Dear Editors:

Please find enclosed the edited manuscript in Word format (file name: answering reviewers)

Title: A Critical Role of Yin-Yang 1 in Autoimmune Hepatitis Through the Regulation of TBX21 Gene Expression Mediated By the T-1993C Polymorphism

Authors: Wei Sun, Hong-Yan Wu, Song Chen

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

Revision has been made according to the suggestions and comments of the reviewers:

Reviewer #1:

(1) **Comment:** How many of the AIH patients were positive for F-actin? Only anti-SMA positivity is not enough for the diagnosis of AIH-1.

Response: In study, Fa-actin was not detected, instead, autoantibodies were

determined by indirect immunofluorescence on murine tissue sections, and a serum titer of 1:100 or greater was considered positive for all antibodies. Among the 20 patients, 15 (75%) had ANA, 3 (15%) had SMA, and 2 (10%) were positive for both (Table 1).None of the patients was seropositive for liver–kidney microsomal 1 antibody (anti-LKM1) or antimitochondrial antibody. These findings justified the diagnosis of AIH-1. Moreover, liver biopsy was performed in each patient. The liver histology of all patients showed interfacial hepatitis or portal inflammation. According to the revised scoring system of the International Autoimmune Hepatitis Group (IAIHG)(Alvarez F, et al. J Hepatol, 1999;31:929–938), all our 20 patients had pretreatment scores exceeding 15, who fuifilled the diagnostic criteria of IAIHG for AIH.

(2) **Comment:** How were their clinical parameters? (incl.: HCV status, comorbidities, smoking and drinking habits, disease onset etc.)

Response: Thanks for your helpful suggestion. We have re-drawn the above-mentioned content , and added a table (Table 1) to show the demographic and clinical parameters of all patients in the **Subject** portion of our revised manuscript.

(3) **Comment:** What can be the role of TBX21 in other AIHs, and overllap syndromes

Response: Thanks for your question. Results from our previous epidemiologic study showed that there was significantly decreased frequency of TBX21-1993C allele in AIH patients, compared with that in healthy controls (3% *vs* 11.8%, Hum Immunol,

2011; 72: 69-73). It is difficult for us to collect more peripheral blood samples of AIH patients with TBX21-1993TC genotype in a short period of time. This is the limitation of this study. To elucidate the relationship between the T-1993C polymorphism and the development of AIH, further detailed analysis of a large number of AIH patients carrying the TC genotype is required. In our previous and present studies, patients with autoimmune overlap syndrome were excluded, thus the role of TBX21 in these autoimmune liver diseases remains to be clarified.

Reviewer #2

(1) **Comment:** few data are shown on the clinical features of patients with AIH-1 used for this study. Therefore, clinical significance of the observed phenomenon is hard to understand.

Response: Thanks for your comments. We have added a table (Table 1) to show the demographic and clinical parameters of all patients. All of the revisions are highlighted in the revised version of manuscript.

(2) **Comment:** Minor point What are the percentages of patients with AIH-1 having TBX21-1993TC allele or -1993TT allele?

Response: Results from our previous case-control study (84 cases and 318 control subjects) showed that 94% of patients with AIH-1 had TBX21 -1993TT genotype and 5% of AIH-1 patients presented -1993TC genotype (Hum Immunol, 2011; 72: 69–73).

Once again, thank you very much for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Dr. Song Chen

Institute of Infectious Diseases, Southwest Hospital

Third Military Medical University

Chongqing 400038, China