

## Format for ANSWERING REVIEWERS

2013/10/07, 2013



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: #TK-Format for original articles-WJH5352R.doc).

**Title:** IL28B polymorphisms and treatment response in HCV patients with PNALT

**Author:** Tatsuo Miyamura, Tatsuo Kanda, Masato Nakamura, Xia Jiang, Shuang Wu, Shingo Nakamoto, Shigeru Mikami, Nobuo Takada, Fumio Imazeki, Osamu Yokosuka

**Name of Journal:** *World Journal of Hepatology*

**ESPS Manuscript NO:** 5352 (00012386)

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 comment from reviewer **00503966**

1. *Response to your comment: "We recommend publication of this paper, though it should be discussed, that dual peginterferon / ribavirin – therapy is no longer the standard therapy for chronic HCV-infection."*

Thank you for your valuable comment. We agree with you. According to your suggestion, we added the following sentence in revised manuscript. "Dual peginterferon/ribavirin therapy is no longer the standard therapy for chronic HCV infection."

(2) The comment from reviewer **00006683**

1. *Response to your comment: " I have minor comments: 1) In pag 8, para 1, lines 4-5: It should read: AST, ALT, GGT levels in the PNALT group were lower compared to those in the abnormal ALT group. 2) In the results of the abstract and in the multivariate analysis section of results, I would change the sentence by saying: SVR was independently predicted by IL28B rs8099917 major type and having EVR in HCV genotype 1-infected patients with PNALT."*

Thank you for your valuable comment. We agree with you. According to your suggestion, we revised our manuscript.

(3) The comment from reviewer **00006675**

1. Response to your comment: ".....Major comment I wonder why the study of rs12979860 was not also carried out in the patients. Minor comment The role of IL28B gene should be described in the introduction."

Thank you for your valuable comment. We agree with you. According to your suggestion, we revised our manuscript.

In DISCUSSION section,

..... PNALT-patients with moderate or severe fibrosis should be treated<sup>[8, 10]</sup>. Tanaka et al.<sup>[14]</sup> has shown that the IL28B SNP rs8099917 TT genotype strongly correlates with treatment response in HCV genotype 1-infected Asian patients. It has also been reported that linkage disequilibrium between the two IL28B SNPs, rs8099917 and rs12979860, is strong in Japanese HCV patients<sup>[30]</sup>. In the present study, IL28B SNP rs8099917 but not IL28B SNP rs12979860 was evaluated.....

In INTRODUCTION section,

..... Genome-wide association studies have revealed a strong relationship between single-nucleotide polymorphisms (SNPs) near interleukin 28B (IL28B) on chromosome 19 and the virologic response to peginterferon plus ribavirin treatment in patients worldwide who are infected with HCV genotype 1<sup>[12-14]</sup> as well as .....

In DISCUSSION section,

..... receive treatment. Baseline plasma interferon-gamma inducible protein-10 (IP-10 or CXCL10) levels are strongly associated with IL28B genotypes<sup>[18]</sup>. Honda et al.<sup>[17]</sup> reported that hepatic interferon-stimulated genes (ISGs) are associated with IL28B genotypes. We have also reported that concomitant assessment of lower-hepatic STAT1-nuclear translocation and IL28B genotypes is useful for the prediction of SVR in HCV-infected patients<sup>[19]</sup>. Additionally, we have recently demonstrated that IL28B induces ISGs that are reportedly associated with the progression of HCV-related pathogenesis and antiviral activities against HCV<sup>[34]</sup>. Further studies will be needed. In a previous study, t.....

3 References and typesetting were corrected

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

Sincerely yours,

A handwritten signature in black ink, appearing to read "Tatsuo Kanda". The signature is written in a cursive, somewhat stylized font.

Tatsuo Kanda, M.D., Ph.D., Associate Professor,  
Department of Gastroenterology and Nephrology, Chiba University,  
Graduate School of Medicine, Chiba 260-8670, Japan.  
kandat-cib@umin.ac.jp