Dear Prof. Yuan Qi,

Thank you very much for your efforts on our work. According to Reviewers' constructive comments, we have carefully checked and revised the relevant contents. The detailed revisions have been highlighted in the revised manuscript, and we hope that the improved manuscript can be reconsidered in the journal. Many thanks for your continued attention again.

Yours sincerely,

Ai-Lan Qin

Reply to Reviewers' comments:

Reviewer 1:

WJG-20161126103922 In the present study, the authors demonstrated change in Th17/Treg ratio in autoimmune liver disease. The results are interesting, and believed to provide readers and investigators with good information.

Comments 1-However, the authors did not present autoantibodies of the patients. It is recommended that analyses on the correlation among Th17/Treg ratio, autoantibody, and clinical features of the disease.

Reply: First of all, thank you very much for your recognition of the scientific value of this article. Our study aimed to discuss the relationship between autoimmune liver disease and immunoragulation cells. Autoantibodies are important in diagnosis of autoimmune liver disease, and they are not affected by control of symptoms or disappear of symptoms. However, these contents are not our aims, and we will perform the relevant study in future. Many thanks for your kind suggestion.

Comments 2-There are many typographical errors. it is recommended that manufacturers of materials and devices should be cited as followings: "material (manufacturer's name, city, province (abbreviated), country)". After that, only manufacturer's name is required when repeatedly cited.

Reply: We are very sorry because of language error. The manuscript has been completely checked and edited by a professional English editing company, and the detailed revisions have been highlighted in the revised manuscript. Thanks.

The certificate of English editing:

Comments 3-Please check the abbreviation of γ-glutamyltransferase, and describe in a consistent

manner: γGGT, γGT or GGT?

Reply: They have been changed to "γ-GT".

Comments 4-In Table 1, P=0.000 is inappropriate. "P<0.001" is recommended. The data of only GLB is described as "mean±SD". You'd better describe in a consistent manner. In addition, full names of the abbreviations should be described below the table.

Reply: We have changed my error and marked it with red in revised manuscript.

The updated Table 1:

Table 1 Liver function in group E.

Liver function	Subgroup EA (n=31)	Subgroup ER (n=11)	*P*
TBIL (μmol/L)	133.10 (55.00,200.20)	17.60 (12.10,24.90)	<0.001
DBIL (μmol/L)	87.20 (38.80,151.10)	7.60 (6.20,15.80)	<0.001
ALT (U/L)	116.00 (47.00,314.00)	28.00 (10.00,56.00)	<0.001
AST (U/L)	103.00 (76.00,343.00)	37.00 (30.00,51.00)	<0.001
ALP (U/L)	128.00 (113.00,173.00)	74.00 (51.00,110.00)	=0.001
γ-GT (U/L)	160.50 (99.75,281.00)	34.00 (16.00,44.00)	<0.001
GLB (g/L)	29.69±5.70	28.89±4.35	0.678

Note: total bilirubin (TBIL), Direct bilirubin (DBIL), glutamic-pyruvic transaminase (ALT), glutamic- oxaloacetic transaminase(AST), alkaline phosphatase(ALP), γ-glutamyltransferase (γ-GT).

Comments 5-I cannot find Table 2. 6) In Table 3, there are no data of Th1 and Th2 mentioned in the title. And why not describe as "mean±SD". 7) It is also recommended that page and line numbers are required in the manuscript.

Reply: Indeed, due to these cases were not normally distributed, they were only described with median. The page and line numbers have been presented in the revised manuscript. Thanks.

Reviewer 2:

Comments 1-Although the role of the T reg is well known, it is important that such works be published. Because AILD are uncommon diseases, it is necessary that scientists from different centers report their research so that the therapeutic result improves even more in the future.

Reply: Thank you very much for your recognition of the scientific value of this article.

Reviewer 3:

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 31586

Manuscript Type: ORIGINAL ARTICLE

Title: Clinical significance of changes in the Th17/Treg ratio in autoimmune liver disease

Authors: Ting-Ting Feng, Ting Zou, Xin Wang, Wei-Feng Zhao, Ai-Lan Qin*

Correspondence to:Ai-Lan Qin

Comments 1-What did this study explore?

Reply: The th-17 cells are induced the differentiation and survival by IL-23, and secrete IL-17, IL-21, IL-22, IL-6, TNF-α, and other cytokines, among which IL-17 can induce other inflammatory cytokines such as IL-6 and TNF-α, and chemokines such as monocyte chemoattractant protein-1, 2 (MCP-1,2), thus causing the local infiltration of inflammatory cells and inflammatory injury of tissues and organs. Th17 cells may be increased due to infection or drug-triggered autoimmune liver cell damage, in which the body secretes a large number of inflammatory factors and induces the Th17 differentiation, thereby exacerbating the inflammatory process of liver cells. TGF-β induces the initial T cells to differentiate into the Foxp3 + Treg cells, thus maintaining immune tolerance and preventing the occurrence of autoimmune diseases. IL-6 or IL-21 and other inflammatory factors are secreted when the body is infected or invaded by pathogens, and inhibit the differentiation of Treg cells together with TGF-β as well as promotethedifferentiation of Th17 cells. So, Th17 / Treg ratio disorder then occurs and then mediates inflammatory responses.We divided the patients with autoimmune liver disease into the remission group, the progression groups, the good prognosis group, and the remitted prognosis group, and observed the changes of Th17 and Treg: on one hand, we can determine the disease conditions and guide the medication based on the patient's Th17 and Treg changes, on the other hand, we can continuously understand the immunological statuses of the patients with different prognosis so as to provide some experimental data. Indeed, the relevant content has been presented in the current version. Thanks.

Comments 2-How did the authors perform all experiments?

Reply: The detailed experiments have been presented as listed below, and the relevant contents are simplified described in the current version. Thanks.

The relevant detailed experiments:

1、reagents

PE-labeled IL-17A monoclonal antibody and Leukocyte Activation Cocktail and FITC-labeled CD4, CD8, and IFN-γ monoclonal antibodies (BD GolgiPlugTM).PE-labeled CD127, CD161, CD279, CD14, and IL-4 monoclonal antibodies, ECD-labeled CD3 monoclonal antibody, PC5-labeled CD25, CD3, CD4, CD2, and CD8 monoclonal antibodies, and

IntraPrepPermeabilization Reagent, including the sheath fluid and the cleaning solution.CD45-FITC / CD3-PC5 / CD4-RDl / CD8-ECD, CD45-FITC / CD3-PC5 / CD56-RD1 / CD19-ECD.

2、**instrument：** Beckman Couler XL AT09010

3、**blood sampling：** 2ml of venous blood was sampled into one heparin-anticoagulant tube, and mixed up-and-down 5 times for future use.

4、**Detection of Th17 and Treg**

30 μl of stimulant (BD Pharmingen ™: 10% heat-inactivated FBS-containing 1640 medium = 1: 50) was added into 50 μl of whole blood and shaken, and incubated at 37 ° C and 5% CO2 for 4-6 h; the mixture was then added 5ul of CD3-ECD and CD8-PC5, respectively, shaken, and incubated in darkness for 15min, followed by shaking and 15-min incubation with 100ul of IntraPrepPermeabilization Reagent1; after shaken with 1ml of PBS, and centrifuged at 1500r / min for 5min, the supernatant was discard, and the residue was added 100ul ofIntraPrepPermeabilization Reagent2 for shaking and 15-min incubation at 37℃and 5% CO_2; 5ul of corresponding antibodies were then added, shaken, and incubated in darkness for 25min； after washed using 2ml of PBS, shaken, and centrifuged at 1500r / min for 5min so as to discard the supernatant（twice）， 500ul of PBS was used to re-suspend the residue for the detection, with CD3-ECD as the gate and counting 3000-5000 cells。

5、labeled antibodies of detected cells

$CD4^+$T cells（$45^+3^+4^+$） and $CD8^+$T cells（$45^+3^+8^+$）: CD45-FITC/CD3-PC5/CD4-RD1/CD8-ECD;

Treg cells（$4^+25^+127^\pm$）: CD4-FITC, CD25-PC5, CD127-PE;

Th17 cells ($3^+8^-IL17^+$): CD3-ECD, CD8-PC5, IL-17A-PE.

Comments 3-How did the authors process all experimental data?

Reply: Indeed, SPSS 20.0 statistical software was used for statistical analysis (SPSS, Inc., Chicago, IL, USA). Normally distributed data are presented as the mean ± standard deviation, whereas non-normally distributed data are presented as medians with the interquartile range (25th–75th percentile). Groups with normally distributed data were compared by using the Student's t-test. Data from the groups with non-normally distributed data were compared by the Mann-Whitney U-test. More than two groups were compared by using the Kruskal-Wallis H-test. Comparisons of group counts were carried out by using the chi-squared test. In all cases, differences between groups were considered to be significant when $P < 0.05$. Thanks.

Comments 4-How did the authors deal with the pre-study hypothesis?

Reply: We divided the patients with autoimmune liver disease into the remission group, the progression groups, the good prognosis group, and the remitted prognosis group, and observed the changes of Th17 and Treg.

Comments 5-What are the novel findings of this study?This file must be signed by the corresponding author and provided in a PDF format.

Reply： To investigate the roles of Th17/Treg in the onset and development of AILD. Thank you.

Comments6-Please provided language certificate by professional English language editing companies. For manuscripts submitted by Non-Native Speakers of English, the authors are required to provide a language editing certificate, which will serve to verify that the language of the manuscript has reached Grade A. You can find the details of the language editing process for manuscripts submitted by Non-Native Speakers of English at http://www.wjgnet.com/bpg/gerinfo/240.

Reply: We are very sorry because of language error. The manuscript has been completely checked and edited by a professional English editing company, and the detailed revisions have been highlighted in the revised manuscript. Thanks.

Comments7-Please provide the grant application form(s). If you can't provide it, please delete this part.Please provide the approved grant application form(s) or funding agency copy of any approval document(s)/letter(s). For manuscripts supported by various foundations (i.e., charitable, not-for-profit organizations), the authors should provide a copy of the full approved grant application form(s) or funding agency copy of any approval document(s)/letter(s), consisting of the information section and body section in PDF format. The approved grant application form(s) or funding agency copy of any approval document(s)/letter(s) will be released online together with the manuscript in order for readers to obtain more information about the study and to increase the likelihood of subsequent citation.

Reply: According to your kind suggestion, the relevant grant application forms have been provided as listed below. Thanks.

The application forms of China Foundation for Hepatitis Prevention and Control (TQGB20150026) and Kejiaoxingwei project of Suzhou (KJXW2016004)

Comments8-This statement must be mentioned in the text, and a certificate of statistical review signed by a biostatistician must be provided in PDF format.Sample wording: The statistical methods of this study were reviewed by [name(s) of individual(s)] from [name(s) of organization(s)]…All files must be signed by the corresponding author and provided in a PDF format.

Reply: Indeed, This study only performed simple grouping and is not one randomized, double-blind, prospective control trial, so only the medians or averages were performed pairwise comparison, and no statistician is necessary.

Comments9-Please write the COMMENTS section at here. See the format in the Format.

COMMENTS (1) Background

Reply: Autoimmune liver disease is a group of liver injuries mediated by abnormal autoimmune disorders,it is very important to improve its recognition and diagnostic level, further clinical research and practice are needed for better diagnosis and treatment of AILD.

(2) Research frontiers: To introduce briefly the current hotspots or important areas in the research field as related to your study.

Reply: To investigate the function of regulatory T cells and the molecular mechanisms in autoimmune diseases using specific signaling pathways as the target molecules.

(3) Innovations and breakthroughs

Reply: We divided the patients with autoimmune liver disease into the remission group, the progression groups, the good prognosis group, and the remitted prognosis group, and observed the changes of Th17 and Treg.

(4) Applications: To summarize the practical applications of your research findings, so that readers may understand the perspectives by which this study will affect the field and future research.

Reply: On one hand, we can determine the disease conditions and guide the medication based on the patient's Th17 and Tregchanges, on the other hand, we can continuously understand the immunological statuses of the patients with different prognosis so as to provide some experimental data.

(5) Terminology: To describe concisely and accurately any terms that may not be familiar to the majority of the readers, but which are essential for understanding your article.

Reply: Autoimmune liver disease (AILD), Flow cytometry：can label related molecules on cell surface, thus distinguishing different cell groups. Biochemical markers and specific proteins：such as total bilirubin (TBIL), direct bilirubin (DBIL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), γ-glutamyltransferase (γ-GT), and globulin (GLB).

Th17 cells：a newly discovered T cell subset capable of secreting interleukin 17 (IL-17), which is of great significance in autoimmune diseases and body defense responses.

Treg cells： a class of T cell subsets capable of controlling autoimmune reactivity, and closely related to autoimmune diseases, so its abnormal expression can lead to autoimmune diseases.

Peer-review

Reply: This is a peer-review paper in the journal.

Comments10-Please provide the decomposable figure of Figures, whose parts are movable and can be edited. So please put the original picture as word or ppt or excel format so that I can edit them easily.

Reply: According to your comments. We have provided the decomposable figure of Figures in the revised manuscript.