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Editorial

The New Insights for Inflammation and Nonalcoholic Fatty Liver Disease

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Nonalcoholic fatty liver disease (NAFLD) is a chronic liver disease associated with the impairment of hepatic lipid metabolism. NAFLD begins as abnormal lipid accumulation in the liver (simple steatosis), and non-alcoholic steatohepatitis (NASH) is a severe stage of NAFLD that can further develop different degrees of hepatic fibrosis and hepatocellular carcinoma. The causes of NAFLD result from lifestyles, polymorphisms, dietary habits and environmental factors.

Cholesterol and fatty acid play critical roles in hepatic lipid metabolism. Hepatic cholesterol accumulation exhibits the imbalance of cholesterol homeostasis caused by increased cholesterol synthesis and decreased cholesterol excretion [1]. The more oxidative derivatives of cholesterol namely oxysterols combined with excessive fatty acid contribute to the pathogenesis of NAFLD by disrupting mitochondrial and hepatocellular function [2,3]. Oxysterols can act as lipid mediators through interacting with receptors, transporters and regulatory proteins [4]. The higher levels of non-esterified fatty acids (NEFA) are positively correlated with de novo lipogenesis of NAFLD [5]. In addition, abnormal hepatic fatty acid synthesis and uptake is accompanied with the expressions of related metabolic genes, including acetyl-CoA carboxylase (ACC), fatty acid synthase (FAS), sterol regulatory element-binding protein 1c (SREBP-1c), and adipose differentiation-related protein (ADRP) [6].

Excessive lipid accumulation in hepatocytes triggers chronic endoplasmic reticulum (ER) stress and induces a series of inflammatory responses and hepatic pathologies.

Additionally, inflammation has been thought to be involved in many liver diseases, including chemical hepatitis (alcohol and toxin), viral hepatitis and NAFLD. The higher expressions of inflammatory cytokines and tumor necrosis factor α (TNFα) are closely related to the progression of NAFLD [7]. Moreover, the impairment of lipid metabolism via the inflammatory signaling of toll-like receptor 4 (TLR4) and nuclear factor κB (NFκB) has been reported in high fat diet (HFD)-induced NAFLD [8].

NEFA also activates hepatic NFκB inflammatory pathway to promote hepatic steatosis under HFD condition [9]. Thus, lipotoxicity-induced hepatic injury through inflammation displays the pathogenesis of NAFLD.

Interestingly, the dietary fat composition (unsaturated fatty acids or saturated fatty acids) can modulate hepatic lipid metabolism, such as fatty acid oxidation and fatty acid synthesis [10]. The well-known dietary omega-3 (ω-3) polyunsaturated fatty acids, namely eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have beneficial effects on the prevention of hepatic inflammation associated with lipid accumulation in NAFLD [11]. In addition, some novel medications and targets can be used as pharmacotherapy for NAFLD because they exhibit therapeutic effects on hepatic lipid metabolism, metabolic or oxidative stress and inflammation, including peroxisome proliferator-activator receptor (PPAR) agonists, bile acid-farnesoid X receptor axis, lipogenesis (fatty acid and triglyceride synthesis) antagonists, antioxidants, anti-inflammation agents and immune modulators [12]. Taken together, understanding the underlying mechanism of inflammation induced by lipid dysfunction can provide new insights for improving the development and progression of NAFLD.

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