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Title: A human liver-chimeric mouse model based on inducible liver injury by diphtheria toxin

Authors: Xiao-Nan Ren, Rong-Rong Ren, Hua Yang, Bo-Yin Qin, Xiu-Hua Peng, Li-Xiang Chen, Shun Li, Meng-Jiao Yuan, Chao Wang, Xiao-Hui Zhou

Correspondence to: Xiao-Hui Zhou, MD, PhD, Professor, Shanghai Public Health Clinical Center, Key Laboratory of Medical Molecular Virology, Ministry of Education and Health, Fudan University, 2901 Caolang Road, Jin Shan District, Shanghai 201508, China. zhouxiaohui@shaphc.org

Telephone: +86-21-37990333

Fax: +86-21-37990333

1 What did this study explore?

Our study explore a novel inducible liver injury mouse model and then utilize this model to establish liver-humanized mice.

2 How did the authors perform all experiments?

We crossed three mouse strains including Alb-cre transgenic mice, inducible diphtheria toxin receptor (DTR) transgenic mice and SCID-beige mice to create Alb-cre/DTR/SCID-beige (ADSB) mice, and then injected with diphtheria toxin (DT) to establish liver injury mouse model. Transplanted human hepatocytes to the liver injury mice to obtain liver-humanized mice. Animals relevant experimental operation are approved by the Institutional Animal Care and Use Committee (IACUC) of Shanghai Public Health Clinical Center, Fudan University.

3 How did the authors process all experimental data?

The photograph of PCR analysis, histological analysis of liver injury and CD68 immunohistochemistry were faithful showed. Statistical analyses, including ALT level and human albumin level were performed using Prism 5.0 software (GraphPad Software, San Diego, CA, United States). A P value of <0.05 was considered significant.

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

We presumed that DT could induce liver injury in the mice with both Alb-cre and DTR transgenes, and crossing those mice to SCID-beige could get immunodeficient background. Thus, in the created ADSB mice, the host liver injury induced by DT would provide the condition to hold transplantation of human hepatocytes, and the immunodeficient background would prevent the rejection of exogenic transplanted human cells.

Then we performed a pilot study and confirmed our pre-study hypothesis.

5 What are the novel findings of this study?

This study setup a novel mouse model of human liver-chimeric based on inducible liver injury system, in which liver injury can be induced by DT injection in DTR transgenic mice. This mouse model might provide a novel platform for liver diseases, such as hepatitis viruses researches and development of antivirals etc.

Thank you again for your assistant.

Sincerely yours,

Xiao-Hui Zhou, MD, PhD, Professor, Shanghai Public Health Clinical Center, Key Laboratory of Medical Molecular Virology, Ministry of Education and Health, Fudan University, 2901 Caolang Road, Jin Shan District, Shanghai 201508, China.

E-mail:zhouxiaohui@shaphc.org

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Fax: +86-21-37990333