

December 19, 2013

Dear editor,

I really appreciate several important comments of two reviewers on my manuscript (Manuscript revision NO: 6715). My responses to reviewers' comments are as follows. I highlighted the changes in my manuscript. Please find enclosed the edited manuscript in Word format. (file name : WJG Review 6715-edited (I.Nakamura) (2013-12).docx).

**Title : Impairment of Innate Immune Responses in Cirrhotic Patients and Treatment by Branched-Chain Amino Acids**

**Author: Ikuo Nakamura**

**Name of Journal : *World Journal of Gastroenterology***

**ESPA Manuscript NO: 6715**

**<Reviewer 00506513>**

- 1. Description of chemical formula of BCAA was added on page 9.**
- 2. Figure 1 was deleted. Alternatively, Table 1 (Impairment of innate immune responses in cirrhotic patients) and Table 2 (Impairment of adaptive immune responses in cirrhotic patients) were produced**
- 3. Several descriptions were revised. (p4, p5, p6, p7, p8, p9 and p13)**

**<Reviewer 01560505>**

**1. The following descriptions were inserted on page 7. <Reduction of NK cell activity might occur partially due to lower frequency of NK cell in peripheral blood<sup>[13]</sup>. However, the mechanisms of diminished NK cell activity was not clarified so far. >**

**2. Other speculated mechanisms of reduction of the risk of HCC development by BCAA are (1) suppression of vascular endothelial growth factor (VEGF)**

expression, (2) Induction of apoptosis of tumor cells through mTORC1 and mTORC2-dependent mechanisms. Details were already described in page 12 and 13.

3. On page 6, the pointed description was revised. <Polymorphonuclear cells (PMNs)>

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

Sincerely yours,



Dec. 19, 2013

Ikuo Nakamura, MD, PhD

Department of Gastroenterology, Tokyo Medical University

Address: 6-7-1, Nishishinjuku, Shinjuku-ku, Tokyo, 160-0023, Japan

Tel: +81-3-3342-6111

Facsimile: +81-3-5381-6654

e-mail: ikuonaka@tokyo-med.ac.jp