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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 14619
Title: Paeoniflorin inhibits human gastric carcinoma cell proliferation through up-regulation microRNA-124 and suppression of PI3K/Akt signaling...
Reviewer's code: 02863741
Reviewer's country: China
Science editor: Jing Yu
Date sent for review: 2014-10-18 12:03
Date reviewed: 2014-12-12 01:59

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

COMMENTS TO AUTHORS

The authors Yongbin Zheng et al., present an interesting study- Paeoniflorin inhibits human gastric carcinoma cell proliferation through up-regulation microRNA-124 and suppression of PI3K/Akt signaling. In general, the experimental methods are sound and the conclusions drawn are appropriate. However, some issues need to be addressed to improve the quality of the article. 1.The authors show that paeoniflorin inhibits MGC-803 cell viability and induces apoptosis. Does paeoniflorin regulate cell cycle? The authors have to clarify it by flow cytometry. 2.Also, the authors have to clarify that whether anti-miR-124 can reverse the effect of paeoniflorin on cell cycle, since miR-124 has been proved to a potent regulator of cell cycle. 3.The authors used miR-124 and anti-miR124 plasmids rather than mimic and inhibitor for overexpression or inhibition of miR-124. What are the transfection efficiencies of the plasmids into MGC-803 cells?

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 14619
Title: Paeoniflorin inhibits human gastric carcinoma cell proliferation through up-regulation microRNA-124 and suppression of PI3K/Akt signaling...
Reviewer's code: 03017207
Reviewer's country: China
Science editor: Jing Yu
Date sent for review: 2014-10-18 12:03
Date reviewed: 2014-12-02 09:19

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

COMMENTS TO AUTHORS

1. MGC-803 cell line was used in all the cell line assays in this manuscript. The authors should show the effects of paeoniflorin on normal gastric mucosa cell lines (GES-1). 2. The authors have showed that the anticancer effects of paeoniflorin on MGC-803 cells. The authors should consider the different roles of paeoniflorin when the gastric carcinoma cell line changes. 3. The authors have mentioned that miR-124 regulates and controls the expression of PI3K, Akt and phospho-Akt in MGC-803 cells. The authors could add more assays to show which is miR-124 target gene in this signaling pathway. 4. Regarding qPCR analysis, the authors do not describe which housekeeping gene was used and do not include the sequence of the primers utilized.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 14619
Title: Paeoniflorin inhibits human gastric carcinoma cell proliferation through up-regulation microRNA-124 and suppression of PI3K/Akt signaling...
Reviewer's code: 02537284
Reviewer's country: Venezuela
Science editor: Jing Yu
Date sent for review: 2014-10-18 12:03
Date reviewed: 2014-11-11 06:16

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

COMMENTS TO AUTHORS

In this work authors presented data suggesting that paeoniflorin is a potential novel therapeutic agent against gastric carcinoma, which inhibits cell viability and induces apoptosis through the up-regulation of miR-124 and suppression of PI3K/Akt signaling. They carried out in vitro assays with the gastric carcinoma cell line MGC-803. It is an interesting study, with a lot of work. However, I think that the manuscript is poorly written; in fact I think it carelessly. for example: ? In the abstract it is said: "The anti-apoptotic activity of paeoniflorin against MGC-803 was measured using both flow cytometry…" anti-apoptotic activity????? ? At the introduction (page 3) it is said: "Therefore, a mutation of PTEN uncouples Akt regulation, resulting in unchecked cell proliferation and tumorigenesis. PTEN can dephosphorylate-PIP3, inhibit PI3K activity, and reduce the concentration of PIP3..." inhibit PI3K activity???? PTEN can be considered a PI3K antagonist but it does not inhibit the PI3K activity. Therefore multiple corrections must be made before accepting the manuscript in WJG. The English and writing should be revised extensively throughout the text. In the introduction, the entire paragraph concerning PI3K/Akt pathway should be reviewed and

corrected. It should be clarified that PP242 is a protein kinase inhibitor. Not all readers need to know it. The discourse made in the introduction seems to lack a connection or association between variables to reach the objective of the study: Gastric cancer, miR-124, paeoniflorin and PI3K / Akt pathway. I mean…the paragraphs are not connected. In the results section (Paeoniflorin promotes apoptosis): What's the meaning of AST? It seems that never it is mentioned. Figure 3: It was not shown figure 3C. In the legend must be placed the meaning of FCM. Figure 4: The text mentions that occurred an inhibition of miR-124 expression, however the figure seems to show a dose-dependent increase of it. Moreover, where the levels of miR-124 after 48 h of treatment with paeoniflorin are shown? It is very confusing…. Figure 5: The text mentions that occurred an increase in the expressions of PI3K, p-Akt and Akt protein after cell treatment with different concentrations of paeoniflorin (5, 10 and 20 μM), however; the figure shows an apparent reduction of the protein levels. What is p-Akt? It is not mentioned anywhere in the text, neither the importance of its detection. With this result authors should not refer as changes in expression levels, since they cannot infer where the drug is acting to reduce the level of protein detected by Western blot. Figure 6: The legend is very poorly written. It was assayed the expression of a housekeeping gene by real-time quantitative RT-PCR? Conclusion: As with the entire manuscript, it should be improved the writing of this section. I consider that it is necessary some additional experiments to say that it was demonstrated that paeoniflorin possesses antitumor activity on gastric cancer cells by inhibiting cell proliferation and stimulating apoptosis via the up-regulation miR-124, and suppression of PI3K/Akt signaling. For example, evaluating apoptosis in the presence of miR-124 overexpression and anti-miR-124. Therefore, authors can only suggest this effect.