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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 15587

**Title:** Low Expression of RASSF6 in Pancreatic Ductal Adenocarcinoma is Associated with Poor Survival

**Reviewer's code:** 03026908

**Reviewer's country:** Spain

**Science editor:** Yuan Qi

**Date sent for review:** 2014-11-29 22:35

**Date reviewed:** 2014-12-12 19:16

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> Accept
<input 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input 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 type="checkbox"/> No	

### COMMENTS TO AUTHORS

COMMENTS TO AUTHORS Abstract (Results): You say "Survival curve revealed that lower RASSF6 expression was correlated with better overall survival" but above you expose that the median survival time of strong positive cases (33 months) is higher than the median survival time of negative cases (11 months) Results (Expression of RASSF6 in tumor cells and correlation with clinicopathological parameters): You write "higher stage tumors demonstrated RASSF6 expression much more frequently" however, in the discussion you determine that using IHC "RASSF6 protein expression was significantly lower in higher T stage tumors" Discussion: You expose "down-regulation of RASSF6 is a predictor of different aggressive tumor behaviours such as advanced T stage, poorly differentiated carcinoma, perineural invasion, and poor survival outcome" but below you write that in your data the RASSF6 expression don't tend to be negative in poorly differentiated tissues.

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

**ESPS manuscript NO:** 15587

**Title:** Low Expression of RASSF6 in Pancreatic Ductal Adenocarcinoma is Associated with Poor Survival

**Reviewer's code:** 03026443

**Reviewer's country:** China

**Science editor:** Yuan Qi

**Date sent for review:** 2014-11-29 22:35

**Date reviewed:** 2014-12-23 09:31

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> Accept
<input 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input 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 type="checkbox"/> No	

### COMMENTS TO AUTHORS

There are several points that need to be addressed: 1) Typos and grammatical errors need to be corrected. 2) Abstract: results: the authors note that the median survival time of strong positive and negative RASSF6 staining groups was 33 months and 11 months. However, survival curve revealed that lower RASSF6 expression was correlated with better overall survival. please check why? Conclusion: low expression of RASSF6 in PDAC is associated with poor survival, so how can it be a biomarker of unfavorable prognosis? 3) Figure 2: the figure purporting to show reduced RASSF6 expression in tumor cells that invaded nerves is unconvincing. Some quantification would be appropriate 4) Results: Page 9: the authors note that the RASSF6 expression were significantly down-regulated in cancer tissues. However, as shown in table 1, higher-stage tumors demonstrated RASSF6 expression much more frequently. Is there any reason? 5) Discussion: Page 10: Please check the result of the relationship between RASSF6 expression and the UICC T stage in PDAC patients (the correlation is positive or negative?) Page 10: ".....down-regulation of RASSF6 is a predictor of different aggressive tumor behaviors such as advanced T stage, poorly differentiated



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carcinoma.....". As shown in table 1, no significant association was observed between RASSF6 expression and tumor differentiation ( $P=0.138$ ). 6) How many patients with a follow up of less than 5 years were included in this study?