Inhibition of ADORA1 attenuates hepatic steatosis by gut

microbiotaderived acetic acid from Astragalus polysaccharides

Ying Hong^{1#}, Ningning Zheng^{1#}, Xuyun He¹, Jing Zhong², Junli Ma¹, Aihua Zhao³, Xiaojiao Zheng³, Yu Gu¹, Jian Yao⁴, Yue Li⁵, Lin Yuan⁶, Min Lin⁶, Xiong Lu⁶, Jinliang Ping⁷, Pengtao Song⁷, Bingbing Li¹, Ruiting Han¹, Lili Sheng⁸, Weidong Zhang⁹, Kan Ding⁴, Jun Liu⁵, Wei Jia^{3,10*} and Houkai Li^{1*}

¹Functional Metabolomic and Gut Microbiome Laboratory, Institute of Interdisciplinary Integrative Medicine Research, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China

²Huzhou Key Laboratory of Molecular Medicine, Huzhou Central Hospital, Huzhou 313000, China

³Shanghai Key Laboratory of Diabetes Mellitus and Center for Translational Medicine, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai 200233, China

⁴Glycochemistry and Glycobiology Laboratory, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China

⁵Department of Endocrinology, Shanghai Fifth People's Hospital affiliated to Fudan University, Shanghai 200240, China

⁶Experiment Center for Science and Technology, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China

⁷Department of Pathology, Huzhou Central Hospital, Huzhou 313000, China ⁸Department of Pathology and Laboratory Medicine, University of California, Davis, Sacramento, California, USA

⁹Department of Phytochemistry, College of Pharmacy, Second Military Medical University, Shanghai 200433, China

*Corresponding author

Wei Jia, University of Hawaii Cancer Center, Honolulu, Hawaii, USA; wjia@cc.hawaii.edu; 808-564-5823.

Houkai Li, Functional Metabolomic and Gut Microbiome Laboratory, Institute for Interdisciplinary Medicine Sciences, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China; houkai1976@126.com; +86-21-5132-2729.

¹⁰University of Hawaii Cancer Center, Honolulu, Hawaii, USA

[#]These authors contributed equally

Abstract

The authors have withdrawn this manuscript, because some data could not be replicated. During the process of subsequent revision of the manuscript, we separated the data into two parts. The majority data of the preprint draft, the anti-NAFLD effect of *Astragalus* polysaccharides (APS) in mice and the contribution of gut microbiota, were independently published in 2021 after substantial revision (doi: https://doi.org/10.1080/19490976.2021.1930874). However, the data on figure 6 (about ARs inhibitors DPCPX orally ameliorating NAFLD in mice, and *Adoral* si-RNA data *in vitro*) could not be fully replicated in subsequent experiments. The most probable reason might be due to the batch differences of mice / cells, or other undetermined factors during experiment. Moreover, we have carried out in-depth studies on the exact role of hepatic A₁R on NAFLD formation, which is opposite to our prior assumption. Therefore, we do not wish this work to be cited as reference for the project. We apologize for any inconvenience caused to our readers. Any questions can be addressed to first/corresponding author.