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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 10401
Title: Genomic aberrations in pancreatic neuroendocrine tumors detected by high-resolution array comparative genomic hybridization
Reviewer code: 02520050
Science editor: Ya-Juan Ma
Date sent for review: 2014-03-30 13:17
Date reviewed: 2014-04-03 18:48

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] 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	[ ] Major revision

COMMENTS TO AUTHORS

This is a very interesting article illustrating the use of genomic analysis to help predict clinical outcomes. A few comments 1. I would move the last sentence of the first paragraph of the methods to results; comparison of he proliferative activity of primary/metastatic lesions belongs in results 2. I would be cautious in relying on the Kaplan Meier analysis with such small sample size. It is likely to be inaccurate. 3. Do the authors believe these chromosomal aberrations are a primary defect or the result of epigenetic influences? Is there a hypothesis about whether this is a causal finding or just an association with oncogenesis and poor outcomes? 4. Are any of the protein products of these genetic aberrations actionable? Translational potential? 5. At least one more figure or table would be helpful

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
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Title: Genomic aberrations in pancreatic neuroendocrine tumors detected by high-resolution array comparative genomic hybridization
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Science editor: Ya-Juan Ma
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] 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 by Gebauer et al. employed high resolution array comparative genomic hybridization (aCGH) to reveal aberrant chromosomal copy number in primary pancreatic neuroendocrine tumors (panNETs) and corresponding metastases. They showed that chromosomal gains were frequently occurred in panNET but not chromosomal loss. By clustering of the aCGH data, they identified two distinct subgroups with distinct subset of genomic chromosomal aberration. They also identified several chromosomal gains that are associated with worse patient survival. This study provides essential information of genomic alteration present in panNET which is yet to be reported, and identifies critical genomic region for further investigation of their role in panNET. They identified two subgroups of primary panNETs after aCGH hybridization, illustrating a small proportion of panNETs harbouring a distinct subset of chromosomal aberrations. If possible, they should also study the association between patient survival and the two subgroups, which is invaluable in further classification of the panNET, as well as future prognostic strategy development. Furthermore, they also detected 2 distinct chromosomal clusters (a and b). However, they have not discussed and illustrated the significance of these two clusters. The author should briefly discuss the significance and implication of the clusters in panNET in the discussion section. During the aCGH data interpretation, they listed out a number of genes lying on the unstable locus that were potentially associated with the development of panNETs (i.e cell-cell adhesion genes and cell cycle genes). In addition to MEN1 gene, we would like to know whether there is other reported panNET-associated genes, such as DAXX and ATRX, that were heavily affected by chromosomal imbalance. Even though

these panNET-associated genes may not lie at the identified unstable locus, it is still worth mentioning so as to exclude the involvement of chromosomal aberration leading to their deregulation. They also attempted to compare the genomic aberration between primary panNETs and corresponding metastases. The author has not stated clearly from whom the 11 metastatic tissues were obtained, leading to the unclear perception of the reader. A table summarizing the origin of the metastases could greatly improve the message conveyed. To the reviewer's assumption, the 11 metastases were obtained from 7 patients that had matched primary tumors in the primary panNET cohort. If this assumption stands, they should include another table for comparison of genomic aberration between the primary and metastatic tumors within an individual patient, even though they have listed out the genomic aberration observed in the primary cohort and metastases cohort. Matched comparison could provide important information for the discovery of genomic aberration critical during disease progression (i.e. lymph node or liver metastasis). Is it possible for the author to extrapolate the progression of panNET from primary tumors to metastases by comparing and contrasting the genes affected by chromosomal aberration? In Fig 2, the sub-population number (n) should be indicated. In addition, Fig 2 is not reader-friendly enough. Figures should be self-explanatory. The author should indicate clearly each sub-figure with appropriate heading, and provide legend to indicate the groups within the sub-figure.