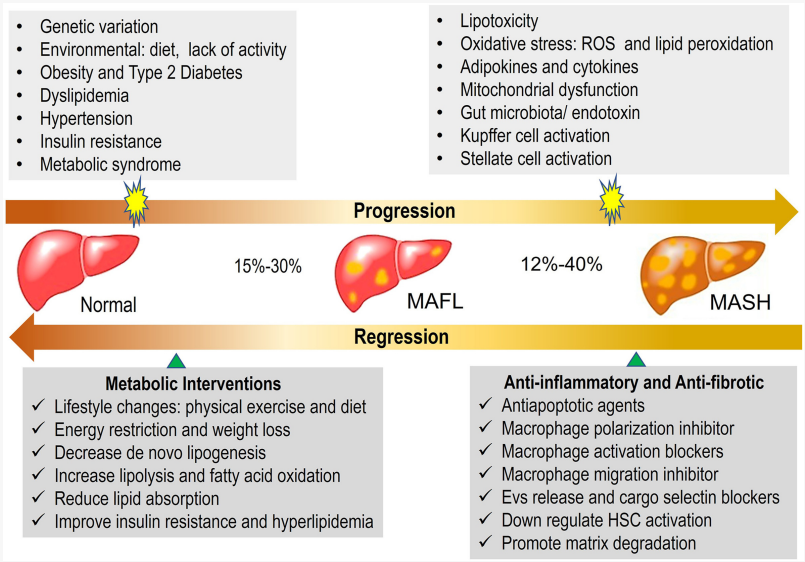
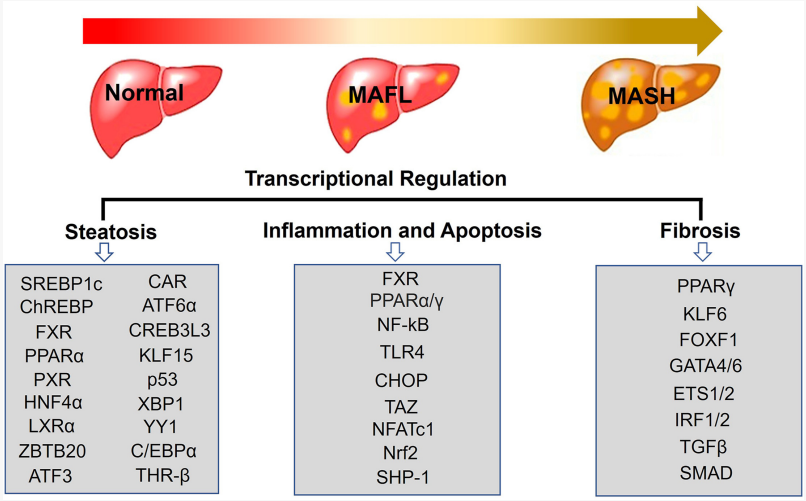
New Avenues for Treating Metabolic Dysfunction-Associated Fatty Liver Disease

SHANNON, CLARE, IRELAND, March 10, 2025 /EINPresswire.com/ -- Metabolic dysfunction-associated fatty liver disease (MAFLD) has become a growing global health concern, affecting millions worldwide. This complex liver disorder ranges from simple steatosis to more severe forms, including metabolic dysfunction-associated steatohepatitis (MASH), which may progress to fibrosis, cirrhosis, and even liver cancer. The latest insights into transcription factors provide a deeper understanding of the disease's progression and potential therapeutic interventions.



The MAFLD spectrum and treatment options for MAFL and MASH.



Transcriptional regulation of steatosis, inflammation, apoptosis, and fibrosis in the progression of MAFLD.

Transcription factors are critical proteins that regulate gene expression, playing a pivotal role in controlling key processes such as lipid metabolism, inflammation, apoptosis, and fibrosis in MAFLD. Several transcription factors, including farnesoid X receptor (FXR), peroxisome proliferator-activated receptors (PPARs), thyroid hormone receptors (THRs), and liver X receptors (LXRs), have emerged as promising drug targets for managing the disease. The ability to modulate hepatic steatosis and fibrosis through these factors presents a new frontier in MAFLD treatment.

Therapeutic advancements have already begun to show promise. FXR agonists such as

obeticholic acid (OCA) have demonstrated potential in reducing liver lipid accumulation and inflammation, though concerns remain over cardiovascular side effects. Meanwhile, resmetirom, a selective THR-β agonist, has received FDA breakthrough therapy designation due to its ability to reduce hepatic steatosis and inflammation. Additionally, dual PPARα/γ agonists, like saroglitazar, have exhibited positive metabolic effects, including improving insulin resistance, reducing liver fat content, and decreasing fibrosis markers.

Inflammation and apoptosis play a crucial role in the progression of MAFLD to MASH, with transcription factors such as NF-κB, CHOP, and TLR4 contributing to disease severity. Strategies targeting these factors could suppress inflammatory responses and limit hepatocyte damage, thereby slowing disease progression. Similarly, addressing hepatic fibrosis, which is the strongest predictor of liver-related mortality, remains a key focus. Transcription factors such as SMADs, FOXF1, and KLF6 regulate fibrosis pathways and present valuable therapeutic targets.

The ongoing development of transcription factor-based drugs is a significant step toward effective, targeted therapies for MAFLD and MASH. The challenge remains in achieving long-term efficacy while minimizing adverse effects. The next phase of research will focus on fine-tuning these therapeutic agents to ensure optimal benefits for patients.

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