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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 11059
Title: Effects of oridonin on nuclear transcription factors and its target genes related inflammatory factors in human BxPC-3 cells
Reviewer code: 00045410
Science editor: Su-Xin Gou
Date sent for review: 2014-05-02 13:34
Date reviewed: 2014-05-29 10:22

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[Y] 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	[ ] Major revision

COMMENTS TO AUTHORS
A well conducted study which carries forward the work done earlier by the authors. It shows that Oridonin extracted from Rabdosia rubescens has anti-inflammatory properties which may be useful in controlling pancreatic cancer . The authors need to shorten discussion by removing statements on background knowledge and focussing on clinical relevance. They could also suggest what could be the implications of their results in planning further studies.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 11059
Title: Effects of oridonin on nuclear transcription factors and its target genes related inflammatory factors in human BxPC-3 cells
Reviewer code: 00417178
Science editor: Su-Xin Gou
Date sent for review: 2014-05-02 13:34
Date reviewed: 2014-06-01 00:45

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] 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)	[Y] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This paper describes the antitumor in vitro effects of oridonin in pancreatic adenocarcinoma. Interestingly, this compound seems to regulate the expression of several nuclear transcription and inflammatory factors. The manuscript is interesting and innovative. Few comments are suggested to improve on the submitted manuscript: - Aberrant constitutive activation of STAT-3 proteins has been frequently detected in pancreatic cancer (Dicitore A. et al. Biochim Biophys Acta. 2014 Jan;1845(1):42-52). This mechanism seems to be a crucial survival pathway, activated by cancer cells, involved in the resistance to biological therapy and chemotherapy (Vitale G. et al. Biotechnol Adv. 2012 Jan-Feb;30(1):169-84. Dicitore A et al. Curr Cancer Drug Targets. 2013 May;13(4):460-71). Indeed, the inhibition of STAT3 activation is able to increase the antitumor activity of several agents. Please, discuss these points and cite related references. In addition, the Authors should underline the potential clinical application and future perspectives arising from the results of the present study. We cannot exclude a future use of oridonin in combination with other biological and chemotherapeutic compounds in pancreatic cancer. - Page 9, Results section: "These results indicated that oridonin … in the STAT3 signal pathway". Please, explain better this point. - There are several typing and grammatical errors in the manuscript. Please, read carefully the paper and correct them.

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ESPS Peer-review Report
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	[Y]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[Y] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

In this study, authors show that treating with oridonin changed in vitro proliferation and various protein expression in BxPC-3 cells. Although some of the changes in protein levels are clearly shown, these results are not sufficient to support the conclusion they reached. Major points 1. Authors are using higher concentrations of oridonin than in other reports to inhibit growth of cancer cell lines. Authors need to confirm this concentration of oridonin does not have toxic effects on normal tissues, especially on epithelial cells. Most of the protein levels are not decreased or only slightly decreased at 8 or 16 μg/ml of oridonin, and substantially decreased at 32 μg/ml of oridonin. Judging from the fact that IC50 is 19.32 μg/ml, 32 μg/ml seems rather high concentration. In addition, authors also need to examine the effect of oridonin on other pancreatic cancer cell lines to discuss pancreatic cancer treatment. Authors show growth inhibition using BxPC-3 cells by MTT assay. In this assay, authors should show whether the growth inhibition was caused by cell death or cell cycle arrest. At least, authors should examine whether apoptosis is increased or not. 2. Authors show changes in protein levels related to NF-kappaB pathway. In order to conclude the activity of this pathway is changed, authors need to perform certain functional assay such as Electrophoresis Mobility Shift Assay (EMSA) or nuclear translocation of NF-kappaB. Authors also need to show the change in apoptosis. 3. IL-1β and IL-33 do not seem to have functionally significant decrease in ELISA assay. Although IL-33 level seems to decrease in western blotting, it is not clear that the decrease is caused by decreased expression, or by simple degradation in apoptosis. In addition, authors did not mention the role of intra-nuclear IL-33 in cancer cells in the manuscript. Authors need to explain the

significance of the amount of intra-nuclear IL-33. If there are previous reports, they should cite them. Although authors mentioned the relation of IL-33 and prognosis in the manuscript, they did not show the evidence of such a relation in this study. Thus, the role of IL-33 in this context is unclear. 4. IL-6 also does not seem to have functionally significant decrease in ELISA. Although p-STAT3 level is decreased in western blotting, they did not show decrease in invasion or metastasis. What they have shown is inhibition of cell growth, which is insufficient to discuss the effect of p-STAT3. 5. BxPC-3 is known to have homozygous deletion of Smad4 gene. Thus, the western blot shown here is thought not to indicate Smad4, but another protein, or non-specific one. Overall, authors showed only growth inhibition in vitro, which seems not convincing to reach their conclusion that the changes in protein levels shown have some therapeutic potential. Minor points Reference 15 is cited as "we found cell apoptosis", but this paper was not written by them. In addition, lots of grammatical errors were found in the manuscript. Authors need to have edited the manuscript by native speakers of English.