

March 16, 2016

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 24979-Revised manuscript).

Title: Development of combined hepatocellular cholangiocarcinoma: many controversies to be addressed

Author: Anqiang Wang, Yongchang Zheng, Juan Wu, Chengpei Zhu, Hanchun Huang, Shanshan Wang, Liangcai Wu, Xueshuai Wan, Haohai Zhang, Ruoyu Miao, Xinting Sang and Haitao Zhao

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 24979

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

1. Format has been updated
2. Revision has been made according to the suggestions of the reviewer

(1) **Suggestion:** language polishing

Response:

Change the word “the” to “this” in “abstract” section, line2

Add a word “the” in “abstract” section, line4

Add words “of this disease” in “abstract” section, line8

Add a word “still” in “introduction” section, line7, paragraph2

Add a word “literature” to “literatures” in “introduction” section, line1, paragraph3

Add a phrase “With the development of medicine” in “Evolution of CHC classification” section, line 1, paragraph 2

Add a word “occurred” in the “origin” section, line1

Add a word “also” in the “protein” section, line9

Add word “the function of” in the “unsolved problems” section, line17

Add word “ for CHC” in the “prognosis” section, last line.

Change the word “diversity” to “numbers” in the “prospective” section, line8

(2) **Suggestion:** some important references should be discussed.

Response:

1. We discussed the reference “Zhu CP, et al, Research progress and prospects of markers for liver cancer stem cells. World J Gastroenterol. 2015 Nov 14; 21(42): 12190-6” in the “protein level” section, line 11

2. We discussed the effect of liver transplantation concerned the reference “Long-term outcome of patients undergoing liver transplantation for mixed hepatocellular carcinoma and cholangiocarcinoma: an analysis of the UNOS database by Vilchez V et al,HPB (Oxford). 2016 Jan; 18(1): 29-34” in the “treatment “ section, line2, paragraph 3

3. We compared the difference of prognosis between CHC and HCC and discussed the reference “Outcomes and prognostic factors of cirrhotic patients with hepatocellular carcinoma after radical major hepatectomy by Zhou L et al (World J Surg. 2007 Sep; 31(9): 1782-7)” in the “prognosis” section, line7

4. We discussed the risk factors of CHC and other liver cancers and cited the reference “Wan XS, et al, Intraductal papillary neoplasm of the bile duct. World J Gastroenterol. 2013 Dec 14; 19(46): 8595-604” in the “clinical features” section, line6,

3. Revision has been made according to the suggestions of the reviewer

(1) Add running title in the text

(2) Add core tip in the text

(3) Provide a language editing certificate

(4) Delete the funding support

(5) All changes are marked in red font

4. 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 on a light-colored rectangular background. The signature reads "Haitao Zhao" in a cursive, slightly slanted script.

Haitao Zhao, MD
Department of Liver Surgery
Peking Union Medical College Hospital
Chinese Academy of Medical Sciences
1 Shuaifuyuan, Wangfujing, Beijing
Fax: +86-10-69156042
E-mail:zhaht@pumch.cn