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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5204
Title: Mass spectrometry to profile serum peptides of hepatocellular carcinoma with bone metastasis
Reviewer code: 00068723
Science editor: Wen, Ling-Ling
Date sent for review: 2013-08-22 20:44
Date reviewed: 2013-09-28 07:25

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 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

The study design and labor are well organized and should be admired. This work would be more attractive if the authors more clearly presented the advantage of these new biomarkers as compared with the current diagnostic strategy, such as CT, MRI, and PET-CT. AFP and prothrombin mean that HCC with bone metastasis is at more advanced stage as compared with HCC without bone metastasis. What do the authors speculate biological significance of the other peptides with peak in HCC with bone metastasis? Autophagy related protein is intriguing. The significant peptides may unveil progression of HCC to bone metastasis. If the involvement of these peptides to bone metastasis is revealed, it would be expected to develop a new strategy to suppress bone metastasis. ROC analysis clearly showed that this model is useful for the diagnosis or prediction of bone metastasis of HCC. Where is the description of the diagnostic model? Discussion should be more compact, focusing on significance of the findings.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5204
Title: Mass spectrometry to profile serum peptides of hepatocellular carcinoma with bone metastasis
Reviewer code: 00011221
Science editor: Wen, Ling-Ling
Date sent for review: 2013-08-22 20:44
Date reviewed: 2013-10-12 00:40

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 language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

The methods of this study appear technically sound but the cross-sectional nature and lack of appropriate controls, specifically HCC patients with non-bone metastases, limit interpretation of the validity of the identified markers. There is no way to conclude that the putative biomarkers are specifically related to bone metastases. There is no way absent a prospective analysis to determine if these are sensitive for early detection of bone metastases. It is unclear what advantage these proteomic markers would have over nuclear bone scans. I'd suggest the authors examine patients with lung metastases but no bone metastases and determine if these markers are specific to bone metastases. If they find a marker that is specific to bone, then I think this is reasonable to publish as long as they don't make any claim that these are valid predictors of bone metastasis development. To make this claim they would need to perform a prospective assessment of patients without initial bone metastases to determine if the marker predicted subsequent development of bone metastases. If so, this would be useful for identifying patients who might benefit from bisphosphonate therapy or increased surveillance.