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Advances in Lipotoxicity Research on Hepatocellular Carcinoma

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Abstract

Hepatocellular carcinoma (HCC), a fifth most continual diagnosed cancer, acquires large amounts of free fatty acids (FAs) to promote cell growth. But how the cancer avoids lipotoxicity is unknown. Here, we discussed some lip toxicity research in HCC. Targeting molecules related to lipotoxicity could be a promising therapeutic approach for HCC.

Keywords: Hepatocellular carcinoma; Endoplasmic reticulum; Altered fatty acid; Free fatty acids; Cholesterol ester; Tricarboxylic acid

Abbreviations:HCC: Hepatocellular Carcinoma; ER: Endoplasmic Reticulum; FA: Fatty Acid; FFAs: Free Fatty Acids; CE: Cholesterol Ester; TA: Tricarboxylic Acid

Global Impact of HCC

Hepatocellular Carcinoma (HCC) is the fifth most continual diagnosed cancer and epidemiological studies have authenticated obesity as a crucial risk factor in its development, recently [1-3]. Endoplasmic Reticulum (ER) and oxidative stress, the dysregulation of adipokines, altered gut microbiota and elevated proinflammatory cytokines have been suggested feasible mechanisms underlie obesity-mediated hepatocarcinogenesis, but the process remains dimness [4-8]. Tumour cells undergo typical metabolic changes to fit to their local environment, what is called "metabolic reprogramming" [9]. The most well-studied of these changes is the Warburg effect, in which tumour cells don't use the normal cellular pathway of mitochondrial oxidative phosphorylation but aerobic glycolysis to exert the energy needed for the synthesis of proteins, nucleic acids and lipids [10]. Altered Fatty Acid (FA) metabolism is another distinction of tumour cells [11].

Lipotoxicity

Lipotoxicity means exposure and accumulation of various lipid species which may cause cellular toxicity or proinflammatory and profibrotic [12]. Relatively small quantities of lipotoxic lipid may exert large negative impact on HCC. While, some others, like omega-3 fatty acids, may decrease lipotoxicity and show a beneficial effect [13]. Potentially lipotoxic molecules include Free Fatty Acids (FFAs) and their derivatives, ceramides [14] diacylglycerol [15] as well ascholesterol [16-18]. FFAs may act in KCs (the resident macrophages of the liver), stellate cells (the cells responsible for most hepatic fibrosis) and hepatocytes [the cells that store most hepatic lipid, including cholesterol and Cholesterol Ester (CE)] and affect insulin signaling, impair membrane function and result in apoptosis [19].

Lipotoxicity Research in HCC

Many studies have reported that lipid metabolism is significantly changed, especially FA synthesis, which is obviously elevated in various types of tumours [20-22]. FAs are synthesized de novo in gross tumour cells, especially in HCC [11,21]. They are essential lipids in cells as they constitute the major structural components of membrane lipids, serve as signalling molecules, an energy source through mitochondria-mediated b-oxidation and Tricarboxylic Acid (TCA) cycle catabolism, storage compounds and incorporation into the cell membrane. However, the enhancive intake of dietary FAs participates with the lipolysis of visceral adipose tissue result in enormous exogenous FA supplies to hepatocytes though the portal vein in obesity [23-26]. This is an extremely feature environment lipid-rich condition for liver cancer, but how the pernicious cells accommodate to it and use it for their recreation is still obscure. Targeting molecules related to lipo toxicity could be a promising therapeutic approach for HCC..

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