

Table SI. Regulatory roles of miRNAs, lncRNAs and circRNAs in the progression of MASLD to HCC.

A, Simple hepatic Steatosis			
ncRNA type and key molecule	Expression pattern ^a	Action and mechanism	(Refs.)
miRNA			
miR-34a	Upregulated; pathogenic	Suppresses PPAR α and thereby impairs fatty acid oxidation, promoting lipid accumulation.	(169)
miR-21	Upregulated; pathogenic	Disrupts lipid homeostasis by targeting PPAR α .	(170)
miR-22	Upregulated; pathogenic	Directly targets SIRT1 and suppresses PPAR α expression, driving lipid accumulation and amplifying TNF- α and IL-6 production.	(171)
miR-155-5p	Upregulated; pathogenic	Induced by NF- κ B; suppresses STC1 and causes mitochondrial dysfunction in hepatocytes, accelerating MASLD progression.	(172)
miR-192-5p	Downregulated; protective	Its downregulation derepresses the target gene SCD1, promoting lipid accumulation.	(173)
lncRNA			
SRA	Pathogenic (direction not reported)	Facilitates lipid accumulation by modulating the p38/JNK phosphorylation balance and directly activating the insulin receptor gene.	(123,124)
Blnc1	Upregulated; pathogenic	Forms a ribonucleoprotein complex with transcription factors to enhance lipogenic gene transcription through the LXR-SREBP1c pathway; liver-specific deletion ameliorates steatosis and insulin resistance in obese mice.	(122)
Gm15622	Upregulated; pathogenic	Acts as a ceRNA sequestering miR-742-3p, thereby derepressing SREBP-1c and accelerating lipogenesis; suppressed by metformin.	(188)
NEAT1	Upregulated; pathogenic	Sponges miR-146a-5p and upregulates ROCK1, promoting hepatocellular lipid accumulation; its downregulation inhibits mTOR/S6K1 signalling, reducing hepatic lipid deposition, inflammation and injury.	(189,191)
MALAT1	Upregulated; pathogenic	Inhibits miR-206, thereby increasing ARNT expression and activating the PPAR α /CD36 pathway to enhance hepatic lipogenesis.	(190)
Mirt2	Downregulated; protective	Sponges miR-34a-5p, resulting in USP10 upregulation and subsequent inhibition of the lipogenic transcription factor SREBP-1.	(193)
circRNA			
circRNA_0046366	Downregulated; protective	Sponges miR-34a and enhances PPAR α -mediated fatty acid β -oxidation, alleviating hepatic steatosis.	(130)
circRNA_0046367	Downregulated; protective	Protects against hepatocyte lipid peroxidation; its reduced expression weakens this protection and promotes lipid accumulation.	(199)
circRNA_0001805	Downregulated; protective	Regulates the miR-106a-5p/miR-320a and ABCA1/CPT1 axes; nanodrug-mediated delivery ameliorates hepatic steatosis in mouse models.	(200)
circ-SLC9A6-126aa	Upregulated; pathogenic	Functional peptide translated from circ-SLC9A6; activates CD36 transcription in an H4K16ac-dependent manner, directly promoting hepatic lipid uptake and deposition.	(127)
B, Steatohepatitis (MASH)			

ncRNA type and key molecule	Expression pattern	Action and mechanism	(Refs.)
miRNA			
miR-9-5p	Upregulated; pathogenic	Delivered to macrophages by hepatocyte-derived extracellular vesicles under lipotoxic conditions; inhibits TGM2, promotes pro-inflammatory M1 polarisation and amplifies IL-1 β , IL-6 and TNF- α production.	(174)
miR-21	Upregulated; pathogenic	Amplifies inflammatory signalling through repression of SMAD7 and PDCD4.	(170)
miR-146a	Protective (direction not reported)	Targets IRAK1/TRAF6 and promotes anti-inflammatory M2 macrophage polarisation.	(175)
miR-690	Downregulated; protective	Targets NADK and promotes anti-inflammatory M2 macrophage polarisation.	(175)
miR-122	Downregulated; protective	Its loss increases inflammatory cytokine expression, including IL-6 and TNF- α , accelerating MASH progression.	(176)
miR-375	Upregulated; pathogenic	Its inhibition exerts protective effects through AdipoR2-dependent regulation of adipokines and suppression of inflammatory cytokine production.	(177)
miR-33	Ablated; pathogenic	Genetic deletion promotes favourable metabolic reprogramming and prevents progression from MASH to HCC.	(178)
lncRNA			
lncSHGL	Downregulated; protective	Recruits hnRNPA1, enhancing calmodulin translation and activating PI3K/AKT, which suppresses gluconeogenesis and inhibits the mTOR/SREBP-1 pathway, thereby reducing lipogenesis.	(134)
GAS5	Upregulated; pathogenic	Highly expressed in MASLD; sponges miR-29a-3p and upregulates NOTCH2, promoting disease progression.	(131)
circRNA			
CiR-EIS	Downregulated; protective	Sponges miR-548m to maintain IGF1 expression and support anti-inflammatory M2-like macrophage polarisation; its downregulation exacerbates MASH-associated inflammation.	(201)
circPI4KB	Downregulated in liver (upregulated in serum); pathogenic	Facilitates extracellular export of miR-122 through a non-canonical mechanism, reducing intracellular miR-122 abundance and indirectly aggravating hepatic lipid accumulation and injury.	(202)
circRNA SCAR	Downregulated; protective	Suppressed by lipids through the ER stress/PGC-1 α axis; its downregulation causes mitochondrial dysfunction and mitochondrial ROS accumulation, promoting fibroblast-mediated metaflammation.	(10)

C, Fibrosis

ncRNA type and key molecule	Expression pattern	Action and mechanism	(Refs.)
miRNA			
miR-21	Upregulated; pathogenic	Represses PPAR α in inflammatory and biliary cells; promotes fibrogenesis and carcinogenesis by targeting PTEN; sustained upregulation reinforces a	(170,179,180)

			lipotoxic and profibrotic programme that can progress toward MASH-related HCC.	
miR-188-5p	Upregulated; pathogenic		Activates the PTEN/PI3K/AKT signalling pathway, exacerbating fibrosis.	(181)
miR-29a	Downregulated; protective		Directly targets fibrogenic mediators such as COL1A1 and dampens TGF- β /SMAD3-driven hepatic stellate cell activation.	(182)
miR-372-3p	Downregulated; protective		Its downregulation in patients with MASH causes loss of repression of AEBP1, a critical driver of HSC activation.	(183)
lncRNA				
NEAT1	Upregulated; pathogenic		Binds miR-129-5p and upregulates PEG3 expression, contributing to HSC activation in MASH.	(192)
GAS5	Downregulated; protective		In experimental fibrosis models, its overexpression sponges miR-23a and restores PTEN expression, suppressing HSC activation (context-dependent role, opposite to that in steatosis).	(194)
circRNA				
circRNA_29981	Upregulated; (function not experimentally validated)	putative not	Markedly upregulated in the MCD-diet-induced NASH mouse model (6.1-fold; confirmed by RT-qPCR); bioinformatic analyses suggest it may regulate HSC activation by sequestering miRNAs including miR-181b-5p, but the mechanism remains to be experimentally validated.	(203)

D, HCC				
ncRNA type and key molecule	Expression pattern		Action and mechanism	(Refs.)
miRNA				
miR-182-5p	Upregulated; pathogenic		Oncogenic; promotes tumour development by inhibiting the tumour suppressors CYLD and FOXO1.	(184)
miR-122	Downregulated; protective		Its silencing is recognised as an early event in malignant transformation.	(155)
miR-223	Ablated; protective		Its loss accelerates progression from MASH to HCC by derepressing inflammatory and oncogenic pathways.	(142)
miR-132	Upregulated; pathogenic		Promotes steatosis and hyperlipidaemia through synergistic suppression of multiple downstream targets; associated with disease severity.	(185)
lncRNA				
H19	Upregulated; pathogenic		Re-induced in NAFLD-related steatosis; enhances lipogenesis via the H19/PTBP1/SREBP1 feed-forward loop (stabilising SREBP1c and promoting its nuclear translocation) and via activation of the MLXIPL network and mTORC1 signalling; also acts as a ceRNA for miR-130a to increase PPAR γ expression.	(125,126,195)
lncTNF	Upregulated; pathogenic		Exacerbates chronic inflammation through NF- κ B activation.	(196)
SNHG20	Upregulated in NAFLD-HCC; pathogenic		Promotes polarisation of Kupffer cells from the antitumour M1 phenotype to the pro-tumour M2 phenotype through STAT6 activation.	(197)
FTX	Downregulated; protective		Tumour suppressor; acts as an immunometabolic checkpoint regulating the M1/M2 Kupffer-cell balance, suppressing the protumorigenic M2 phenotype, reducing inflammation and inhibiting carcinogenesis.	(161)

LINC01468	Upregulated; pathogenic	Functions as a molecular scaffold promoting CUL4A-linked ubiquitination and degradation of the phosphatase SHIP2, thereby activating the oncogenic AKT/mTOR pathway.	(133)
lnc-OXAR	Upregulated; pathogenic	Regulated by the m6A-WTAP/IGF2BP2 axis; enhances Ku70/CSTA-mediated DNA damage repair and mediates oxaliplatin resistance in MASH-HCC.	(198)
circRNA circSMEK1	Downregulated; protective	Tumour-suppressive through the hnRNPK-IGF2-AKT signalling axis; serum levels show diagnostic potential for MASH-HCC.	(204)

^aExpression pattern reports, for each ncRNA entry, the direction of expression change and the functional role of the endogenous ncRNA in the corresponding disease stage, where available. 'Upregulated' and 'downregulated' denote the directional change in ncRNA abundance reported in the cited study; 'ablated' denotes that the evidence derives from genetic deletion or antisense knockdown experiments; 'pathogenic' and 'protective' denote the functional role attributed to the endogenous ncRNA by gain- or loss-of-function studies, that is, whether its presence aggravates or ameliorates the disease phenotype, respectively. Thus, for example, 'Downregulated; protective' indicates an ncRNA whose expression decreases during disease progression and whose loss contributes to disease development. Entries marked 'direction not reported' reflect studies in which the original work characterised the ncRNA primarily in functional terms without reporting consistent directional expression data. Entries marked 'putative' denote a proposed mechanism supported only by bioinformatic analyses that has not yet been experimentally validated. ABCA1, ATP-binding cassette transporter A1; AdipoR2, adiponectin receptor 2; AEBP1, adipocyte enhancer-binding protein 1; AKT, protein kinase B; ARNT, aryl hydrocarbon receptor nuclear translocator; CD36, cluster of differentiation 36; ceRNA, competing endogenous RNA; circRNA, circular RNA; COL1A1, collagen type I α 1 chain; CPT1, carnitine palmitoyltransferase 1; CSTA, cystatin A; CUL4A, cullin 4A; CYLD, cylindromatosis; ER, endoplasmic reticulum; FTX, five prime to Xist; HCC, hepatocellular carcinoma; hnRNPA1, heterogeneous nuclear ribonucleoprotein A1; hnRNPK, heterogeneous nuclear ribonucleoprotein K; HSC, hepatic stellate cell; IGF, insulin-like growth factor; IL, interleukin; IRAK1, interleukin-1 receptor-associated kinase 1; JNK, c-Jun N-terminal kinase; lncRNA, long non-coding RNA; LXR, liver X receptor; MALAT1, metastasis-associated lung adenocarcinoma transcript 1; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MCD, methionine-choline-deficient; miRNA, microRNA; MLXIPL, MLX-interacting protein-like; mTOR, mechanistic target of rapamycin; mTORC1, mTOR complex 1; NADK, NAD kinase; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; ncRNA, non-coding RNA; NEAT1, nuclear paraspeckle assembly transcript 1; NF- κ B, nuclear factor κ B; PDCD4, programmed cell death 4; PEG3, paternally expressed gene 3; PGC-1 α , peroxisome proliferator-activated receptor γ coactivator 1- α ; PI3K, phosphoinositide 3-kinase; PPAR, peroxisome proliferator-activated receptor; PTBP1, polypyrimidine tract-binding protein 1; PTEN, phosphatase and tensin homologue; ROCK1, Rho-associated coiled-coil containing protein kinase 1; ROS, reactive oxygen species; RT-qPCR, reverse transcription-quantitative polymerase chain reaction; S6K1, ribosomal protein S6 kinase β -1; SCAR, steatohepatitis-associated circRNA ATP5B regulator; SCD1, stearoyl-CoA desaturase 1; SHIP2, SH2-containing inositol 5-phosphatase 2; SIRT1, sirtuin 1; SLC9A6, solute carrier family 9 member A6; SNHG20, small nucleolar RNA host gene 20; SRA, steroid receptor RNA activator; SREBP-1c, sterol regulatory element-binding protein 1c; STC1, stanniocalcin 1; TGF- β , transforming growth factor β ; TGM2, transglutaminase 2; TNF- α , tumour necrosis factor α ; TRAF6, TNF receptor-associated factor 6; USP10, ubiquitin-specific peptidase 10; WTAP, Wilms tumour 1-associating protein.