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Prof. Lian-Sheng Ma, President and Company Editor-in-Chief  
World J Gastroenterology  
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My ID is 00503536

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4278-review.doc). We have revised our invited Editorial entitled "Branched-chain amino acids in liver diseases" according to the reviewers.

**Title:** Branched-chain amino acids in liver diseases

**Author:** Kazuto Tajiri, Yukihiro Shimizu

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

**ESPS Manuscript NO:** 4278

We have listed the answers below (underlined), and revised portions in the manuscripts are also underlined. We believe that those revisions are satisfactory for the reviewers.

**Reviewer #00054465**

This is a very comprehensive review of the potential efficacy of branched chained amino acids in liver disease. There are 103 references yet not included is the World J Gastroenterol 2012 September 7; 18(33): 4486-4490 authored by Toru Ishikawa. This manuscript covers much of the same ground and clearly in a table demonstrates the key human studies and gives number of patients enrolled, duration of therapy and outcome. this allows the reader to assess the strength of the data presented. This study was much clearer and let the reader know the state of the art. This manuscript under review needs to be much stronger to add to the literature or to improve on Ishikawa. Perhaps they could

present all the potential benefits of BCAAs as based on animal data, then look at the strength of the human data for each of these outcomes. Could they present a meta-analysis of the human data? The reader needs to know the strength of the human data as we know all that can be done in animals does not translate to the human. To improve on Ishikawa they need to revise with a more indepth analysis of the human clinical trials.

We summarized all the important reports on basic analysis and clinical utilization on BCAAs, both human and animal study, including Ishikawa's review. Newly added portions are underlined. A comprehensive lists of the results of RCTs are now summarized in Table 1.

#### **Reviewer # 00742311**

This is a review article on BCAA in liver diseases. The topics are clearly presented and most comments are sound and acceptable. However some references are old, with 20 and even 30 years, and should be replaced by more recent ones. At that time laboratory methods were not as reliable as nowadays, therefore results become questionable. There are also a few language problems. Parenteral nutrition is sometimes written Parental Nutrition, or else as Hyperalimentation, an expression that became obsolete and is not used anymore.

We again searched the reports on the analyses for the serum concentrations of BCAAs and AAs in patients with liver diseases including PubMed and the standard (major) textbooks for hepatology. However, all of the reports regarding the serum BCAAs concentrations are old. Other reviews also cited only old references. We corrected Parenteral Nutrition and Hyperalimentation as indicated.

#### **Reviewer # 00009221**

I think that the review is complete and suggestive, for researchers, of future investigations. Only some old references should be changed, if possible, by adding more recent data.

We again searched the reports on the analyses for the serum concentrations of BCAAs and AAs in patients with liver diseases using PubMed and the major textbooks. However, all of the reports regarding the serum BCAAs concentrations are old. Other reviews also cited only old references.

We hope the manuscript is now acceptable for publication in your Journal. We are looking forward to hearing from you soon.

Best regards,

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