Commentary

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Journal of Clinical and Molecular Pathology

2020
Vol.4 No.1:25

DOI: 10.36648/molecular-pathology.4.1.25

Commentary on Hepatic CD147 knockout modulates liver steatosis and up-regulates autophagy in high-fat-diet-induced NAFLD mice

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Received date: April 09, 2020; **Accepted date:** April 16, 2020; **Published date:** April 27, 2020

Citation: Chen ZN (2020) Commentary on Hepatic CD147 knockout modulates liver steatosis and up-regulates autophagy in high-fat-diet-induced NAFLD mice. J Clin Mol Pathol Vol. 4 No.1: 01

Keywords: Hepatic CD147; Non-alcoholic; Fatty liver disease; Liver transplantation

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The current work "Hepatic CD147 knockout modulates liver steatosis and up-regulates autophagy in high-fat-diet-induced NAFLD mice" reported the expression of CD147 in liver tissues of non-alcoholic fatty liver disease [1]. Non-alcoholic fatty liver disease, also known as metabolic (dysfunction) associated fatty liver disease, has emerged as the most common form of chronic liver disorder worldwide ADDIN NE [2]. Over 90% of obese, 60% of diabetic and up to 20% normal-weight people develop NAFLD, which is the main cause of chronic liver disease, and the second most common reason for liver transplantation ADDIN NE [3]. However, the pathogenesis of NAFLD still remains largely unclear. Accumulating evidence indicates that increased uptake of free fatty acids (FFA) into the liver, decreased lipid catabolism, enhanced de novo lipogenesis and impaired autophagy may contribute to the pathogenesis of NAFLD ADDIN NE [4-7].

At present, the most effective treatment of NAFLD is diet control and exercise to reduce body fat ADDIN NE [8]. There is no effective drug treatment for NASH yet. On June 9th this year, FDA will hold an advisory committee meeting on whether to approve intercept's obeticholic acid. Obeticholic acid is a specific steroid FXR agonist based on the structural modification of cholic acid. It was approved in 2016 in the United States for the treatment of primary biliary cholangitis. In February 2019, in a phase 3 clinical trials for NASH patients, obeticholic acid significantly improved liver fibrosis in NASH patients, reaching the main end point of the study. It is the first NASH drug in research that has achieved success in phase 3 clinical trials so far ADDIN NE [9].

In the current work, Lou and her colleagues investigated that molecule CD147 modulates liver steatosis and autophagy in high-fat-diet-induced NAFLD mouse models for the first time. In this study, a high-fat diet emplored to induce a mouse model with metabolic parameters similar to those of human NAFLD ADDIN NE [10]. The researchers compared the liver tissues of 16 NAFLD patients with 6 normal adults. The preliminary results showed that the expression of CD147 was negative in normal liver samples, while the expression was positive in 16 fatty liver samples. They also performed the immunohistochemical staining for the paraffin sections of liver tissues from NAFLD patients, and found that the up-regulated CD147 was negatively correlated with the expression of LC3, while it was positively correlated with the expression of protein P62. Although the study had the limitation of a small sample size for the NAFLD patients and Normal Donors, the results indicate that CD147 has potential diagnostic and therapeutic significance in NAFLD.

Further study in NAFLD mouse model showed that hepatic specific CD147 knockout could alleviate HFD-induced liver steatosis and increase autophagy in NAFLD in mice, and CD147-mediated reduction in hepatocyte autophagy correlated with PI3K/AKT/mTOR signaling pathway. The results revealed that impaired autophagy not only affects hepatocyte metabolism but also induces steatosis. The obtained results are also vital to understand the role of CD147 in the development of NAFLD, suggesting that CD147 might be a potential target for NAFLD treatment in future.

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