Informatics in Biology, Health, and Food

Interdisciplinary Explorations in Life Science

Volume 2. Number 2. Dec. 2025 DOI: 10.22034/ibhf.2025.553840.1036

Review Article

From Fibrosis to Cancer: Emerging Role of the lncRNA MIAT in Liver Pathophysiology and Therapy

Reza Sahebi[1,2]*, Reyhaneh Shaban Hashemabadi[3], Fatemeh Izanlo[3]

[1] Metabolic Syndrome Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

[2] Department of Molecular Medicine, School of Advanced Technologies, Shahrekord University of Medical Sciences, Shahrekord, Iran

[3] Department of Biology, Islamic Azad University of Mashhad, Mashhad, Iran.

Received: 2025/10/17 **Accepted:** 2025/11/17 **Online Published:** 2025/11/17

Abstract

The long noncoding RNA (lncRNA) myocardial infarction-associated transcript (MIAT) has emerged as a potential regulator of the pathogenesis of various liver diseases, including hepatocellular carcinoma (HCC), liver fibrosis, cirrhosis, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), chronic hepatitis C virus (HCV) infection, and chronic liver disease (CLD). This review summarizes evidence showing that MIAT is overexpressed in liver disease tissues, both in human patients and in animal models. In these contexts, MIAT functions as a competing endogenous RNA (ceRNA), sponging microRNAs such as miR-3085-5p, miR-214, miR-411-5p, miR-520d-3p, miR-22-3p, and miR-149-5p. These interactions activate key signaling pathways, including the Hippo/YAP, Wnt/β-catenin, TGF-β/Smad, PI3K/AKT, NF-κB, and STAT3/PD-L1 pathways which collectively promote HSCs activation, epithelial mesenchymal transition (EMT), extracellular matrix (ECM) deposition, and cell proliferation. In HCC, MIAT expression is correlated with advanced tumor stage, poor clinical prognosis, and resistance to targeted therapies such as sorafenib. In liver fibrosis and other CLDs, MIAT sustains inflammatory and oxidative stress responses, thereby linking diverse etiologies, including viral infection and metabolic syndrome. Moreover, MIAT modulates hepatitis C virus (HCV) replication by suppressing innate immune signaling through RIG-I/IRF3 inhibition while enhancing hepatic lipogenesis. Unlike other lncRNAs, such as H19, NEAT1, and TUG1, MIAT uniquely integrates inflammatory, fibrogenic, and oncogenic pathways. Circulating MIAT can also serve as a noninvasive biomarker for early diagnosis and prognostic assessment. Therapeutically, MIAT silencing via siRNAs, antisense oligonucleotides (ASOs), or CRISPR-based strategies has demonstrated both antifibrotic and antitumor efficacy in preclinical models. Key limitations include disease-specific variability and insufficient validation in human studies.

Keywords: MIAT noncoding RNA; HCC; Hepatic scarring; Nonalcoholic steatohepatitis; Hepatitis C; Hepatic inflammation.

Cite this article: Sahebi R, Shaban Hashemabadi R, Izanlo F. From Fibrosis to Cancer: Emerging Role of the lncRNA MIAT in Liver Pathophysiology and Therapy. *Informatics in Biology, Health, and Food*. 2025;2(2):143-157.

Corresponding authors: Reza Sahebi **Email**: Rezasahebi@mshdiau.ac.ir

Introduction

Long noncoding RNAs (lncRNAs) have emerged as key regulators of hepatic pathophysiology through their diverse interactions with transcription factors, chromatin modifiers, and microRNAs (1). These lncRNAs regulate gene expression via either cis- or trans-acting mechanisms. They modulate transcriptional and posttranscriptional processes by promoting chromatin remodeling, repressing transcription, and stabilizing mRNAs (2). In the hepatic microenvironment, lncRNAs coordinate intercellular signaling among hepatocytes, Kupffer cells, hepatic stellate cells, and endothelial cells, shaping the complex networks that promote fibrosis and tumorigenesis (3). The dysregulation of specific lncRNAs, such as HULC, MALAT1, and MIAT, highlights their dual utility as biomarkers and active mediators of hepatic disease progression. Elucidating their mechanistic contributions thus provides a foundational framework for understanding disease etiology and pinpointing novel therapeutic targets (4). Emerging evidence underscores the pivotal role of MIAT in modulating signaling pathways essential for liver fibrosis and hepatocellular carcinoma (HCC) development. In addition, the Hippo/YAP pathway is known to be involved in animal models of fibrosis and in in vitro hepatic stellate cell (HSC) studies (5). MIAT influences other fibrogenic cascades, including the transforming growth factor-beta (TGF-β)/Smad and phosphatidylinositol-3-kinase (PI3K)/AKT pathways. TGF-β is a key regulator of fibrosis. It induces MIAT expression in HSCs, creating a feedback loop that strengthens fibrogenic signals (6). Additionally, MIAT enhances AKT phosphorylation, promoting cell survival and resistance to apoptosis during fibrogenesis (7). These interconnected interactions position MIAT as a key regulator of hepatic fibrogenic signaling, with profound implications for fibrosis resolution and oncogenic transformation. Moreover, HOTAIR acts as a potent regulator of hepatic stellate cell activation, as shown in in vitro and animal studies, enhancing fibrogenesis through multiple mechanisms, including the epigenetic silencing of antifibrotic genes via DNMT1 and the modulation of the TGF-β/Smad and PI3K/AKT signaling pathways. By downregulating miR- 29b, HOTAIR promotes PTEN hypermethylation and increases extracellular matrix deposition. Similarly, MIAT may exert comparable effects in in vitro HSC models by amplifying TGF-β-driven fibrogenic responses in hepatic stellate cells, suggesting that both lncRNAs contribute to a self-reinforcing profibrotic network that accelerates liver fibrosis progression (8). Furthermore, MIAT functions as a competing endogenous RNA (ceRNA), sequestering various microRNAs, including miR-214, in (in vitro) HSC models (9). MIAT modulates the translation of fibrosis-associated target genes via miR-3085-5p and simultaneously acts as a molecular scaffold, coordinating transcriptional, posttranscriptional, and epigenetic mechanisms to drive a profibrotic cellular phenotype. In hepatocellular carcinoma, MIAT exhibits oncogenic properties, with clinical studies reporting its upregulation in tumor tissues compared with adjacent nontumorous liver parenchyma (10). Additionally, MIAT drives cancer cell proliferation, migration, and angiogenesis through the activation of the Wnt/β-catenin and Notch signaling pathways (5). Moreover, its contribution to metabolic reprogramming, particularly in augmenting glycolytic flux and inhibiting mitochondrial apoptosis, is associated with the metabolic adaptability of MIAT, which underpins tumor advancement (11). Accordingly, MIAT has emerged as a potential prognostic biomarker and therapeutic target in HCC on the basis of preliminary clinical data. Advancements in transcriptomic profiling and bioinformatics have enabled the detection of circulating lncRNAs, including MIAT, in plasma and serum, paving the way for their application as noninvasive biomarkers (12). Although the presence of MIAT in exosomes has not been fully validated, accumulating evidence suggests that exosomal lncRNAs can serve as stable and noninvasive biomarkers for liver fibrosis and HCC. Combining such lncRNA-based markers with established indicators such as alpha-fetoprotein (AFP) or fibrotic gene panels may improve diagnostic precision and facilitate personalized medicine strategies (13). Standardizing detection protocols and validating them in expansive

clinical cohorts are imperative for successful clinical implementation. Therapeutically, MIAT represents a promising target for mitigating hepatic fibrosis and tumor progression. Preclinical investigations have demonstrated that the modulation of MIAT expression via small interfering RNAs (siRNAs), antisense oligonucleotides (ASOs), and CRISPR-Cas9 genome editing effectively suppresses MIAT activity in animal models, highlighting its potential as a molecular intervention in liver disease (14, 15). Nanoparticle-based delivery platforms have further improved the specificity and bioavailability of these interventions, reducing off-target effects. Prospective research exploring MIAT inhibition in conjunction with conventional antifibrotic or antineoplastic agents may yield synergistic outcomes, advancing combination therapies. Critical evaluations of pharmacodynamics, tissue biodistribution, and long-term safety are essential to bridge these preclinical insights into clinical applications (15, 16).

In conclusion, the lncRNA MIAT appears to be an important regulator within the molecular framework of liver fibrosis, cirrhosis, and hepatocellular carcinoma. MIAT has diverse functions in signal transduction, epigenetic changes, and noncoding RNA networks. These findings highlight its central role in liver disease. Although significant strides have been made, unresolved challenges persist, notably in characterizing its upstream regulators, cell type-specific activities, and interactions with environmental stressors such as viral infections or metabolic perturbations. Tackling these knowledge gaps via integrative multiomics methodologies and sophisticated molecular modeling will enrich our comprehension of the contributions of MIATs to liver disease and expedite the evolution of innovative diagnostic and therapeutic paradigms. This review aims to comprehensively elucidate the regulatory roles of the lncRNA MIAT in liver diseases, with a particular focus on its interactions with inflammatory, fibrotic, and oncogenic pathways.

Role of the lncRNA MIAT in the Pathobiology and Clinical Applications of HCC

The Hepatocellular carcinoma remains one of the most aggressive and lethal forms of liver malignancy and is among the leading causes of cancer-related deaths worldwide. Despite advancements in diagnostic imaging and targeted therapy, the prognosis of HCC patients remains dismal due to late-stage diagnosis, tumor heterogeneity, and high recurrence rates. Early detection and understanding of the molecular mechanisms underlying tumorigenesis are therefore essential for improving patient outcomes. Long noncoding RNAs (lncRNAs) have recently emerged as crucial regulators in liver cancer biology, orchestrating diverse cellular processes such as tumor initiation, progression, angiogenesis, and immune modulation through transcriptional, posttranscriptional, and epigenetic mechanisms. Among these, the MIAT has gained attention for its potential roles in regulating oncogenic pathways in HCC pathobiology (17, 18). Accumulating evidence indicates that MIAT is markedly overexpressed in HCC tissues compared with adjacent normal liver tissue, with elevated levels correlated with advanced tumor stage, vascular invasion, and poor prognosis (19). Mechanistically, MIAT exerts its oncogenic influence by functioning as a competing endogenous RNA (ceRNA) and epigenetic modulator, integrating multiple signaling cascades that drive hepatic tumor progression. One of the key pathways involves the MIAT/miR-214/β-catenin–EZH2 regulatory axis. MIAT acts as a molecular sponge for miR-214, a tumor-suppressive miRNA that negatively regulates β-catenin and the histone methyltransferase enhancer of zeste homolog 2 (EZH2) (9). MIAT sequesters miR-214. This activates the Wnt/β-catenin pathway and increases EZH2 expression. As a result, EZH2 silences tumor suppressor genes via histone H3K27 trimethylation (9, 20, 21). In addition to its role in proliferation and epigenetic regulation, MIAT also contributes to immune evasion, a hallmark of cancer progression. The MIAT/miR-411-5p/STAT3/PD-L1 signaling axis has been shown to play a central role in modulating immune checkpoint expression. By sponging miR-411-5p, MIAT indirectly

enhances signal transducer and activator of transcription 3 (STAT3) expression, which transcriptionally upregulates programmed death-ligand 1 (PD-L1) expression in HCC cells. Elevated PD-L1 levels suppress CD8+ cytotoxic T lymphocyte activity, thereby enabling tumor cells to evade immune surveillance in human HCC samples and in vitro cell lines (20-21). Thus, MIAT has emerged as a critical regulator of immune checkpoint pathways, linking noncoding RNA regulation with tumor immune microenvironment remodeling. Furthermore, MIAT modulates metastatic potential through the MIAT/miR-520d-3p/EPHA2 signaling pathway (22). Ephrin type-A receptor 2 (EPHA2), a receptor tyrosine kinase implicated in tumor invasion and angiogenesis, is a direct downstream effector of miR-520d-3p in multiple independent cohorts (23). MIAT-mediated suppression of miR-520d-3p results in EPHA2 upregulation, which in turn promotes EMT, enhances migratory capability, and accelerates metastasis formation (22, 23). Clinical analyses have demonstrated that high MIAT expression and reduced miR-520d-3p levels are associated with poorer overall survival, emphasizing their prognostic significance in HCC (22). Importantly, experimental silencing of MIAT or overexpression of miR-520d-3p attenuates tumor cell migration and invasiveness, highlighting this axis as a potential therapeutic target (23). At the intersection of tumor progression and cellular senescence, MIAT influences the miR-22-3p/SIRT1/p53-p21/p16-pRb signaling network. In this context, MIAT functions as a ceRNA for miR-22-3p, resulting in the derepression of SIRT1, an NAD^+-dependent histone deacetylase that inhibits the tumor-suppressive p53/p21 and p16/pRb pathways. The activation of SIRT1 by MIAT leads to the suppression of senescence-associated cell cycle arrest and the evasion of apoptosis, thereby promoting tumor survival and proliferation (24). Conversely, MIAT silencing triggers the activation of senescence pathways and the release of senescence-associated secretory phenotype (SASP) factors, which collectively inhibit tumor growth and induce immunogenic clearance (25). This complex regulatory network underscores the role of MIAT in modulating the balance between tumor proliferation and cellular senescence in HCC(22). From a clinical perspective, MIAT has considerable diagnostic and prognostic potential. Circulating MIAT levels in plasma or serum-derived exosomes have been proposed as noninvasive biomarkers on the basis of human plasma/serum studies (10).

lncRNA MIAT and Liver Fibrosis

Fibrosis occurs due to an imbalance in ECM production and breakdown. This process is driven mainly by HSCs turning into active, contractile cells that produce excess ECM (17, 26, 27). Persistent injury arising from etiologies such as NASH, chronic viral hepatitis (HBV and HCV infection), alcohol-induced liver damage, or biliary obstruction initiates a cascade of inflammatory and oxidative stress responses. These factors, in turn, activate intracellular signaling pathways that perpetuate HSC activation, collagen deposition, and tissue stiffening (28, 29). If unresolved, fibrosis progresses to cirrhosis, a stage characterized by extensive scarring, vascular remodeling, and regenerative nodule formation, predisposing the liver to failure and HCC (30-32). Consequently, elucidating the molecular mechanisms governing HSC activation and ECM accumulation is vital for developing effective antifibrotic therapies. Recent transcriptomic studies have revealed that noncoding RNAs (ncRNAs), particularly long noncoding RNAs (lncRNAs), are critical regulators of hepatic fibrogenesis. LncRNAs modulate gene expression at multiple levels, including chromatin remodeling, transcription, RNA stability, and translation (33). Functionally, they can act as molecular decoys, scaffolds, or guides, influencing transcription factors and chromatin-modifying complexes. Furthermore, by functioning as competing endogenous RNAs (ceRNAs), lncRNAs sequester microRNAs (miRNAs), thereby derepressing target messenger RNAs and altering downstream signaling cascades (9, 17, 34-36). In the hepatic

context, dysregulated lncRNAs contribute to diverse cellular processes ranging from hepatocyte apoptosis and inflammatory cytokine release to HSC activation and EMT, which together orchestrate fibrotic remodeling. This expanding body of evidence underscores lncRNAs as master regulators of fibrogenesis and promising therapeutic targets for liver disease. Among the lncRNAs implicated in liver fibrosis, MIAT has been implicated as a profibrotic mediator in preclinical studies. Recent studies have demonstrated that MIAT expression is markedly upregulated in human fibrotic tissues and in activated HSCs in vitro. Functional assays revealed that MIAT silencing via adenoviral short hairpin RNA (Ad-shMIAT) significantly attenuated HSC proliferation, migration, and contractility while reducing ECM deposition. These findings indicate that MIAT acts as a central regulator of HSC activation and fibrogenic signaling. Mechanistically, MIAT exerts its fibrogenic effects primarily through posttranscriptional regulation within the cytoplasm of HSCs. RNA immunoprecipitation (RIP) and fluorescence in situ hybridization (FISH) analyses have shown that MIAT is predominantly localized in the cytoplasm, where it functions as a miRNA sponge. A key regulatory interaction involves miR-3085-5p, miR-3085-5p, a microRNA that negatively regulates the Hippo/YAP signaling pathway, a critical regulator of cell proliferation and EMT by binding to miR-3085-5p. MIAT binds to and sequesters miR-3085-5p, thereby preventing YAP degradation(5). This pathway is now recognized as a crucial mechanism linking noncoding RNA regulation to cytoskeletal remodeling, ECM synthesis, and fibrogenic progression. In addition to its impact on YAP-mediated EMT, MIAT influences cellular processes related to oxidative stress and apoptosis resistance, which sustain chronic fibrogenic activation (37). Elevated MIAT expression has been shown to suppress ferroptosis, a regulated form of cell death characterized by lipid peroxidation and iron accumulation (38). By downregulating ferroptotic mediators and maintaining mitochondrial homeostasis, MIAT contributes to HSC survival under profibrotic conditions. This antiferroptotic activity not only facilitates ECM deposition but also perpetuates the inflammatory milieu that fuels fibrosis progression (39). The dual function of MIAT in promoting EMT while inhibiting programmed cell death highlights its potential role as a regulator of fibrogenic persistence and tissue scarring in chronic liver injury. From a translational perspective, MIAT presents substantial promise as both a diagnostic biomarker and a therapeutic target. Circulating MIAT levels, which are detectable in serum and plasma, could serve as noninvasive indicators of fibrosis severity or progression, complementing existing diagnostic tools such as elastography and serum fibrosis panels. Therapeutically, targeted silencing of MIAT through antisense oligonucleotides (ASOs), small interfering RNAs (siRNAs), or CRISPR-based gene-editing platforms has shown encouraging results in preclinical models, reducing collagen deposition and restoring normal hepatic architecture. Furthermore, combination strategies integrating MIAT inhibition with antifibrotic agents such as TGF-β or YAP pathway inhibitors could yield synergistic effects, offering a new paradigm for the management of liver fibrosis and cirrhosis. Nonetheless, comprehensive mechanistic studies and controlled clinical trials are needed to evaluate the safety, efficacy, and delivery strategies of MIAT-targeted interventions (5).

lncRNA MIAT and Chronic Liver Diseases

Chronic liver diseases (CLDs) encompass a spectrum of progressive hepatic disorders, including liver fibrosis, cirrhosis, chronic hepatitis, and alcoholic liver disease, all of which represent major risk factors for HCC. Persistent hepatic injury resulting from viral infection, alcohol abuse, metabolic dysfunction, or autoimmune insult leads to sustained cycles of inflammation, hepatocyte death, and regenerative proliferation. Over time, these events promote the activation of HSCs, excessive ECM deposition, and architectural remodeling of liver tissue, ultimately progressing toward cirrhosis and carcinogenesis. The cellular and molecular heterogeneity of CLDs underscores the need to identify upstream regulators that coordinate fibrogenic, inflammatory, and oncogenic pathways. In this context, long noncoding RNAs (lncRNAs), which act through transcriptional,

posttranscriptional, and epigenetic mechanisms, have emerged as key modulators of hepatic homeostasis and disease progression (40). In addition to acting as simple modulators, lncRNAs function in diverse ways: they can act as molecular scaffolds to assemble chromatin-modifying complexes, serve as competing endogenous RNAs (ceRNAs) to sponge microRNAs and derepress target genes, guide transcription factors to specific genomic loci, or influence mRNA stability and translation. In the liver, lncRNAs play critical roles in regulating lipid homeostasis (e.g., triglyceride and cholesterol metabolism), fibrotic pathways (e.g., ECM deposition and HSC activation), inflammatory responses, and oncogenic processes leading to diseases such as NAFLD, fibrosis, and HCC (14). For example, certain lncRNAs modulate de novo lipogenesis and hepatic stellate cell proliferation, whereas others influence apoptosis suppression and angiogenesis during aging-associated liver diseases (41). Among the lncRNAs implicated in hepatic pathophysiology, MIAT has gained increasing attention for its potential role in chronic liver injury and fibrogenesis. Accumulating evidence has demonstrated that MIAT expression is markedly upregulated in fibrotic and cirrhotic liver tissues, as well as in activated HSCs, and is strongly correlated with the accumulation of collagen and the expression of fibrotic markers such as α-smooth muscle actin (α-SMA) and type I collagen (Col1A1). Experimental knockdown of MIAT significantly attenuates HSC proliferation, migration, and ECM deposition both in vitro and in vivo, confirming its profibrotic role in the pathogenesis of CLD (40). HSC activation is regulated primarily by well-known signaling pathways, including the TGF-β/Smad pathway, which induces fibrogenic gene expression and ECM synthesis, and the Hippo/YAP pathway, which promotes HSC contractility and survival during fibrosis progression (42-44). These observations suggest that MIAT functions not only as a downstream effector of chronic hepatic injury but also as an active molecular driver sustaining fibrogenic and inflammatory cascades. Mechanistically, MIAT exerts its regulatory effects primarily through posttranscriptional modulation of signaling pathways that govern HSC activation and EMT. A pivotal mechanism involves the MIAT/miR-3085-5p/YAP1 signaling axis. MIAT functions as a competing endogenous RNA (ceRNA) in both in vitro and animal studies (38). This axis integrates noncoding RNA regulation with mechanotransductive and transcriptional control mechanisms central to liver fibrogenesis, establishing MIAT as a master regulator of HSC plasticity. In addition to its fibrogenic effects, MIAT likely contributes to broader aspects of chronic hepatic pathophysiology, including inflammation, oxidative stress, and metabolic dysregulation. Chronic liver injury is characterized by a persistent inflammatory milieu driven by Kupffer cell activation, cytokine release, and infiltration of immune cells. Preliminary evidence suggests that MIAT may influence inflammatory signaling networks by interacting with the nuclear factor κB (NF-κB) and STAT3 pathways, both of which are pivotal in promoting hepatocellular injury and fibrogenic progression. Given that MIAT modulates immune checkpoint molecules and STAT3 activation in HCC, similar mechanisms may operate at earlier stages of CLD, facilitating immune evasion and chronic inflammation within the hepatic microenvironment. Furthermore, MIAT may regulate oxidative stress responses by altering mitochondrial function and redox homeostasis, potentially through the Nrf2/HO-1 axis, which activates antioxidant enzymes such as GPX4 (to prevent lipid peroxidation and ferroptosis) and SOD2 (to scavenge mitochondrial superoxide) (45, 46). This regulation could mitigate oxidative damage in conditions such as alcoholic and viral liver disease, where mitochondrial dysfunction exacerbates pathology, although direct human validation is needed (47, 48). Although direct evidence linking MIAT to alcoholic liver disease (ALD) and chronic viral hepatitis remains limited, its well-established role in fibrosis and cirrhosis strongly implies a broader contribution to other CLD phenotypes. In alcohol-related liver injury, acetaldehyde-induced oxidative stress and lipid peroxidation activate HSCs via the TGF-β- and YAP-dependent pathways, in which MIAT is known to exert regulatory control. Similarly, in chronic hepatitis B and C infections, inflammatory

cytokines and viral proteins induce epigenetic alterations and noncoding RNA dysregulation, potentially engaging MIAT in the regulation of the immune response and fibrotic progression. Therefore, MIAT may act as a convergent molecular node that integrates fibrogenic, inflammatory, and immune-mediated signals across diverse etiologies of chronic liver injury (49, 50). The interplay between MIAT-mediated fibrosis and hepatocarcinogenesis further highlights its importance in CLD progression. Chronic fibrotic remodeling establishes a protumorigenic microenvironment characterized by persistent inflammation, angiogenesis, and genomic instability. By promoting HSC activation, EMT, and YAP1-driven transcription, MIAT may indirectly facilitate the transition from chronic liver injury to malignant transformation. The elevated MIAT expression observed in both cirrhotic and HCC tissues supports this continuum, suggesting that MIAT may serve as a molecular link between fibrogenesis and tumorigenesis. Thus, targeting MIAT could mitigate not only fibrotic progression but also the risk of HCC development in patients with advanced CLD (5).

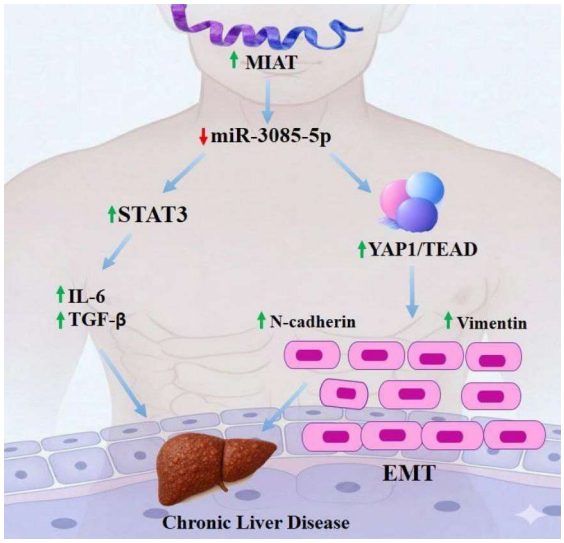

Figure 1. Signaling pathway of the lncRNA MIAT in chronic liver disease.

lncRNA MIAT in NAFLD Progression and NASH Pathogenesis

NAFLD has become the most prevalent chronic liver disorder globally, affecting approximately 25–30% of the adult population. It is closely associated with obesity, insulin resistance, and type 2 diabetes mellitus, which are core components of metabolic syndrome(51, 52). NAFLD encompasses a spectrum ranging from simple steatosis to its more aggressive inflammatory subtype, NASH, which is characterized by hepatocyte ballooning, lobular inflammation, and progressive fibrosis. NASH may culminate in cirrhosis, liver failure, and HCC if it is unresolved(53-55). The pathogenesis of NAFLD and its progression to NASH involves a complex interplay between metabolic, inflammatory, and fibrogenic pathways. Recent evidence has revealed long noncoding RNAs (lncRNAs) as key molecular regulators in this transition, orchestrating gene expression networks that modulate lipid metabolism, oxidative stress, and hepatic fibrogenesis(56, 57). Among these, myocardial infarction–associated transcript (MIAT) has emerged as an important regulator linking metabolic dysregulation to inflammatory and fibrotic signaling in NAFLD and NASH. MIAT expression is upregulated in fibrotic human livers and in experimental models, and MIAT knockdown reduces hepatic stellate cell activation and collagen accumulation in vivo. Mechanistically, MIAT has been shown to act as a competing endogenous RNA (ceRNA) that sponges miR-149-5p in macrophages, and miR-149-5p in turn regulates proinvasive/profibrotic targets such as MMP9 in liver cancer models, suggesting a plausible MIAT/miR-149-5p/MMP9 axis that could be relevant to ECM remodeling in the liver. Taken together, this

ceRNA-mediated modulation may contribute to extracellular matrix remodeling, hepatic inflammation, and fibroblast/hepatic stellate cell activation hallmark processes in NASH progression(58-61). In addition to its ceRNA activity, MIAT profoundly influences the intracellular signaling cascades that govern inflammatory and oxidative stress responses. Elevated MIAT expression activates the nuclear factor κB (NF-κB) pathway, resulting in increased transcription of proinflammatory cytokines, including tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6). These cytokines amplify hepatic inflammation, recruit immune cells, and exacerbate hepatocellular injury. Concurrently, MIAT enhances oxidative stress by upregulating NADPH oxidase 4 (NOX4), which elevates reactive oxygen species (ROS) generation, induces mitochondrial dysfunction, and triggers hepatocyte apoptosis, which represents a central mechanism driving the histopathological progression from simple steatosis to NASH(62, 63). Moreover, MIAT modulates key metabolic and fibrogenic signaling pathways. By repressing miR-149-5p, MIAT indirectly activates the phosphatidylinositol-3-kinase (PI3K)/AKT pathway, increasing hepatocyte survival and promoting insulin resistance, a major metabolic process involved in NAFLD progression. Sustained activation of this pathway further stimulates HSC activation and collagen synthesis, thereby aggravating liver fibrosis (46). In addition, MIAT interacts with the miR-3085-5p/yes-associated protein 1 (YAP1) axis, promoting HSC proliferation, ECM accumulation, and EMT. Inhibition of MIAT suppresses YAP1 expression and attenuates EMT, underscoring the pivotal role of MIAT in fibrogenic remodeling and tissue stiffening characteristic of advanced NASH (5).

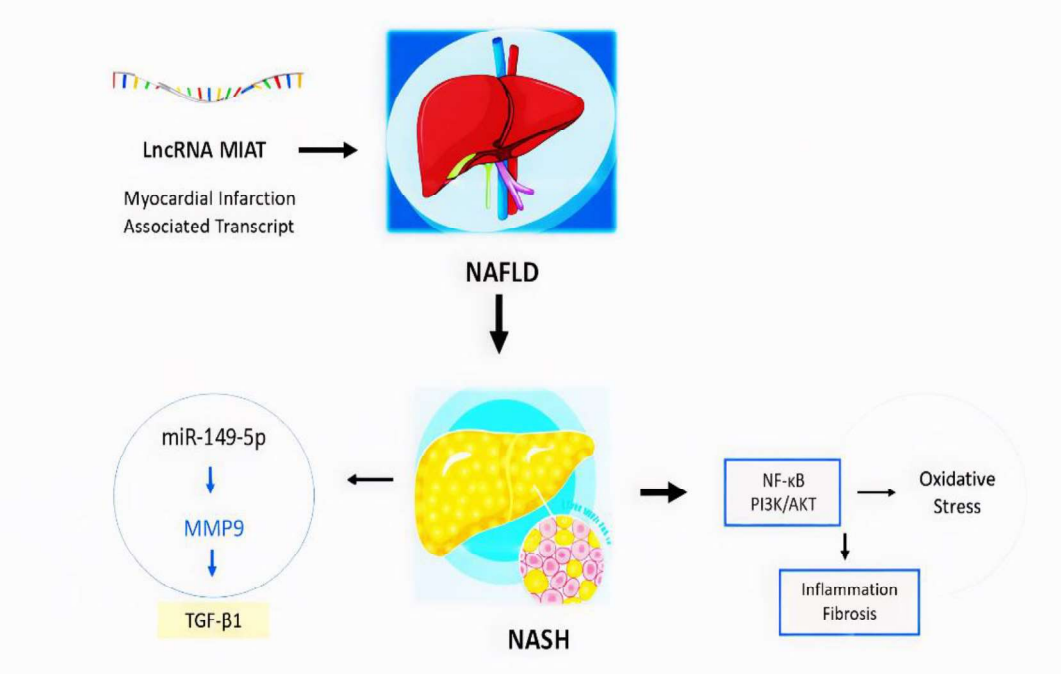

Figure 2. Signaling pathway of lncRNA MIAT in NAFLD progression and NASH pathogenesis.

lncRNA MIAT in Hepatitis C Virus (HCV) Infection

Recent studies have revealed a significant increase in the expression of the lncRNA MIAT in patients with occult hepatitis C virus (OCI) infection compared with individuals harboring active HCV infection and healthy controls. This upregulation is positively correlated with both disease severity and viral replication, implicating MIAT as a key molecular regulator of HCV pathogenesis. Mechanistically, MIAT contributes to HCV infection by modulating lipid metabolism and innate immune responses, two central processes in the viral life cycle. MIAT interacts with the retinoid X receptor alpha (RXRA) signaling pathway to promote lipogenesis and lipid droplet formation, thereby facilitating viral assembly and release. In parallel, MIAT suppresses critical antiviral mediators, including retinoic acid-inducible gene I (RIG-I) and interferon regulatory factor 3 (IRF3), both of which are essential components of the type I interferon (IFN-I) signaling cascade. Through this suppression, MIAT acts as a proviral factor, promoting viral replication and persistence. The lncRNA MIAT interferes with innate immune signaling by binding to regulatory proteins such as protein phosphatase methylesterase-1 (PME-1) and cystatin B (CSTB). These interactions enhance the demethylation and inactivation of protein phosphatase 2A (PP2A), leading to reduced phosphorylation of IRF3 and subsequent inhibition of IFN-β production. The attenuation of this antiviral pathway weakens the host's innate immune defense, enabling efficient viral replication and contributing to the progression of HCV-associated liver disease. In addition, MIAT promotes lipid biosynthesis by upregulating lipogenic gene expression through the transcriptional activation of signal transducer and activator of transcription 3 (STAT3), a process essential for HCV packaging and secretion (64). Several other lncRNAs are intimately involved in regulating the HCV life cycle and the host antiviral response, with the exception of MIAT. For example, GAS5 inhibits the viral NS3 protease and enhances host antiviral defenses, whereas lncRNAs such as HOTAIR and HULC, both of which are upregulated by HCV proteins, participate in the modulation of lipid metabolism and viral egress (65-68). Moreover, interferon-stimulated lncRNAs, including NRIR, LUARIS, and lncITPRIP-1, have been shown to regulate immune gene transcription and interferon-stimulated gene (ISG) expression, exerting either antiviral or proviral effects depending on the context (69).

lncRNA MIAT in Inflammation

The lncRNA MIAT has emerged as a pivotal regulator of inflammatory processes across diverse tissues and pathological contexts. Accumulating evidence suggests that MIAT plays a dual role in inflammation: it is transcriptionally upregulated in response to inflammatory stimuli and, in turn, actively amplifies inflammatory signaling, thereby establishing a positive feedback loop between MIAT expression and inflammation. This bidirectional functionality positions MIAT as a central mediator of inflammation in various disease models, including sepsis-induced cardiac injury, rheumatoid arthritis, podocyte injury, pneumonia, and allergic disorders. In lipopolysaccharide (LPS)-induced sepsis models, MIAT expression is markedly elevated in cardiac tissues and correlates with increased levels of proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β) (70). These findings indicate that MIAT acts as a sensitive responder to inflammatory cues, with its expression potentially reflecting the intensity of the inflammatory response. Mechanistically, MIAT functions as a molecular sponge for miR-330-5p, resulting in the activation of TNF receptor-associated factor 6 (TRAF6) and subsequent stimulation of the NF-κB signaling pathway, which amplifies cytokine production and reinforces the inflammatory cascade. In collagen-induced arthritis models, MIAT is significantly upregulated in both synovial tissues and cardiac muscle. In J774A.1 macrophages, MIAT silencing led to increased IL-1β and TNF-α levels but decreased IL-6 expression, underscoring the context-dependent regulatory nature of MIAT in inflammation (71). Interestingly, activation of the NLRP3 inflammasome was associated with reduced MIAT expression, whereas inhibition of the ATP–P2X7 receptor pathway restored its levels, suggesting an intricate and dynamic regulatory

mechanism under inflammatory stress. In high glucose-induced podocyte injury, MIAT regulates Toll-like receptor 4 (TLR4) expression by sponging miR-130a-3p. Silencing MIAT alleviated inflammatory and apoptotic responses, whereas deletion of miR-130a-3p or overexpression of TLR4 abrogated these effects, confirming the biological relevance of the MIAT/miR-130a-3p/TLR4 axis in renal inflammation (72). Similarly, in LPS-stimulated macrophages, MIAT modulates autophagy and inflammatory signaling via the miR-30a-5p/SOCS1 pathway, where MIAT knockdown increases apoptosis, reduces autophagy, and alters cytokine expression profiles (73). In pneumonia models, MIAT enhances inflammation by sponging miR-147a, leading to the upregulation of NKAP and the activation of NF-κB, which elevates IL-1β, IL-6, and TNF-α production. Conversely, MIAT silencing exerts a protective, anti-inflammatory effect(74). Furthermore, MIAT contributes to Th17-mediated allergic responses by suppressing miR-10b-5p, thereby promoting Th17 cell differentiation, eosinophil infiltration, and increased secretion of IL-4, IL-6, and IL-17, effects that are reversed upon miR-10b-5p overexpression (75). In LPS-induced chondrocyte injury, MIAT inhibits miR-488-3p, resulting in the derepression of SOX11, activation of NF-κB, decreased cell viability, increased apoptosis, and elevated levels of proinflammatory cytokines. MIAT silencing effectively reverses these detrimental effects, underscoring its proinflammatory potential (76).

Discussion

Liver diseases encompass a broad spectrum of metabolic and inflammatory conditions, including NAFLD, NASH, fibrosis, cirrhosis, viral hepatitis, and HCC. Accumulating evidence highlights the pivotal role of lncRNAs in orchestrating the molecular crosstalk among metabolic, inflammatory, and fibrotic pathways within the liver. Among these, the lncRNA MIAT has emerged as a multifaceted regulator involved in hepatocarcinogenesis, fibrogenesis, and immune modulation. MIAT is consistently overexpressed in HCC tissues and exerts pleiotropic effects on tumor biology, promoting proliferation, migration, EMT, and immune evasion while suppressing cellular senescence. Mechanistically, it mediates these processes through several molecular axes, such as MIAT/miR-214/β-catenin–EZH2, MIAT/miR-411-5p/STAT3/PD-L1, and MIAT/miR-22-3p/SIRT1/p53-p21/p16-pRb, collectively enhancing tumor progression and immune escape. Furthermore, in hepatic fibrosis, MIAT accelerates HSC proliferation and ECM accumulation by sponging miR-3085-5p and activating the YAP/EMT pathway. Through these mechanisms, MIAT links fibrotic remodeling and oncogenic signaling, underscoring its central role as a molecular hub bridging liver inflammation, fibrosis, and carcinogenesis. Interestingly, the biological activity of MIAT is not restricted to hepatic malignancy or fibrosis but extends to inflammatory regulation, as demonstrated in diverse tissues. Inflammatory stimuli such as LPS, TNF-α, or hyperglycemia upregulate MIAT, which, in turn, amplifies cytokine production through feedback activation of the NF-κB, TRAF6, or TLR4 signaling cascades. These findings collectively suggest that MIAT acts both as a responder and as an important factor of inflammation, an attribute that likely contributes to chronic inflammatory states underpinning liver pathology. By simultaneously engaging in proinflammatory, metabolic, and fibrogenic signaling, MIAT appears to serve as an integrative regulator that connects systemic inflammation to hepatic disease progression (9, 77).

Comparison with other lncRNAs in liver diseases

Compared with other well-characterized lncRNAs, MIAT has both overlapping and distinct functional profiles. H19, for example, governs hepatic lipid and glucose metabolism primarily via the TGF-β and SREBP1c pathways, with a predominant role in NAFLD and NASH pathogenesis(78). NEAT1 influences macrophage activation, immune cell infiltration, and inflammasome assembly in HCC and fibrotic liver injury through the

modulation of NF-κB signaling(79). In contrast, TUG1 mainly regulates apoptosis and proliferation in HCC through PI3K/AKT and Wnt/β-catenin signaling, indicating minimal involvement in fibrotic or metabolic dysfunction(80). MIAT distinguishes itself by spanning multiple domains of liver pathology ranging from metabolic dysfunction and inflammation to fibrogenesis and malignancy through the regulation of diverse miRNA-mRNA networks. It operates as a "bridging molecule", integrating distinct pathological processes that are often studied in isolation. This broad spectrum of regulatory effects positions MIAT as a unique molecular node whose targeting may offer a more holistic therapeutic advantage than approaches focusing on single-pathway lncRNAs.

Limitations and Future Perspectives

Despite substantial progress, several limitations warrant attention. Most current data on MIATs are derived from animal models or in vitro systems, necessitating rigorous validation in human cohorts(19). Moreover, the regulatory networks of MIAT exhibit context-dependent variability in its downstream targets, and interacting miRNAs differ among metabolic, fibrotic, and neoplastic environments. The specificity and sensitivity of MIAT as a diagnostic or prognostic biomarker remain to be fully established compared with those of other lncRNAs. Future studies should employ multiomics profiling, single-cell transcriptomics, and longitudinal patient analyses to map the dynamic expression and functional interactions of MIATs throughout disease progression. In addition, therapeutic exploration using antisense oligonucleotides or small interfering RNAs targeting MIAT could offer valuable insights into its translational potential. Understanding how MIAT integrates metabolic and immune cues to drive liver pathology will be essential for developing next-generation RNA-based therapeutics.

Conclusion

In conclusion, this review establishes the lncRNA MIAT as a pivotal molecular mediator that orchestrates inflammation, fibrogenesis, and tumorigenesis across the full continuum of liver diseases from early metabolic dysregulation in NAFLD/NASH to advanced stages of cirrhosis and HCC. Unlike previous studies limited to descriptive expression analyses, this work integrates mechanistic insights across multiple signaling pathways, offering a systems-level understanding of MIAT's biological importance. The innovative aspect of this review lies in highlighting MIAT as a multifunctional regulatory hub rather than a disease-specific marker. By unifying its roles in inflammation, fibrosis, and oncogenesis, MIAT has emerged as a compelling diagnostic, prognostic, and therapeutic target. Future clinical validation will be essential to translate these insights into effective MIAT-targeted interventions capable of modulating complex hepatic disease networks and improving patient outcomes.

References

1.Uchida S, Kauppinen S. Long non-coding RNAs in liver cancer and nonalcoholic steatohepatitis. Non-Coding RNA. 2020;6(3):34. doi: doi:10.3390/ncrna6030034

2.Statello L, Guo C-J, Chen L-L, Huarte M. Gene regulation by long non-coding RNAs and its biological functions. Nature reviews Molecular cell biology. 2021;22(2):96-118. doi:10.1038/s41580-020-00315-9.

3.Li Y, Wu J, Liu R, Zhang Y, Li X. Extracellular vesicles: catching the light of intercellular communication in fibrotic liver diseases. Theranostics. 2022;12(16):6955. doi: 10.7150/thno.77256

4.Abam F, Ghorbian S. The dual role of LncRNAs in hepatocellular carcinoma: friend and foe. Gastroenterology & Endoscopy. 2024;2(4):186-95. doi:10.1016/j.gande.2024.06.001

5.Zhan Y, Tao Q, Meng Q, Zhang R, Lin L, Li X, et al. LncRNA-MIAT activates hepatic stellate cells via regulating Hippo pathway and epithelial-to-mesenchymal transition. Communications Biology. 2023;6(1):285. doi: 10.1038/s42003-023-04670-z

6.Ding X, Zhu X-L, Xu D-H, Li S, Yang Q, Feng X, et al. NPM promotes hepatotoxin-induced fibrosis by inhibiting ROS-induced apoptosis of hepatic stellate cells and upregulating lncMIAT-induced TGF-β2. Cell Death & Disease. 2023;14(8):575. doi: 10.1038/s41419-023-06043-0

7.Zhu W, Cui Y, Qiu J, Zhang X, Gao Y, Shang Z, et al. Exploring the Therapeutic Potential of TGF-β Inhibitors for Liver Fibrosis: Targeting Multiple

Signaling Pathways. Journal of Clinical and Translational Hepatology. 2025;13(7):588. doi: 10.14218/JCTH.2025.00029

8.Ganguly N, Chakrabarti S. Role of long non-coding RNAs and related epigenetic mechanisms in liver fibrosis. International Journal of Molecular Medicine. 2021;47(3):23. doi: 10.3892/ijmm.2021.4856

9.Huang X, Gao Y, Qin J, Lu S. lncRNA MIAT promotes proliferation and invasion of HCC cells via sponging miR-214. American Journal of Physiology-Gastrointestinal and Liver Physiology. 2018;314(5):G559-G65. doi: 10.1152/ajpgi.00242.2017

10.Elmasri RA, Rashwan AA, Gaber SH, Rostom MM, Karousi P, Yasser MB, et al. Puzzling out the role of MIAT LncRNA in hepatocellular carcinoma. Non-coding RNA Research. 2024;9(2):547-59. doi:10.1016/j.ncrna.2024.01.006

11.Fang K, Xu H, Yuan S, Li X, Chen X, Fan X, et al. LncRNA mediated metabolic reprogramming: The chief culprits of solid tumor malignant progression: An update review. Nutrition & Metabolism. 2024;21(1):89. 10.1186/s12986-024-00866-0

12.Toden S, Goel A. Non-coding RNAs as liquid biopsy biomarkers in cancer. British journal of cancer. 2022;126(3):351-60. doi:10.1038/s41416-021-01672-8

13.Zhang Q, Li H, Liu Y, Li J, Wu C, Tang H. Exosomal non-coding RNAs: new insights into the biology of hepatocellular carcinoma. Current Oncology. 2022;29(8):5383-406. doi:10.3390/curroncol29080427

14.Wang Z, Yang X, Gui S, Yang F, Cao Z, Cheng R, et al. The roles and mechanisms of lncRNAs in liver fibrosis. Frontiers in pharmacology. 2021;12:779606. doi:10.3389/fphar.2021.779606

15.Chen Y, Li Z, Chen X, Zhang S. Long non-coding RNAs: from disease code to drug role. Acta Pharmaceutica Sinica B. 2021;11(2):340-54. doi:10.1016/j.apsb.2020.10.001

16.Gu L, Zhang F, Wu J, Zhuge Y. Nanotechnology in drug delivery for liver fibrosis. Frontiers in molecular biosciences. 2022;8:804396. doi:10.3389/fmolb.2021.804396

17.Da C-m, Gong C-Y, Nan W, Zhou K-S, Wu Z-L, Zhang H-H. The role of long non-coding RNA MIAT in cancers. Biomedicine & Pharmacotherapy. 2020;129:110359. doi:10.1016/j.biopha.2020.110359.

18.Wang Y, Zeng J, Chen W, Fan J, Hylemon PB, Zhou H. Long noncoding RNA H19: a novel oncogene in liver cancer. Non-coding RNA. 2023;9(2):19. doi:10.3390/ncrna9020019

19.Wang Y, Fu L, Lu T, Zhang G, Zhang J, Zhao Y, et al. Clinicopathological and prognostic significance of long non-coding RNA MIAT in human cancers: a review and meta-analysis. Frontiers in genetics. 2021;12:729768.

20.Shi Z, Jin S, Liu X, Jiang M, Fang Y, Khadaroo PA, et al. The epigenetic regulatory network of long noncoding RNAs in hepatocellular carcinoma. Genes & Diseases. 2025:101534. doi:10.1016/j.gendis.2025.101534

21.Liang W, Zhao Y, Meng Q, Jiang W, Deng S, Xue J. The role of long non-coding RNA in hepatocellular carcinoma. Aging (Albany NY). 2024;16(4):4052. doi:10.18632/aging.205523.

22.Xiang Y, Huang Y, Sun H, Pan Y, Wu M, Zhang J. Deregulation of miR-520d-3p promotes hepatocellular carcinoma development via lncRNA MIAT regulation and EPHA2 signaling activation. Biomedicine & Pharmacotherapy. 2019;109:1630-9. doi: 10.1016/j.biopha.2018.11.014

23.Zhang Y, Tian F, Zhao J. MiR-520d-3p suppresses the proliferation and epithelial-mesenchymal transition of cervical cancer cells by targeting ZFP36L2. Heliyon. 2023;9(8). doi:10.1016/j.heliyon.2023.e18789

24.Zhao L, Hu K, Cao J, Wang P, Li J, Zeng K, et al. lncRNA miat functions as a ceRNA to upregulate sirt1 by sponging miR-22-3p in HCC cellular senescence. Aging (Albany NY). 2019;11(17):7098. doi:10.18632/aging.102240

25.Cai X, Guillot A, Liu H. Cellular senescence in hepatocellular carcinoma: the passenger or the driver? Cells. 2022;12(1):132. doi:10.3390/cells12010132

26.Bataller R, Brenner DA. Liver fibrosis. The Journal of clinical investigation. 2005;115(2):209-18. doi:10.1172/JCI24282

27.Parola M, Pinzani M. Liver fibrosis: Pathophysiology, pathogenetic targets and clinical issues. Molecular aspects of medicine. 2019;65:37-55. doi:10.1016/j.mam.2018.09.00

28.Böttcher K, Pinzani M. Pathophysiology of liver fibrosis and the methodological barriers to the development of anti-fibrogenic agents. Advanced drug delivery reviews. 2017;121:3-8. doi: 10.1016/j.addr.2017.05.016

29.Friedman SL. Hepatic stellate cells: protean, multifunctional, and enigmatic cells of the liver. Physiological reviews. 2008;88(1):125-72. doi:10.1152/physrev.00013.2007.

30.Chen L-L. Linking long noncoding RNA localization and function. Trends in biochemical sciences. 2016;41(9):761-72. doi:10.1016/j.tibs.2016.07.003

31.Yang Z, Jiang S, Shang J, Jiang Y, Dai Y, Xu B, et al. LncRNA: Shedding light on mechanisms and opportunities in fibrosis and aging. Ageing research

reviews. 2019;52:17-31. doi:10.1016/j.arr.2019.04.001
32. Bridges MC, Daulagala AC, Kourtidis A. LNCcation: lncRNA localization and function. Journal of Cell Biology. 2021;220(2):e202009045. doi:10.1083/jcb.202009045
33. Yao L, Zhou B, You L, Hu H, Xie R. LncRNA MIAT/miR-133a-3p axis regulates atrial fibrillation and atrial fibrillation-induced myocardial fibrosis. Molecular Biology Reports. 2020;47(4):2605-17. doi:10.1007/s11033-020-05347-0
34. Liu Z, Wang H, Cai H, Hong Y, Li Y, Su D, et al. Long non-coding RNA MIAT promotes growth and metastasis of colorectal cancer cells through regulation of miR-132/Derlin-1 pathway. Cancer Cell International. 2018;18(1):59. doi.org/10.1186/s12935-017-0477-8.
35. Liu J, Cao G, Liu J, Zhao X, Cao H. Long non-coding RNA MIAT knockdown potentiates the therapeutic effect of transcatheter arterial embolization in liver cancer by regulating the miR-203a/HIF-1α axis. Oncology Reports. 2020;44(2):722-34. doi:10.3892/or.2020.7618
36. Ma S, Meng Z, Chen R, Guan K-L. The Hippo pathway: biology and pathophysiology. Annual review of biochemistry. 2019;88(1):577-604. doi.10.1146/annurev-biochem-013118-111829
37. He Z, Yang D, Fan X, Zhang M, Li Y, Gu X, et al. The roles and mechanisms of lncRNAs in liver fibrosis. International journal of molecular sciences. 2020;21(4):1482. doi:10.3390/ijms21041482
38. Chen Q, Ji H, Lin Y, Chen Z, Liu Y, Jin L, et al. LncRNAs regulate ferroptosis to affect diabetes and its complications. Frontiers in Physiology. 2022;13:993904. doi:10.3389/fphys.2022.993904
39. Xu L, Zhang L, Xiang Y, Zhang X. Knockdown of lncRNA NEAT1 suppresses streptococcus pneumoniae-induced ferroptosis in alveolar epithelial cells by regulating the Nrf2-GPX4 pathway. Toxicon. 2024;243:107705. doi:10.1016/j.toxicon.2024.107705
40. Mattick JS, Amaral PP, Carninci P, Carpenter S, Chang HY, Chen L-L, et al. Long non-coding RNAs: definitions, functions, challenges and recommendations. Nature reviews Molecular cell biology. 2023;24(6):430-47. doi:10.1038/s41580-022-00566-8
41. Zarandi PK, Ghiasi M, Heiat M. The role and function of lncRNA in ageing-associated liver diseases. RNA biology. 2025;22(1):1-8. doi:10.1080/15476286.2024.2440678
42. Zhang Y, Ren L, Tian Y, Guo X, Wei F, Zhang Y. Signaling pathways that activate hepatic stellate cells during liver fibrosis. Frontiers in Medicine. 2024;11:1454980. doi:10.3389/fmed.2024.1454980
43. Bedair Dewidar CM, Dooley S, Meindl-Beinker N. TGF-β in Hepatic Stellate Cell Activation and Liver Fibrogenesis—Updated 2019. Cells. 2019;8(11):1419. doi:10.3390/cells8111419
44. Garg A, Agostinis P. Immunogenic Cell Death in Cancer: From Benchside Research to Bedside Reality. Lausanne: Frontiers Media. doi:10.3389/fimmu.2016.00110
45. Chen Y, Jiang Z, Li X. New insights into crosstalk between Nrf2 pathway and ferroptosis in lung disease. Cell Death & Disease. 2024;15(11):841. doi:10.1038/s41419-024-07224-1
46. Li N, Hao L, Li S, Deng J, Yu F, Zhang J, et al. The NRF-2/HO-1 signaling pathway: a promising therapeutic target for metabolic dysfunction-associated steatotic liver disease. Journal of Inflammation Research. 2024:8061-83. doi:10.2147/JIR.S490418
47. Grivennikov SI, Karin M. Dangerous liaisons: STAT3 and NF-κB collaboration and crosstalk in cancer. Cytokine & growth factor reviews. 2010;21(1):11-9. doi:10.1016/j.cytogfr.2009.11.005
48. He G, Karin M. NF-κB and STAT3–key players in liver inflammation and cancer. Cell research. 2011;21(1):159-68. doi:10.1038/cr.2010.183.
49. Gao R, Mao J. Noncoding RNA-Mediated Epigenetic Regulation in Hepatic Stellate Cells of Liver Fibrosis. Non-coding RNA. 2024;10(4):44. doi:10.3390/ncrna10040044
50. Zhang Y, Luo G, Zhang Y, Zhang M, Zhou J, Gao W, et al. Critical effects of long non-coding RNA on fibrosis diseases. Experimental & molecular medicine. 2018;50(1):e428-e. doi:10.1038/emm.2017.223
51. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—meta - analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73-84. doi:10.1002/hep.28431
52. Powell EE, Wong VW-S, Rinella M. Non-alcoholic fatty liver disease. The Lancet. 2021;397(10290):2212-24. doi:10.1016/S0140-6736(20)32511-3
53. Han SK, Baik SK, Kim MY. Non-alcoholic fatty liver disease: Definition and subtypes. Clinical and molecular hepatology. 2022;29(Suppl):S5. doi:10.3350/cmh.2022.0424
54. Anstee QM, Reeves HL, Kotsiliti E, Govaere O, Heikenwalder M. From NASH to HCC: current concepts and future challenges. Nature reviews Gastroenterology & hepatology. 2019;16(7):411-28. doi.org/10.1038/s41575-019-0145-7
55. Huang DQ, El-Serag HB, Loomba R. Global epidemiology of NAFLD-related HCC: trends, predictions, risk factors and prevention. Nature reviews Gastroenterology & hepatology. 2021;18(4):223-38. doi:10.1038/s41575-020-00381-6

56.Matboli M, Gadallah SH, Rashed WM, Hasanin AH, Essawy N, Ghanem HM, et al. mRNA-miRNA-lncRNA regulatory network in nonalcoholic fatty liver disease. International journal of molecular sciences. 2021;22(13):6770. doi:10.3390/ijms22136770.
57.Zeng Q, Liu C-H, Wu D, Jiang W, Zhang N, Tang H. LncRNA and circRNA in patients with non-alcoholic fatty liver disease: a systematic review. Biomolecules. 2023;13(3):560. doi:10.3390/biom13030560.
58.Ye Z-m, Yang S, Xia Y-p, Hu R-t, Chen S, Li B-w, et al. LncRNA MIAT sponges miR-149-5p to inhibit efferocytosis in advanced atherosclerosis through CD47 upregulation. Cell death & disease. 2019;10(2):138. doi:10.1038/s41419-019-1409-4.
59.Liu G, Yin L, Ouyang X, Zeng K, Xiao Y, Li Y. M2 m 157 ges promote HCC cells invasion and migration via miR-149-5p/MMP9 signaling. Journal of Cancer. 2020;11(5):1277. doi:10.7150/jca.35444.
60.Ren F-j, Yao Y, Cai X-y, Cai Y-t, Su Q, Fang G-y. MiR-149-5p: an important miRNA regulated by competing endogenous RNAs in diverse human cancers. Frontiers in Oncology. 2021;11:743077. doi.10.3389/fonc.2021.743077
61.Jia W, Xie G, Jia W. Bile acid–microbiota crosstalk in gastrointestinal inflammation and carcinogenesis. Nature reviews Gastroenterology & hepatology. 2018;15(2):111-28. doi:10.1038/nrgastro.2017.119.
62.Magee N, Zou A, Zhang Y. Pathogenesis of nonalcoholic steatohepatitis: interactions between liver parenchymal and nonparenchymal cells. BioMed research international. 2016;2016(1):5170402. doi:10.1155/2016/5170402.
63.Godoy-Matos AF, Silva Júnior WS, Valerio CM. NAFLD as a continuum: from obesity to metabolic syndrome and diabetes. Diabetology & metabolic syndrome. 2020;12(1):60. doi:10.1186/s13098-020-00570-y.
64.Rashad N, Soliman SA, Obaya AA, Elshamy AM, El Helaly AM, Hussien MH, et al. Clinical significance of LncRNA-MIAT as a non-invasive diagnostic marker of non-Hodgkin's lymphoma associated with occult hepatitis C virus infection. African journal of gastroenterology and hepatology. 2023;6(1):1-18. doi:10.21608/ajgh.2023.187817.1028.
65.Qian X, Xu C, Zhao P, Qi Z. Long non-coding RNA GAS5 inhibited hepatitis C virus replication by binding viral NS3 protein. Virology. 2016;492:155-65.
doi:10.1016/j.virol.2016.02.020
66.Murray CL, Jones CT, Rice CM. Architects of assembly: roles of Flaviviridae non-structural proteins in virion morphogenesis. Nature reviews microbiology. 2008;6(9):699-708.
doi:10.1038/nrmicro1928
67.Li Z-q, Gu X-y, Hu J-x, Ping Y, Li H, Yan J-y, et al. Hepatitis C virus core protein impairs metabolic disorder of liver cell via HOTAIR-Sirt1 signalling. Bioscience reports. 2016;36(3):e00336. doi.10.1042/BSR20160088
68.Sharma G, Tripathi SK, Das S. lncRNA HULC facilitates efficient loading of HCV‐core protein onto lipid droplets and subsequent virus‐particle release. Cellular Microbiology. 2019;21(10):e13086. doi:10.1111/cmi.13086.
69.Unfried JP, Fortes P. LncRNAs in HCV infection and HCV-related liver disease. International Journal of Molecular Sciences. 2020;21(6):2255. doi:10.3390/ijms21062255.
70.Xing P-C, An P, Hu G-Y, Wang D-L, Zhou M-J. LncRNA MIAT promotes inflammation and oxidative stress in sepsis-induced cardiac injury by targeting miR-330-5p/TRAF6/NF-κB axis. Biochemical Genetics. 2020;58(5):783-800. doi:10.1007/s10528-020-09976-9.
71.Wang Z, Kun Y, Lei Z, Dawei W, Lin P, Jibo W. LncRNA MIAT downregulates IL-1 β , TNF-α to suppress macrophage inflammation but is suppressed by ATP-induced NLRP3 inflammasome activation. Cell Cycle. 2021;20(2):194-203. doi:10.1080/15384101.2020.1867788
72.Zhang M, Zhao S, Xu C, Shen Y, Huang J, Shen S, et al. Ablation of lncRNA MIAT mitigates high glucose-stimulated inflammation and apoptosis of podocyte via miR-130a-3p/TLR4 signaling axis. Biochemical and Biophysical Research Communications. 2020;533(3):429-36. doi:10.1016/j.bbrc.2020.09.034.
73.Sun L, Yang K, Wang L, Wu S, Wen D, Wang J. LncRNA MIAT suppresses inflammation in LPS-induced J774A. 1 macrophages by promoting autophagy through miR-30a-5p/SOCS1 axi. Scientific Reports. 2024;14(1):22608. doi:10.1038/s41598-024-73607-1.
74.Liu M, Li W, Song F, Zhang L, Sun X. Silencing of lncRNA MIAT alleviates LPS-induced pneumonia via regulating miR-147a/NKAP/NF-κB axis. Aging (Albany NY). 2020;13(2):2506. doi:10.18632/aging.202284.
75.Ma Z, Lian H, Lin X, Li Y. LncRNA MIAT promotes allergic inflammation and symptoms by targeting MiR-10b-5p in allergic rhinitis mice. American Journal of Rhinology & Allergy. 2021;35(6):781-9. doi:10.1177/1945892421998143.

76. Pan W, Wang H, Ruan J, Zheng W, Chen F, Kong J, et al. lncRNA myocardial infarction-associated transcript (MIAT) knockdown alleviates LPS-induced chondrocytes inflammatory injury via regulating miR-488-3p/sex determining region Y-related HMG-box 11 (SOX11) axis. Open life sciences. 2021;16(1):511-22. doi:10.1515/biol-2021-0023.
77. Zhang X, Pan B, Qiu J, Ke X, Shen S, Wang X, et al. lncRNA MIAT targets miR‐411‐5p/STAT3/PD‐L1 axis mediating hepatocellular carcinoma immune response. International Journal of Experimental Pathology. 2022;103(3):102-11. doi:10.1111/iep.12440.
78. Wang Y, Hylemon PB, Zhou H. Long noncoding RNA H19: a key player in liver diseases. Hepatology. 2021;74(3):1652-9. doi:10.1002/hep.31765.
79. Xu S, Dong W. RETRACTED: LncRNA NEAT1 targets miR‐125/ADAM9 mediated NF‐κB pathway in inflammatory response of rosacea. Skin Research and Technology. 2024;30(7):e13630. doi:10.1111/srt.13630.
80. Zhou H, Sun L, Wan F. Molecular mechanisms of TUG1 in the proliferation, apoptosis, migration and invasion of cancer cells. Oncology letters. 2019;18(5):4393-402. doi:10.3892/ol.2019.10848.