ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 5401

Title: Caspase-3 Expression In Metastatic Lymph Node is a Potential Prognostic Marker for Resected Esophageal Squamous Cell Carcinoma

Reviewer code: 00227606

Science editor: Ma, Ya-Juan

Date sent for review: 2013-09-09 16:56

Date reviewed: 2013-09-14 04:15

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

COMMENTS TO AUTHORS

1. The antibodies used in this study are able to recognize the pro-caspase 3 and active caspapse 3. It is very important to include the data using active caspase 3 antibodies.   2. Activation of caspase 3 is a indication of cell apoptosis. Why in ESCC, there is an increased expression of caspase 3? The authors should distinguish the pro-caspase 3 and the cleaved caspase 3 in this study.

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Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5401
Title: Caspase-3 Expression In Metastatic Lymph Node is a Potential Prognostic Marker for Resected Esophageal Squamous Cell Carcinoma
Reviewer code: 00041286
Science editor: Ma, Ya-Juan
Date sent for review: 2013-09-09 16:56
Date reviewed: 2013-09-15 22:32

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

COMMENTS TO AUTHORS

This is an interesting study analysing caspase-3 expression related to clinical outcomes of esophageal SCC. Its main result is related to Caspase-3 expression in lymphatic metastasis and its relationship with disease specific survival. However, there are some issues that should be clarified before considering it for publication. 1. The sentence at the end of the methods "We chose one lymph node randomly per case from 42 patients which have more than one satisfied the afore-mentioned criteria." is not clear. the whole patients selection is not clear. I suggest a flow chart as figure 1. 2. 42 cases with failure matching... were they the same as above? how many patients were finally and actually evaluated? 42 patients are a small sample size for a 5 predictors multivariate analysis 3. how was defined the expression score thresholds of 80 and 160? literture, ROC curves, convention...? 4. no mention of neoadjuvant therapy, which is now standard terapy for ESCC. How many of these patients had it? these patients should be considered as a separate group since caspase 3 expression might be strongly influenced by this therapy. If no patients had neoadjuvant therapy this should be stated and discussed. The clinical validity of these findings might be rather weakened in this case. 5. Mann-Whitney does not measure correlation but differences. Please, correct the statement. 6. Please, avoid pe value and numbers in the discussion section 7. which cell population was stained in tumors and lymph nodes? tumor cells, TILs, mesenchimal cells, endothelium...? This data may add furthr clues about the meaning of caspase 3 expression.

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Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5401
Title: Caspase-3 Expression In Metastatic Lymph Node is a Potential Prognostic Marker for Resected Esophageal Squamous Cell Carcinoma
Reviewer code: 00071702
Science editor: Ma, Ya-Juan
Date sent for review: 2013-09-09 16:56
Date reviewed: 2013-09-18 14:49

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
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		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

Comments: Esophageal squamous cell carcinoma is one of the most common tumors in the world. There is an imperative need to understand the molecular mechanism and develop new therapeutic strategies. The approach adopted in the study is different though not unique. In the "Introduction", the authors must focus on the fact that why this study is important and how this is different. Much of the generalized account describing the association of protein expression patters observed in various cancers must be deleted. The concept/hypothesis must be introduced in the second paragraph of the introduction. In the "Methodology" segment, describe how were the false positives and negatives determined? What were the precise false positives and negatives rates observed? What was the dilution used for primary antibodies? What protocols were adopted to negate inter and intra observership bias? These points need to be included. In "Results", provide a better quality photograph for caspase expression. Legend to figure 2 & 3 must be elaborated and major inference observed should be highlighted. Did the authors use cell-specific markers to precisely note the variability of caspase expression within a heterogenous region ? Well, I do not quite agree (as it might be premature at this point of time) with the authors that caspase could prove to be a better prognostic marker for ESCC, therefore superlative statements must be amended in the "Discussion" segment accordingly. What exactly is the cause of this increase in caspase expression metastatic lymph node ? A hypothesis should be provided in the "conclusion" segment, it might help to significantly elevate the impact of the manuscript.

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Title: Caspase-3 Expression In Metastatic Lymph Node is a Potential Prognostic Marker for Resected Esophageal Squamous Cell Carcinoma
Reviewer code: 00006789
Science editor: Ma, Ya-Juan
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
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COMMENTS TO AUTHORS

Title: Caspase-3 Expression In Metastatic Lymph Node is a Potential Prognostic Marker for Resected Esophageal Squamous Cell Carcinoma Reviewer comments: In the paper by Wang et al, the authors analysed Casaspe 3 expression by immunohistochemistry in esophageal squamous cell carcinoma primary tumors (PT) and in metastatic lymph nodes (PMLN). They showed that caspase 3 expression is significantly higher in metastatic lymph nodes that in PT. They conclude that high levels of caspase 3 expression levels is a maker of poor prognosis while high levels of caspase 3 expression in PT is a marker of good prognosis. Thus one will expect that those patients with high expression levels in PT will have low expression levels in PMLN and viceversa. However attending to the data on figure 3 this is not the case and the data differ substantially between the two graphs, although the statistical significance I similar. Since the patients with better survival attending to caspase 3 expression in PT are 88 while attending to PMLN are 28. It will be interesting to see graphically the correlation between caspase 3 expression in PT and PMLN for each patient and if it correlates with the survival Some comments   The authors should include the pictures of more patients tissue in particular those showing high levels of caspase 3 expression in PT and low levels in in PMLN. The way the authors have evaluated caspase 3 staining intensity is not very objective, could it be done using an automatic analyser? Could the authors analyse caspase 3 expression by other means like RT-PCR, western blot? Several PMLN have been taken for the same patient, all of them have the same level of caspase 3 expression.   The authors indicate in the abstract that they have analysed 122 cases with primary tumors and paired metastatic lymph nodes, however in the material and methods section they indicate they were 42 cases with failure matching. Thus, they have analysed 122 cases with primary

tumors and paired metastatic lymph nodes or 80. The authors should indicate in table 3 that in the low expression group are included the negative patient.