

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 45590

**Title:** Seven-senescence associated gene signature predicts overall survival for Asian patients with hepatocellular carcinoma

**Reviewer's code:** 00188507

**Reviewer's country:** Japan

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2019-01-29

**Date reviewed:** 2019-01-29

**Review time:** 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

The author presented the development of senescence-associated genes signatures which could be related to the prognosis of HCC patients. Although the data from the basic research is relatively poor, based on the novelty of this work, it could be further



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considered for publication with the modification regarding the points below. Major The focus is interesting but the bridge to the clinica data set is poor. The information of liver cirrhosis level, child pugh score, AFP-L3 (%), background liver disease should be included in the tables and be compared. Minor A lot of typos. for e.g., 1. Introduction outcome and adopt effective strategies 2. Methods Differential gene expression analysis The differential expression gene (DEG) analysis 3. The median was used as a cutoff value for classification

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- ☐ The same title
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- ☐ Plagiarism
- ☐ No

##### ***BPG Search:***

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- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 45590

**Title:** Seven-senescence associated gene signature predicts overall survival for Asian patients with hepatocellular carcinoma

**Reviewer's code:** 03479773

**Reviewer's country:** Japan

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2019-01-29

**Date reviewed:** 2019-02-04

**Review time:** 2 Hours, 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

The authors aimed at developing a signature of senescence-associated genes that predict patients' survival and concluded that the 7 genes signature can predict the survival of Asian HCC patients. The data was organized well and the interpretation of the results is



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reasonable. My comments are as follows. <Major> What is the clinical benefit of measuring the 7 gene signatures especially regarding cost-benefit. Do the authors have any data regarding the staging, treatment history and pathological information of the patients? If so, are there any relationship between the gene signature and these clinical information? Why do the authors set the cut-off value as the median of all patient's risk scores? <Minor> "COMCLUSION" must be corrected to "CONCLUSION" in the abstract.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 45590

**Title:** Seven-senescence associated gene signature predicts overall survival for Asian patients with hepatocellular carcinoma

**Reviewer's code:** 00013213

**Reviewer's country:** Egypt

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2019-01-29

**Date reviewed:** 2019-02-05

**Review time:** 1 Hour, 7 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
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			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

Your manuscript points to the investigational methods adopted by your team to develop a gene score that can diagnose and predict survival of HCC. However some remarks about your study are presented here: 1-At introduction section, you have not listed a

reference referring to the fact that AFP can predict the OS. 2-At introduction, the statement: cellular senescence is considered a proliferating somatic cell that responds to.....etc, is not understandable. 3- At introduction, no listed reference that indicate your statement about the role of RAS activation in senescence. 4- At methods, both the survival analysis and the time dependent ROC curve are essentially statistical analysis and can be included with the statistical analysis. 5-At discussion section, you have not discussed in a simple clear way the value and meaning of your results. For example how to explain the meaning of the upregulation of the seven SAGs in HCC where you have mentioned that abrogation of senescence leads to development and aggressiveness of HCC. This is your explanation statement: (The potential explanation might be that due to the number of senescent cells increasing, the expression of 7- SAG signature is decreased, while patients with high expression indicate a higher proliferation rate and poorer OS); which is not satisfactory to explain the paradox. 6- At results, in the validation group, AFP was not a significant risk for HCC on multiple analyses. 7- You have not illuminated the relevance of your gene score whether it is related essentially to pathogenesis of HCC or otherwise it acts as a predictor and prognostic marker for HCC. The AUC of both AFP and your sophisticated SAG score are not greatly different. Thus the routine daily use of your gene score will not be applicable. 8- Major language revision is warranted. 9- Lastly, I wonder if the corresponding author can be more than one.

## INITIAL REVIEW OF THE MANUSCRIPT

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