

Jul. 25th. 2017

RE: MS#32657

Jing Yu, Science Editor, Editorial Office
Lian-Sheng Ma, President and Company
The World Journal of Gastroenterology

Dear Dr. Jing Yu and Dr. Lian-Sheng Ma:

Subject: Submission of revised paper **“STAT3 deficiency prevents hepatocarcinogenesis and promotes biliary proliferation in thioacetamide-induced liver injury.”** (MS#32657) as a research article in *World Journal of Gastroenterology*

We thank referees for careful reading our manuscript. In response to the Referees' useful comments, we have revised the manuscript. Our responses are given in a point-by-point manner below. After native editing, changes to the manuscript are shown highlight in yellow.

We hope the revised version is now suitable for publication and look forward to hearing from you.

Sincerely,

Takafumi Yoshida, M.D., PhD.

Assistant Professor.

Division of Gastroenterology, Department of Medicine; Liver Cancer Research

Division, Research Center for Innovative Cancer Therapy, Kurume University School of Medicine

Response to Reviewer #1:

Reviewer #1: It is very written manuscript and need Minor revision. Fig1B and D seems no statistical significance, the data need to be revised.

According to reviewer's comment, we re-evaluated with increased specimens and confirmed statistical significance (revised Fig1C and E). To demonstrate clearly the difference, we replaced error bar of standard deviation with that of standard error.

Fig1A and C, Fig2A, Fig3A and B, Fig4A and Fig5C need add bar.
We added scale bar in the indicated figures.

Response to Reviewer #1:

Reviewer #2: The authors provided evidence showing that STAT3 may mediate carcinogen-induced HCC in mouse model. Hepatocyte-specific deletion of STAT3 reduced compensatory proliferation and cancer formation in response to TAA. Additional test indicated that deficiency of STAT3 enhanced YAP activation and SOX9 expression, which may contribute to the enhanced formation of biliary ductular structures. The manuscript was well-written; the results are straightforward. However, some weaknesses need to be addressed.

1. Please provided genotyping data of the hepatocytes/liver tissues of wt and STAT3dhep;

According to reviewer's comment, we performed immunoblotting analysis to confirm deficiency of STAT3 with isolated hepatocytes (revised Fig1A).

2. The discussion should be shortened with an emphasis on how STAT3 signal is linked to SOX9/YAP. structure formation

We shortened discussion and added a description about the link between STAT3 and SOX9/YAP.