

Apoptosis-inducing factor deficient mice fail to develop hepatic steatosis under high fat high fructose diet or bile duct ligation

A study conducted at DBT's National Institute of Immunology (NII), New Delhi tried to find that mitochondria dysfunction could trigger inflammation of the liver. Thus, the study tried to evaluate the apoptosis inducing factor a protein that regulate the permeability of the mitochondrial membrane, function as respiratory chain and an antioxidant.

A mouse model system, Harlequinmouse (Hq Mice) that has defect in apoptosis inducing factor was employed in the present study for investigating the role of AIF in the development of NAFLD. The Hq mice were fed high fat high fructose (HFHF) diet and ligation of bile duct to create inflammation in liver. Further, pathophysiology of NAFLD in mouse model system was evaluated.

Based on the study, team tried to understand that Hq mice failed to develop diet induced hepatic steatosis, suggestive of a role of AIF mediated pathway in the initiation and progression of liver inflammation. Thus, partial loss of AIF appears to be hepato protective.

The study involves the pathophysiology of NAFLD (Non-alcoholic fatty liver diseases) commonly called as fatty liver. This disease includes simple fatty liver (steatosis) where the fat is deposited in the liver and diagnosed accidentally during regular health check-up. This condition is usually reversible by life style modifications. If not controlled, this leads to non-alcoholic steatohepatitis (NASH) where the liver gets further damaged and it develops in fibrosis (scarring of liver) and if not controlled it leads to cirrhosis – the most severe stage, occurring after years of inflammation, where the liver shrinks and liver stops working properly and may lead to liver cancer.

There are several mechanisms that cause steatosis (fatty changes). a. It includes increase in fat supply to the liver, b. decreased fat export from the liver, c. decreased free fat oxidation from the mitochondria and causing stress to liver cells, and d. by increased fatty acid production from carbohydrate food. Apart from this, various cytokines and gut microbes have some role in initiating this process.

Hepatocytes (Liver cells) are normally rich in mitochondria and each hepatocyte contains about 800 mitochondria occupying about 18% of the entire liver cell volume. Mitochondria are the power house of the liver cell. Mitochondria play an important role in hepatocyte metabolism. They help for the oxidation of fatty acids and production of ATP (energy for cells). There are many reasons to indicate that hepatic mitochondrial dysfunction could lead pathogenesis of liver causing NAFLD. Mitochondrial dysfunction may not only cause fat accumulation, but also may lead to the generation of ROS and cytokine production contributing to progression of NAFLD by inducing liver inflammation and fibrosis.

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