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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
Ms: 2839
Title: Dietary-suppression of hepatic lipogenic enzyme expression in intact male transgenic mice
Reviewer code: 00503516
Science editor: s.x.gou@wjgnet.com
Date sent for review: 2013-03-20 09:26
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS

COMMENTS TO AUTHORS:

Notarnicola et all. studied the effects of three diets based on olive oil and olive oil diet supplemented with lovastatin and orlistat on hepatic lipogenic enzymes expression in mice. They show that the enzymes Fatty Acid Synthase, -hydroxyl-3-methyl-glutaryl CoA reductase and farnesyl pyrophosphate synthase have reduced activity and expression level compared to animal feed with normal diet. Given the fact that these enzymes tend to be over-expressed in tumor cells, these finding suggest that the three diets may have an anti-proliferative and anti-tumor effect. Major point The findings are of potential interest but the author claim: ”we confirmed the role of lipogenic enzymes as markers of cell proliferation (discussion page 10 lines 2-3 from bottom)” is not supported by the data reported. Whereas convincing evidence are shown with regard to the reduction of the activity of the three considered lipogenic enzymes, no evidences of reduced cell proliferation (in the liver) are reported. To substantiate their claim, the authors should provide evidences of reduced cell proliferation, for example by measuring the expression level of cell cycle related genes such as E2F1, cyclin E, cyclin A and B etc. in the same liver samples used to measure the expression of the lipogenic enzymes. Minor point In the abstract, the “conclusion” are not logically connected to the “aim”; to make the connection between the “aim” and the “conclusion” more clear, the “aim” should be rephrased introducing the concept of the relation between the expression of the lipogenic enzymes and cell proliferation.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
Ms: 2839
Title: Dietary-suppression of hepatic lipogenic enzyme expression in intact male transgenic mice
Reviewer code: 00037961
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS

CONFIDENTIAL COMMENTS TO EDITOR:

To aim of this research is to study the effects of three diets based on olive oil and olive oil diet supplemented with lovastatin and orlistat on hepatic lipogenic enzymes expression in ApcMin/+ mice which are divided randomly into 4 groups of 10 animals per group that were fed for 10 weeks: Concentration of olive oil used was 12%; lovastatin 5mg/Kg; orlistat 50 mg/Kg and SD group that was fed a standard diet. The activity of lipogenic enzymes and their gene expression were evaluated by radiometric and real-time RT-PCR assay. Results show that all the dietary managed treated groups significantly reduced hepatic levels of Fatty Acid Synthase, farnesyl pyrophosphate synthase and 3-hydroxyl-3-methyl-glutaryl CoA reductase activity and gene expression when compared with the mice fed the standard diet. The data confirm the role of lipogenic enzymes as markers of cell proliferation, suggesting that appropriate dietary management alone or with drugs can be a feasible approach to counteract hepatic cell proliferation in mice. Comments: This is a straightforward study done well in mice by these standard techniques in these transgenic animals. The rationale for the study is well justified. The outcome of the study results justified their hypothesis and objectives. The conclusions however indicate that the observed effects could serve as markers for hepatic cell proliferation although no direct experiments have been conducted to justify this conclusion. Major comments: The results section in addition to the current data also indicated histological analysis with no data provided. It will be important to show these data or remove the statement from the results section altogether. Other comments: The paper is well written and the English langauage meets the standards. The data and the statistics are clear. The references are all in order. Recommend: Approval with revisions.

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COMMENTS TO AUTHORS:

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
Ms: 2839
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Reviewer code: 00467187
Science editor: s.x.gou@wjgnet.com
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
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[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS

CONFIDENTIAL COMMENTS TO EDITOR:

The study was poorly designed and the data were inconclusive. The concept is not novel and the study lacked innovation.

COMMENTS TO AUTHORS:

In this manuscript, the authors investigated inhibition of lipogenic enzymes in the mouse liver by olive oil alone or in combination with lovastatin or orlistat. The data demonstrated that olive oil had strong inhibition of selected lipogenic enzymes in the liver in mRNA expression and enzymatic activity. The effects of olive oil in combination with lovastatin or orlistat were variable with or without enhancement. Based on these findings, the authors concluded that appropriate dietary management alone or with selected drugs can be a feasible approach to counteract hepatic cell proliferation, implying that the approach could be used for treatment of hepatocellular carcinoma or other cancers. However, the study was simple and poorly designed. There were no data to prove that cell proliferation was inhibited. Importantly, the intense of the study was to investigate the potential use of olive oil alone or with other drugs for cancer treatment or prevention. The authors studied the effects in the normal liver only instead of cancer. The effects on the normal liver cannot be absolutely applied to the effects on cancer cells because hepatocytes are usually quiescent in adult liver in the absence of damage. Therefore, effects on the selected lipogenic enzymes are insufficient to conclude inhibition of liver cell proliferation. Direct evidence is required, including cell proliferative markers, apoptosis, and related signaling pathways. It is also required to validate that these effects occur in hepatocellular carcinoma cells in vivo. Another deficiency of the study is that the effects of lovastatin or orlistat alone were not tested. Therefore, it is unclear whether the results of the combinations of olive oil with the drugs were synergistic effects or just the effects of drugs alone. Also, the rationale of these combinations was not well addressed in the manuscript. The

authors should consider to look at the effects on normal intestinal cells and adenoma in the animal model used in the study, which may be more interesting. The interpretation and discussion of the results need to be improved in the manuscript.