

Format for ANSWERING REVIEWERS

June 10, 2015



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 17600-review.doc).

Title: Blood DNA methylation markers in prospectively identified hepatocellular carcinoma from a case-control study at Taiwan

Author: Hui-Chen Wu, Jing Shen, Hwai-I Yang, Wei-Yann Tsai, Chien-Jen Chen¹, Regina M. Santella

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 17600

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) IRB approval was obtained from both Columbia and Taiwan.

Familial clustering of HBV infection is one of the major concerns worldwide especially in Chinese population. Therefore we often observed HCC occurring in several members from one family. It is interesting to know whether the authors observed HCC patients from one families? if yes, do they show similar DNA methylation in those patients? are there any differences in the DNA methylation between HCC patients from different families and those from one family?

(2)?? The sum of the number of female and male in case and control group isn't equal to 159 and 312, respectively in table 1. Why? 2. In table 2, the differences of mean methylation values between cases and controls were analyzed. But, why did authors use median (not mean) as cutoff value in table 3? Were the values passed the normality test? 3. There are some spelling errors in the text (page 3, "ca be used" should be instead of "can be used", page 8, "cg1272601 methylation above" should be instead of "cg10272601 methylation above", for instance) .

None of the cases were from the same family

An error in numbers in table 1 has been fixed

Because of the relatively small number of subjects, they were dichotomized around the median for some analyses

Spelling errors have been fixed and the typo in the cg number has been fixed

(3) none

(4) none

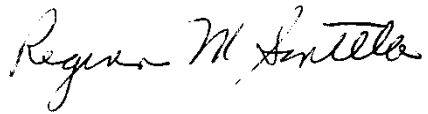
(5) The error in hypomethylated sites was corrected. It is 31 not 32.

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3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely,

A handwritten signature in black ink, reading "Regina M. Santella". The signature is written in a cursive, flowing style with a large initial 'R'.

Regina M. Santella, PhD
Professor of Environmental Health Sciences

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