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315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Clinical Oncology

ESPS Manuscript NO: 7233

Title: The mRNA expression of Dok 1-6 in human breast cancer

Reviewer code: 02446338

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-09 16:30

Date reviewed: 2013-11-19 19:26

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

General comments This work tackles a novel and interesting issue: the expression profile of DOK proteins in breast cancer. The importance of this study lies in that by first time it is suggested a role of DOK proteins as tumour suppressors in breast cancer. Even though this point should be demonstrated with specific experiments, the findings depicted in this manuscript open the door to further investigations on the use of DOK proteins as possible diagnostic/prognostic biomarkers and hypothetical drug targets. Overall, the manuscript is well written and shows a good presentation, although the authors may consider adding plots depicting the most interesting findings. Specific comments Title: correct. Abstract: correct. Materials and methods: 1. The authors declare in text to have collected 112 breast cancer samples (all from different patients?). However, in table 1 containing clinical and pathological data, the total counts differ with the figure provided in text. In this way, the sum of patients by node status and tumour type is 127; the sum of patients by tumour grade is 125; by TNM staging, 121; by NPI, 122; and by clinical outcome, 118. 2. Given the high incidence of breast cancer and the feasibility to recruit participants, the sample size of 112 patients can be considered moderate. In addition, the population of patients recruited shows an important imbalance towards early stages and ductal histology. 3. Is this a multicentre study? The authors should explain the origin of samples utilised in the study. 4. The authors use a standard and well established technique (qRT-PCR) to perform the analyses. 5. In relation to controls, the authors do not provide any data. However, to evaluate the conclusions of this study, the authors should provide data about the mean age (with SD) of patients and controls. The age of patients and controls should be similar (using t test) in order to avoid interference in results. 6. Following the minimum information for publication of quantitative real-time PCR experiments (MIQE) guidelines (Bustin SA,



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et al. Clin Chem. 2009 Apr;55(4):611-22), the standard terminology for “housekeeping” genes is “reference” genes. 7. What kind of quantification was used in this study: absolute or relative? If absolute (i.e., using a standard), it is not necessary perform then normalization against any reference (housekeeping) gene. 8. The authors depict the use of Pearson’s correlation, but this test was not utilized in this study. Results: 1. Regarding the sample size, the inclusion of >100 patients (112?) can be considered sufficient to perform this exploratory study. 2. How many replicates were performed for each sample and analysis? Were the experiments performed in duplicate? In triplicate? 3. Why the SD provided in tables 3 and 4 is 2-, 3- and even 4-fold the corresponding mean? It is usual convention that the coefficient of variation (i.e., SD/mean) should not exceed 1/3 (0.33) to consider data as suitable. However, in this study the data seem to have an alarming dispersion, which may represent an important pitfall for deriving acceptable statistical conclusions. 4.

Following with the previous point, there are some mean comparisons in which the variances of samples seem to be quite different in value (the authors can compare variances using F test). In cases where compared groups have different variances, the t test can only be applied with the Welch’s correction. Discussion: correct. References: correct. Tables: correct. Figures: The article does not include figures or plots.



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ESPS Peer-review Report

Name of Journal: World Journal of Clinical Oncology

ESPS Manuscript NO: 7233

Title: The mRNA expression of Dok 1-6 in human breast cancer

Reviewer code: 02445418

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-09 16:30

Date reviewed: 2013-11-25 09:51

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The analysis and discussion need to address the relation of DOK 1-6 to ER, PR HER2 etc



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ESPS Peer-review Report

Name of Journal: World Journal of Clinical Oncology

ESPS Manuscript NO: 7233

Title: The mRNA expression of Dok 1-6 in human breast cancer

Reviewer code: 02445925

Science editor: Zhai, Huan-Huan

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Date reviewed: 2013-12-03 07:36

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The authors of the study analyzed the expression profile of DOK 1-6 in breast cancer specimen and non-cancerous mammary tissue. The mRNA expression level of DOK1-6 is evaluated against pathological and prognostic parameters as well as clinical outcome. The results depict a correlation between decreased DOK-2 and 6 expressions and increasing TNM-Stage. Furthermore higher DOK-2 expression is associated with significant lower chance of local and distant disease recurrent within the following 10-year period. Here the authors could demonstrate the role of DOK-2 and 6 as a potential tumor suppression in breast cancer. The study is well done and the results are written in a conclusive way. I can recommend to publish this paper.



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ESPS Peer-review Report

Name of Journal: World Journal of Clinical Oncology

ESPS Manuscript NO: 7233

Title: The mRNA expression of Dok 1-6 in human breast cancer

Reviewer code: 02446263

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-09 16:30

Date reviewed: 2013-12-05 23:41

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

In the present manuscript, the authors analyzed the expression of DOKs in breast cancer samples. The manuscript may be interesting to researchers working in the field, but need a major revision because it present flaws both in data presentation/analysis and in the corresponding discussion. Mayor compulsory revisions. - The way data are presented in tables 3 and 4 is not in agreement with the statistical analysis performed. Mann-Whitney U-test does not use means and SD, please correct. -The number of patients with clinical outcome other than “disease-free” is relatively small. However, for DOK 2, 4, and 6 the authors conclude that there is a statistical difference in recurrence or survival. Does this coincide with microarray studies compiled in public databases? - Discussion is poor. It is not focused on the presented results but in other data published elsewhere. For example, DOK-2 and DOK-6 belong to different subfamilies with different functional relevance on proliferation but the authors found similar correlations with TNM stage for both molecules; there is no discussion at all about the apparent paradox. They do not offer a serious discussion either about the lack of differences in DOK expression between cancerous and normal tissue, they just present and hypothesis that lacks of support (no quotes). Minor essential revisions -Authors completely omit any information about DOK-7 in the introduction. There is no rationale for the evaluation of 6 members of the family and left one unstudied. - A large number of quoted papers are older than 10 years. Can more recent literature be quoted instead?