

## 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.

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.

Lipotoxicity Genetic variation Oxidative stress: ROS and lipid peroxidation Environmental: diet, lack of activity Adipokines and cytokines Obesity and Type 2 Diabetes Mitochondrial dysfunction Gut microbiota/ endotoxin Hypertension Kupffer cell activation Insulin resistance Stellate cell activation Metabolic syndrome Progression 12%-40% 15%-30% MAFL MASH Regression Metabolic Interventions Anti-inflammatory and Anti-fibrotic Antiapoptotic agents ✓ Lifestyle changes: physical exercise and diet Macrophage polarization inhibitor Energy restriction and weight loss Decrease de novo lipogenesis Macrophage activation blockers Macrophage migration inhibitor Increase lipolysis and fatty acid oxidation Evs release and cargo selectin blockers Reduce lipid absorption Down regulate HSC activation Improve insulin resistance and hyperlipidemia Promote matrix degradation The MAFLD spectrum and treatment options for MAFL and MASH. **Normal Transcriptional Regulation** Inflammation and Apoptosis **Fibrosis** Steatosis **FXR** CAR **PPARy** PPARα/γ **ChREBP** ATF6α KLF6 CREB3L3 NF-kB FXR FOXF1 TLR4 PPARα KLF15 GATA4/6 p53 CHOP PXR ETS1/2 HNF4α XBP1 TAZ IRF1/2 LXRα YY1 NFATc1 TGFβ ZBTB20 C/EBPa Nrf2 **SMAD** ATF3 THR-β Transcriptional regulation of steatosis, inflammation,

apoptosis, and fibrosis in the progression of MAFLD.

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- $\beta$  agonist, has received FDA breakthrough therapy designation due to its ability to reduce hepatic steatosis and inflammation. Additionally, dual PPAR $\alpha$ / $\gamma$  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-kB, 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.

#####

Genes & Diseases publishes rigorously peer-reviewed and high quality original articles and authoritative reviews that focus on the molecular bases of human diseases. Emphasis is placed on hypothesis-driven, mechanistic studies relevant to pathogenesis and/or experimental therapeutics of human diseases. The journal has worldwide authorship, and a broad scope in basic and translational biomedical research of molecular biology, molecular genetics, and cell biology, including but not limited to cell proliferation and apoptosis, signal transduction, stem cell biology, developmental biology, gene regulation and epigenetics, cancer biology, immunity and infection, neuroscience, disease-specific animal models, gene and cell-based therapies, and regenerative medicine.

Scopus CiteScore: 7.3 Impact Factor: 6.9

######

More information: <a href="https://www.keaipublishing.com/en/journals/genes-and-diseases/">https://www.keaipublishing.com/en/journals/genes-and-diseases/</a> Editorial Board: <a href="https://www.keaipublishing.com/en/journals/genes-and-diseases/editorial-board/">https://www.keaipublishing.com/en/journals/genes-and-diseases/editorial-board/</a>

All issues and articles in press are available online in ScienceDirect (<a href="https://www.sciencedirect.com/journal/genes-and-diseases">https://www.sciencedirect.com/journal/genes-and-diseases</a>). Submissions to Genes & Disease may be made using Editorial Manager (<a href="https://www.editorialmanager.com/gendis/default.aspx">https://www.editorialmanager.com/gendis/default.aspx</a>).

Print ISSN: 2352-4820 eISSN: 2352-3042

CN: 50-1221/R

Contact Us: editor@genesndiseases.com

X (formerly Twitter): @GenesNDiseases (<a href="https://x.com/GenesNDiseases">https://x.com/GenesNDiseases</a>)

######

## Reference

Shuwei Hu, Yingjie Ai, Chencheng Hu, Fathima N. Cassim Bawa, Yanyong Xu, Transcription factors, metabolic dysfunction-associated fatty liver disease, and therapeutic implications, Genes & Diseases, Volume 12, Issue 3, 2025, 101372, <a href="https://doi.org/10.1016/j.gendis.2024.101372">https://doi.org/10.1016/j.gendis.2024.101372</a>

## Funding Information:

National Natural Science Foundation of China 32271218

Genes & Diseases Editorial Office Genes & Diseases + +86 23 6571 4691 editor@genesndiseases.com

This press release can be viewed online at: https://www.einpresswire.com/article/792401598

EIN Presswire's priority is source transparency. We do not allow opaque clients, and our editors try to be careful about weeding out false and misleading content. As a user, if you see something we have missed, please do bring it to our attention. Your help is welcome. EIN Presswire, Everyone's Internet News Presswire™, tries to define some of the boundaries that are reasonable in today's world. Please see our Editorial Guidelines for more information.

© 1995-2025 Newsmatics Inc. All Right Reserved.