are increasing and leading to various health-related complications, including hepatocellular carcinoma. The Gifu team explored molecular mechanisms that link obesity to hepatocarcinogenesis by C57BL/KsJ-db/db (db/db) obese mice model. They also tried to reduce hepatic steatosis and hepatocarcinogenesis by Green tea catechins, Branched-chain amino acids and Acyclic retinoid. The review is interesting and based on their continue works and findings in this field. Comments 1. Please give a section to discuss weight reduction as one of the therapeutic policy. 2. The authors recommend Green tea catechins, Branched-chain amino acids and Acyclic retinoid to be potential agents in management of NASH or NASH related HCC. Please discuss the rational of long term use with these agents in human.