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7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
 Telephone: +1-925-223-8242 Fax: +1-925-223-8243
 E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 33581
Title: Spontaneous regression of hepatocellular carcinoma: A mini-review
Reviewer’s code: 00051373
Reviewer’s country: Taiwan
Science editor: Ze-Mao Gong
Date sent for review: 2017-02-20
Date reviewed: 2017-02-20

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The current mini-review is a very interesting manuscript to describe the possible mechanism on the spontaneous regression of HCC and would like to show out a new generation of immunotherapies. This manuscript is well written. Herein, only one point to be concern that because this is not an original article, the references should need to mention in the possible factors of tumor hypoxia in table 2.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 33581

Title: Spontaneous regression of hepatocellular carcinoma: A mini-review

Reviewer's code: 03017809

Reviewer's country: China

Science editor: Ze-Mao Gong

Date sent for review: 2017-02-20

Date reviewed: 2017-02-25

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

In this study, Dr Sakamaki et al reviewed the cases of spontaneous regression of hepatocellular carcinoma and analyzed the mechanism of spontaneous regression. They provided some new information to the current therapy of hepatocellular carcinoma. Generally, this manuscript is well written and of great interests for clinical readers. Actually, the manuscript is potential acceptable for publication. However, some minor issues should be improved. Minor comments: 1. It would be better if the authors explain the definition of spontaneous regression of hepatocellular carcinoma in introduction section. 2. When discussing the mechanisms of spontaneous regression in HCC, the authors should explore more roles of hypoxia in the pathophysiology of HCC. 3. Please make a confirmation that how many patients were recruited in this review. 4. Some typos and grammar errors should be further corrected.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 33581

Title: Spontaneous regression of hepatocellular carcinoma: A mini-review

Reviewer's code: 02540515

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2017-02-20

Date reviewed: 2017-03-01

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
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		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Reviewer : This paper examined the mechanisms of spontaneous tumor regression by summarizing 24 case report literatures, which provide valuable insight into therapies of Hepatocellular carcinoma. However, there are some problems with the paper. Overall:

- The authors should state the similarity between the spontaneous tumor regression and therapies of HCC by explaining about each mechanisms more in detail.
- Are there any necessary literatures of references except for that of published in recent 5-years?
- The authors should refer literatures which state about spontaneous regression tumor histopathologically diagnosed not only by diagnostic imaging.
- The authors should state that the written informed consent was obtained from the patient/the patient's family. Abstract P3, line 15 In the manuscript, the authors state that "immunotherapies". What are the immunotherapies? Please provide examples about that. Introductions Please expand the introduction so that it is longer than the abstract. For example, further information on the incidence and prognosis of hepatocellular carcinoma, and background on what is currently known about the pathogenic



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mechanism of hepatocellular carcinoma necrosis could be included. Materials and methods P5, line12 In the manuscript, the authors state that "PubMed". Please confirm all company detail in the materials and methods. These should include Company name, City, State and Country. Epidemiology P6, line10-11 In the manuscript, the authors state that "regional difference in the world and the higher frequency of spontaneous regression in the Asian countries". If it is possible, please state the cause of that result. Clinical Course P8 In the manuscript Authors' case is stated. Please show more examination such as blood test, abdominal ultrasound, Magnetic Resonance Imaging. Hypoxia page9 Is it appropriate if thromboses and rapid growth, hepatic arterioportal shunts are categorized in Hypoxia? They are causes of ischemic change, so do they mean not only hypoxia but also poor nutrition and dehydration, etc.? Immunological Reaction P10, line3-4 Immunological mechanism was stated in the latter half of this paragraph, are "Abstinence of alcohol and smoking, herbal medicines, prolonged fever, antidiabetics, and vitamin K administration" the same mechanism? Prognosis P11, line13-17 The author should additionally state about relapse of HCC and viable persistence of tumor cell for the reason of "additional therapies" after the last sentence. Figure Legends Figure1. There are images of lymph node metastasis before and after the tumor regression, are they mean spontaneous regression happened in the lymph node too? If so, what is the mechanism? Does it happen caused by Hypoxia or Immunological reaction?



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 33581

Title: Spontaneous regression of hepatocellular carcinoma: A mini-review

Reviewer's code: 00182703

Reviewer's country: Romania

Science editor: Ze-Mao Gong

Date sent for review: 2017-02-20

Date reviewed: 2017-03-05

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The theme of this review is interesting and useful for scientist and practitioners. Unfortunately the authors studied a single database and only in the last 5 years. So they could find and analyze a small number of cases. Spontaneous regressions had also been in the past. They can also be found in other places. The authors could not provide physiological explanations additional to those contained in the analyzed articles. Thus, the topic remains open for future studies. There are several grammatical errors that must be corrected.