

Format for ANSWERING REVIEWERS



June 8, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 10804-review.doc).

Title: A novel mutation in a Chinese patient with progressive familial intrahepatic cholestasis type 3

Author: Hao-Zhe Sun, Hong Shi, Shun-Cai Zhang, Xi-Zhong Shen

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 10804

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) The differential diagnosis between PFIC 3 and PFIC 1-2 was added on page 7, the first paragraph of the discussion. The clinical, biochemical and histological results indicated the diagnosis of PFIC 3 and led to the genetic analysis of the ABCB4 gene accordingly.

(2) Explanation for why the patient with heterozygous mutation developed autosomal recessive disease was explained on page 9-10, the 5<sup>th</sup> paragraph of the discussion.

(3) Explanation for why the patient does not have any family history was added on page 11.

(4) MDR3 liver immunostaining might be helpful to select PFIC candidates for whom genotyping could be proposed to confirm the diagnosis. However, normal liver immunostaining of MDR3 does not preclude a gene defect, as a mutation may induce loss of function, but with normal synthesis and expression. Because of the reasons explained in the first paragraph of the discussion (page 8), immunostaining of MDR3 was not performed. Genetic analysis of the ABCB4 gene was performed.

(5) Combined with the patient's clinical (present symptomatically at a later age), biochemical (markedly elevated GGT), histological (presence of ductular proliferation), radiologic findings (bile ducts not dilated), and ABCB4 gene analysis, the diagnosis of PFIC was confirmed. Due to personal reasons, the patient's parents declined to be tested. Finding heterozygous mutations of the parents are helpful for prenatal diagnosis but are not indispensable for the diagnosis of the patients.

3 References and typesetting were corrected

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

Sincerely yours,

A handwritten signature in black ink, appearing to be 'Hong Shi'.

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