

Multifaceted roles of miR-124 in cancer: Molecular mechanisms and clinical prospects (Review)

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Abstract. MicroRNAs (miRNAs or miRs) are a class of small non-coding RNAs that are critical regulators of gene expression. By targeting messenger RNAs, they play essential roles in various biological processes, including development, differentiation, immunity, metabolism and apoptosis. miRNA dysregulation is often associated with tumorigenesis and cancer progression. miR-124, a miRNA predominantly and specifically expressed in the central nervous system, is commonly downregulated in various cancers. It inhibits multiple malignant traits, including tumor growth, metastasis, stemness and chemoresistance. Furthermore, miR-124 influences the tumor microenvironment and modulates antitumor immune responses. These diverse functions highlight their

significant potential for clinical application. Its expression is modulated by various upstream factors, including transcription factors, signaling pathways, epigenetic modifications, and other non-coding RNAs. However, the precise mechanisms governing this upstream regulation require further investigation. Despite this, the translational application of miR-124 for early cancer diagnosis and therapy faces several significant challenges, including improving its stability and bioavailability and developing effective *in vivo* delivery systems. The present study provides a comprehensive overview of the multifaceted roles of miR-124 in cancer, elucidating its underlying molecular mechanisms and exploring its clinical potential. By synthesizing the current literature, it was aimed to consolidate the current understanding of miR-124 and identify promising avenues for future research.

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Abbreviations: miR or miRNA, microRNA; TME, tumor microenvironment; CSCs, cancer stem cells; ceRNA, competing endogenous RNA; lncRNA, long non-coding RNA; OCT4, octamer-binding transcription factor 4; EMT, epithelial-mesenchymal transition; SNAI1, Snail family transcriptional repressor 1; PI3K/AKT, phosphatidylinositol 3-kinase/protein kinase b; PD-L1, programmed death-ligand 1; SP1, specificity protein 1; STAT3, signal transducer and activator of transcription 3; CDK6, cyclin-dependent kinase 6; CAFs, cancer-associated fibroblasts; NF-κB, nuclear factor kappa B; HIF-1α, hypoxia inducible factor 1 alpha; 5-mC, 5-methylcytosine; LNPs, lipid nanoparticles; AAV, adeno-associated virus; AuNPs, gold nanoparticles

Key words: miR-124, cancer, biological function, upstream regulatory mechanisms, delivery systems

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1. Introduction

MicroRNAs (miRNAs or miRs) constitute a class of small non-coding RNAs, typically ~22 nucleotides in length, that are essential for gene regulation. They primarily modulate gene expression by base-pairing with target messenger RNAs (mRNAs), resulting in either translational repression or mRNA degradation (1). A single miRNA can regulate multiple target genes, thereby exerting pleiotropic effects. Consequently, miRNAs are pivotal in various physiological and pathological processes, such as morphogenesis, disease progression and tumorigenesis (2). Among them, miR-124 is a highly conserved miRNA found in various species and tissues. It is often downregulated in numerous cancers, where it acts as a tumor suppressor by inhibiting multiple oncogenic

pathways (3). These pathways include cell proliferation, metastasis, stemness, drug resistance, and modulation of the tumor microenvironment (TME) and immune response (4). Moreover, recent research suggests that miR-124 plays a pivotal role in regulating genes involved in metabolism and contributes to the metabolic reprogramming observed in tumors (5).

This discovery highlights its functional complexity in diverse physiological and pathological contexts. In cancer, the upstream regulatory mechanisms of miR-124 constitute a complex, multi-layered network that is regulated by transcription factors, epigenetic modifications, competing endogenous RNA (ceRNA) networks, and various signaling pathways (6,7). These mechanisms collectively and precisely modulate miR-124 expression, thereby affecting numerous downstream target genes and signal transduction pathways. miR-124 has emerged as a promising therapeutic target due to its fundamental tumor-suppressive function. Research has implicated miR-124 in cancer diagnosis, therapeutic response, and prognosis assessment, underscoring its significant potential as both a biomarker and a therapeutic target (3). A comprehensive investigation into the functional mechanisms of miR-124 in tumor progression is poised to significantly advance the development of personalized medicine and targeted therapies, thereby paving the way for novel clinical interventions. Despite the significant challenges associated with miR-124 translation into clinical practice, a systematic examination of miR-124 and its regulatory network is anticipated to significantly enrich our understanding of cancer biology.

2. Multifaceted roles of miR-124 in tumors

miR-124, a broad-acting tumor suppressor, plays a crucial role in tumorigenesis and cancer progression, as evident by its consistent downregulation in various human cancers (3,8). miR-124 is involved in numerous biological processes during tumorigenesis and progression, attributed to its multifaceted regulatory capabilities. It directly inhibits the proliferation, migration and invasion of tumor cells. Furthermore, miR-124 exerts tumor-suppressive effects across multiple fronts by modulating cancer stemness, drug sensitivity, TME remodeling and immune responses. This chapter systematically elucidates the roles and mechanisms underlying miR-124 in tumor growth, metastasis, stemness maintenance, drug resistance, microenvironment regulation and immune modulation. It also elaborates on its complex regulatory network, thereby providing a theoretical foundation for developing miR-124-based diagnostic and therapeutic strategies.

Suppression of tumor growth and metastasis by miR-124. miR-124 is an important tumor suppressor frequently down-regulated in various cancers. Its primary role is to inhibit the progression of malignant tumors, particularly by targeting tumor growth and metastasis (9). This inhibitory effect is mediated by a sophisticated regulatory network that concurrently targets multiple critical nodes within complementary and synergistic signaling pathways (3,10,11). The tumor-suppressive activity of miR-124 is characterized by three hallmark features. First, the systematic, cancer-type-specific nature of miR-124 target selection facilitates its simultaneous inhibition of essential proliferative processes and tissue-specific invasive

behaviors. Particularly, miR-124 suppresses key pathways that regulate cell cycle progression and proliferation by targeting widely acting oncoproteins, such as signal transducer and activator of transcription 3 (STAT3) (3), enhancer of zeste homolog 2 (EZH2) (12), cyclin-dependent kinase 6 (CDK6) (13), and SET and MYND domain containing 3 (14). Furthermore, it affects tissue-specific factors, including androgen receptor in prostate cancer (PC) (15,16), Forkhead box Q1 in nasopharyngeal carcinoma and breast cancer (BC) (17-19), integrin subunit beta 1 in osteosarcoma (20), and receptor tyrosine kinase like orphan receptor 2 in medulloblastoma (21,22) thereby disrupting cancer-type-specific migration, invasion, and survival signaling pathways.

This coordinated regulation of both universal and context-dependent targets enables miR-124 to effectively suppress tumor progression across various cancer types. Second, the wide spectrum of miR-124 activity underlies its tumor-suppressive effects, extending beyond cancer cells themselves by directly targeting and remodeling the metastatic microenvironment. For instance, miR-124 in oral cancer inhibits the tumor-promoting functions of cancer-associated fibroblasts (CAFs) by downregulating C-C motif chemokine ligand 2 and interleukin-8 (23). In BC, miR-124 disrupts the formation of the bone metastatic niche by targeting interleukin-11 (24). Furthermore, in non-small cell lung cancer, exosome-mediated intercellular transmission of miR-124 facilitates the spatiotemporal extension of its tumor-suppressive effects (25,26). Through these multifaceted mechanisms, miR-124 effectively inhibits metastasis at both local and systemic levels. Third, the significant therapeutic potential of miR-124 is underscored by the intricate nature of upstream regulatory mechanisms and the extensive scope of its functional network. miR-124 expression is modulated by ceRNA molecules, including long non-coding RNAs (lncRNAs) SND1-IT1 (27) and LINC00240 (28), indicating the complex layers of its regulatory control. The concurrent targeting of multiple critical nodes by miR-124 that promote metastasis, such as IQ Motif Containing GTPase activating protein 1 in colorectal cancer (CRC) (29), arrestin domain containing 1 in hepatocellular carcinoma (HCC) (30), and histidine rich carboxyl terminus 1 in gastric cancer (GC) (31), suggests that restoring or simulating miR-124 function could be a promising multi-target therapeutic strategy. This approach can inhibit tumor growth and metastasis, thereby improving patient prognosis. Collectively, these findings underscore the consistent role of miR-124 in tumor suppression across diverse cancer types, underscoring its broad therapeutic applicability.

Modulation of cancer stem cell (CSC) properties by miR-124. CSCs are a minor yet critical subpopulation within tumors, distinguished by their ability to self-renew and to differentiate into multiple lineages. These cells play a crucial role in tumor initiation, metastasis and therapeutic resistance (32,33). miR-124 significantly affects the self-renewal and differentiation capabilities of CSCs by regulating key target genes (34). Notably, the dysregulation of miR-124-mediated pathways is strongly associated with the emergence of resistance in CSCs to standard chemotherapy and radiotherapy (35). Studies have demonstrated that the natural compound sulforaphane

(SFN), in addition to its wide-ranging antitumor effects, can particularly improve the transcription of miR-124. This upregulation leads to the downregulation of essential stemness genes, including β -catenin, SRY-box transcription factor 2 and octamer-binding transcription factor 4 (Oct4). Consequently, SFN significantly reduces stemness and the self-renewal capacity of CSCs (36). miR-124 exerts a significant inhibitory effect on CSCs, as observed across various tumors. For instance, miR-124 directly downregulates the expression of the junctional adhesion molecule A in nasopharyngeal carcinoma, thereby reducing stem cell-like characteristics of tumor cells and increasing their sensitivity to radiotherapy (37). In HCC, miR-124 inhibits CSC proliferation and reverses sorafenib resistance (38).

The regulatory mechanisms of miR-124 demonstrate significant heterogeneity across various cancer types. In glioblastoma (GBM), miR-124 directly targets the oncogene EPH receptor A2 by disrupting AlkB homolog 5-mediated N6-methyladenosine RNA modification, thereby inhibiting tumor cell stemness and tumorigenic potential (39). This discovery highlights a novel epitranscriptomic mechanism of miR-124 regulation. Conversely, circular RNA circ-trichorhinophalangeal syndrome type 1 functions as a molecular sponge in PC, sequestering miR-124, thereby indirectly upregulating EZH2 expression and enhancing stem cell-like characteristics. However, the exogenous reintroduction of miR-124 counteracts the EZH2-mediated epigenetic silencing pathway, thereby reducing tumor stemness and improving patient prognosis (40). Collectively, these findings clarify the critical role of the circRNA-miRNA-epigenetic axis in regulating stemness from a ceRNA perspective. The significant metastatic potential of CSCs is closely linked to their tumorigenic properties, a highly aggressive characteristic primarily attributed to their ability to undergo epithelial-mesenchymal transition (EMT). It is a process deeply embedded in their intrinsic cellular plasticity. miR-124 partially mitigates the metastatic potential of CSCs by inhibiting EMT. EMT endows cells with migratory and invasive capabilities and is a fundamental mechanism by which CSCs facilitate metastasis. Mechanistically, miR-124 has been demonstrated to directly target key transcription factors that induce EMT, such as Zinc Finger E-Box Binding Homeobox 1 and Snail Family Transcriptional Repressor 1 (SNAIL) (20,41). For instance, miR-124 reduces SNAIL expression in osteosarcoma, thereby attenuating transforming growth factor-beta-induced EMT and reducing metastatic potential (20). miR-124 disrupts the CSC-induced metastatic cascade by simultaneously suppressing both stemness and EMT, underscoring its critical role as a tumor suppressor.

In conclusion, miR-124 modulates numerous signaling pathways to play a critical inhibitory role in maintaining stemness in various CSCs. These findings provide new insights into the heterogeneity and plasticity of CSCs and establish a theoretical basis for the development of miR-124-based precision therapies. Despite the cancer-type specificity of miR-124 mechanisms, targeting miR-124 or its associated pathways offers a promising universal approach to overcoming resistance to tumor therapies. Future research should focus on elucidating the specific targets of miR-124 and the interactions between the pathways it regulates in different TMEs. These

endeavors will be indispensable for advancing the clinical translation of miR-124-based therapeutic strategies.

Role of miR-124 in reversing tumor drug resistance. Tumor drug resistance is characterized by the ability of cancer cells to endure chemotherapy, targeted therapy, and other anticancer agents, resulting in reduced therapeutic efficacy and unfavorable patient outcomes (42,43). Recent advances in cancer therapeutics have highlighted the importance of miR-124 in modulating drug resistance (44). miR-124 exhibits multifaceted regulatory functions in counteracting tumor drug resistance. miR-124 improves drug sensitivity by targeting pro-survival signaling pathways at the cellular level. Notably, miR-124, a key negative regulator of the Janus kinase-signal transducer and activator of transcription pathway, suppresses the expression of the glycosyltransferase beta-1,4-galactosyltransferase 1, thereby reversing chemotherapy resistance in tumor cells (45). In liver cancer, miR-124 enhances the sensitivity of HCC cells to sorafenib by inhibiting the AKT serine/threonine kinase 2/sirtuin 1 pathway, thereby activating Forkhead Box O3a-mediated apoptosis. Furthermore, miR-124 directly targets TNF receptor-associated factor 6, negatively regulating the nuclear factor kappa B (NF- κ B) pathway and thereby counteracting pro-survival signaling-induced drug resistance (46,47). Regarding the DNA damage response, miR-124 improves the efficacy of genotoxic agents, such as temozolomide, by impairing the DNA repair mechanisms of tumor cells, a phenomenon particularly well-documented in glioma (48,49). Moreover, miR-124 suppresses CSC characteristics. For instance, in BC, it diminishes stemness and doxorubicin resistance by disrupting the STAT3/hypoxia inducible factor 1 alpha (HIF-1 α) signaling axis (50,51). Given its influence on TME and cell death regulation, miR-124 modulates immune microenvironment dynamics and pyroptosis-related processes, which, in turn, affect the response to gemcitabine chemotherapy in bladder cancer (52,53). In conclusion, miR-124 significantly enhances the efficacy of various anticancer agents by orchestrating multiple mechanisms, including apoptosis, DNA repair, stemness, the TME, and epigenetic modifications. These diverse functions highlight miR-124 as a promising therapeutic target for combating drug resistance.

Although miR-124 significantly reverses drug resistance in preclinical studies, its translation from experimental findings to clinical application is hindered by numerous obstacles. As elaborated in subsequent sections, these challenges are predominantly related to delivery systems, stability and targeting strategies. The systematic resolution of these issues could establish miR-124 as an innovative and effective therapeutic approach to overcome tumor drug resistance.

Modulation of the TME by miR-124. TME is a complex ecosystem comprising tumor cells, immune cells, stromal cells, the extracellular matrix (ECM), soluble factors, and physicochemical conditions such as hypoxia and acidic pH. This intricate assembly facilitates tumor proliferation, invasion, metastasis and drug resistance (54-56). miRNAs are crucial regulators within the TME, and their expression and activity are tightly controlled by various TME components while simultaneously contributing to TME

reprogramming. Among these, miR-124 assumes a central regulatory role within this intricate network (57). Within the immune microenvironment, miR-124 downregulates the expression of pro-inflammatory factors, including tumor necrosis factor- α and interleukin-1 β . This reduction in tumor-associated inflammation subsequently reduces the risk of tumor initiation and progression (58,59). Furthermore, miR-124 directly modulates macrophage polarization by inhibiting M1 markers and promoting the M2 phenotype, thereby reprogramming the immune microenvironment and affecting tumor progression (60,61). miR-124 regulates T-cells by inhibiting TH17 cell differentiation. Notably, miR-124 demonstrates both anti-inflammatory and antitumor properties in models of colitis-associated CRC (62,63). In the metabolic microenvironment, miR-124 is an important link between metabolic reprogramming and inflammatory responses. Particularly, in CRC, cell energy utilization and signal secretion through lipid metabolic reprogramming are affected by a regulatory network involving the RNA-binding protein HuR, miR-124, and its target gene, the vitamin D receptor (VDR). Subsequently, this process affects immune cell infiltration and function, including VDR signaling-induced macrophage polarization (64,65). Regarding the ECM and physicochemical microenvironment, emerging evidence indicates that miR-124 is involved in cell-matrix interactions and stress responses. lncRNA MALAT1 activates the phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT) pathway through the miR-124/laminin subunit gamma 1 axis. This mechanism, initially identified in tissue repair, suggests that MALAT1 may contribute to tumor ECM remodeling and regulation of the metastatic microenvironment (66,67).

In conclusion, miR-124 is crucial to prevent the formation of a pro-TME by regulating various mechanisms, including immune responses, metabolic reprogramming and physicochemical properties. miR-124 precisely modulates inflammatory factors, metabolic pathways, and immune differentiation, through its post-transcriptional regulatory functions, underscoring its potential as a viable target for therapies targeting the TME. Notably, the regulatory effects of miR-124 on immune cells are highly context-dependent, and the specific outcomes vary based on tumor type and microenvironmental signals. Therefore, future research should focus on elucidating the role of miR-124 within specific components of the TME, such as CAFs, ECM and hypoxic niches, to elucidate its functional diversity across various contexts, thereby facilitating its precise translation in tumor immunology and microenvironment-targeted therapeutic strategies.

Modulation of tumor immunity by miR-124. miR-124 regulates tumor immunity by coordinating multicellular and multipathway synergistic effects. It enhances antitumor immune responses by simultaneously targeting both immune and tumor cells (68). In the adaptive immune system, miR-124 enhances the CD8⁺ T-cell-mediated clearance of tumor cells and facilitates the production and function of effector CD4⁺ T-cells by inhibiting the STAT3 signaling pathway (69-71). Furthermore, miR-124 increases the cytotoxic activity of natural killer (NK) cells by modulating the LINC00240/miR-124/STAT3/MHC Class I polypeptide-related sequence A axis (28). In neuro-immunity, miR-124 regulates microglial activation via the

MALAT1/miR-124/SGK axis in myeloid immune cells (72). Similarly, miR-124 may reverse the immunosuppressive microenvironment by affecting the polarization state of tumor-associated macrophages through this mechanism. Moreover, miR-124 directly influences tumor cells by downregulating immune checkpoint molecules, including programmed death-ligand 1 (PD-L1), while simultaneously upregulating the expression of pro-inflammatory factors. This dual action impedes immune evasion and facilitates the immune cell infiltration (61,73). Furthermore, miR-124-regulated JAK/STAT and NF- κ B signaling pathways act as 'bridge pathways' that connect inflammation and cancer in autoimmune diseases, thereby reinforcing the critical role of miR-124 in tumor immunology (74-76). In summary, miR-124 emerges as a critical therapeutic target that can reverse the immunosuppressive microenvironment and modulate antitumor immune responses through its integrated multicellular and multipathway regulatory mechanisms. The development of effective regulatory strategies, including nanoparticle-based or natural compound-derived delivery systems, has the potential to advance the field of cancer immunotherapy significantly.

miR-124 demonstrates significant functional pleiotropy and context-dependent effects in regulating the immune system. miR-124 can manifest diverse and occasionally contradictory biological functions in distinct TME niches and among various immune cell subsets. As aforementioned, miR-124 facilitates macrophage polarization towards the M2 phenotype, primarily indicating its regulatory role in mitigating inflammatory damage and preserving tissue homeostasis within specific microenvironmental contexts. Conversely, this section highlights its capacity to counteract tumor immune suppression by targeting key immune checkpoint molecules, such as STAT3 and PD-L1, thereby augmenting the effector functions of CD8⁺ T-cells and NK cells. This functional plasticity demonstrates the complex role of miR-124 as a microenvironment-responsive regulator. Its ultimate effect is not an intrinsic property of the molecule itself. However, it is influenced by the spatiotemporal dynamics of the tumor type, immune cell subset status, the repertoire of microenvironmental signals, and intercellular interactions. Consequently, it is imperative to analyze the immunomodulatory mechanisms of miR-124 across distinct pathophysiological contexts, avoiding a reductionist binary perspective on its function.

In summary, miR-124 acts as an important tumor suppressor by regulating tumor growth, metastasis, stemness, drug resistance and immune responses. Its multifaceted functions are systematically cataloged in Table I and schematically summarized in Fig. 1, highlighting its central role in cancer biology.

3. Upstream regulatory mechanisms of miR-124 in tumors

The upstream regulatory mechanisms of miR-124 in tumors comprise a complex network, including transcription factors, signaling pathways, epigenetic modifications, and competitive interactions with non-coding RNAs. Understanding this intricate network is a primary focus of contemporary research efforts. The transcriptional regulation of miR-124 involves a coordinated interplay of various transcription factors and oncogenic signaling pathways (Fig. 2).

Table I. Multifunctional roles of miR-124 in cancer.

Functional category	Key mechanisms of action	Critical targets/regulatory axes	Associated cancers
Inhibition of tumor growth and metastasis	Suppresses tumor cell proliferation and invasion; impairs the pre-metastatic niche	STAT3 (13), EZH2 (14), CDK6 (15), SMYD3 (16), AR (17,18), Foxq1 (19-21), ITGB1 (22), ROR2 (23,24); CCL2/IL-8 in CAFs (25); IL-11 in bone metastasis (26); Exosome-mediated transfer (27,28); lncRNA SND1-IT1/LINC00240 (ceRNA) (29,30); IQGAP1 (31), ARRDC1 (32), HRCT1 (33)	Prostate cancer, nasopharyngeal carcinoma, breast cancer, osteosarcoma, medulloblastoma, oral squamous cell carcinoma, non-small cell lung cancer
Reduction of cancer stem cell stemness	Inhibits self-renewal and multi-lineage differentiation potential	β -catenin, Sox-2, Oct4 (via SFN induction) (38); JAMA (39); EPHA2 (via ALKBH5/m6A) (41); EZH2 (via circ-TRPS1 sponge) (20)	Nasopharyngeal carcinoma, liver cancer, glioblastoma, prostate cancer
Reversal of tumor drug resistance	Enhances chemosensitivity by promoting drug-induced apoptosis and impairing DNA damage repair	B4GALT1/JAK-STAT (45); AKT2/SIRT1/FOXO3a and TRAF6/NF- κ B axes (46,47); DNA repair mechanisms in glioma (48,49); STAT3/HIF-1 α axis (50,51); TME/Pyroptosis in bladder cancer (52,53)	Liver cancer, glioma, breast cancer, bladder cancer
Modulation of TME	Reprograms the TME by regulating immune cell polarization, inflammatory factors, metabolic reprogramming, and ECM remodeling	TNF- α /IL-1 β (58,69); Macrophage polarization (M1/M2) (60,61); TH17 cell differentiation (62,63); HuR/miR-124/VDR axis (metabolic reprogramming) (64,65); lncRNA-Malat1/miR-124/Lamc1 axis (ECM remodeling) (66,67)	Colorectal cancer, oral cancer, breast cancer
Regulation of tumor immunity	Potentiates antitumor immunity by enhancing T and NK cell activity and suppressing immune checkpoint expression	STAT3 in T cells (69-71); LINC00240/miR-124/STAT3/MICA axis in NK cells (28); MALAT1/miR-124/SGK axis in microglia/TAMs (72); PD-L1 downregulation (61,73); JAK/STAT & NF- κ B bridge pathways (74-76)	Various solid tumors and hematological malignancies

TME, tumor microenvironment; ECM, extracellular matrix; STAT3, signal transducer and activator of transcription 3; EZH2, enhancer of zeste homolog 2; CDK6, cyclin-dependent kinase 6; SMYD3, SET and MYND domain containing 3; AR, androgen receptor; ITGB1, integrin subunit beta 1; ROR2, receptor tyrosine kinase like orphan receptor 2; CAFs, cancer-associated fibroblasts; CCL2, C-C motif chemokine ligand 2; IQGAP1, IQ motif containing GTPase activating protein 1; ARRDC1, arrestin domain containing 1; HRCT1, histidine rich carboxyl terminus 1; SOX2, SRY-box transcription factor 2; PD-L1, programmed death-ligand 1; OCT4, octamer-binding transcription factor 4; HIF-1 α , hypoxia inducible factor 1 alpha; NF- κ B, nuclear factor kappa B; JAMA, junctional adhesion molecule A; SIRT1, sirtuin 1; FOXO3a, forkhead box O3.

Transcriptional and signaling pathway-mediated upstream regulation of miR-124 in tumors. The expression of miR-124 in tumors is regulated by a complex network of transcription factors and signaling pathways. miR-124 regulation can be categorized into repressive and activating mechanisms at the transcriptional level. Several cancer-associated transcription factors, such as HIF-1 α , RE1-silencing transcription factor (77) and c-Myc (78,79), directly inhibit miR-124 expression by binding to cis-regulatory elements, particularly the miR-124 promoter. Similarly, stemness factors, such as SRY-Box transcription factor 9 (80), specificity

protein 1 (SP1) (81,82) and OCT4 (83), repress transcription by directly interacting with promoters. Collectively, these mechanisms maintain cellular stemness, inhibit differentiation, and promote malignant progression. Conversely, tumor suppressor factors, such as p53 (84) and the neural differentiation factor neuronal differentiation 1 (85), significantly induce miR-124 expression. The role of p53 is particularly significant, as it directly activates miR-124 transcription and participates in a signaling crosstalk network involving the p53-miR-124 axis, NF- κ B and iASPP, thereby affecting therapeutic response (86,87).

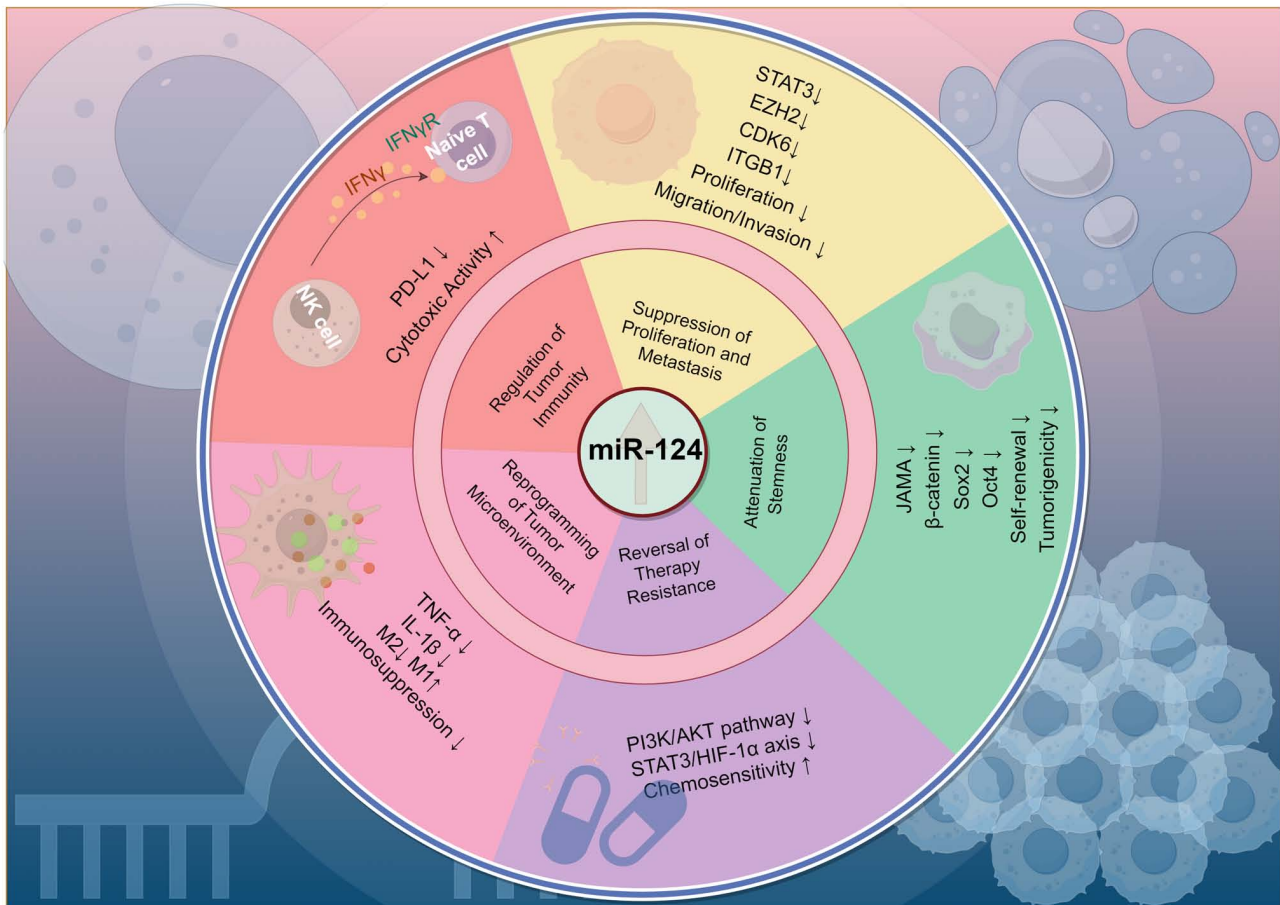


Figure 1. Comprehensive summary of the tumor-suppressive functions of miR-124. This figure summarizes the key functional roles of miR-124 discussed throughout this section, including inhibition of tumor growth and metastasis, modulation of cancer stem cell properties, reversal of drug resistance, and regulation of the tumor microenvironment and antitumor immunity. This figure was created using FigDraw. miR, microRNA; PD-L1, programmed death-ligand 1; EZH2, enhancer of zeste homolog 2; JAMA, junctional adhesion molecule A; ITGB1, integrin subunit beta 1; OCT4, octamer-binding transcription factor 4; SOX2, SRY-box transcription factor 2; HIF-1 α , hypoxia inducible factor 1 alpha; CDK6, cyclin-dependent kinase 6.

In cancer, miR-124 expression is intricately regulated through various key signaling pathways, forming a complex repressive network. Evidence suggests that the transcription of miR-124 is cooperatively suppressed by several core oncogenic pathways. This upstream regulatory network integrates critical signaling cascades, including Wnt/ β -catenin (88), PI3K/Akt (22,26), Notch (89) and EGF/MEK/ERK (90,91). miR-124 targeting through multiple pathways highlights its crucial role in maintaining cellular homeostasis. Consequently, miR-124 inactivation is a critical mechanism by which cancer cells maintain their malignant phenotype. Furthermore, NF- κ B, a transcription factor and a canonical inflammatory pathway, negatively regulates miR-124 upon activation. This regulatory mechanism is particularly important in tumorigenesis and the establishment of the TME (92-94). By coordinated suppression of their expression, evolutionarily conserved signaling pathways contribute to the prevalent silencing of miR-124 in tumors. This regulatory framework provides a basis for therapeutic targeting of upstream regulatory nodes of miR-124.

In summary, miR-124 expression in tumors is meticulously regulated by a complex, finely tuned multi-layered regulatory network. The frequent silencing of this molecule results from direct suppression by oncogenic transcription factors, such as

c-Myc and HIF-1 α , the functional loss of tumor suppressors, such as p53, and collaborative suppression through numerous signaling pathways, including Wnt/ β -catenin, PI3K/Akt and NF- κ B. There is extensive crosstalk between these regulatory elements. For instance, the p53-miR-124 axis regulates NF- κ B while concurrently inhibiting miR-124 expression. Furthermore, signaling pathways such as Wnt and PI3K/Akt can activate transcription factors, including c-Myc and SP1, which subsequently increase the transcriptional repression of miR-124, thereby establishing a multi-layered regulatory network. A comprehensive analysis of the composition and dynamic regulation of this network will clarify the crucial role of miR-124 in tumorigenesis and provide a theoretical basis for developing restorative therapeutic strategies targeting this regulatory system.

Epigenetic silencing mechanisms of miR-124 expression. Epigenetic modification is a crucial mechanism regulating miR-124 expression (95). At the epigenetic level, DNA methylation, such as CpG island hypermethylation in promoter regions, and histone modifications, including repressive methylation or deacetylation, can silence the miR-124 gene locus. Furthermore, certain non-coding RNAs, such as lncRNAs, may indirectly contribute to the silencing or functional

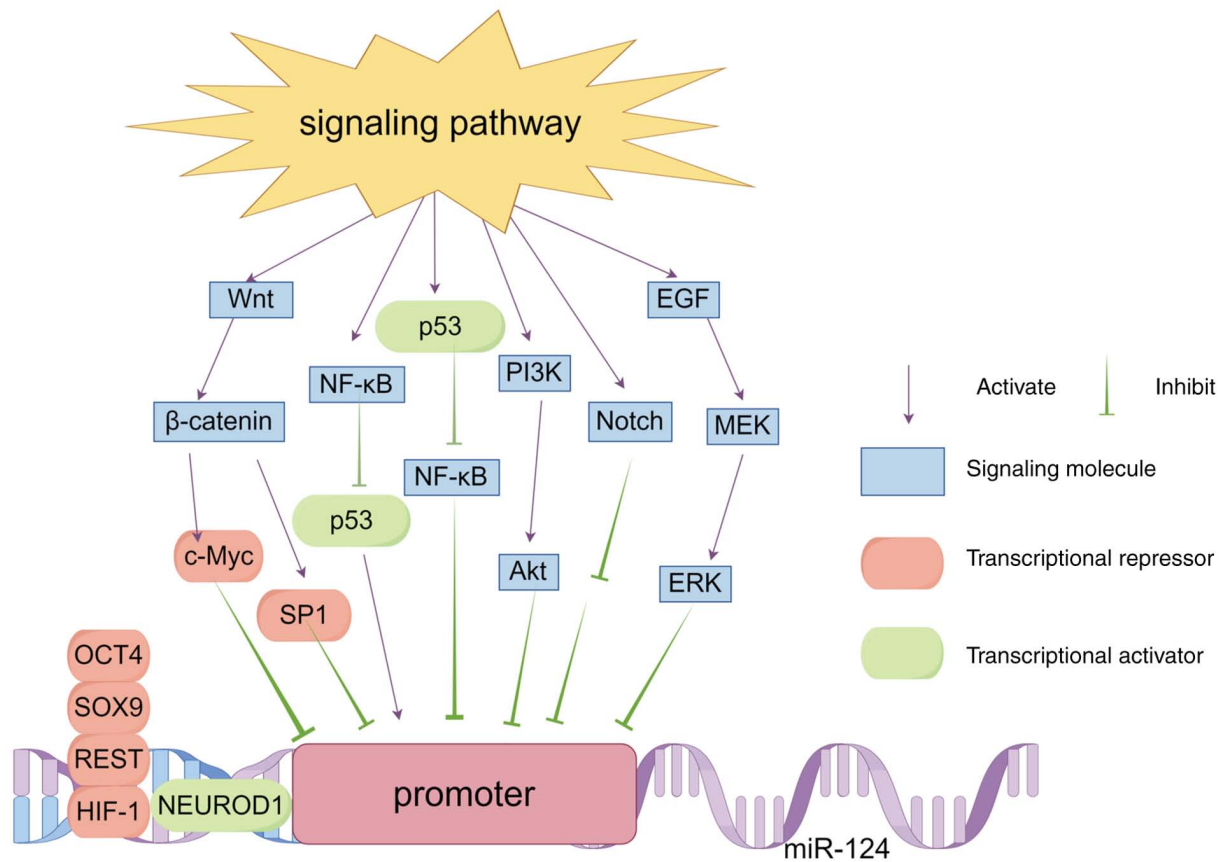


Figure 2. Regulatory network of transcription factors and upstream signaling pathways controlling miR-124 transcription. This schematic diagram illustrates the sophisticated network orchestrated by key transcription factors (for instance, c-Myc, p53 and HIF-1 α) and core signaling pathways (for instance, Wnt/ β -catenin, PI3K/Akt and NF- κ B), which fine-tunes miR-124 transcription through multiple layers of crosstalk. Dysregulation of this network and the consequent disruption of miR-124 expression are important pathogenic events in cancer. This figure was created using FigDraw. miR, microRNA; HIF-1 α , hypoxia inducible factor 1 α ; NF- κ B, nuclear factor kappa B; OCT4, octamer-binding transcription factor 4; SOX9, SRY-box transcription factor 9; NEUROD1, neural differentiation factor neuronal differentiation 1; SP1, specificity protein 1; REST, RE1-silencing transcription factor.

inhibition of miR-124 through mechanisms, such as ceRNA networks (96,97).

Hypermethylation of CpG islands in the promoter region of the miR-124 gene is primarily responsible for its transcriptional silencing. DNA methyltransferases facilitate the formation of 5-methylcytosine (5-mC), which directly obstructs the binding of transcription factors to promoter regions. Furthermore, 5-mC recruits repressive complexes, including methyl-CpG-binding domain proteins, leading to chromatin condensation and subsequent gene silencing. The molecular mechanism underlying this epigenetic silencing is illustrated in Fig. 3. Research has demonstrated that miR-124 expression is silenced through promoter hypermethylation, a critical epigenetic mechanism, in various cancers, including pancreatic adenocarcinoma, cutaneous T-cell lymphoma and oral squamous cell carcinoma. This silencing promotes malignant progression and underscores its potential as a diagnostic biomarker (98-100).

Histone modifications play a direct, crucial role in the transcriptional silencing of miR-124. In acute lymphoblastic leukemia, the miR-124 locus, including miR-124-1, miR-124-2 and miR-124-3, exhibits a characteristic repressive histone modification profile. This profile is characterized by enrichment of repressive histone marks and depletion of activating marks. Particularly, elevated levels of repressive histone modifications,

including H3K9me2, H3K9me3 and H3K27me3, facilitate the recruitment of complexes, such as heterochromatin protein 1 and Polycomb repressive complex 2, thereby promoting heterochromatin formation. Simultaneously, a significant reduction in activating marks, including H3K4me3 and acetylated histone H3 (AcH3), maintains a transcriptionally repressed state. Functionally, the histone deacetylase inhibitor trichostatin A can reverse the loss of AcH3 and partially restore miR-124 expression. This mechanism of histone modification-mediated regulation is illustrated in Fig. 4. These histone modifications synergize with DNA methylation mechanisms, establishing a feedback loop that stably silences miR-124. Consequently, this silencing leads to aberrant expression of its target gene, CDK6, contributing to leukemia progression (101).

Research has demonstrated that the functional activity of miR-124 is influenced by post-transcriptional regulation of lncRNAs via a ceRNA mechanism (102). Numerous lncRNAs, including H19 imprinted maternally expressed transcript (103), nuclear paraspeckle assembly transcript 1 (104), OIP5 antisense RNA 1 (105) and MALAT1 (72), have been identified as 'molecular sponges' that sequester miR-124. This sequestration alleviates miR-124-mediated repression of downstream target genes and regulates the related signaling pathways. A schematic representation of this critical regulatory axis of lncRNA-miR-124 interaction in tumorigenesis is illustrated

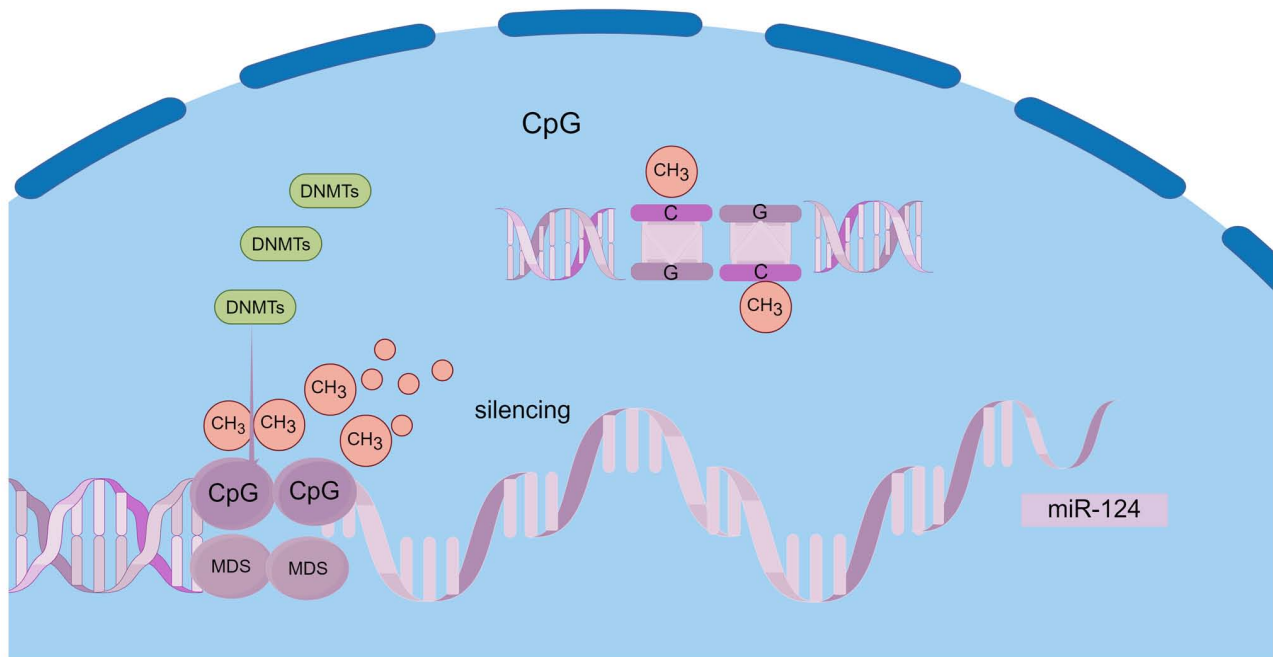


Figure 3. Epigenetic silencing of miR-124 via DNA methylation in cancer. This model illustrates the key steps in DNMT-mediated hypermethylation of CpG islands in the miR-124 promoter region. This process involves the addition of methyl groups to cytosine bases, forming 5-mC, which impedes transcription factor binding and recruits methyl-CpG binding domain proteins, leading to chromatin compaction and stable transcriptional silencing of miR-124. This figure was created using FigDraw. miR, microRNA; DNMT, DNA methyltransferase.

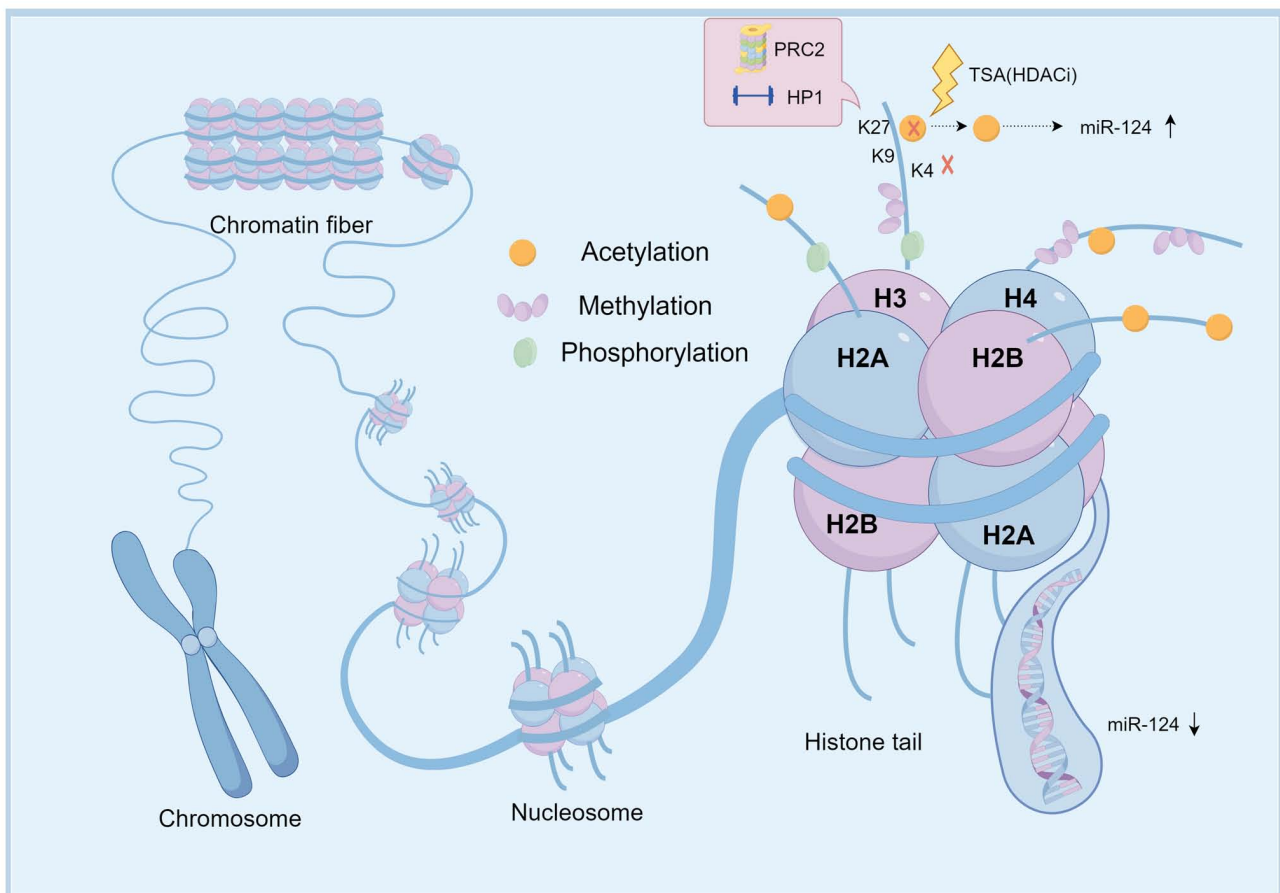


Figure 4. Histone modification-mediated epigenetic regulation of miR-124 in cancer. This model illustrates the dynamic balance between activating and repressive histone marks at the miR-124 locus. Enrichment of repressive marks, including H3K9me3 and H3K27me3, recruits protein complexes such as HP1 and PRC2, leading to chromatin condensation and gene silencing. Conversely, HDAC inhibitors (for instance, TSA) can promote an open chromatin state by increasing histone acetylation, thereby reactivating miR-124 expression. This figure was created using FigDraw. miR, microRNA; HP1, heterochromatin protein 1; PRC2, polycomb repressive complex 2; HDAC, histone deacetylase; TSA, trichostatin A.

Table II. Key upstream regulators of miR-124 expression and activity.

Regulatory layer	Regulatory type	Representative factors	Effect on miR-124	Associated cancers/context
Transcriptional regulation	Transcription factors (repressive)	c-Myc 78,79), HIF-1 α (77), REST (77), SOX9 (80), SP1 (81,82), OCT4 (83)	Repression	Ubiquitous in various cancers
	Transcription factors (activatory)	p53 (84), NEUROD1 (85)	Activation	Inactivation contributes to miR-124 downregulation
	Signaling pathways	Wnt/ β -catenin (88), PI3K/Akt 22,26), Notch (89), EGF/MEK/ERK (90,91), NF- κ B (92-94)	Repression	Ubiquitous in various cancers
Epigenetic regulation	DNA methylation	Promoter hypermethylation (by DNA methyltransferases) (98-100)	Repression	Pancreatic cancer, cutaneous T-cell lymphoma, oral squamous cell carcinoma
Post-transcriptional regulation (ceRNA network)	Histone modifications	H3K9me3, H3K27me3; H3K4me3, AcH3 (101)	Repression	Acute lymphoblastic leukemia
	ceRNAs	lncRNAs: H19 (103), NEAT1 (104), OIP5-AS1 (105), MALAT1 (72)	Functional inhibition (sponging)	Gastric cancer, glioma, prostate cancer

ceRNAs, competing endogenous RNAs; lncRNA, long non-coding RNA; miR, microRNA; SP1, specificity protein 1; NEAT1, nuclear paraspeckle assembly transcript 1; OCT4, octamer-binding transcription factor 4; HIF-1 α , hypoxia inducible factor 1 alpha; NF- κ B, nuclear factor kappa B; NEUROD1, neural differentiation factor neuronal differentiation 1; REST, RE1-silencing transcription factor; AcH3, acetylated histone H3.

in Fig. 5. These findings highlight the key role of the ceRNA network in the precise regulation of miR-124 and enhance our understanding of non-coding RNA interactions, thereby providing novel insights into disease modulation. Future research should elucidate the context-dependent dynamics of ceRNA regulation and its modifications in pathological conditions, and explore the translational potential of ceRNA-based targeted therapies.

A complex multi-layered network of upstream regulators that regulate miR-124 expression and activity is comprehensively summarized in Table II.

4. Potential clinical applications of miR-124 in cancer therapy

Dual role of miR-124 as a predictive biomarker and therapeutic target. The significantly reduced expression of miR-124 across various cancers underscores its potential use as a biomarker for cancer diagnosis and prognostic evaluation (106). The quantification of miR-124 levels in serum or tumor tissue enables early tumor detection and has the potential to predict patient survival rates and recurrence risk. Wang *et al* (107) reported a significant downregulation of serum miR-124 expression in patients with bladder cancer. Increased miR-124 levels were associated with early-stage disease, smaller tumor size, absence of lymph node metastasis and improved survival outcomes. Moreover, miR-124 was identified as an independent prognostic factor, underscoring its

potential as a diagnostic and prognostic biomarker for bladder cancer (107). Numerous studies in translational research have investigated the diagnostic potential of miR-124 when used in conjunction with other miRNAs. For instance, a systematic analysis of 14 miRNAs in the serum of patients with BC identified a specific panel of miRNAs, including miR-124, miR-96, miR-183, miR-195, miR-15a and miR-16, which has significant diagnostic value for differentiating early-stage BC patients from healthy individuals. This finding was corroborated by an independent external cohort (n=115), producing an area under the curve of 0.889 and an accuracy rate of 86.14%. These results highlight the significant potential of integrating miR-124 with other miRNAs to improve early detection rates of BC (108). The clinical relevance of miR-124 is substantiated by its essential biological functions, primarily through the modulation of critical signaling pathways. In addition to its diagnostic applications, miR-124 exhibits significant promise in modulating chemosensitivity and mitigating drug resistance. In advanced GC, studies have demonstrated that low serum miR-124 expression is significantly associated with poor tumor differentiation, advanced TNM stage and chemotherapy resistance. Mechanistically, miR-124 modulates chemosensitivity by downregulating the PI3K/AKT/mTOR signaling pathway. These findings indicate that miR-124 is a predictive biomarker and a promising therapeutic target for overcoming drug resistance (109).

In conclusion, miR-124 is a multifunctional molecule with integrated diagnostic, prognostic and therapeutic guidance

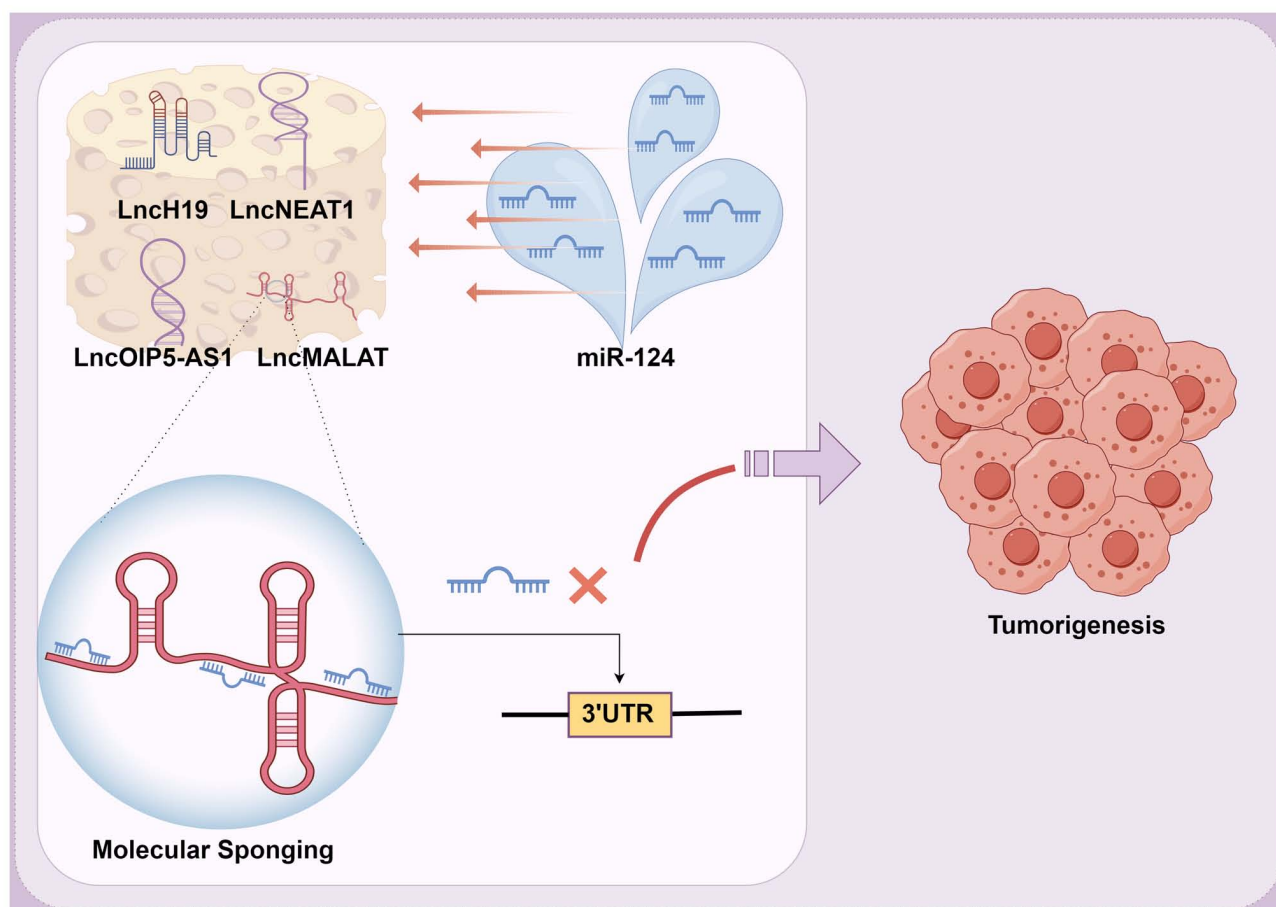


Figure 5. Epigenetic regulation of miR-124 by lncRNAs as molecular sponges in tumorigenesis. This schematic illustrates the competing endogenous RNA mechanism, in which specific lncRNAs, including H19, NEAT1 and MALAT1, act as molecular sponges to sequester miR-124. This interaction prevents miR-124 from binding its target mRNAs, thereby derepressing oncogenic signaling pathways and contributing to tumor development. This figure was created using FigDraw. miR, microRNA; lncRNA, long non-coding RNA; H19, H19 imprinted maternally expressed transcript; NEAT1, nuclear paraspeckle assembly transcript 1; UTR, untranslated region.

capabilities, offering significant promise for the clinical management of cancer. However, the therapeutic efficacy of most related research is currently restricted to the preclinical stage due to several significant challenges, including suboptimal *in vivo* delivery efficiency, insufficient tissue targeting specificity, and inadequate molecular stability. Future research should prioritize the development of efficient and safe targeted delivery systems, such as lipid nanoparticles (LNPs) or exosomal vectors. Furthermore, it is imperative to elucidate the critical role of miR-124 within tumor drug resistance networks and its synergistic interactions with current chemotherapeutic and targeted agents. Moreover, research should focus on developing precise therapeutic strategies based on molecular subtyping to identify patient subgroups that are most likely to benefit from miR-124-based interventions. Investigating miR-124-based gene therapies or oligonucleotide drugs will be essential for translating these findings from the bench to the bedside.

Carrier system-based therapeutic strategies for miR-124 in tumor treatment. Carrier-based delivery strategies for miR-124 are a promising development in tumor gene therapy. Current delivery systems include LNPs, polymeric carriers, inorganic nanoparticles, and viral vectors, such as adeno-associated

virus and lentiviral vectors, and exosomes. These carriers exhibit structural and functional diversity, providing a versatile toolkit for delivering miR-124. Collectively, they facilitate the transition of this strategy from basic research to clinical applications.

Among synthetic nanocarriers, LNPs have attracted significant attention owing to their adjustable physicochemical properties and favorable biocompatibility. For instance, an LNP system developed with the novel ionizable lipid S-Ac7-DOG effectively encapsulates and delivers miR-124, significantly improving its stability and intracellular delivery efficiency (110). Moreover, liposomal nanocarriers facilitate co-delivery strategies, such as concurrent encapsulation of miR-124 and the chemotherapeutic agent SN38, resulting in synergistic therapeutic effects in the treatment of HCC (111). Polymeric carriers, such as cationic polymeric nanoparticles, have been demonstrated to effectively deliver miR-124 into PC cells, leading to a significant reduction in tumorigenicity and demonstrating significant therapeutic potential (112). Inorganic nanomaterials also have significant potential for miR-124 delivery. Although studies particularly targeting miR-124 are currently sparse in the literature, various inorganic nanoplatforms have been successfully used to deliver other functional miRNAs, such as miR-206. The

Table III. Delivery systems for microRNA-124 in cancer therapy with clinical challenges.

Delivery system	Representative carrier	Core advantages	Key challenges
LNPs	Ionizable LNP	Highest industrial maturity, suitable for systemic administration, facile surface modification	Limited target specificity, potential acute toxicity
Polymeric nanoparticles	PEI, PLGA	High design flexibility, capable of stimulus-responsive release	Cytotoxicity concerns, complex <i>in vivo</i> behavior
Inorganic nanoparticles	AuNPs, AAV	High stability, potential for theranostic applications	Poor biodegradability and long-term toxicity risks
Viral vectors	AAV, lentivirus	Sustained and high-efficiency expression, Inherent tissue tropism	Immunogenicity, limited cargo capacity, Insertional mutagenesis concerns
Exosomes	MSC-derived exosomes	Innately low immunogenicity, superior biodistribution and barrier-penetrating capacity	Major hurdles in scalable production and quality control, low drug loading efficiency

LNPs, lipid nanoparticles; AuNPs, gold nanoparticles; MSNs, mesoporous silica nanoparticles; AAV, adeno-associated virus.

design principles and technical expertise derived from these studies offer valuable insights into the development of miR-124-specific delivery systems. Gold nanoparticles (AuNPs) exhibit excellent biocompatibility, ease of functionalization, and distinctive optical properties, which facilitate efficient miRNA loading and targeted delivery via surface modifications. Research indicates that PEGylated AuNPs can efficiently deliver miR-206 mimics, thereby inhibiting BC progression (113). This suggests that analogous strategies could be used to improve the stability and tumor-targeting properties of miR-124. Mesoporous silica nanoparticles, known for their high stability, adjustable pore size, and flexible surface chemistry, present opportunities for high-capacity encapsulation and controlled release of miR-124 (114). Furthermore, carbon-based materials, including graphene oxide and carbon nanotubes, have attracted significant interest as innovative platforms for miRNA delivery owing to their exceptional electrical properties and easily functionalizable surfaces (115). The combined advantages of these inorganic carriers, including stability, loading capacity, and functional versatility, provide a robust foundation for developing efficient and targeted miR-124 delivery systems.

Compared with synthetic carriers, viral vectors are distinguished by their superior transfection efficiency. Lentiviral vectors facilitate stable overexpression of miR-124 in human lung fibroblasts, which effectively suppress downstream target genes (85). Conversely, AAV vectors enable tissue-specific delivery of miR-124, resulting in significant antitumor effects by inhibiting oncogenes, such as sphingosine kinase 1, and consequently remodeling the TME (116). Exosomes, endogenous nanovesicles, offer distinct advantages for targeted delivery. For instance, exosomes engineered with rabies virus glycoprotein can cross the blood-brain barrier and deliver miR-124 to regions affected by cerebral ischemia. This targeted delivery enhances neural repair and mitigates injury (117), providing proof of concept for the clinical translation of this strategy.

In summary, critical strategies to enhance the therapeutic efficacy of miR-124 focus on improving its stability and bioavailability, as well as on developing efficient and safe delivery systems. To improve stability, chemical modifications, such as 2'-O-methylation or phosphorothioate linkages, can be used. Alternatively, encapsulation within nuclease-resistant carriers can prolong its half-life. Incorporating functional components, such as ionizable lipids or cell-penetrating peptides, can improve bioavailability by increasing cellular uptake and endosomal escape efficiency. The development of delivery systems requires a balance between targeting specificity and safety. Surface modification of carriers with targeting ligands, such as peptides, antibodies, or aptamers, can increase tumor accumulation while minimizing off-target effects. Furthermore, stimuli-responsive carriers (for instance, pH-, reactive oxygen species-, or enzyme-sensitive materials) facilitate the controlled release of miR-124 within the TME. It is anticipated that the clinical translation of miR-124 in precision oncology will be significantly advanced by integrating personalized delivery strategies with multimodal combination therapies. The core characteristics, advantages and challenges of the major delivery systems developed for miR-124 are provided in Table III.

Current status and future challenges of miR-124 in clinical translation. Although numerous miRNA-based therapeutics have progressed to phase I/II clinical trials, research particularly targeting miR-124 remains relatively underdeveloped. Regulatory bodies, such as the U.S. Food and Drug Administration or the National Medical Products Administration of China, have not yet granted clinical approval for any pharmaceutical agent that directly targets miR-124 or incorporates it as an active ingredient. Most current studies are limited to the preclinical stage, with a primary focus on validating miR-124-based diagnostic markers and therapeutic strategies. These efforts include the development of nanoparticle delivery systems for conditions such as HCC and

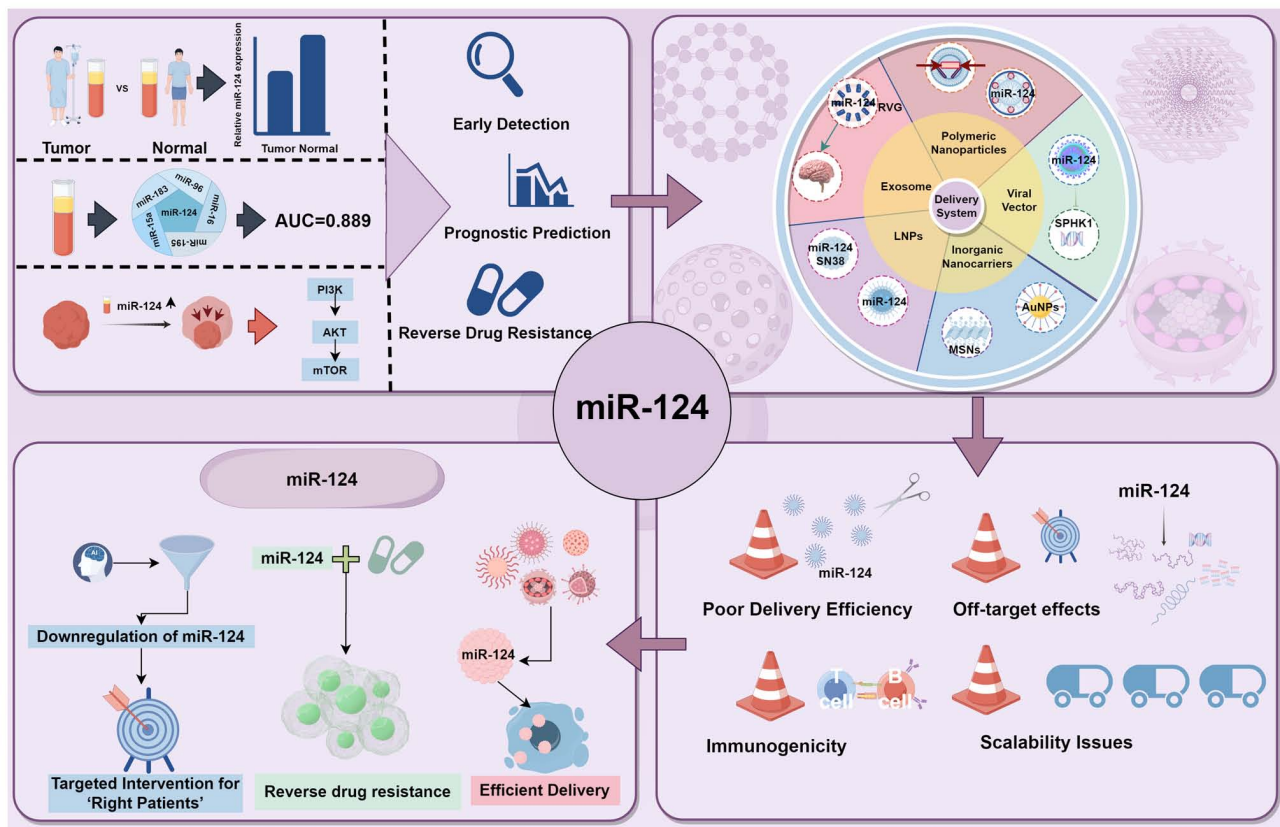


Figure 6. Translational landscape of miR-124 in cancer therapy: From biological mechanisms to clinical applications. This schematic integrates the core concepts discussed in this section, revealing the potential of miR-124 as a diagnostic/prognostic biomarker and therapeutic agent, currently developed delivery systems, including LNP, viral vectors, and exosomes, key challenges in clinical translation, and future development prospects. This figure was created using FigDraw. LNP, lipid nanoparticles; miR, microRNA; AuNP, gold nanoparticles; MSN, mesoporous silica nanoparticles; AUC, area under the curve; SPHK1, sphingosine kinase 1; RVG, rabies virus glycoprotein.

GBM, using both cellular and animal models. Although these studies provide preliminary evidence suggesting the potential for clinical translation, numerous critical challenges must be overcome to realize this potential. The most important challenge is the delivery system. Serum nucleases can degrade unmodified miRNA molecules, limiting their ability to selectively access target cells. Therefore, the development of safe, stable and targeted delivery carriers, such as LNP, exosomes, or viral vectors, is a primary challenge. Furthermore, there is a significant risk of off-target effects and adverse side effects, as miR-124 can regulate numerous downstream target genes. Moreover, exogenous RNA molecules may elicit immunogenic responses, and the *in vivo* pharmacokinetic properties, including distribution, metabolism and stability, require comprehensive evaluation. Furthermore, establishing large-scale production and quality control systems that comply with clinical standards remains an unmet requirement. Consequently, it is anticipated that the clinical translation of miR-124-based therapies will focus on three principal directions. First, the integration into precision medicine frameworks will enable the identification of patient subgroups characterized by low miR-124 expression through molecular subtyping, thereby enabling targeted interventions. Second, combination with standard chemotherapy or targeted agents may improve therapeutic efficacy by functioning as chemosensitizers or by reversing resistance. Third, it is expected that advancements in delivery technologies, such as nanomaterials and engineered

exosomes, will accelerate clinical translation. Despite these challenges, miR-124 remains a highly promising therapeutic strategy, particularly considering the recent advancements in RNA therapeutics. The overarching journey from bench to bedside for miR-124, including its dual roles as a biomarker and therapeutic target, as well as current delivery strategies and translational challenges, is comprehensively summarized in Fig. 6.

5. Future perspectives

Prospective studies of miR-124 in oncology present significant potential, particularly in precision medicine, targeted therapy, elucidation of underlying mechanisms, and biomarker development. First, it is anticipated that miR-124-level-based personalized therapeutic strategies will be developed as understanding of miR-124 expression profiles across various cancer types advances. This precision medicine approach could improve patient response rates to therapy and reduce unnecessary side effects, thereby improving the overall quality of life. Second, it is imperative to optimize the targeted delivery systems for miR-124 to ensure its efficient release and high bioavailability within the TME. Current research primarily focuses on various nanocarriers, including liposomes, polymeric nanoparticles and viral vectors, to enhance the specificity and accumulation of miR-124 in tumor tissues. Furthermore, the development

of functionalized nanoparticles presents innovative strategies to improve miR-124 delivery, potentially enabling controlled release through external stimuli, such as light or magnetic fields, thereby increasing treatment precision. In mechanistic studies, it is essential to elucidate the precise molecular mechanisms by which miR-124 influences tumorigenesis and metastasis. This involves a comprehensive understanding of its interactions with key signaling pathways, such as PI3K/Akt, Wnt/ β -catenin and NF- κ B, as well as the array of target genes it regulates. These studies will provide novel insights into tumor biology and may guide the development of novel targeted therapeutic strategies. Moreover, integrating miR-124 with conventional chemotherapeutic agents or immunotherapies represents a promising avenue for research. Empirical evidence indicates that miR-124 can improve the sensitivity of tumor cells to specific chemotherapeutic agents, thereby overcoming drug resistance and improving overall therapeutic efficacy. Future clinical trials should prioritize the assessment of the safety and efficacy of such combination therapies to provide more targeted treatment options for patients with cancer. Furthermore, miR-124, as a potential biomarker, offers significant application prospects for early cancer diagnosis, prognostic evaluation, and therapeutic monitoring. A systematic analysis of the correlation between miR-124 expression and the clinical characteristics of patients will provide significant support for the diagnosis and treatment of cancer. In summary, the future of miR-124 in cancer research is highly promising. However, advancing this field will require more in-depth fundamental research and multi-disciplinary collaborations to facilitate its effective translation from bench to bedside. With the progression of technologies and ongoing research, miR-124 is poised to emerge as a novel biomarker and therapeutic target in cancer therapy.

6. Conclusion

miR-124 is a critical miRNA that has a multifaceted role in cancer research. Its significant functions include suppression of tumor growth, regulation of metastasis and cancer stemness, modulation of drug resistance, remodeling of the TME, and modulation of immune responses. These diverse functions offer novel insights into the complex mechanisms underlying tumorigenesis and cancer progression. Recent studies suggest that miR-124 activity is modulated by multiple upstream signaling pathways. Moreover, the broad spectrum of its downstream target genes highlights its potential as a therapeutic target. Despite these advancements, the specific roles of miR-124 in different cancer types and its clinical applications warrant further comprehensive studies. Future studies should aim to elucidate the precise mechanisms by which miR-124 affects tumor biology and explore its practical applications in cancer therapy, including its potential as a biomarker and in the development of therapeutic strategies. miR-124 is expected to improve the prognosis and quality of life of patients with cancer by providing novel therapeutic avenues through the integration of fundamental research and clinical practice. In conclusion, miR-124 is poised to remain a focus of future research and clinical practice due to its significant clinical potential and multifaceted roles in oncology.

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Availability of data and materials

Not applicable.

Authors' contributions

JG conceptualized the study, developed methodology, conducted investigation, performed formal analysis, wrote the original draft and visualized data. YXL conceptualized and supervised the study, provided resources, wrote, reviewed and edited the manuscript, conducted project administration, and acquired funding. XPY validated data, wrote, reviewed and edited the manuscript, and supervised the study. YYG performed software analysis, validated and curated data. PYC conducted investigation and data curation. WYX performed formal analysis and data visualization. YXT wrote, reviewed and edited the manuscript. ZYW provided resources, contributed to the study design, and reviewed the manuscript. All authors read and approved the final version of the manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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