Chronic liver diseases: What new insights are there?

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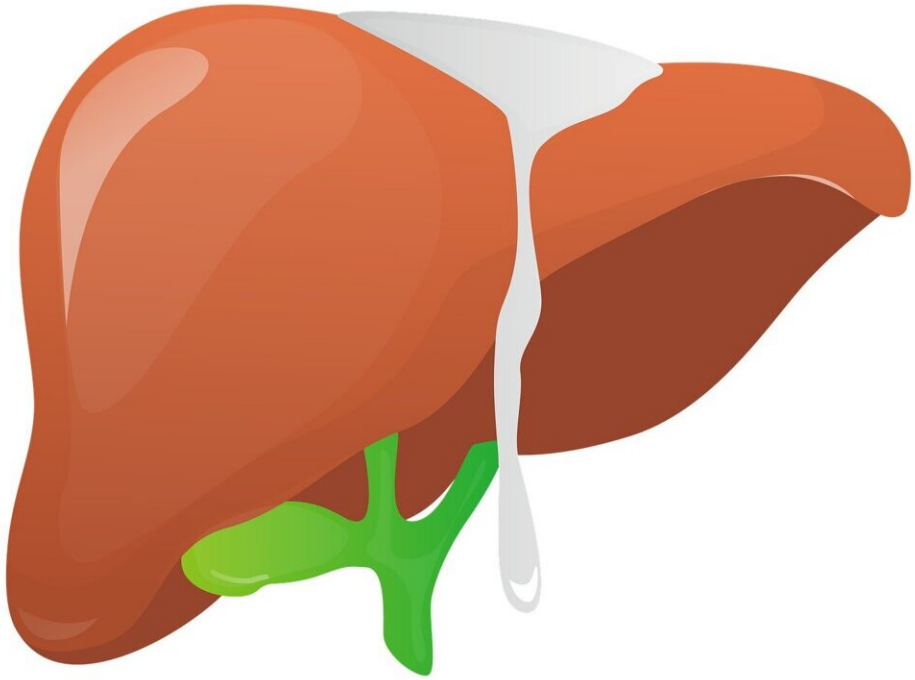

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Fatty liver diseases (FLD) have become a significant health concern worldwide, affecting millions. The two most common types of FLD are non-alcoholic fatty liver disease (NAFLD) and alcoholic-associated liver

disease (ALD).

NAFLD is associated with obesity, insulin resistance, and metabolic syndrome, while ALD is caused by excessive alcohol consumption. Both NAFLD and ALD can progress to liver fibrosis, cirrhosis, and, ultimately, hepatocellular carcinoma (HCC), a primary liver cancer with a poor prognosis.

Significant progress has been made in understanding the pathogenesis of FLD and HCC over the past decade. This has led to the identification of novel therapeutic targets for preventing and treating these diseases.

The fifth Chinese American Liver Society (CALS)/Society of Chinese Bioscientists in America (SCBA) Hepatology Division Annual Symposium, which was held virtually on 21–22 October 2022, focused on recent insights into the pathogenesis of FLD and HCC, as well as the therapeutic targets that have emerged from these studies.

Non-coding RNAs (ncRNAs) are diverse RNA molecules that do not code for proteins. NcRNAs have been shown to play essential roles in the pathogenesis of FLD and HCC. For example, microRNAs (miRNAs) are small ncRNAs that can regulate gene expression at the post-transcriptional level. miRNAs have been implicated in all aspects of FLD and HCC pathogenesis, including steatosis, inflammation, fibrosis, and carcinogenesis.

Autophagy is a cellular process that removes damaged organelles and proteins. Autophagy is essential for maintaining cellular homeostasis and preventing cell death. However, impaired autophagy has been linked to the development and progression of FLD and HCC. For example, studies have shown that hepatocyte-specific autophagy deficiency can lead to steatosis and inflammation.

Extrahepatic signaling refers to communication between the liver and other organs in the body. Extrahepatic signaling plays a vital role in regulating liver metabolism and inflammation. Disruption of extrahepatic signaling has been implicated in the pathogenesis of FLD and HCC. For example, studies have shown that obesity-related changes in adipose tissue signaling can promote the development of NAFLD.

Macrophages are a type of immune cell that plays a crucial role in inflammation. Macrophages are present in the liver and can be activated by a variety of stimuli, including steatosis, injury, and infection. The heterogeneity of macrophages in these diseases were discussed via single cell RNA sequencing. For example, studies have shown that TREM2+CD9+ NASH-associated macrophages are activated in patients with NAFLD and HCC.

In addition to the factors discussed above, other potential therapeutic targets for FLD and HCC include:

- Bile acid metabolism
- Oxidative stress
- Apoptosis
- Angiogenesis
- Epigenetic regulation

The fifth CALS/SCBA Hepatology Division Annual Symposium highlighted the latest research on these and other therapeutic targets for FLD and HCC. This research can potentially lead to new and more effective treatments for these devastating diseases.

Related research is published in the journal *eGastroenterology*.

More information: Yankai Wen et al, Recent insights into the pathogenesis and therapeutic targets of chronic liver diseases,

eGastroenterology (2023). DOI: 10.1136/egastro-2023-100020