miR-100: A key tumor suppressor regulatory factor in human malignant tumors (Review)

LIANG ZHANG[1*], JIULING ZHANG[1*], XUE ZHANG[2], SHUANG LIU[2], CHUNYU QI[2,3] and SHENGYU GAO[1]

[1]Department of General Surgery I, The First Affiliated Hospital of Jiamusi University, Jiamusi, Heilongjiang 154002, P.R. China; [2]School of Basic Medical Sciences, Jiamusi University, Jiamusi, Heilongjiang 154002, P.R. China; [3]Department of Infection, The First Affiliated Hospital of Jiamusi University, Jiamusi, Heilongjiang 154002, P.R. China

Received November 1, 2024; Accepted January 2, 2025

DOI: 10.3892/ijmm.2025.5508

Abstract. MicroRNA (miRNA/miR)-100 is a crucial tumor-suppressive miRNA that serves a pivotal role in the initiation and progression of various malignancies. miR-100 regulates cancer cell proliferation, migration, invasion and apoptosis by targeting oncogenes, and acts as a molecular sponge to regulate long non-coding RNAs and circular RNAs, thereby influencing processes such as glycolysis, autophagy and resistance to chemotherapy/radiotherapy. Furthermore, miR-100 suppresses tumor progression by modulating key signaling pathways, including the PI3K/AKT and Wnt/β-catenin signaling pathways. miR-100 exhibits potential for early cancer diagnosis, particularly in cancer types such as gastric and lung cancer, where it can serve as a non-invasive biomarker for early screening. As a therapeutic target, restoring miR-100 expression can enhance the efficacy of chemotherapy or targeted therapy, thereby improving patient prognosis. Although challenges remain in its clinical application, including delivery systems and safety concerns, ongoing research suggests that miR-100 holds promise for personalized treatment and early diagnosis. Given that cancer remains a global health challenge, research on miR-100 provides hope for cancer therapy, particularly in China, where the mortality rates of malignancies such as gastric, lung and liver cancer continue to rise, further emphasizing its potential for clinical translation.

Correspondence to: Professor Shengyu Gao, Department of General Surgery I, The First Affiliated Hospital of Jiamusi University, 348 Dexiang Street, Jiamusi, Heilongjiang 154002, P.R. China
E-mail: 208113045@stu.jmsu.edu.cn

*Contributed equally

Key words: microRNA-100, non-coding RNA, competing endogenous RNA, tumor biology, radiotherapy resistance, signaling pathway, diagnostic marker, cancer prognosis

Contents

1. Introduction

Despite progress in cancer prevention, early detection and treatment, cancer remains a major unresolved global medical challenge (1,2). In 2020, the leading causes of cancer-related deaths in China included lung cancer, liver cancer, gastric cancer (GC), breast cancer (BC) and colorectal cancer (CRC), with liver cancer mortality rising from third place in 2018 to second place in 2020 (3). Globally, cancer incidence continues to rise, placing increasing pressure on public health systems and healthcare infrastructure (4). The initiation and progression of malignancies are primarily driven by dysregulation of gene expression, especially within critical regulatory pathways involving cell proliferation, survival and apoptosis (5). Although there has been some advancement in understanding these molecular mechanisms, the complexity and heterogeneity of cancer still pose major challenges for effective treatment.

In this context, non-coding RNAs (ncRNAs), including microRNAs (miRNAs/miRs), long non-coding RNAs (lncRNAs) and circular RNAs (circRNAs), have gained widespread attention due to their crucial roles in gene expression regulation and modulation of tumor behavior (6). Among ncRNA molecules, miRNAs are the most extensively studied. They serve crucial roles in regulating key biological processes in cancer, including cell proliferation, apoptosis, migration and invasion (7,8). Initially considered 'transcriptional noise'

or 'junk DNA', ncRNAs, including miRNAs, have now been proven to be essential for numerous cellular processes and diseases, particularly cancer (9). Among these miRNAs, miR-100 is involved in the biological processes of multiple cancer types (10).

miR-100 (MI0000102), located on human chromosome 11 [chr11:122152229-122152308(-)], is part of the let-7-C gene cluster. This miRNA has two mature forms, hsa-miR-100-5p and hsa-miR-100-3p, which are derived from the 5' and 3'arms of the precursor miR-100, respectively (10). miR-100 is frequently dysregulated in cancer and has been shown to act as a tumor suppressor in various malignancies, including ovarian cancer (OC), prostate cancer (PCa), thyroid cancer (TC), bladder cancer and GC (10-14). miR-100 inhibits cancer cell proliferation, migration and invasion, while promoting apoptosis by targeting multiple genes involved in these processes (11-15). For example, Zhang *et al* (11) showed that miR-100 inhibited the proliferation and cell cycle of FTC-133 cells by targeting RB protein serine phosphatase from chromosome 3 (RBSP3). Additionally, miR-100 has been identified as a key regulator of the cancer cell response to chemotherapy and radiotherapy, enhancing the chemosensitivity and radiosensitivity of CRC, lung cancer, and head and neck squamous cell carcinoma (15,16).

miR-100 exerts its effects by targeting the 3'untranslated regions (UTRs) of various key genes involved in growth signaling and stress responses. For example, miR-100 has been shown to directly regulate the mTOR pathway, a critical signaling axis involved in cell metabolism, proliferation and survival (17). By downregulating key genes such as insulin-like growth factor 1 receptor (IGF1R), fibroblast growth factor receptor 3 (FGFR3) and polo-like kinase 1 (PLK1), miR-100 regulates cell cycle progression, autophagy and chemotherapy resistance (10,17). Furthermore, miR-100 influences the tumor microenvironment through interactions with lncRNAs and circRNAs (10). These RNA molecules act as molecular sponges, regulating multiple cellular processes, including glycolysis, oxidative stress and tumor progression (18). Through its effects on these pathways, miR-100 has emerged as a promising therapeutic target in cancer treatment, especially for overcoming chemotherapy resistance and improving the efficacy of traditional therapies (10).

In addition to its role in malignancies, miR-100 is also associated with a variety of non-cancerous diseases. The expression levels of miR-100 are elevated in conditions such as hypertrophic cardiomyopathy, type 1 and type 2 diabetes, osteoporosis, and osteoarthritis (19-22). Furthermore, miR-100 has been shown to regulate apoptosis in different cell types, including retinal pigment epithelial cells, and serves a crucial role in normal cellular functions, including embryo implantation and germ cell proliferation (23-26). These findings further highlight the diverse biological roles of miR-100 and its potential as a therapeutic target, with applications not only in cancer but also in other diseases.

In conclusion, miR-100 represents a promising biomarker for cancer diagnosis, prognosis and treatment. Its multifaceted role in regulating critical signaling pathways related to tumorigenesis, therapeutic resistance and cancer progression underscores its potential as a target for precision medicine. Further research into the molecular mechanisms underlying the functions of miR-100 will provide deeper insights into its therapeutic applications and may lead to the development of novel RNA-based cancer therapies, as well as its use in other diseases.

2. Molecular mechanisms of miR-100 in cancer

miR-100 was first identified in *Drosophila* in 2003 and is derived from the let-7-C gene cluster (27). miR-100 is located on the distal fragile site FRA11F of the 11q13 amplification region on human chromosome 11 (28). In numerous malignancies, miR-100 regulates tumor cell proliferation, migration and invasion by targeting the 3'-UTR of its target genes (29). The specific mechanism by which miR-100 regulates gene expression involves post-transcriptional modulation through base pairing of its seed sequence with the 3'-UTR of target mRNAs. miR-100 is initially transcribed in the nucleus by RNA polymerase II as primary miRNA, which is subsequently processed by the Drosha and Dicer enzymes into mature miRNA. These mature miRNAs are incorporated into the RNA-induced silencing complex (RISC). Within the RISC, miR-100 utilizes its seed sequence to bind highly complementarily to target mRNAs, resulting in either mRNA degradation or translational repression. This regulatory mechanism effectively controls protein expression levels and influences various cellular processes (Fig. 1A) (29). For instance, miR-100 inhibits the migration and invasion of renal cancer cells by downregulating NADPH oxidase 4 (NOX4) (30) and acts as a tumor suppressor in CRC by suppressing leucine rich repeat containing G protein-coupled receptor 5 (LGR5) expression (31). Additionally, the online databases ENCORI (https://rnasysu.com/encori/), miRDB (https://mirdb.org/), TargetScan (https://www.targetscan.org/vert_80/), Diana-TarBase (https://diana.imis.athena-innovation.gr/) and miRTarBase (https://mirtarbase.cuhk.edu.cn/) predicted 385 downstream target genes targeted by miR-100 (Fig. 1B). Accumulating evidence suggests that miR-100 serves a critical role in the molecular regulation of various cancer types and serves as an important regulator in tumor biology (29-32).

3. miR-100 as a molecular sponge in the competing endogenous RNA (ceRNA) network

The ceRNA network regulates the interaction of transcripts post-transcriptionally through the competition of shared miRNAs. The ceRNA network functionally connects mRNA encoding proteins with ncRNAs, including miRNAs, lncRNAs, pseudogenes and circRNAs (32). Studies have shown that miRNAs often act as molecular sponges for lncRNAs and circRNAs within the ceRNA network, thereby regulating the transcription or degradation of protein-coding genes. This regulation affects various biological processes, including cell proliferation, migration, invasion, angiogenesis, autophagy and drug resistance (32-35).

For example, the upregulation of lncRNA HAGLROS activates the PI3K/AKT/mTOR pathway through the miR-100/autophagy related 14 axis, promoting the progression of nasopharyngeal carcinoma (NPC) (36). Additionally, lncRNA HAGLROS inhibits miR-100 and upregulates SNF2

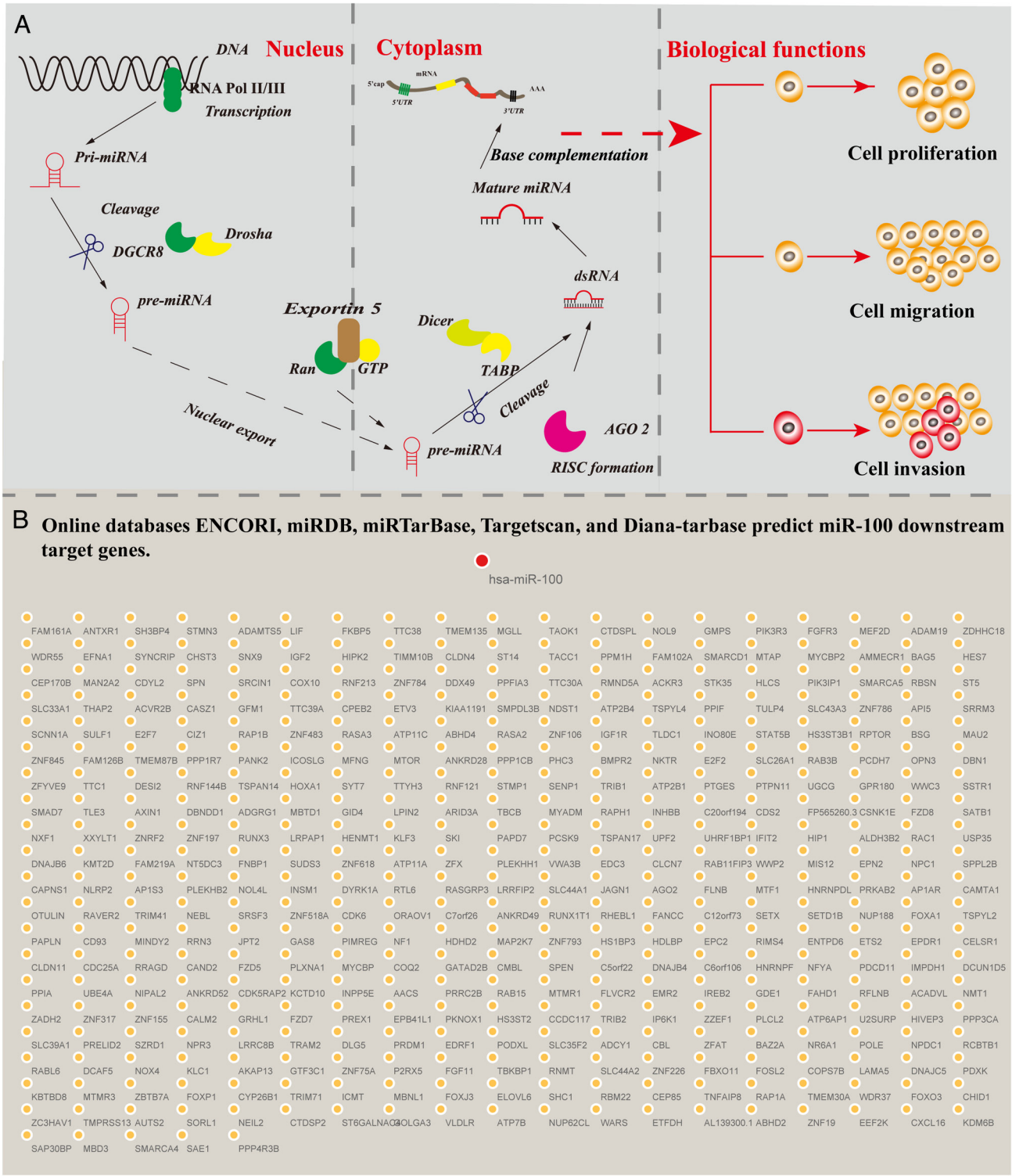

Figure 1. Targeting mechanism and downstream targets of miR-100 in cancer. (A) Mechanisms of miRNA-mediated regulation of mRNA. (B) Online database prediction of proteins encoded by miR-100 downstream targets. dsRNA, double-stranded RNA; miR/miRNA, microRNA; UTR, untranslated region.

related chromatin remodeling ATPase 5 (SMARCA5), enhancing the malignant phenotype of non-small cell lung cancer (NSCLC) cells (37). Yang *et al* (38) found that lncRNA HAGLROS, as a molecular sponge for miR-100, regulated the expression of mTOR and zinc and ring finger 2, thereby affecting the mTOR signaling pathway in OC, making it a potential biomarker for early diagnosis and prognosis. Shu *et al* (39) demonstrated that in diffuse large B-cell lymphoma, lncRNA HAGLROS promoted tumor cell proliferation, migration and invasion by inhibiting miR-100. Similarly, lncRNA SDCBP2-AS1 delays the progression of OC through miR-100 targeting of ependymin related 1 (40). Chen *et al* (41) found that lncRNA HAGLROS, by competitively binding miR-100, activated the mTORC1 signaling pathway, inhibiting autophagy and promoting excessive proliferation of GC cells, thereby maintaining their

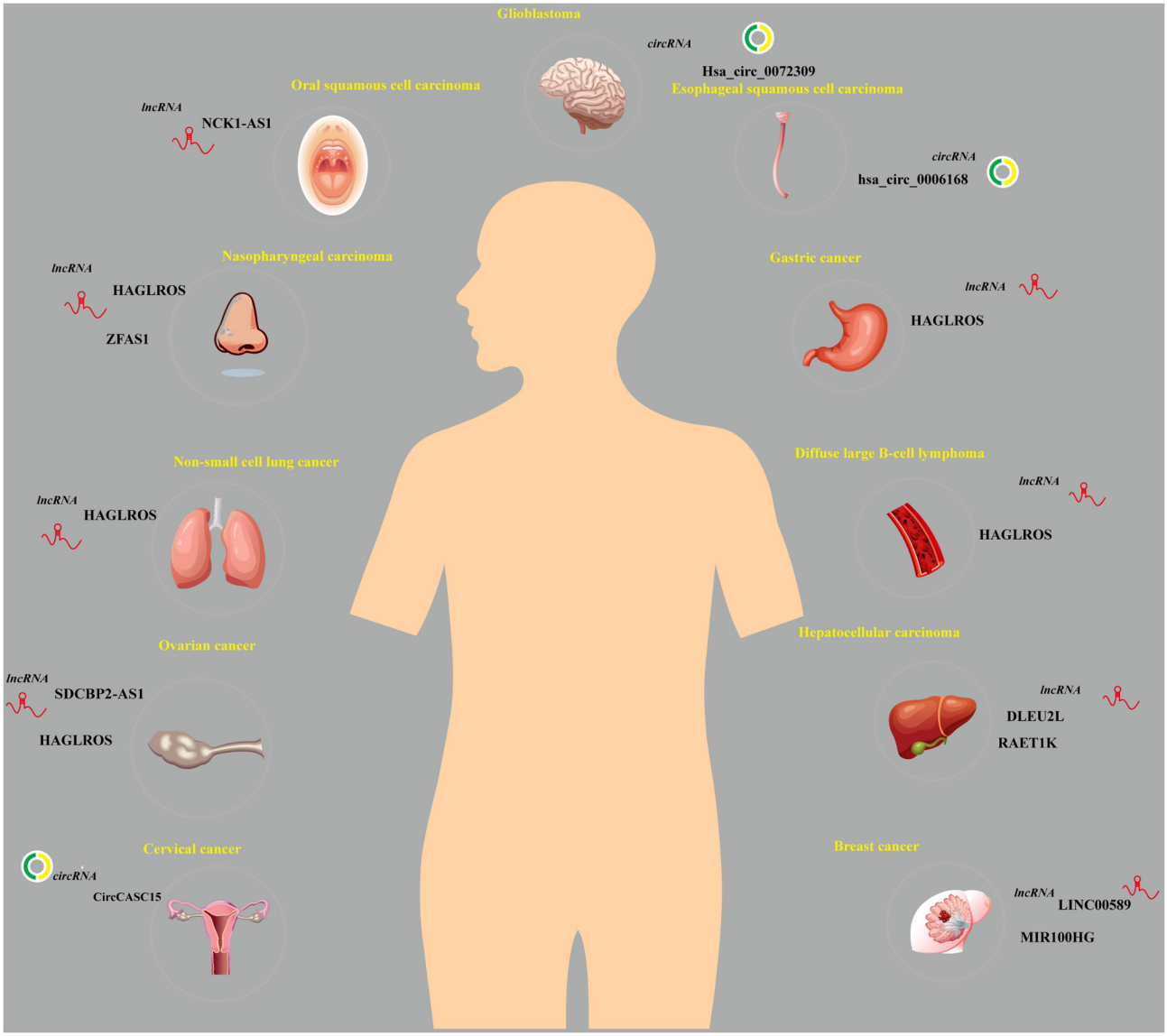

Figure 2. Interaction of miR-100 with lncRNAs and circRNAs. circRNA, circular RNA; lncRNA, long non-coding RNA; miR, microRNA.

malignant phenotype. Furthermore, Peng *et al* (42) reported that lncRNA ZFAS1 regulated the m6A methyltransferase METTL3 through miR-100, influencing autophagy and tumor progression in NPC.

The targeting of miR-100 by lncRNAs is not limited to autophagy. miR-100 has also been described as an important diagnostic marker in cancer. For example, Le *et al* (43) found that the plasma levels of lncRNA NCK1-AS1 were elevated in patients with oral squamous cell carcinoma, and its expression was negatively associated with miR-100. Shi *et al* (44) established the lncRNA DLEU2L-miR-100-5p-TAO kinase 1 ceRNA network and found that this network was associated with the prognosis of hepatocellular carcinoma (HCC), suggesting it may serve as a foundation for clinical prognostic models. Furthermore, Zhou *et al* (18) demonstrated that lncRNA RAET1K, through miR-100, activated hypoxia inducible factor 1 subunit α and regulated glycolysis in HCC cells.

miR-100 is also involved in cancer stem cell-like properties and therapeutic resistance. For example, Bai *et al* (45) found that lncRNA LINC00589 regulated trastuzumab resistance and multidrug resistance in BC through the miR-100-discs large MAGUK scaffold protein 5 axis, while miR-100, derived from lncRNA MIR100HG, mediated resistance to anti-EGFR monoclonal antibody and everolimus by activating the Wnt/β-catenin signaling pathway (46).

miR-100 also functions as a sponge for circRNAs in malignant tumors. For example, hsa_circ_0006168 serves as a molecular sponge for miR-100 and promotes the proliferation, migration and invasion of esophageal squamous cell carcinoma (ESCC) by regulating mTOR (47). Yuan *et al* (48) found that hsa_circ_0072309 enhanced autophagy and temozolomide sensitivity in glioblastoma multiforme (GBM) through miR-100. Additionally, CircCASC15 regulates radioresistance in cervical cancer (CC) through the miR-100/mTOR axis (49).

In conclusion, miR-100 acts as a molecular sponge for both lncRNAs and circRNAs, serving a pivotal role in tumorigenesis, progression and therapeutic resistance (Fig. 2; Table I).

Table I. miR-100 ceRNA network and its role in cancer.

First author/s, year	ceRNA	Associated cancer	Control mechanism	(Refs.)
Zhang *et al*, 2020	HAGLROS	Nasopharyngeal carcinoma	Activates the PI3K/AKT/mTOR pathway to promote tumor progression	(36)
Li *et al*, 2021		Non-small cell lung cancer	Inhibits miR-100 and upregulates SMARCA5 to enhance malignancy	(37)
Yang *et al*, 2019		Ovarian cancer	Regulates mTOR and ZNRF2 via miR-100 to affect mTOR signaling	(38)
Shu *et al*, 2022		Diffuse large B-cell lymphoma	Promoting DLBCL onset and progression by inhibiting miR-100 expression	(39)
Chen *et al*, 2018		Gastric cancer	Competes for miR-100 binding and activates mTORC1, suppressing autophagy and promoting cell proliferation	(41)
Liu *et al*, 2021	SDCBP2-AS1	Ovarian cancer	Regulation of miR-100 and its target gene EPDR1 delays malignant progression of ovarian cancer	(40)
Peng *et al*, 2022	ZFAS1	Nasopharyngeal carcinoma	Regulates m6A methyltransferase METTL3 via miR-100 to affect autophagy and tumor progression	(42)
Le *et al*, 2020	NCK1-AS1	Oral squamous cell carcinoma	Plasma levels are inversely associated with miR-100, potentially serving as a diagnostic biomarker for cancer	(43)
Shi *et al*, 2021	DLEU2L	Hepatocellular carcinoma	miR-100 acts as a sponge and regulates prognosis in patients with hepatocellular carcinoma	(44)
Zhou *et al*, 2020	RAET1K	Hepatocellular carcinoma	Activates HIF1A via miR-100 to regulate glycolysis	(18)
Bai *et al*, 2022	LINC00589	Breast cancer	Regulates drug resistance via the miR-100-DLG5 axis, involving trastuzumab and multi-drug resistance	(45)
Lu *et al*, 2017	MIR100HG	Colorectal cancer	MIR100HG-derived miR-100 enhances cetuximab resistance in colorectal cancer cells by activating the Wnt/β-catenin signaling pathway	(46)
Shi *et al*, 2019	hsa_circ_0006168	Esophageal squamous cell carcinoma	Regulates mTOR via miR-100 to promote proliferation, migration and invasion	(47)
Yuan *et al*, 2022	hsa_circ_0072309	Glioblastoma	Enhances autophagy and temozolomide sensitivity via miR-100	(48)
Yao et al, 2022	CircCASC15	Cervical cancer	Regulates radioresistance via the miR-100/mTOR axis	(49)

ceRNA, competing endogenous RNA; circ, circular RNA; DLG5, discs large MAGUK scaffold protein 5; EPDR1, ependymin related 1; HIF1A, hypoxia inducible factor 1 subunit α; miR, microRNA; SMARCA5, SNF2 related chromatin remodeling ATPase 5; TAOK1, TAO kinase 1; ZNRF2, zinc and ring finger 2.

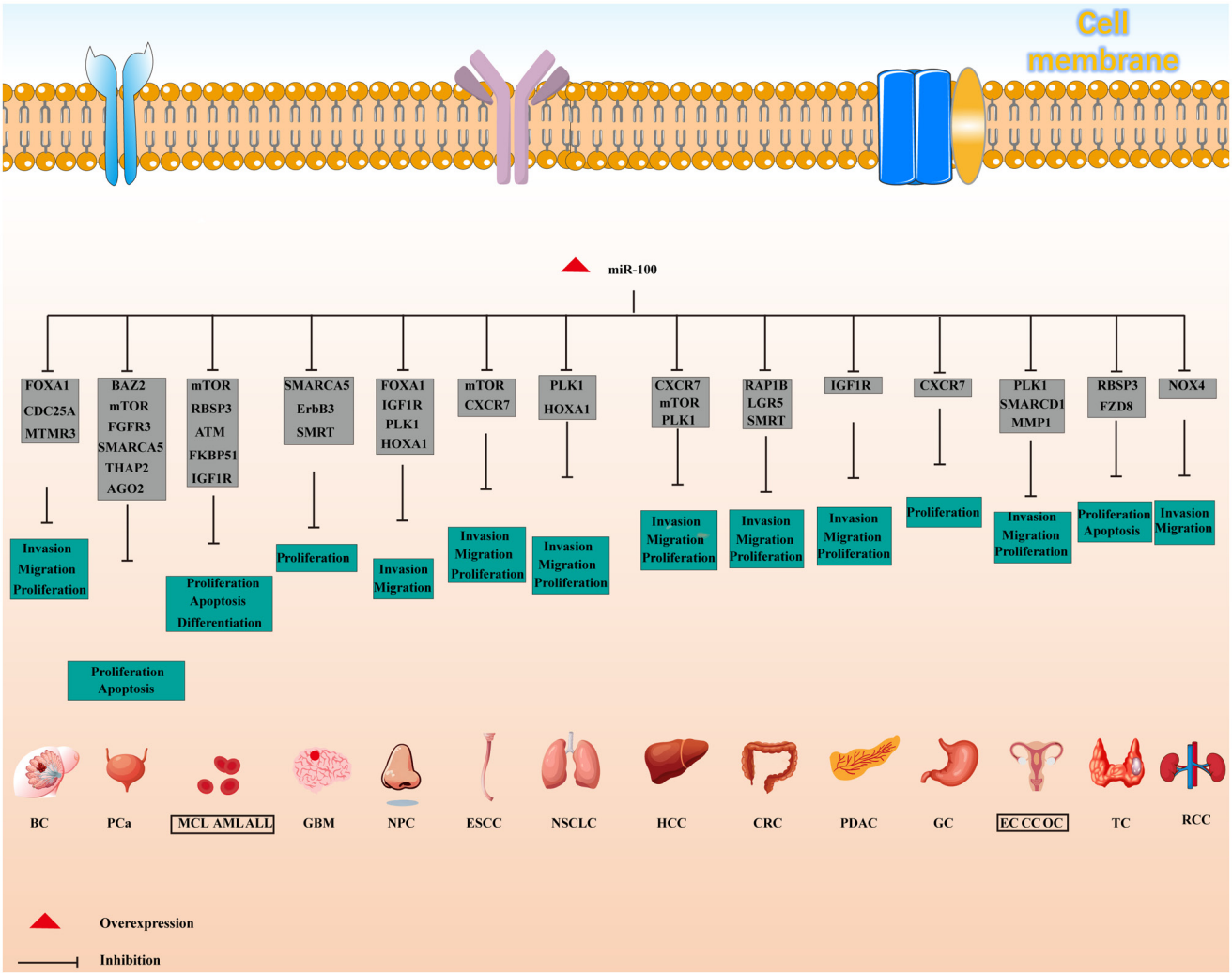

Figure 3. Biological effects and molecular targets of miR-100 in various cancer types. ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; BC, breast cancer; CC, cervical cancer; CRC, colorectal cancer; EC, endometrial cancer; ESCC, esophageal squamous cell carcinoma; GBM, glioblastoma multiforme; GC, gastric cancer; HCC, hepatocellular carcinoma; MCL, mantle cell lymphoma; miR, microRNA; NPC, nasopharyngeal carcinoma; NSCLC, non-small cell lung cancer; OC, ovarian cancer; PCa, prostate cancer; PDAC, pancreatic ductal adenocarcinoma; TC, thyroid cancer.

4. Role of miR-100 in cancer development

The present review emphasizes the broad role of miR-100 in the ceRNA network. Beyond acting as a molecular sponge in the ceRNA axis, modulating cancer-related processes, numerous studies have indicated that dysregulation of miR-100 is strongly associated with the onset and progression of various cancer types (Table II). Specifically, miR-100 serves a central role in regulating key biological processes, including cell proliferation, apoptosis, migration, invasion, metastasis and cell cycle progression, by modulating the expression of multiple downstream target genes in malignant tumor cells (10,50). These findings provide compelling evidence for the molecular mechanisms through which miR-100 influences cancer biology. Related studies are summarized in Fig. 3 and Table II, laying the foundation for further exploration of the function of miR-100 in tumorigenesis.

Mantle cell lymphoma (MCL). MCL is an aggressive B-cell lymphoma that accounts for 5-7% of malignant lymphomas in Western Europe, with an annual incidence of 1-2 cases per 100,000 individuals in 2017 (51). The median age of onset is 65 years, with a male-to-female ratio of ~3:1 (51). Lin *et al* (52) demonstrated that miR-100 is downregulated in MCL tissues and cells, suggesting its potential role as a tumor suppressor. Lin *et al* (52) revealed that miR-100 overexpression decreased mTOR mRNA and protein levels, thereby inhibiting cell proliferation, inducing apoptosis. Notably, mTOR knockdown can reverse these effects, confirming mTOR as a key downstream target of miR-100 (52). These findings underscore the crucial role of miR-100 in MCL progression through the modulation of the mTOR pathway, offering novel insights into the molecular mechanisms and potential therapeutic strategies for MCL.

Acute myeloid leukemia (AML). AML is a heterogeneous hematologic malignancy characterized by the abnormal proliferation of hematopoietic stem cells in the bone marrow (53). Approximately 150-200 children aged 0-16 years are diagnosed with AML annually in Japan (52). Sun *et al* (54) demonstrated that miR-100 was highly expressed in clinical samples and cell lines of adult AML, where it inhibited cell

Table II. miR-100 target genes and their mechanisms in different cancer types.

First author/s, year	Cancer type	miR-100 target gene	Mechanism of action of miR-100	(Refs.)
Lin *et al*, 2020	Mantle cell lymphoma	mTOR cell cycle arrest.	Inhibits mTOR expression to suppress cell proliferation, induce apoptosis and cause G_1 phase	(52)
Sun *et al*, 2020; Zheng *et al*, 2012	Acute myeloid leukemia	RBSP3, ATM, pRB-E2F1	Inhibits RBSP3 to regulate the RB-pRB-E2F1 pathway, and inhibits cell proliferation and migration. Inhibits ATM to block cell proliferation and induce apoptosis	(54,55)
Li *et al*, 2013	Acute lymphoblastic leukemia	FKBP51, IGF1R, mTOR	Inhibits FKBP51, IGF1R and mTOR signaling pathways to suppress cell proliferation and induce apoptosis	(57)
Alrfaei *et al*, 2020; Alrfaei *et al*, 2013	Glioblastoma	SMARCA5, ErbB3, SMRT/NCOR2	Targets SMARCA5 and ErbB3 to inhibit cell viability and proliferation, extending survival	(59,60)
Peng *et al*, 2020; He *et al*, 2020; Sun *et al*, 2018; Shi *et al*, 2010	Nasopharyngeal carcinoma	FOXA1, HOXA1, IGF1R, PLK1	Regulates FOXA1, HOXA1 and PLK1 to inhibit cell proliferation and tumor growth	(63-66)
Liu *et al*, 2012; Han *et al*, 2020	Non-small cell lung cancer	PLK1, HOXA1	Inhibits PLK1 and HOXA1 expression to suppress tumor progression	(68,69)
Zhang *et al*, 2014; Sun *et al*, 2013; Zhou *et al*, 2016;	Esophageal squamous cell carcinoma	mTOR, CXCR7	Inhibits mTOR signaling and CXCR7 to regulate cell proliferation, migration and invasion, and suppress tumor growth	(71-74)
Zhou *et al*, 2014 Ge *et al*, 2021; Zhou *et al*, 2016; Chen *et al*, 2013	Hepatocellular carcinoma	CXCR7, mTOR, PLK1	Targets CXCR7, mTOR and PLK1 to inhibit tumor growth and cell proliferation	(77-79)
Cao *et al*, 2018; Chen *et al*, 2015	Gastric cancer	CXCR7	Targets CXCR7 to inhibit cell proliferation and tumor metastasis, potentially serving as a diagnostic and therapeutic marker	(81,83)
Peng *et al*, 2014; Zhou *et al*, 2015; Fujino *et al*, 2017	CRC	RAP1B, LGR5	Inhibits RAP1B and LGR5 to suppress CRC cell proliferation, migration and invasion	(31,87,88)
Huang *et al*, 2013; Dobre *et al*, 2021	Pancreatic ductal adenocarcinoma	IGF1R	Modulates IGF1R to regulate pancreatic cancer cell metastasis, potentially serving as an early diagnostic and therapeutic marker	(91,92)
Liu *et al*, 2022; Chen *et al*, 2017	Renal cell carcinoma	NOX4, mTOR	Inhibits NOX4 and mTOR expression to suppress cell migration and invasion, promoting apoptosis	(30,95)
Wang *et al*, 2014; Nabavi *et al*, 2017; Ye *et al*, 2020	Prostate cancer	BAZ2, mTOR, FGFR3, SMARCA5, THAP2	Modulates multiple genes to inhibit tumor growth, migration and invasion, exerting tumor-suppressive effects	(99-101)

Table II. Continued.

First author/s, year	Cancer type	miR-100 target gene	Mechanism of action of miR-100	(Refs.)
Ma and Han, 2022	Thyroid cancer	FZD8	Targets FZD8 to inhibit papillary thyroid cancer cell proliferation and suppress cancer progression	(104)
Xie *et al*, 2021; Gebeshuber and Martinez, 2013; Li *et al*, 2022; Gong *et al*, 2015	Breast cancer	FOXA1, CDC25A, MTMR3	Inhibits FOXA1, CDC25A and MTMR3 to suppress breast cancer cell proliferation, migration and invasion, and promote apoptosis	(106-109)
Schoutrop *et al*, 2022	Ovarian cancer	PLK1	Inhibits PLK1 to suppress ovarian cancer cell growth and proliferation, and promote apoptosis	(112)
Huang *et al*, 2021; Li *et al*, 2011	Cervical cancer	SATB1, AKT/mTOR, PLK1	miR-100 inhibits cervical cancer progression by targeting SATB1 and PLK1, thereby inhibiting proliferation, migration and invasion of cervical cancer cells	(114,115)
Takebayashi *et al*, 2020	Endometrial cancer	SMARCD1	miR-100-5p promotes cell invasion by attenuating SMARCD1 expression	(118)

BAZ2, bromodomain adjacent to zinc finger domain 2; CDC25A, cell division cycle 25A; CRC, colorectal cancer; CXCR7, chemokine (C-X-C motif) receptor 7; E2F1, E2F transcription factor 1; ErbB3, erb-b2 receptor tyrosine kinase 3; FGFR3, fibroblast growth factor receptor 3; FKBP51, FKBP prolyl isomerase 5; FOXA1, forkhead box A1; FZD8, frizzled class receptor 8; HOXA1, homeobox A1; IGF1R, insulin-like growth factor 1 receptor; LGR5, leucine rich repeat containing G protein-coupled receptor 5; miR, microRNA; MTMR3, myotubularin related protein 3; SMRT/NCOR2, nuclear receptor corepressor 2; NOX4, NADPH oxidase 4; PLK1, polo-like kinase 1; RB-pRB-E2F1, retinoblastoma protein-phosphorylated retinoblastoma protein-E2F1 transcription factor; RBSP3, RB protein serine phosphatase from chromosome 3; SATB1, SATB homeobox 1; SMARCA5, SNF2 related chromatin remodeling ATPase 5; SMARCD1, SWI/SNF related BAF chromatin remodeling complex subunit D1; THAP2, THAP domain containing 2.

differentiation and promoted proliferation by targeting RBSP3. The miR-100/RBSP3-retinoblastoma protein-E2F transcription factor 1 signaling pathway is involved in the pathogenesis of AML (54). Furthermore, miR-100 expression is elevated in pediatric AML bone marrow and cell lines, and its inhibition suppresses cell proliferation and induces apoptosis by preventing ATM activation (55). These findings highlight the pathogenic role of miR-100 in AML and suggest its potential as a diagnostic and therapeutic target for this malignancy.

Acute lymphoblastic leukemia (ALL). ALL is the most common pediatric malignancy, and characterized by abnormal clonal proliferation of lymphocytes (56). Precursor B-cells account for 80-85% of cases, with T-cells and mature B-cells less frequently involved (56,57). Li *et al* (57) indicated that miR-100 was downregulated in clinical tissues of patients with ALL, and its low expression was associated with poor 5-year overall survival (OS) rates. Further investigation revealed that overexpression of miR-100 inhibited ALL cell proliferation and induced apoptosis by suppressing FKBP prolyl isomerase 5 (FKBP51) and the IGF1R/mTOR signaling pathway (57). These findings suggest a key role for miR-100 in ALL and its potential as a therapeutic target to improve patient prognosis.

GBM. GBM is the most common and aggressive primary brain tumor in adults (58,59). Despite advances in treatment, including maximal safe resection, radiotherapy and chemotherapy, the prognosis remains poor, with a median OS time of 14-20 months (58). Research has shown that miR-100 is downregulated in GBM cells. Overexpression of miR-100 reduces cell viability and proliferation, inhibits tumor growth, and suppresses SMARCA5 and Erb-B3 receptor tyrosine kinase 3 activation (59). Additionally, Alrfaei *et al* (60) demonstrated that miR-100 targeted nuclear receptor corepressor 2, reducing tumor growth and extending survival in GBM animal models. These results suggest that miR-100 may serve a critical role in GBM progression and could be a potential therapeutic target for improving survival outcomes.

NPC. NPC is a squamous cell carcinoma originating from the nasopharyngeal epithelium (61). In 2018, ~129,079 new cases of NPC were diagnosed globally, resulting in 72,987 deaths (62). The development of NPC is influenced by factors such as dietary habits, lifestyle, environmental exposure, ethnicity and Epstein-Barr virus infection (61,62). Peng *et al* (63) demonstrated that miR-100 was typically downregulated in NPC tissues, and its expression was associated with tumor malignancy. Overexpression of miR-100 leads to the downregulation of forkhead box A1 (FOXA1) and promotes the malignant invasion of NPC cells (63). Additionally, He *et al* (64) confirmed that miR-100 inhibited NPC cell growth and proliferation by targeting homeobox A1 (HOXA1), and exogenous miR-100 expression suppressed xenograft tumor growth. Furthermore, Sun *et al* (65) reported that miR-100 inhibited NPC cell migration and invasion by targeting IGF1R, while Shi *et al* (66) found that high PLK1 expression in most NPC samples was associated with a higher risk of recurrence, with miR-100 inhibiting tumor growth through the regulation of PLK1.

NSCLC. Lung cancer remains the leading cause of cancer-related deaths in the United States, with ~247,270 new cases reported in 2020, including 130,340 in men and 116,930 in women (67). In NSCLC, miR-100 is widely recognized as a tumor suppressor (68,69). Liu *et al* (68) indicated that miR-100 was downregulated in NSCLC tissues, and its reduced expression was closely associated with advanced clinical stage, higher tumor grade and lymph node metastasis. Additionally, low miR-100 expression may serve as a predictive marker for poor prognosis in NSCLC. Mechanistically, miR-100 exerts its tumor-suppressive effect by post-transcriptionally regulating PLK1 expression (68). Han *et al* (69) further confirmed that miR-100 inhibited NSCLC progression both *in vitro* and *in vivo* by targeting HOXA1. The mechanism was that miR-100 inhibited the activation of the Wnt/β-catenin pathway by targeting HOXA1, thereby reducing cell migration, invasion and proliferation (69).

ESCC. ESCC is the sixth leading cause of cancer-related deaths globally, with ~544,000 deaths reported in 2020 (70). miR-100 is downregulated in ESCC and is closely related to lymph node metastasis and increased invasiveness (71). Zhang *et al* (71) have shown that miR-100 regulates the migration and invasion of ESCC cells by targeting mTOR and suppressing the expression of tumor-associated genes. Sun *et al* (72) further confirmed the direct targeting relationship between miR-100 and mTOR. Zhou *et al* (73) found that miR-100 inhibited the proliferation and tumor growth of esophageal cancer cells by targeting chemokine (C-X-C motif) receptor 7 (CXCR7). Additionally, in 120 ESCC tissue samples, low expression levels of miR-100 were associated with advanced stage, distant metastasis and deep invasion (74), highlighting its potential as a diagnostic marker and therapeutic target for esophageal cancer progression.

HCC. HCC is the most common type of primary liver cancer, accounting for ~90% of liver cancer cases (75). The main risk factors for HCC include chronic hepatitis B virus infection and subsequent liver cirrhosis (75). Due to the lack of specific early symptoms and diagnostic biomarkers, the majority of patients are diagnosed at an advanced stage, with only 10-20% suitable for curative surgical resection, leading to a generally poor prognosis (46). Studies have shown that miR-100 serves an important tumor-suppressive role in HCC (76-79). Ge *et al* (77) found that miR-100 inhibited HCC cell proliferation, invasion and migration by targeting CXCR7. Zhou *et al* (78) further demonstrated that low miR-100 expression was associated with blood vessel encapsulated tumor clusters (VETC), venous invasion and microthrombosis in HCC tissues. In VETC-2 and Hepa1-6 mouse models, miR-100 expression inhibited VETC formation, thereby reducing tumor metastasis. Furthermore, miR-100 inhibits tumor growth by targeting mTOR and blocking the mTOR-p70S6K signaling pathway, as well as by regulating PLK1 to suppress angiopoietin 2 protein levels (79).

GC. GC is a common malignancy globally, with its complexity arising from the combination of environmental and genetic factors (80,81). Age is a risk factor for GC, with a median age at diagnosis of 70 years (80). Due to the asymptomatic and non-specific nature of early-stage GC, most patients are

diagnosed at an advanced stage, leading to poor prognosis (81). Increasing research has focused on the molecular mechanisms underlying GC. miR-100 has been found to be downregulated in GC (81,82). Cao *et al* (82) found that miR-100 inhibited the proliferation of GC cells by targeting CXCR7, and its expression was closely associated with lymph node metastasis, tumor size and stage. Furthermore, Chen *et al* (83) confirmed the role of miR-100 as a tumor suppressor in GC progression, highlighting its potential in molecular diagnostics and targeted therapy. These studies provide key insights into the molecular mechanisms of GC and lay the groundwork for exploring novel therapeutic targets.

CRC. CRC is the third most common cancer worldwide and the fourth leading cause of cancer-related deaths (84). Dietary and lifestyle factors are considered major contributors to the rising incidence of CRC (84). The incidence of newly diagnosed CRC in China accounts for 49.3% of the global total, while the related mortality represents 58.3% of global CRC-related deaths (84,85). The 5-year relative survival rate stands at 57% (84,85). Approximately 11% of CRC cases present with metastasis (85). Preventive colonoscopy remains the most effective strategy for CRC prevention (86). Previous studies have highlighted non-invasive biomarkers, with miR-100 emerging as a potential candidate for CRC diagnosis. For example, Peng *et al* (87) found that miR-100 regulated SW620 CRC cell proliferation and invasion by modulating RAP1B expression. Similarly, Zhou *et al* (31) demonstrated that miR-100 was downregulated in colon cancer tissues and suppressed cell viability, proliferation, migration and invasion by targeting LGR5. Furthermore, Fujino *et al* (88) reported that miR-100 was downregulated in early CRC and was closely associated with lymph node metastasis. miR-100 inhibited the activation of the Wnt/β-catenin signaling pathway by targeting HOXA1, thereby reducing the migratory and invasive capabilities of cancer cells. These findings underscore the critical role of miR-100 in CRC pathogenesis and its potential as a diagnostic and therapeutic target. Further exploration of the mechanisms of miR-100 will provide deeper insights into the molecular pathology of CRC and support the development of early detection and personalized treatment strategies.

Pancreatic ductal adenocarcinoma (PDAC). PDAC is a highly fatal malignancy and is expected to become the leading cause of pancreatic cancer-related deaths in the U.S. by 2030. Currently, ~90% of patients with PDAC are diagnosed at advanced stages, with tumors often having spread beyond the pancreas and >50% presenting with distant metastases (89). Early diagnosis is crucial for improving prognosis (89). In the past decade, advances in basic and translational research have deepened the understanding of the biological processes underlying pancreatic cancer, which are gradually being applied to improve diagnostic and therapeutic strategies (89,90). Huang *et al* (91) found that miR-100 served a key role in PDAC cell metastasis by regulating IGF1R. Dobre *et al* (92) further validated this mechanism, supporting the involvement of miR-100 in PDAC molecular pathology. These studies suggest that miR-100 may serve as a potential biomarker for early diagnosis and targeted therapy in PDAC, providing valuable insights for clinical application.

Renal cell carcinoma (RCC). RCC is the third most common cancer of the urinary system, accounting for 3% of cancers in women and 5% in men, representing ~90% of all kidney cancers (93). Approximately 400,000 new RCC cases are reported annually worldwide (30,93,94). RCC is associated with a poor prognosis, since ~30% of patients present with metastasis at diagnosis, and another 30% develop metastasis during follow-up (91,92). Research has shown that miR-100 inhibits RCC cell invasion and migration by downregulating NOX4 expression (30). Additionally, Chen *et al* (95) found that miR-100 was highly expressed in RCC tissues. miR-100 inhibited cell viability, promoted apoptosis, and inhibited migration and invasion by inhibiting mTOR. These findings highlight the dual role of miR-100 in RCC and suggest its potential as a diagnostic, prognostic and therapeutic target. Further investigation of the molecular mechanisms of miR-100 will provide valuable insights for personalized treatment strategies in RCC.

PCa. PCa is one of the most common malignancies worldwide and a leading cause of cancer-related death (96). Although most PCa cases are diagnosed as localized or indolent, ~20% of patients present with high-risk cancer that may progress to fatal disease (97). The role of miR-100 in PCa has garnered increasing attention. Leite *et al* (98) first demonstrated that miR-100 expression decreased during the progression of localized PCa to advanced metastatic stages. Wang *et al* (99) further revealed that miR-100 affected PCa cell migration and invasion by regulating AGO2. Additionally, Nabavi *et al* (100) reported that miR-100 inhibits PCa cell apoptosis, while Ye *et al* (101) found that miR-100-5p downregulation suppressed cell proliferation, migration and invasion by targeting mTOR. These studies underscore the critical role of miR-100 in PCa progression and suggest its potential as a diagnostic, prognostic and therapeutic target. Further research into the molecular mechanisms of miR-100 will provide essential support for precision treatment strategies for patients with high-risk PCa.

TC. TC is one of the fastest-growing malignancies globally, with its incidence steadily rising over the past 30 years (102). Although the overall mortality rate remains stable, some rare subtypes, such as anaplastic TC, remain a clinical challenge due to their high invasiveness and limited treatment options (103). The role of miRNAs in TC has attracted widespread attention. Zhang *et al* (11) found that overexpression or knockdown of miR-100 inhibited the translation of RBSP3, thereby promoting follicular thyroid carcinoma cell proliferation. Furthermore, Ma and Han (104) found that miR-100 was downregulated in papillary thyroid carcinoma (PTC) tissues and cells. Overexpression of miR-100 inhibits the proliferation and migration, and promotes apoptosis of PTC, which may be achieved by inhibiting the expression of fragile fission class receptor 8 (104). These findings highlight the critical roles of miR-10 and miR-100 in the progression of different TC subtypes, suggesting their potential as molecular targets for diagnosis and treatment. Further investigation into the molecular mechanisms of these miRNAs may pave the way for the development of precision therapies for TC.

BC. BC is the leading cause of morbidity and mortality in women worldwide (105). In 2020, BC surpassed lung cancer as the most common malignancy globally, accounting for 15.5% of all cancer-related deaths in women (105). Despite the central role of surgery, radiotherapy and chemotherapy in treatment, research has increasingly focused on the role of miRNAs in BC. Xie *et al* (106) demonstrated that miR-100 was downregulated in BC, and its overexpression suppressed the proliferation, migration and invasion of BC cells by inhibiting FOXA1 expression. Additionally, Gebeshuber and Martinez (107) found that stable overexpression of miR-100 reduced insulin like growth factor 2 expression and inhibited tumor growth. Li *et al* (108) also demonstrated that miR-100 inhibited proliferation, migration and invasion by targeting cell division cycle 25A (CDC25A), while promoting apoptosis. Gong *et al* (109) identified myotubularin related protein 3 (MTMR3) as another downstream target of miR-100, mediating apoptosis in BC cells. These studies collectively highlight the key role of miR-100 in inhibiting BC progression through the regulation of multiple downstream targets, including FOXA1, CDC25A and MTMR3. Given its tumor-suppressive effect, miR-100 offers a potential molecular target for BC diagnosis and treatment, providing novel directions for precision medicine.

OC. OC is one of the leading causes of cancer-related death in women and the second most common cancer in women over the age of 40 years (110). The high mortality rate is primarily due to most patients being diagnosed at advanced stages, emphasizing the need for early diagnostic markers to improve prognosis (111). Studies have indicated that miR-100 serves an important role in OC, especially in epithelial OC (EOC) (110,111). For example, Schoutrop *et al* (112) found that miR-100 exerted tumor-suppressive effects in EOC by targeting PLK1, inhibiting tumor cell growth and proliferation. Nam *et al* (113) further confirmed that miR-100 expression was differential in EOC, suggesting its involvement in OC development and progression. These findings suggest that miR-100 may serve as an early diagnostic biomarker and therapeutic target for OC. Further research into the molecular mechanisms of miR-100 may provide novel directions for precise diagnosis and targeted therapy.

CC. CC is the fourth most common malignant tumor among women worldwide, following BC, CRC and lung cancer (114). Although progress has been made in CC screening and prevention, its incidence and mortality remain high in a number of regions, particularly in low-and middle-income countries (114,115). Huang *et al* (114) found that miR-100 was downregulated in CC tissues, with reverse transcription-quantitative PCR indicating lower expression levels of miR-100. It was shown that overexpression of miR-100 effectively inhibited the proliferation, migration and invasion of CC cells (114). Li *et al* (115) confirmed that the downregulation of miR-100 promoted the progression of CC, at least partially by losing its inhibitory effect on the target gene PLK1. These findings suggest that miR-100 acts as a tumor suppressor in CC, and its mechanism may involve the regulation of key target genes such as PLK1. The potential diagnostic and therapeutic value of miR-100 provides a novel direction for personalized medicine in CC and may offer effective molecular targets for improving patient prognosis.

Endometrial cancer (EC). EC is the sixth most common cancer in women (116). In 2020, there were 417,000 new cases of EC worldwide, with a lifetime risk of ~3% for women, and the median age at diagnosis is 61 years (116). Although most patients are diagnosed early and achieve good prognosis through routine surgery, EC remains the only gynecologic malignancy with an increasing mortality rate (117). The role of miRNAs in EC has garnered increasing attention. Takebayashi *et al* (118) found that transfection of hsa-miR-100 enhanced the invasiveness and proliferative capacity of normal endometrial stromal cells (NESCs). It was shown that SWI/SNF related BAF chromatin remodeling complex subunit D1 (SMARCD1) and MMP-1 are key downstream targets of miR-100. Specifically, miR-100 promoted the invasion and migration of NESCs by inhibiting SMARCD1 expression and activating MMP-1 (118). These findings suggest that miR-100 promotes EC invasion and migration via the SMARCD1/MMP-1 pathway. Further investigation of the molecular mechanisms of miR-100 will not only aid the understanding of the progression of EC but may also provide potential diagnostic and therapeutic targets for the disease.

5. Diagnostic and prognostic value of miR-100

The continued rise in global cancer mortality is not only due to the poor prognosis of cancer itself, but is also closely related to late diagnosis due to the hidden nature of different cancer types. Most patients with cancer are diagnosed when the disease is already in an unresectable stage, which underscores the importance of finding novel diagnostic methods or biomarkers (119). Over the past decade, research on potential cancer biomarkers has grown exponentially, offering hope for early diagnosis and improving clinical prognosis (119-121). Early diagnosis and effective monitoring of treatment responses are crucial for successful cancer management. However, traditional tumor biopsy methods lack sufficient sensitivity and specificity for early detection and ongoing monitoring (121). Therefore, identifying early diagnostic biomarkers is essential for improving the early detection and treatment of malignant tumors.

Studies have highlighted miR-100 as a potential diagnostic biomarker for various cancer types (122-131). For instance, Wang *et al* (122) found that miR-100 was highly expressed in the plasma of patients with BC, and receiver operating characteristic (ROC) curve analysis showed that it had high diagnostic efficiency for early BC. Fuso *et al* (123) confirmed this finding. In HCC, Jin *et al* (124) observed upregulation of miR-100, suggesting that it may serve as a biomarker for HCC. Similarly, Qureshi *et al* (125) found that miR-100 was downregulated in the plasma of patients with bladder cancer, with expression levels associated with clinical features such as microscopic hematuria, cytological examination, cystoscopy and TNM staging. Ludwig *et al* (126) reported that miR-100 was highly expressed in the serum of patients with Wilms tumor, with ROC analysis showing a diagnostic sensitivity of 0.90. Blanca *et al* (127) found that miR-100 was a prognostic biomarker for non-invasive bladder cancer. Furthermore, Yamanaka *et al* (128) revealed that miR-100 serves an

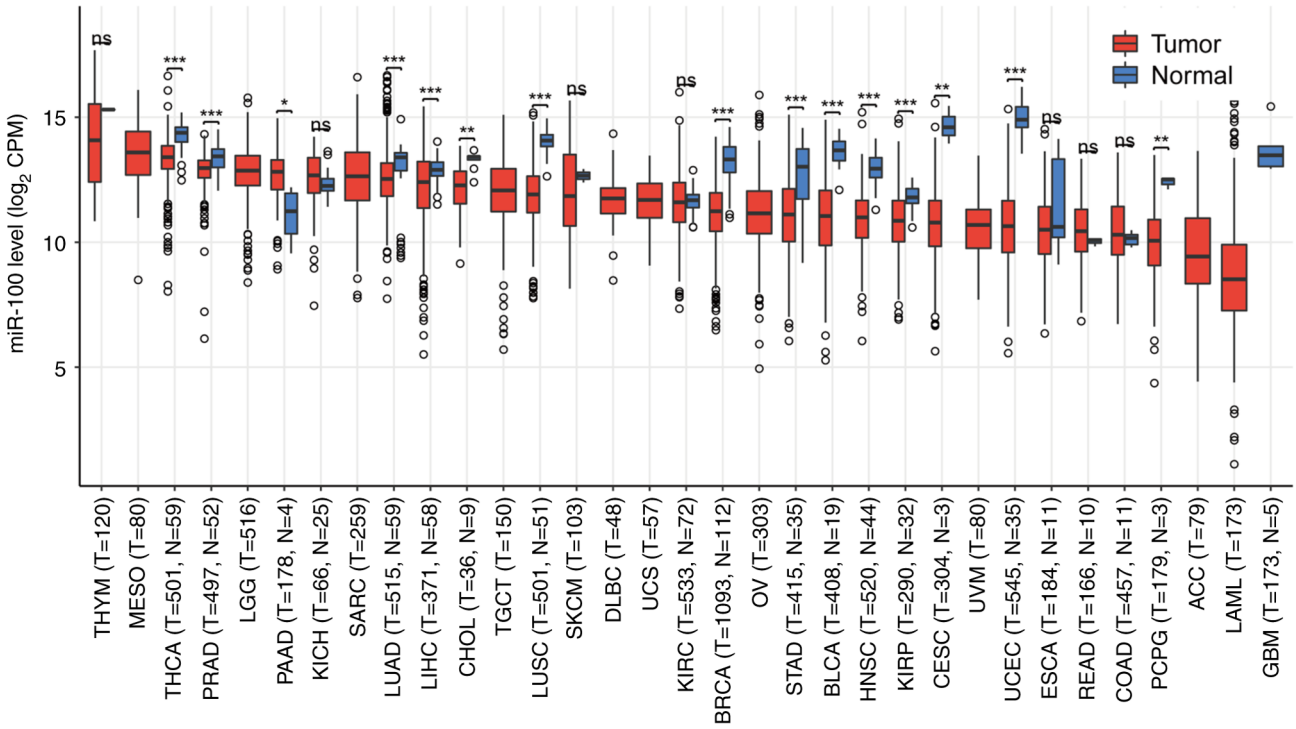

Figure 4. miR-100 expression in tumor and adjacent normal tissue samples from TCGA. Wilcoxon rank-sum test. ***P<0.001; **P<0.01; *P<0.05. CPM, counts per million; miR/miRNA, microRNA; ns, not significant (P>0.05); TCGA, The Cancer Genome Atlas; T, tumor; N, normal.

important role in bladder cancer progression, with reduced expression associated with shorter progression-free survival and OS, suggesting its potential in risk stratification for bladder cancer. In addition to the aforementioned studies, miR-100 has also been recognized as a potential diagnostic marker for CRC (129,130), GC (131), PCa (132), oral cancer (133) and esophageal cancer (134,135).

In addition to its diagnostic role, miR-100 also has prognostic implications in cancer. For example, Wang *et al* (136) found that high miR-100 expression in renal clear cell carcinoma (RCC) tissues was associated with tumor T staging and metastasis, and high miR-100 expression was an independent poor prognostic factor for the OS and cancer-specific survival of patients with RCC. Liu *et al* (137) suggested that miR-100 could serve as a biomarker for predicting lymph node metastasis in patients with GC. Furthermore, He *et al* (138) analyzed The Cancer Genome Atlas (TCGA) and Gene Expression Omnibus datasets, finding that low miR-100 levels were associated with poor clinical features and prognosis in patients with HCC. miR-100 was identified as an independent risk factor for recurrence and OS after liver resection (138). Zhou *et al* (78) further demonstrated that high miR-100 expression in HCC was associated with tumor grade, lymph node metastasis, late TNM stage and recurrence, indicating its negative prognostic significance. In pediatric AML, Hassan *et al* (139) reported that upregulation of miR-100 was associated with poor relapse-free survival and poor OS, positioning it as a negative prognostic marker for AML.

While these findings provide strong support for the potential of miR-100 as an early diagnostic and prognostic biomarker for cancer, several challenges remain to be addressed. First, although the high diagnostic value of miR-100 has been observed in various cancer types, most of the current research is focused on *in vitro* experiments and animal models, with a lack of large-scale clinical trial validation (119-121). Whether these early findings can be replicated in clinical applications, especially in real-world environments with large population heterogeneity, still requires further validation. For example, the differential expression of miR-100 in different populations (for example, different ethnicities and sex) may affect its application as a universal marker (126,127). Secondly, the sensitivity and specificity of miR-100 as a biomarker remain key issues in current research, particularly how to ensure diagnostic accuracy in cases of low early disease burden (10). Additionally, technical challenges such as improving the stability of miR-100 in blood and standardizing its detection processes remain bottlenecks for its broader application.

In addition, pan-cancer data from TCGA (https://www.cancer.gov/tcga) were analyzed using R (version 4.2.1; R Core Team) and trends in miR-100 expression across various cancer types were identified. As shown in Fig. 4, miR-100 expression differed significantly in several cancer types, including lung cancer and TC. Furthermore, ROC analysis of the TCGA pan-cancer database revealed that miR-100 exhibited an area under the curve >0.5 in cancer types such as TC (TCGA-THCA), HCC (TCGA-LIHC), bladder urothelial carcinoma (TCGA-BLCA), breast invasive carcinoma (TCGA-BRCA), and head and neck squamous cell carcinoma (TCGA-HNSC) (Fig. 5), indicating its high sensitivity and specificity as a potential diagnostic marker. However, further multi-center, large-scale clinical studies are required to validate these findings and optimize the use of miR-100 as a clinical biomarker.

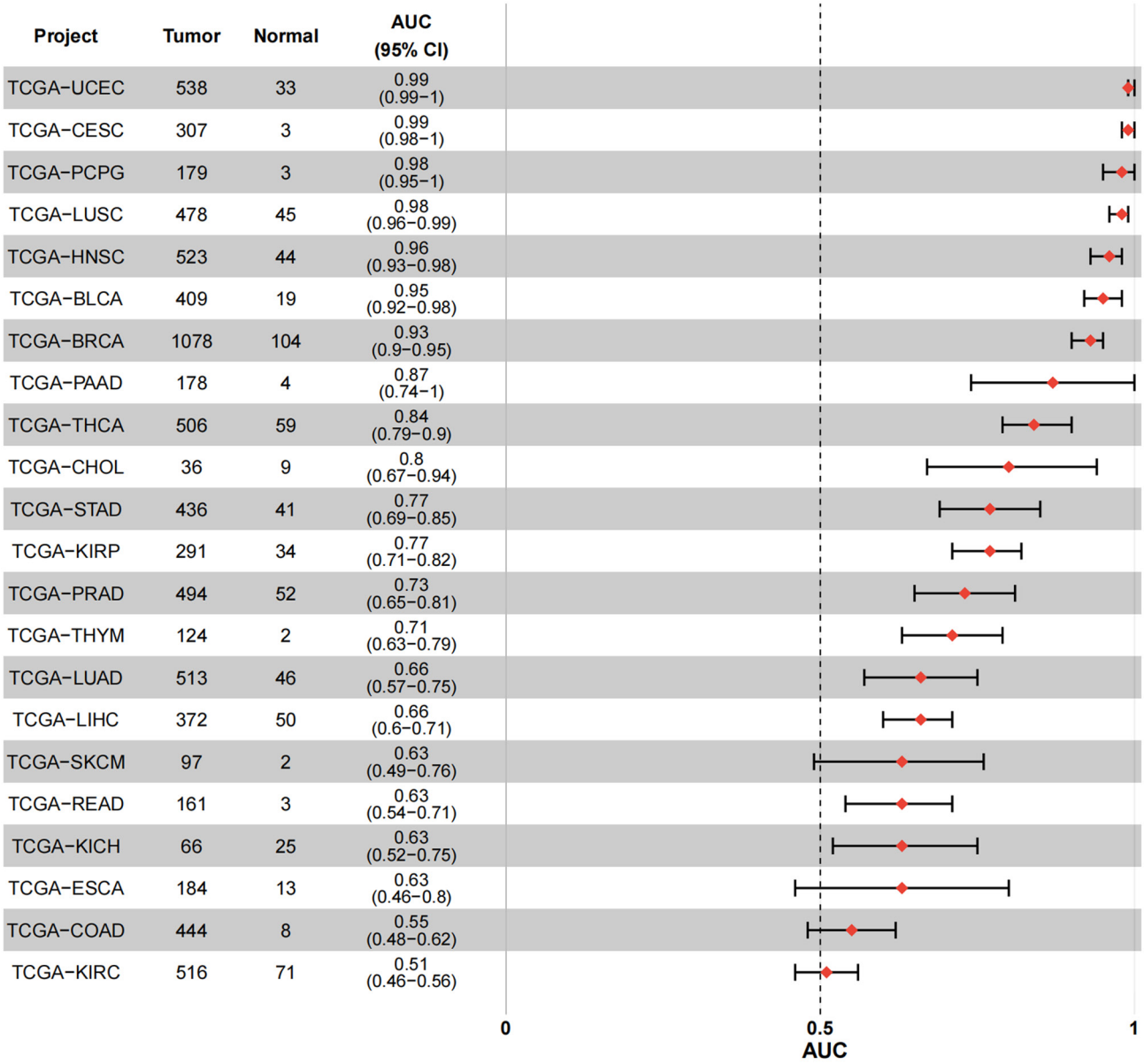

Figure 5. Receiver operating characteristic curve analysis of microRNA-100 expression in tumor and normal samples from TCGA. AUC, area under the curve; TCGA, The Cancer Genome Atlas.

In conclusion, miR-100 serves a crucial role in cancer diagnosis and prognosis, showing clinical potential. Although current studies provide preliminary evidence for the use of miR-100 as an early diagnostic and prognostic biomarker, key issues such as sensitivity, specificity, population applicability and clinical validation need to be addressed before it can be widely used in clinical practice. With future clinical trials and technical optimization, miR-100 is expected to become an important tool in precision cancer diagnosis and treatment.

6. miR-100 and chemotherapy/radiotherapy resistance in cancer

Although progress has been made in cancer treatment, chemotherapy remains a major treatment modality for advanced cancer. However, chemotherapy resistance continues to be one of the key obstacles affecting treatment outcomes (140,141). miRNAs serve an increasingly important role in regulating cancer cell responses to treatment, especially in the mechanisms of chemotherapy resistance, where they influence drug responses by targeting and modulating the expression of relevant genes (140-142).

miR-100 serves a complex role in regulating the sensitivity and resistance to chemotherapy in various cancer types. For example, miR-100 enhances the chemotherapy sensitivity of GBM cells to cisplatin and temozolomide by targeting FGFR3 (142). In small cell lung cancer (SCLC), Xiao *et al* (143) found that the downregulation of miR-100 was negatively associated with HOXA1 expression, suggesting that miR-100 serves a key role in regulating SCLC cell survival and chemotherapy resistance. Similarly, miR-100 restores the sensitivity of docetaxel-resistant lung adenocarcinoma SPC-A1 cells to docetaxel by targeting PLK1 (144). In head and neck squamous cell carcinoma, miR-100 has also been found to be

associated with docetaxel resistance (16). In cisplatin-resistant OC cells, miR-100 restores sensitivity to cisplatin by targeting mTOR and PLK1, inhibiting cell proliferation and inducing apoptosis (145). Similarly, Liu *et al* (146) found that miR-100 enhanced the sensitivity of osteosarcoma cells to cisplatin by targeting IGF1R. In NSCLC, the downregulation of miR-100 may increase resistance to ALK inhibitors (such as crizotinib and lorlatinib), presenting a therapeutic challenge (147). At the same time, the downregulation of miR-100 promotes paclitaxel resistance by increasing the expression of β-tubulin V-type, suggesting its potential as a target for paclitaxel combination therapy (148). The role of miR-100 in radiotherapy should also not be overlooked. In CRC, upregulation of miR-100 enhances cell sensitivity to radiation, possibly by promoting radiation-induced apoptosis and DNA double-strand breaks (15). In childhood acute lymphoblastic leukemia, downregulation of miR-100 contributes to vincristine resistance, and its upregulation effectively reverses this resistance, restoring the anticancer efficacy of vincristine (149). Furthermore, the overexpression or knockout of miR-100 can regulate ATM expression and alter cell sensitivity to ionizing radiation (150).

The role of miR-100 in cancer chemotherapy and radiotherapy underscores its complex regulatory function, which is influenced by tumor type, therapeutic agents and the specific characteristics of cancer cells. Specifically, miR-100 expression in different cancer types may be influenced by various factors, including the drug resistance characteristics of tumor cells and changes in the tumor microenvironment. Therefore, the mechanism of action of miR-100, as a potential therapeutic target, warrants further investigation. In summary, the role of miR-100 in chemotherapy and radiotherapy underscores its crucial function in regulating cancer cell proliferation and drug resistance. In-depth studies on the mechanisms of miR-100 and its interactions with chemotherapy drugs and radiotherapy will provide valuable insights for overcoming resistance in cancer treatment and offer novel directions for future cancer therapeutic strategies.

7. miR-100 and signaling pathways

Cellular signal transduction serves a pivotal role in mediating cellular responses to both internal and external stimuli. Various intracellular signaling pathways are essential for regulating biological processes and gene expression. Although these pathways do not directly engage in transcription, they ultimately influence gene expression by modulating the activity of transcription factors (151). Increasing evidence suggests that miRNAs serve a crucial role in regulating these signaling pathways in both normal and cancer cells (10,152,153). Pathways such as the Hippo, Myc, Notch, TGFβ, p53, epithelial-to-mesenchymal transition (EMT) and Wnt/β-catenin pathways are closely associated with tumorigenesis and cancer progression (154). Tumor-specific alterations in these pathways often serve as potential targets for developing targeted therapies (155).

miR-100 and the EMT pathway. miR-100 serves a critical role in regulating EMT, a process where cells transition from an epithelial to a mesenchymal phenotype. This transition enhances cancer cell migration, invasion and metastasis (99,156,157). Studies have shown that miR-100 inhibits EMT by regulating multiple key molecules (99,156,157). For instance, Wang *et al* (99) demonstrated that the loss of miR-100 enhanced the migration and invasiveness in PCa cells, and promoted the EMT process. This suggests that miR-100 may suppress EMT by regulating the expression of epithelial markers such as E-cadherin, and mesenchymal markers such as N-cadherin and Vimentin (99). In addition, the well-known EMT-promoting factors zinc finger E-box binding homeobox (ZEB)1 and ZEB2 induce EMT by repressing E-cadherin expression, whereas miR-100 inhibits these transcription factors, thereby suppressing EMT (156). Specifically, miR-100-mediated inhibition of SMARCA5 suppresses E-cadherin, thereby inhibiting the EMT process in breast cancer cells (156). In addition, Yang *et al* (157) found that miR-100 inactivation, in conjunction with arsenic exposure, activated the EMT process, promoting the malignant transformation and invasiveness of BEAS-2B lung cells. These findings suggest that miR-100 inhibits cancer cell migration and invasion by regulating EMT-related factors however, its loss or reduced expression may exacerbate malignant transformation.

miR-100 and the AKT/mTOR pathway. The AKT/mTOR signaling pathway serves a vital role in tumor cell proliferation, survival and metabolism. miR-100 inhibits tumor cell migration and invasion by regulating key molecules within this pathway (158). Chen *et al* (95) demonstrated that miR-100 inhibited mTOR signaling activation, slowing migration and invasion in RCC cells. The mechanism is that miR-100 reduces cellular metabolic activity by directly targeting mTORC1 activation, which further inhibits cell proliferation (95). Additionally, miR-100 suppresses AKT phosphorylation, which reduces downstream mTOR activity, thereby inhibiting tumor cell proliferation and migration (95). These findings suggest that miR-100 not only slows tumor cell proliferation by inhibiting mTORC1 activity but also limits metabolic activity and invasiveness, positioning it as a potential target for anticancer therapy.

miR-100 and the PI3K/AKT pathway. The PI3K/AKT signaling pathway is involved in various processes, including cell proliferation, survival and migration (159). miR-100 regulates the PI3K/AKT pathway to inhibit cancer cell proliferation and promote apoptosis (57). Li *et al* (57) demonstrated that miR-100 targeted IGF1R and FKBP51 to inhibit PI3K/AKT pathway activation, thereby inhibiting cell proliferation and promoting apoptosis in ALL cells. These findings provide compelling evidence for the potential of miR-100 as an anticancer factor.

miR-100 and the Wnt/β-catenin pathway. The Wnt/β-catenin signaling pathway serves a critical role in tumor cell proliferation, differentiation and metastasis. miR-100 regulates key molecules within the Wnt/β-catenin pathway to suppress tumor cell proliferation and migration (160). Liu *et al* (146) demonstrated that miR-100 targeted IGF1R to inhibit the Wnt/β-catenin pathway, slowing the proliferation and migration of osteosarcoma cells. IGF1R, an upstream activator of the Wnt/β-catenin pathway, is inhibited by miR-100, which reduces β-catenin activation and decreases Wnt signaling,

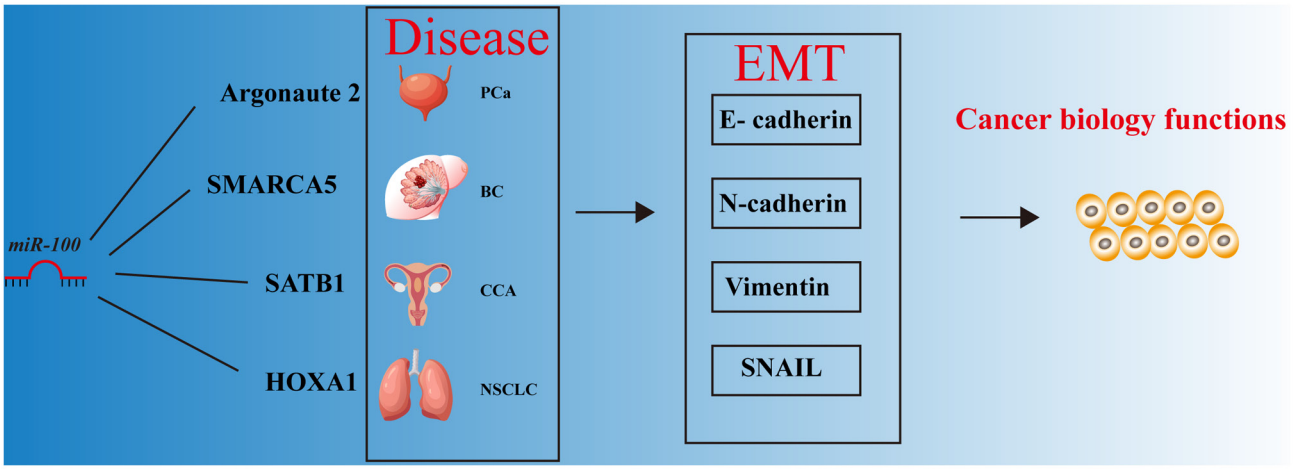

Figure 6. Involvement of miR-100 in the EMT process in cancer. BC, breast cancer; CCA, cholangiocarcinoma; EMT, epithelial-to-mesenchymal transition; HOXA1, homeobox A1; miR, microRNA; NSCLC, non-small cell lung cancer; PCa, prostate cancer; SATB1, SATB homeobox 1; SMARCA5, SWI/SNF-related, matrix-associated actin-dependent regulator of chromatin, subfamily A, member 5.

thereby slowing tumor progression (146). Additionally, Peng *et al* (161) found that miR-100 regulated GC cell proliferation and migration by targeting bone morphogenetic protein receptor type 2. These studies underscore the essential role of miR-100 in regulating the Wnt/β-catenin pathway and its potential as a therapeutic target in cancer.

miR-100 and the Notch signaling pathway. The Notch signaling pathway is critical for cell fate determination, proliferation and EMT (161). Yang *et al* (162) demonstrated that miR-100 regulated the Notch signaling pathway to modulate apoptosis and proliferation in GC cells. Activation of the Notch pathway is closely associated with cancer cell proliferation, metastasis and EMT. Downregulation of miR-100 may lead to abnormal activation of the Notch pathway, promoting tumor progression. By directly inhibiting the expression of Notch receptors, miR-100 reduces Notch signaling, suppressing cancer cell proliferation and metastasis (162). Huang *et al* (163) found that miR-100 downregulated SATB homeobox 1 (SATB1) expression, which in turn inhibited the AKT/mTOR and Notch signaling pathways, suppressing the EMT process and tumor invasiveness. SATB1, a transcription factor involved in several tumor-related signaling pathways, is directly downregulated by miR-100, inhibiting Notch pathway activity and reducing tumor cell proliferation and metastasis. STAT3, a critical transcription factor in tumor progression, is also downregulated by miR-100, further slowing tumor cell proliferation and metastasis (163). Further research into the relationship between miR-100 and the Notch signaling pathway may provide novel therapeutic strategies for cancer treatment.

miR-100 and the MAPK signaling pathway. The MAPK pathway in cancer transmits extracellular signals from the cell membrane to intracellular targets, serving a pivotal role in regulating various biological processes associated with tumorigenesis (164). For example, Liu *et al* (146) demonstrated that miR-100 was downregulated in osteosarcoma. miR-100 inhibits osteosarcoma cell proliferation, migration and invasion by directly targeting IGF1R and suppressing its expression, thereby modulating the downstream MAPK signaling pathway (146).

As shown in Figs. 6 and 7, miR-100 regulates tumor growth, migration and invasion through multiple signaling pathways, including the EMT, AKT/mTOR, mTOR/STAT1/Notch, PI3K/AKT, MAPK and Wnt/β-catenin signaling pathways. By targeting key molecules in these pathways, miR-100 inhibits cancer cell proliferation, migration and metastasis. However, its role may vary across different cancer types, suggesting the need for further investigation of its specific mechanisms in various tumor contexts (57,99,146,156-163). The multifaceted regulatory role of miR-100 provides insights into tumorigenesis and offers potential targets and strategies for cancer therapy. In conclusion, the role of miR-100 in these key signaling pathways was illustrated, further emphasizing its therapeutic potential in oncology.

8. Role of miR-100 in cancer progression and its potential as a diagnostic biomarker

The present review highlights the role of miR-100 in cancer progression by targeting multiple protein-coding genes that regulate cancer cell proliferation, invasion and metastasis. In addition to directly modulating gene expression, miR-100 also alters the tumor microenvironment dynamics by influencing specific signaling pathways (99,156,157). Notably, miR-100 expression levels in cancer are associated with early diagnosis and prognosis of patients (78,119-138,165), emphasizing its importance in understanding cancer biology and its potential as an early diagnostic biomarker.

Previous studies have shown that miR-100 suppresses tumor cell proliferation and invasion by downregulating specific target genes, ultimately reducing tumor metastasis (166,167). The present findings further emphasize the potential of miR-100 in cancer research and its clinical applications. However, several key issues remain unresolved. For instance, the tissue-specific expression patterns of miR-100 and its potential regulatory mechanisms are not fully understood (168). Additionally, although the role of miR-100 in

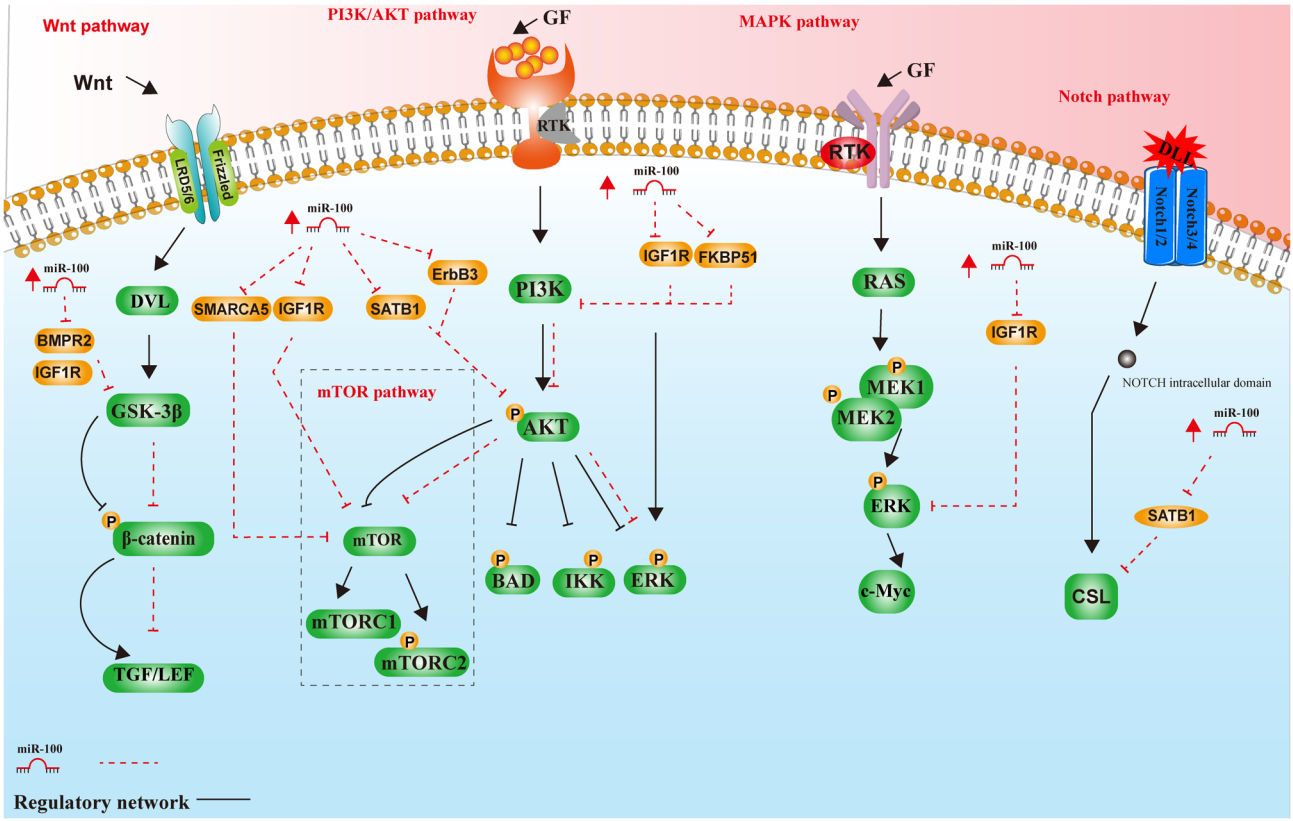

Figure 7. Downstream signaling pathways regulated by miR-100. miR, microRNA.

cancer progression is becoming clearer, its precise function in downstream signaling pathways requires further investigation. The variability in miR-100 effects across different experimental systems highlights the need for standardized protocols to ensure the reproducibility and reliability of results (169,170).

Controversial findings. Despite its tumor-suppressive effects in various cancer types, some controversial studies suggest that miR-100 may serve an oncogenic role in certain cancer contexts. For example, overexpression of miR-100 has been linked to tumor progression and poor prognosis in NSCLC (171), contrasting sharply with its tumor-suppressive effects in GC and peripheral T-cell lymphoma (106-108). This dual role may be attributed to cancer heterogeneity and differences in the genes targeted by miR-100 in different cellular environments. Furthermore, research indicates that the role of miR-100 in various cancer types may be influenced by differential regulation of its downstream signaling pathways, such as the PI3K/AKT, mTOR and Wnt/β-catenin pathways, further complicating its biological functions (172). For comparison, miR-21 and miR-155 are two other miRNAs that have been extensively studied in cancer, each exhibiting distinct roles. miR-21 and miR-155 are commonly upregulated as oncogenic miRNAs in various tumors, where miR-21 contributes to anti-apoptotic, proliferative and invasive processes, thereby enhancing drug resistance in tumor cells. By contrast, miR-155 promotes tumor progression and immune evasion by modulating the immune microenvironment (173,174). These functional differences underscore the critical importance of understanding the specific role of each miRNA within a given cancer context.

Regarding therapeutic strategies, the restoration of miR-100 is typically achieved by delivering its mimics or agonists to inhibit tumor growth and enhance the effectiveness of chemotherapy or targeted therapies. Conversely, therapeutic approaches for miR-21 and miR-155 primarily focus on restoring normal cellular functions by inhibiting their expression through anti-miRNA strategies (175,176).

Therefore, a comparative analysis of miR-100, miR-21 and miR-155 provides valuable insights into the distinct mechanisms these miRNAs are associated with in different cancer contexts. This comparison has implications for optimizing therapeutic strategies and improving clinical outcomes.

9. Future directions and research needs

Future research should focus on clarifying the role of miR-100 as a specific cancer biomarker and evaluating its therapeutic potential. Comparative studies with other cancer-related miRNAs will help deepen the understanding of the unique mechanisms and therapeutic significance of miR-100. Investigating the tissue-specific roles of miR-100 in different cancer types is crucial for its clinical application, particularly in early diagnosis and prognosis. Further exploration of the dual role of miR-100 and mechanistic insights will contribute to a more comprehensive understanding of its potential as a therapeutic target.

Incorporating the latest high-quality studies into this field will enhance the understanding of the clinical application of miR-100. This includes refining its role as a diagnostic or prognostic

biomarker in specific cancer types and exploring its potential as a therapeutic target. In conclusion, addressing the existing controversies and improving experimental methodologies will contribute to bridging the gap between experimental research and clinical practice. These advancements will pave the way for translating experimental findings into clinical applications.

10. Conclusion

As a tumor-suppressive miRNA, miR-100 serves a critical role in the initiation and progression of various cancer types. miR-100 inhibits tumor cell proliferation, migration and invasion by regulating oncogene expression and multiple signaling pathways, such as the PI3K/AKT and Wnt/β-catenin pathways. miR-100 holds great promise as an early diagnostic biomarker in cancer. Its stable presence in body fluids such as blood and urine makes it a potential non-invasive tool for early screening (121-126). The aberrant expression of miR-100 is closely associated with the development of tumors such as gastric and lung cancer, making it an ideal candidate for early detection.

In personalized therapy, the restoration of miR-100 expression can inhibit cancer cell proliferation and invasion, enhancing the efficacy of chemotherapy or targeted therapies. However, the clinical application of miR-100 still faces challenges, including the optimization of delivery systems and safety assessments. Future research should focus on developing efficient delivery vectors to improve the stability and biocompatibility of miR-100 for clinical use.

In conclusion, miR-100 has potential as both a biomarker and a therapeutic target for early diagnosis and personalized treatment.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

Not applicable.

Authors' contributions

XZ and SL contributed to the literature search and selected the studies for inclusion. JZ, LZ and SG drafted the manuscript. XZ, SL and CQ critically revised the content of the paper. JZ and LZ conceived the topic of review for the study and revised the manuscript. Data authentication is not applicable. All authors read and approved the final version of the manuscript.

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.

References

1. Siegel RL, Miller KD, Wagle NS and Jemal A: Cancer statistics, 2023. CA Cancer J Clin 73: 17-148, 2023.
2. Cao M, Li H, Sun D and Chen W: Cancer burden of major cancers in China: A need for sustainable actions. Cancer Commun (Lond) 40: 205-210, 2020.
3. Cao W, Chen HD, Yu YW, Li N and Chen WQ: Changing profiles of cancer burden worldwide and in China: A secondary analysis of the global cancer statistics 2020. Chin Med J (Engl) 134: 783-791, 2021.
4. Toden S, Zumwalt TJ and Goel A: Non-coding RNAs and potential therapeutic targeting in cancer. Biochim Biophys Acta Rev Cancer 1875: 188491, 2021.
5. Chen B, Dragomir MP, Yang C, Li Q, Horst D and Calin GA: Targeting non-coding RNAs to overcome cancer therapy resistance. Signal Transduct Target Ther 7: 121, 2022.
6. Saw PE, Xu X, Chen J and Song EW: Non-coding RNAs: The new central dogma of cancer biology. Sci China Life Sci 64: 22-50, 2021.
7. Calin GA, Dumitru CD, Shimizu M, Bichi R, Zupo S, Noch E, Aldler H, Rattan S, Keating M, Rai K, *et al*: Frequent deletions and down-regulation of micro-RNA genes miR15 and miR16 at 13q14 in chronic lymphocytic leukemia. Proc Natl Acad Sci USA 99: 15524-15529, 2002.
8. Lee RC, Feinbaum RL and Ambros V: The C. elegans heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14. Cell 75: 843-854, 1993.
9. Wightman B, Ha I and Ruvkun G: Posttranscriptional regulation of the heterochronic gene lin-14 by lin-4 mediates temporal pattern formation in C. elegans. Cell 75: 855-862, 1993.
10. Li C, Gao Y, Zhang K, Chen J, Han S, Feng B, Wang R and Chen L: Multiple roles of microRNA-100 in human cancer and its therapeutic potential. Cell Physiol Biochem 37: 2143-2159, 2015.
11. Zhang S, Deng B, Zhang Y and Jiang N: Expression of miR-100 and RBSP3 in FTC-133 cells after exposure to 131I. Nucl Med Commun 35: 932-938, 2014.
12. Wang S, Xue S, Dai Y, Yang J, Chen Z, Fang X, Zhou W, Wu W and Li Q: Reduced expression of microRNA-100 confers unfavorable prognosis in patients with bladder cancer. Diagn Pathol 7: 159, 2012.
13. Wang G, Yang L, Hu M, Hu R, Wang Y, Chen B, Jiang X and Cui R: Comprehensive analysis of the prognostic significance of Hsa-miR-100-5p and its related gene signature in stomach adenocarcinoma. Front Cell Dev Biol 9: 736274, 2021.
14. Yang XD, Xu XH, Zhang SY, Wu Y, Xing CG, Ru G, Xu HT and Cao JP: Role of miR-100 in the radioresistance of colorectal cancer cells. Am J Cancer Res 5: 545, 2015.
15. Qin X, Yu S, Zhou L, Shi M, Hu Y, Xu X, Shen B, Liu S, Yan D and Feng J: Cisplatin-resistant lung cancer cell-derived exosomes increase cisplatin resistance of recipient cells in exosomal miR-100-5p-dependent manner. Int J Nanomedicine 12: 3721-3733, 2017.
16. Dai Y, Xie CH, Neis JP, Fan CY, Vural E and Spring PM: MicroRNA expression profiles of head and neck squamous cell carcinoma with docetaxel-induced multidrug resistance. Head Neck 33: 786-791, 2011.
17. Zeng J, Wang L, Zhao J, Zheng Z, Peng J, Zhang W, Wen T, Nie J, Ding L and Yi D: MiR-100-5p regulates cardiac hypertrophy through activation of autophagy by targeting mTOR. Hum Cell 34: 1388-1397, 2021.
18. Zhou Y, Huang Y, Hu K, Zhang Z, Yang J and Wang Z: HIF1A activates the transcription of lncRNA RAET1K to modulate hypoxia-induced glycolysis in hepatocellular carcinoma cells via miR-100-5p. Cell Death Dis 11: 176, 2020.
19. Assmann TS, Recamonde-Mendoza M, De Souza BM and Crispim D: MicroRNA expression profiles and type 1 diabetes mellitus:systematic review and bioinformatic analysis. Endocr Connect 6: 773-790, 2017.
20. Pek SL, Sum CF, Lin MX, Cheng AK, Wong MT, Lim SC and Tavintharan S: Circulating and visceral adipose miR-100 is down-regulated in patients with obesity and Type 2 diabetes. Mol Cell Endocrinol 427: 112-123, 2016.

21. Ai L, Yi W, Chen L, Wang H and Huang Q: Xian-Ling-Gu-Bao protects osteoporosis through promoting osteoblast differentiation by targeting miR-100-5p/KDM6B/RUNX2 axis. In Vitro Cell Dev Biol Anim 57: 3-9, 2021.
22. Kelch S, Balmayor ER, Seeliger C, Vester H, Kirschke JS and van Griensven M: miRNAs in bone tissue correlate to bone mineral density and circulating miRNAs are gender independent in osteoporotic patients. Sci Rep 7: 15861, 2017.
23. Wu J, Kuang L, Chen C, Yang J, Zeng WN, Li T, Chen H, Huang S, Fu Z, Li J, *et al*: miR-100-5p-abundant exosomes derived from infrapatellar fat pad MSCs protect articular cartilage and ameliorate gait abnormalities via inhibition of mTOR in osteoarthritis. Biomaterials 206: 87-100, 2019.
24. Chang YS, Chang YC, Chen PH, Li CY, Wu WC and Kao YH: MicroRNA-100 mediates hydrogen peroxide-induced apoptosis of human retinal pigment epithelium ARPE-19 cells. Pharmaceuticals 14: 314, 2021.
25. Tan Q, Shi S, Liang J, Cao D, Wang S and Wang Z: Endometrial cell-derived small extracellular vesicle miR-100-5p promotes functions of trophoblast during embryo implantation. Mol Ther-Nucleic Acids 23: 217-231, 2021.
26. Huang YL, Huang GY, Lv J, Pan LN, Luo X and Shen J: miR-100 promotes the proliferation of spermatogonial stem cells via regulating Stat3. Mol Reprod Dev 84: 693-701, 2017.
27. Sempere LF, Sokol NS, Dubrovsky EB, Berger EM and Ambros V: Temporal regulation of microRNA expression in Drosophila melanogaster mediated by hormonal signals and broad-Complex gene activity. Dev Biol 259: 9-18, 2003.
28. Henson BJ, Bhattacharjee S, O'Dee DM, Feingold E and Gollin SM: Decreased expression of miR-125b and miR-100 in oral cancer cells contributes to malignancy. Genes Chromosomes Cancer 48: 569-582, 2009.
29. Gao S, Liu S, Wei W, Qi Y and Meng F: Advances in targeting of miR-10-associated lncRNAs/circRNAs for the management of cancer. Oncolo Lett 25: 89, 2023.
30. Liu X, Zhong L, Li P and Zhao P: MicroRNA-100 enhances autophagy and suppresses migration and invasion of renal cell carcinoma cells via disruption of NOX4-dependent mTOR pathway. Clin Transl Sci 15: 567-575, 2022.
31. Zhou MK, Liu XJ, Zhao ZG and Cheng YM: MicroRNA-100 functions as a tumor suppressor by inhibiting Lgr5 expression in colon cancer cells. Mol Med Rep 11: 2947-2952, 2015.
32. Qi X, Zhang DH, Wu N, Xiao JH, Wang X and Ma W: ceRNA in cancer: Possible functions and clinical implications. J Med Genet 52: 710-718, 2015.
33. Basera A, Hull R, Demetriou D, Bates DO, Kaufmann AM, Dlamini Z and Marima R: Competing Endogenous RNA (ceRNA) Networks and Splicing Switches in Cervical Cancer: HPV Oncogenesis, Clinical Significance and Therapeutic Opportunities. Microorganisms 10: 1852, 2022.
34. Zhang C, Zhou Y, Zhang B, Sheng Z, Sun N, Yuan B and Wu X: Identification of lncRNA, miRNA and mRNA expression profiles and ceRNA Networks in small cell lung cancer. BMC Genomics 24: 217, 2023.
35. Qin L, Li B, Wang S, Tang Y, Fahira A, Kou Y, Li T, Hu Z and Huang Z: Construction of an Immune-related prognostic signature and lncRNA-miRNA-mRNA ceRNA network in acute myeloid leukaemia. J Leukoc Biol 116: 146-165, 2024.
36. Zhang W, Zhang Y and Xi S: Upregulation of lncRNA HAGLROS enhances the development of nasopharyngeal carcinoma via modulating miR-100/ATG14 axis-mediated PI3K/AKT/mTOR signals. Artif Cells Nanomed Biotechnol 47: 3043-3052, 2019.
37. Li L, Zhu H, Li X, Ke Y, Yang S and Cheng Q: Long non-coding RNA HAGLROS facilitates the malignant phenotypes of NSCLC cells via repressing miR-100 and up-regulating SMARCA5. Biomed J 44 (6 Suppl 2): S305-S315, 2021.
38. Yang M, Zhai Z, Zhang Y and Wang Y: Clinical significance and oncogene function of long noncoding RNA HAGLROS overexpression in ovarian cancer. Arch Gynecol Obstet 300: 703-710, 2019.
39. Shu L, Guo K, Lin ZH and Liu H: Long non-coding RNA HAGLROS promotes the development of diffuse large B-cell lymphoma via suppressing miR-100. J Clin Lab Anal 36: e24168, 2022.
40. Liu X, Liu C, Zhang A, Wang Q, Ge J, Li Q and Xiao J: Long non-coding RNA SDCBP2-AS1 delays the progression of ovarian cancer via microRNA-100-5p-targeted EPDR1. World J Surg Oncol 19: 199, 2021.
41. Chen F, Wu P, Xia R, Yang J, Huo XY, Gu DY, Tang CJ, De W and Yang F: STAT3-induced lncRNA HAGLROS overexpression contributes to the malignant progression of gastric cancer cells via mTOR signal-mediated inhibition of autophagy. Mol Cancer 17: 6, 2018.
42. Peng J, Zheng H, Liu F, Wu Q and Liu S: The m6A methyltransferase METTL3 affects autophagy and progression of nasopharyngeal carcinoma by regulating the stability of lncRNA ZFAS1. Infect Agent Cancer 17: 1, 2022.
43. Le F, Ou Y, Luo P and Zhong X: LncRNA NCK1-AS1 in plasma distinguishes oral ulcer from early-stage oral squamous cell carcinoma. J Biol Res (Thessalon) 27: 16, 2020.
44. Shi Y, Zhang DD, Liu JB, Yang XL, Xin R, Jia CY, Wang HM, Lu GX, Wang PY, Liu Y, *et al*: Comprehensive analysis to identify DLEU2L/TAOK1 axis as a prognostic biomarker in hepatocellular carcinoma. Mol Ther Nucleic Acids 23: 702-718, 2021.
45. Bai W, Peng H, Zhang J, Zhao Y, Li Z, Feng X, Zhang J, Liang F, Wang L, Zhang N, *et al*: LINC00589-dominated ceRNA networks regulate multiple chemoresistance and cancer stem cell-like properties in HER2+breast cancer. NPJ Breast Cancer 8: 115, 2022.
46. Lu Y, Zhao X, Liu Q, Li C, Graves-Deal R, Cao Z, Singh B, Franklin JL, Wang J, Hu H, *et al*: lncRNA MIR100HG-derived miR-100 and miR-125b mediate cetuximab resistance via Wnt/β-catenin signaling. Nat Med 23: 1331-1341, 2017.
47. Shi Y, Guo Z, Fang N, Jiang W, Fan Y, He Y, Ma Z and Chen Y: hsa_circ_0006168 sponges miR-100 and regulates mTOR to promote the proliferation, migration and invasion of esophageal squamous cell carcinoma. Biomed Pharmacother 117: 109151, 2019.
48. Yuan F, Zhang S, Sun Q, Ye L, Xu Y, Xu Z, Deng G, Zhang S, Liu B and Chen Q: Hsa_circ_0072309 enhances autophagy and TMZ sensitivity in glioblastoma. CNS Neurosci Ther 28: 897-912, 2022.
49. Yao T, Yao Y, Chen Z, Peng Y, Zhong G, Huang C, Li J and Li R: CircCASC15-miR-100-mTOR may influence the cervical cancer radioresistance. Cancer Cell Int 22: 165, 2022.
50. Hill M and Tran N: miRNA interplay: Mechanisms and consequences in cancer. Dis Model Mech 14: dmm047662, 2021.
51. Silkenstedt E, Linton K and Dreyling M: Mantle cell lymphoma-advances in molecular biology, prognostication and treatment approaches. Br J Haematol 195: 162-173, 2021.
52. Lin L, Huang Y, Zhuang W, Lin P and Ma X: miR-100 inhibits cell proliferation in mantle cell lymphoma by targeting mTOR. Exp Hematol Oncol 9: 25, 2020.
53. Nepstad I, Hatfield KJ, Grønningsæter IS and Reikvam H: The PI3K-Akt-mTOR signaling pathway in human acute myeloid leukemia (AML) cells. Int J Mol Sci 21: 2907, 2020.
54. Sun Y, Wang H and Luo C: MiR-100 regulates cell viability and apoptosis by targeting ATM in pediatric acute myeloid leukemia. Biochem Biophys Res Commun 522: 855-861, 2020.
55. Zheng YS, Zhang H, Zhang XJ, Feng DD, Luo XQ, Zeng CW, Lin KY, Zhou H, Qu LH, Zhang P and Chen YQ: MiR-100 regulates cell differentiation and survival by targeting RBSP3, a phosphatase-like tumor suppressor in acute myeloid leukemia. Oncogene 31: 80-92, 2012.
56. Chang JH, Poppe MM, Hua CH, Marcus KJ and Esiashvili N: Acute lymphoblastic leukemia. Pediatr Blood Cancer 68 (Suppl 2): e28371, 2021.
57. Li XJ, Luo XQ, Han BW, Duan FT, Wei PP and Chen YQ: MicroRNA-100/99a, deregulated in acute lymphoblastic leukaemia, suppress proliferation and promote apoptosis by regulating the FKBP51 and IGF1R/mTOR signalling pathways. Br J Cancer 109: 2189-2198, 2013.
58. Ou A, Yung WKA and Majd N: Molecular mechanisms of treatment resistance in glioblastoma. Int J Mol Sci 22: 351, 2020.
59. Alrfaei BM, Clark P, Vemuganti R and Kuo JS: MicroRNA miR-100 decreases glioblastoma growth by targeting SMARCA5 and ErbB3 in tumor-initiating cells. Technol Cancer Res Treat 19: 1533033820960748, 2020.
60. Alrfaei BM, Vemuganti R and Kuo JS: microRNA-100 targets SMRT/NCOR2, reduces proliferation, and improves survival in glioblastoma animal models. PLoS One 8: e80865, 2013.
61. Guo R, Mao YP, Tang LL, Chen L, Sun Y and Ma J: The evolution of nasopharyngeal carcinoma staging. Br J Radiol 92: 20190244, 2019.
62. Lee HM, Okuda KS, González FE and Patel V: Current perspectives on nasopharyngeal carcinoma. Adv Exp Med Biol 1164: 11-34, 2019.

63. Peng Q, Zhang L, Li J, Wang W, Cai J, Ban Y, Zhou Y, Hu M, Mei Y, Zeng Z, *et al*: FOXA1 suppresses the growth, migration, and invasion of nasopharyngeal carcinoma cells through repressing miR-100-5p and miR-125b-5p. J Cancer 11: 2485-2495, 2020.
64. He W, Huang Y, Jiang CC, Zhu Y, Wang L, Zhang W, Huang W, Zhou T and Tang S: miR-100 inhibits cell growth and proliferation by targeting HOXA1 in nasopharyngeal carcinoma. Onco Targets Ther 13: 593-602, 2020.
65. Sun X, Liu X, Wang Y, Yang S, Chen Y and Yuan T: miR-100 inhibits the migration and invasion of nasopharyngeal carcinoma by targeting IGF1R. Oncol Lett 15: 8333-8338, 2018.
66. Shi W, Alajez NM, Bastianutto C, Hui AB, Mocanu JD, Ito E, Busson P, Lo KW, Ng R, Waldron J, *et al*: Significance of Plk1 regulation by miR-100 in human nasopharyngeal cancer. Int J Cancer 126: 2036-2048, 2010.
67. Alexander M, Kim SY and Cheng H: Update 2020: Management of non-small cell lung cancer. Lung 198: 897-907, 2020.
68. Liu J, Lu KH, Liu ZL, Sun M, De W and Wang ZX: MicroRNA-100 is a potential molecular marker of non-small cell lung cancer and functions as a tumor suppressor by targeting polo-like kinase 1. BMC Cancer 12: 519, 2012.
69. Han W, Ren X, Yang Y, Li H, Zhao L and Lin Z: microRNA-100 functions as a tumor suppressor in non-small cell lung cancer via regulating epithelial-mesenchymal transition and Wnt/β-catenin by targeting HOXA1. Thorac Cancer 11: 1679-1688, 2020.
70. Nagata Y, Yamamoto S and Kato K: Immune checkpoint inhibitors in esophageal cancer: Clinical development and perspectives. Hum Vaccin Immunother 18: 2143177, 2022.
71. Zhang N, Fu H, Song L, Ding Y, Wang X, Zhao C, Zhao Y, Jiao F and Zhao Y: MicroRNA-100 promotes migration and invasion through mammalian target of rapamycin in esophageal squamous cell carcinoma. Oncol Rep 32: 1409-1418, 2014.
72. Zhou F, Tan F, Gao Y, Sun N, Xu X, Shao K and He J: MicroRNA-99a/100 promotes apoptosis by targeting mTOR in human esophageal squamous cell carcinoma. Med Oncol 30: 411, 2013.
73. Zhou SM, Zhang F, Chen XB, Jun CM, Jing X, Wei DX, Xia Y, Zhou YB, Xiao XQ, Jia RQ, *et al*: miR-100 suppresses the proliferation and tumor growth of esophageal squamous cancer cells via targeting CXCR7. Oncol Rep 35: 3453-3459, 2016.
74. Zhou S, Yang B, Zhao Y, Xu S, Zhang H and Li Z: Prognostic value of microRNA-100 in esophageal squamous cell carcinoma. J Surg Res 192: 515-520, 2014.
75. Nagaraju GP, Dariya B, Kasa P, Peela S and El-Rayes BF: Epigenetics in hepatocellular carcinoma. Semin Cancer Biol 86: 622-632, 2022.
76. Ren Z, Ma X, Duan Z and Chen X: Diagnosis, therapy, and prognosis for hepatocellular carcinoma. Anal Cell Pathol (Amst) 2020: 8157406, 2020.
77. Ge Y, Shu J, Shi G, Yan F, Li Y and Ding H: miR-100 suppresses the proliferation, invasion, and migration of hepatocellular carcinoma cells via targeting CXCR7. J Immunol Res 2021: 9920786, 2021.
78. Zhou HC, Fang JH, Shang LR, Zhang ZJ, Sang Y, Xu L, Yuan Y, Chen MS, Zheng L, Zhang Y and Zhuang S: MicroRNAs miR-125b and miR-100 suppress metastasis of hepatocellular carcinoma by disrupting the formation of vessels that encapsulate tumour clusters. J Pathol 240: 450-460, 2016.
79. Chen P, Zhao X and Ma L: Downregulation of microRNA-100 correlates with tumor progression and poor prognosis in hepatocellular carcinoma. Mol Cell Biochem 383: 49-58, 2013.
80. Machlowska J, Baj J, Sitarz M, Maciejewski R and Sitarz R: Gastric cancer: Epidemiology, risk factors, classification, genomic characteristics and treatment strategies. Int J Mol Sci 21: 4012, 2020.
81. Wei L, Sun J, Zhang N, Zheng Y, Wang X, Lv L, Liu J, Xu Y, Shen Y and Yang M: Noncoding RNAs in gastric cancer: Implications for drug resistance. Mol Cancer 19: 62, 2020.
82. Cao Y, Song J, Ge J, Song Z, Chen J and Wu C: MicroRNA-100 suppresses human gastric cancer cell proliferation by targeting CXCR7. Oncol Lett 15: 453-458, 2018.
83. Chen Z, Liu X, Hu Z, Wang Y, Liu M, Liu X, Li H, Ji R, Guo Q and Zhou Y: Identification and characterization of tumor suppressor and oncogenic miRNAs in gastric cancer. Oncol Lett 10: 329-336, 2015.
84. Zhang N, Hu X, Du Y and Du J: The role of miRNAs in colorectal cancer progression and chemoradiotherapy. Biomed Pharmacother 134: 111099, 2021.
85. Zhao W, Dai S, Yue L, Xu F, Gu J, Dai X and Qian X: Emerging mechanisms progress of colorectal cancer liver metastasis. Front Endocrinol (Lausanne) 13: 1081585, 2022.
86. Czauderna C, Luley K, von Bubnoff N and Marquardt JU: Tailored systemic therapy for colorectal cancer liver metastases. Int J Mol Sci 22: 11780, 2021.
87. Peng H, Luo J, Hao H, Hu J, Xie SK, Ren D and Rao B: MicroRNA-100 regulates SW620 colorectal cancer cell proliferation and invasion by targeting RAP1B. Oncol Rep 31: 2055-2062, 2014.
88. Fujino Y, Takeishi S, Nishida K, Okamoto K, Muguruma N, Kimura T, Kitamura S, Miyamoto H, Fujimoto A, Higashijima J, *et al*: Downregulation of micro RNA-100/micro RNA-125b is associated with lymph node metastasis in early colorectal cancer with submucosal invasion. Cancer Sci 108: 390-397, 2017.
89. Wood LD, Canto MI, Jaffee EM and Simeone DM: Pancreatic cancer: Pathogenesis, screening, diagnosis, and treatment. Gastroenterology 163: 386-402.e1, 2022.
90. Jiang S, Fagman JB, Ma Y, Liu J, Vihav C, Engstrom C, Liu B and Chen C: A comprehensive review of pancreatic cancer and its therapeutic challenges. Aging (Albany NY) 14: 7635-7649, 2022.
91. Huang JS, Egger ME, Grizzle WE and McNally LR: MicroRNA-100 regulates IGF1-receptor expression in metastatic pancreatic cancer cells. Biotech Histochem 88: 397-402, 2013.
92. Dobre M, Herlea V, Vlăduţ C, Ciocîrlan M, Balaban VD, Constantinescu G, Diculescu M and Milanesi E: Dysregulation of miRNAs targeting the IGF-1R pathway in pancreatic ductal adenocarcinoma. Cells 10: 1856, 2021.
93. Deleuze A, Saout J, Dugay F, Peyronnet B, Mathieu R, Verhoest G, Bensalah K, Crouzet L, Laguerre B, Belaud-Rotureau MA, *et al*: Immunotherapy in renal cell carcinoma: The future is now. Int J Mol Sci 21: 2532, 2020.
94. Li F, Aljahdali IAM, Zhang R, Nastiuk KL, Krolewski JJ and Ling X: Kidney cancer biomarkers and targets for therapeutics: Survivin (BIRC5), XIAP, MCL-1, HIF1α, HIF2α, NRF2, MDM2, MDM4, p53, KRAS and AKT in renal cell carcinoma. J Exp Clin Cancer Res 40: 254, 2021.
95. Chen P, Lin C, Quan J, Lai Y, He T, Zhou L, Pan X, Wu X, Wang Y, Ni L, *et al*: Oncogenic miR-100-5p is associated with cellular viability, migration and apoptosis in renal cell carcinoma. Mol Med Rep 16: 5023-5030, 2017.
96. Adamaki M and Zoumpourlis V: Prostate cancer biomarkers: From diagnosis to prognosis and precision-guided therapeutics. Pharmacol Ther 228: 107932, 2021.
97. Leite KR, Tomiyama A, Reis ST, Sousa-Canavez JM, Sañudo A, Dall'Oglio MF, Camara-Lopes LH and Srougi M: MicroRNA-100 expression is independently related to biochemical recurrence of prostate cancer. J Urol 185: 1118-1122, 2011.
98. Leite KR, Morais DR, Reis ST, Viana N, Moura C, Florez MG, Silva IA, Dip N and Srougi M: MicroRNA 100: A context dependent miRNA in prostate cancer. Clinics (Sao Paulo) 68: 797-802, 2013.
99. Wang M, Ren D, Guo W, Wang Z, Huang S, Du H, Song L and Peng X: Loss of miR-100 enhances migration, invasion, epithelial-mesenchymal transition and stemness properties in prostate cancer cells through targeting Argonaute 2. Int J Oncol 45: 362-372, 2014.
100. Nabavi N, Saidy NRN, Venalainen E, Haegert A, Parolia A, Xue H, Wang Y, Wu R, Dong X, Collins C, *et al*: miR-100-5p inhibition induces apoptosis in dormant prostate cancer cells and prevents the emergence of castration-resistant prostate cancer. Sci Rep 7: 4079, 2017.
101. Ye Y, Li SL and Wang JJ: miR-100-5p downregulates mTOR to suppress the proliferation, migration, and invasion of prostate cancer cells. Front Oncol 10: 578948, 2020.
102. Chen DW, Lang BHH, McLeod DSA, Newbold K and Haymart MR: Thyroid cancer. Lancet 401: 1531-1544, 2023.
103. Şah Ünal FT, Gökçay Canpolat A, Elhan AH, Sevim S, Sak SD, Emral R, Demir O, Güllü S, Erdoğan MF, Çorapçıoğlu D and Şahin M: Cancer rates and characteristics of thyroid nodules with macrocalcification. Endocrine 84: 1021-1029, 2024.
104. Ma P and Han J: Overexpression of miR-100-5p inhibits papillary thyroid cancer progression via targeting FZD8. Open Med (Wars) 17: 1172-1182, 2022.
105. Trapani D, Ginsburg O, Fadelu T, Lin NU, Hassett M, Ilbawi AM, Anderson BO and Curigliano G: Global challenges and policy solutions in breast cancer control. Cancer Treat Rev 104: 102339, 2022.

106. Xie H, Xiao R, He Y, He L, Xie C, Chen J and Hong Y: MicroRNA-100 inhibits breast cancer cell proliferation, invasion and migration by targeting FOXA1. Oncol Lett 22: 816, 2021.
107. Gebeshuber CA and Martinez J: miR-100 suppresses IGF2 and inhibits breast tumorigenesis by interfering with proliferation and survival signaling. Oncogene 32: 3306-3310, 2013.
108. Li X, Ren Y, Liu D, Yu X and Chen K: Role of miR-100-5p and CDC25A in breast carcinoma cells. PeerJ 9: e12263, 2022.
109. Gong Y, He T, Yang L, Yang G, Chen Y and Zhang X: The role of miR-100 in regulating apoptosis of breast cancer cells. Sci Rep 5: 11650, 2015.
110. Throwba H PK, Unnikrishnan L, Pangath M, Vasudevan K, Jayaraman S, Li M, Iyaswamy A, Palaniyandi K and Gnanasampanthapandian D: The epigenetic correlation among ovarian cancer, endometriosis and PCOS: A review. Crit Rev Oncol Hematol 180: 103852, 2022.
111. Volkova LV, Pashov AI and Omelchuk NN: Cervical carcinoma: Oncobiology and biomarkers. Int J Mol Sci 22: 12571, 2021.
112. Schoutrop E, Moyano-Galceran L, Lheureux S, Mattsson J, Lehti K, Dahlstrand H and Magalhaes I: Molecular, cellular and systemic aspects of epithelial ovarian cancer and its tumor microenvironment. Semin Cancer Biol 86: 207-223, 2022.
113. Nam EJ, Yoon H, Kim SW, Kim H, Kim YT, Kim JH, Kim JW and Kim S: MicroRNA expression profiles in serous ovarian carcinoma. Clin Cancer Res 14: 2690-2695, 2008.
114. Huang C, Qin X, Zhao N, Jin H, Zhang S and Yang H: Erratum: MicroRNA-100 functions as a tumor suppressor in cervical cancer via downregulating the SATB1 expression and regulating AKT/mTOR signaling pathway and epithelial-to-mesenchymal transition. Oncol Lett 22: 741, 2021.
115. Li BH, Zhou JS, Ye F, Cheng XD, Zhou CY, Lu WG and Xie X: Reduced miR-100 expression in cervical cancer and precursors and its carcinogenic effect through targeting PLK1 protein. Eur J Cancer 47: 2166-2174, 2011.
116. Crosbie EJ, Kitson SJ, McAlpine JN, Mukhopadhyay A, Powell ME and Singh N: Endometrial cancer. Lancet 399: 1412-1428, 2022.
117. Chen C, Zhang Q and Kong B: miRNA-576-5p promotes endometrial cancer cell growth and metastasis by targeting ZBTB4. Clin Transl Oncol 25: 706-720, 2023.
118. Takebayashi K, Nasu K, Okamoto M, Aoyagi Y, Hirakawa T and Narahara H: hsa-miR-100-5p, an overexpressed miRNA in human ovarian endometriotic stromal cells, promotes invasion through attenuation of SMARCD1 expression. Reprod Biol Endocrinol 18: 31, 2020.
119. Valihrach L, Androvic P and Kubista M: Circulating miRNA analysis for cancer diagnostics and therapy. Mol Aspects Med 72: 100825, 2020.
120. O'Neill RS and Stoita A: Biomarkers in the diagnosis of pancreatic cancer: Are we closer to finding the golden ticket? World J Gastroenterol 27: 4045-40875, 2021.
121. Wang H, Meng Q, Qian J, Li M, Gu C and Yang Y: RNA-based diagnostic markers discovery and therapeutic targets development in cancer. Pharmacol Ther 234: 108123, 2022.
122. Wang S, Li L, Yang M, Wang X, Zhang H, Wu N, Jia K, Wang J, Li M, Wei L and Liu J: Identification of three circulating MicroRNAs in plasma as clinical biomarkers for breast cancer detection. J Clin Med 12: 322, 2022.
123. Fuso P, Di Salvatore M, Santonocito C, Guarino D, Autilio C, Mulè A, Arciuolo D, Rinninella A, Mignone F, Ramundo M, *et al*: Let-7a-5p, miR-100-5p, miR-101-3p, and miR-199a-3p hyper-expression as potential predictive biomarkers in early breast cancer patients. J Pers Med 11: 816, 2021.
124. Jin Y, Wong YS, Goh BKP, Chan CY, Cheow PC, Chow PKH, Lim TKH, Goh GBB, Krishnamoorthy TL, Kumar R, *et al*: Circulating microRNAs as potential diagnostic and prognostic biomarkers in hepatocellular carcinoma. Sci Rep 9: 10464, 2019.
125. Qureshi A, Fahim A, Kazi N, Farsi Kazi SA and Nadeem F: Expression of miR-100 as a novel ancillary non-invasive biomarker for early detection of bladder carcinoma. J Pak Med Assoc 68: 759-763, 2018.
126. Ludwig N, Nourkami-Tutdibi N, Backes C, Lenhof HP, Graf N, Keller A and Meese E: Circulating serum miRNAs as potential biomarkers for nephroblastoma. Pediatr Blood Cancer 62: 1360-1367, 2015.
127. Blanca A, Sanchez-Gonzalez A, Requena MJ, Carrasco-Valiente J, Gomez-Gomez E, Cheng L, Cimadamore A, Montironi R and Lopez-Beltran A: Expression of miR-100 and miR-138 as prognostic biomarkers in non-muscle-invasive bladder cancer. APMIS 127: 545-553, 2019.
128. Yamanaka Z, Sasaki T, Yamanaka A, Kato K and Nishi H: Circulating and tissue miR-100 acts as a potential diagnostic biomarker for cervical cancer. Cancer Biomark 32: 551-558, 2021.
129. Bahnassy AA, Salem SE, El-Sayed M, Khorshid O, Abdellateif MS, Youssef AS, Mohanad M, Hussein M, Zekri AN and Ali NM: MiRNAs as molecular biomarkers in stage II egyptian colorectal cancer patients. Exp Mol Pathol 105: 260-271, 2018.
130. Wang X, Chen L, Jin H, Wang S, Zhang Y, Tang X and Tang G: Screening miRNAs for early diagnosis of colorectal cancer by small RNA deep sequencing and evaluation in a Chinese patient population. Onco Targets Ther 9: 1159-1166, 2016.
131. Gong Y, Yang G, Wang Q, Wang Y and Zhang X: NME2 is a master suppressor of apoptosis in gastric cancer cells via transcriptional regulation of miR-100 and other survival factors. Mol Cancer Res 18: 287-299, 2020.
132. Damodaran M, Chinambedu Dandapani M, SimonDuraiRaj, SandhyaSundaram, VenkatRamanan S, Ramachandran I and Venkatesan V: Differentially expressed miR-20, miR-21, miR-100, miR-125a and miR-146a as a potential biomarker for prostate cancer. Mol Biol Rep 48: 3349-3356, 2021.
133. Jakob M, Mattes LM, Küffer S, Unger K, Hess J, Bertlich M, Haubner F, Ihler F, Canis M, Weiss BG and Kitz J: MicroRNA expression patterns in oral squamous cell carcinoma: Hsa-mir-99b-3p and hsa-mir-100-5p as novel prognostic markers for oral cancer. Head Neck 41: 3499-3515, 2019.
134. Zhao JY, Wang F, Li Y, Zhang XB, Yang L, Wang W, Xu H, Liu DZ and Zhang LY: Five miRNAs considered as molecular targets for predicting esophageal cancer. Med Sci Monit 21: 3222, 2015.
135. Zhang HC and Tang KF: Clinical value of integrated-signature miRNAs in esophageal cancer. Cancer Med 6: 1893-1903, 2017.
136. Wang G, Chen L, Meng J, Chen M, Zhuang L and Zhang L: Overexpression of microRNA-100 predicts an unfavorable prognosis in renal cell carcinoma. Int Urol Nephrol 45: 373-379, 2013.
137. Liu HT, Wang YW, Xing AY, Shi DB, Zhang H, Guo XY, Xu J and Gao P: Prognostic value of microRNA signature in patients with gastric cancers. Sci Rep 7: 42806, 2017.
138. He QL, Qin SY, Tao L, Ning HJ and Jiang HX: Prognostic value and prospective molecular mechanism of miR-100-5p in hepatocellular carcinoma: A comprehensive study based on 1,258 samples. Oncol Lett 18: 6126-6142, 2019.
139. Hassan NM, Refaat LA, Ismail GN, Abdellateif M, Fadel SA and AbdelAziz RS: Diagnostic, prognostic and predictive values of miR-100 and miR-210 in pediatric acute lymphoblastic Leukemia. Hematology 25: 405-413, 2020.
140. Nussinov R, Tsai CJ and Jang H: Anticancer drug resistance: An update and perspective. Drug Resist Updat 59: 100796, 2021.
141. Bukowski K, Kciuk M and Kontek R: Mechanisms of multidrug resistance in cancer chemotherapy. Int J Mol Sci 21: 3233, 2020.
142. Luan Y, Zhang S, Zuo L and Zhou L: Overexpression of miR-100 inhibits cell proliferation, migration, and chemosensitivity in human glioblastoma through FGFR3. Onco Targets Ther 8: 3391-3400, 2015.
143. Xiao F, Bai Y, Chen Z, Li Y, Luo L, Huang J, Yang J, Liao H and Guo L: Downregulation of HOXA1 gene affects small cell lung cancer cell survival and chemoresistance under the regulation of miR-100. Eur J Cancer 50: 1541-1554, 2014.
144. Feng B, Wang R and Chen LB: MiR-100 resensitizes docetaxel-resistant human lung adenocarcinoma cells (SPC-A1) to docetaxel by targeting Plk1. Cancer Lett 317: 184-191, 2012.
145. Guo P, Xiong X, Zhang S and Peng D: miR-100 resensitizes resistant epithelial ovarian cancer to cisplatin. Oncol Rep 36: 3552-3558, 2016.
146. Liu Y, Zhu ST, Wang X, Deng J, Li WH, Zhang P and Liu BS: MiR-100 inhibits osteosarcoma cell proliferation, migration, and invasion and enhances chemosensitivity by targeting IGFIR. Technol Cancer Res Treat 15: NP40-NP48, 2016.
147. Lai Y, Kacal M, Kanony M, Stukan I, Jatta K, Kis L, Norberg E, Vakifahmetoglu-Norberg H, Lewensohn R, Hydbring P and Ekman S: miR-100-5p confers resistance to ALK tyrosine kinase inhibitors Crizotinib and Lorlatinib in EML4-ALK positive NSCLC. Biochem Biophys Res Commun 511: 260-265, 2019.
148. Lobert S, Jefferson B and Morris K: Regulation of β-tubulin isotypes by micro-RNA 100 in MCF7 breast cancer cells. Cytoskeleton 68: 355-362, 2011.

149. Moqadam FA, Lange-Turenhout EAM, Ariës IM, Pieters R and den Boer ML: MiR-125b, miR-100 and miR-99a co-regulate vincristine resistance in childhood acute lymphoblastic leukemia. Leuk Res 37: 1315-1321, 2013.
150. Ng WL, Yan D, Zhang X, Mo YY and Wang Y: Over-expression of miR-100 is responsible for the low-expression of ATM in the human glioma cell line: M059J. DNA Repair (Amst) 9: 1170-1175, 2010.
151. Zhou B, Lin W, Long Y, Yang Y, Zhang H, Wu K and Chu Q: Notch signaling pathway: Architecture, disease, and therapeutics. Signal Transduct Target Ther 7: 95, 2022.
152. Lee YJ, Kim WR, Park EG, Lee DH, Kim JM, Shin HJ, Jeong HS, Roh HY and Kim HS: Exploring the key signaling pathways and ncRNAs in colorectal cancer. Int J Mol Sci 25: 4548, 2024.
153. Peng WX, Koirala P and Mo YY: LncRNA-mediated regulation of cell signaling in cancer. Oncogene 36: 5661-5667, 2017.
154. Park JH, Pyun WY and Park HW: Cancer metabolism: Phenotype, signaling and therapeutic targets. Cells 9: 2308, 2020.
155. Song SK, Jung WY, Park SK, Chung CW and Park Y: Significantly different expression levels of microRNAs associated with vascular invasion in hepatocellular carcinoma and their prognostic significance after surgical resection. PLoS One 14: e0216847, 2019.
156. Chen D, Sun Y, Yuan Y, Han Z, Zhang P, Zhang J, You MJ, Teruya-Feldstein J, Wang M, Gupta S, *et al*: miR-100 induces epithelial-mesenchymal transition but suppresses tumorigenesis, migration and invasion. PLoS Genet 10: e1004177, 2014.
157. Yang J, Chen Z, Wang X, Xu M, Fang H, Li F, Liu Y, Jiang Y, Ding Y, Li J and Wang S: Inactivation of miR-100 combined with arsenic treatment enhances the malignant transformation of BEAS-2B cells via stimulating epithelial-mesenchymal transition. Cancer Biol Ther 18: 965-973, 2017.
158. Huang C, Qin X, Zhao N, Jin H, Zhang S and Yang H: (Corrigendum) MicroRNA-100 functions as a tumor suppressor in cervical cancer via downregulating the SATB1 expression and regulating AKT/mTOR signaling pathway and epithelial-to-mesenchymal transition. Oncol Lett: 22, 2021.
159. Glaviano A, Foo ASC, Lam HY, Yap KCH, Jacot W, Jones RH, Eng H, Nair MG, Makvandi P, Geoerger B, *et al*: PI3K/AKT/mTOR signaling transduction pathway and targeted therapies in cancer. Mol Cancer 22: 138, 2023.
160. Song P, Gao Z, Bao Y, Chen L, Huang Y, Liu Y, Dong Q and Wei X: Wnt/β-catenin signaling pathway in carcinogenesis and cancer therapy. J Hematol Oncol 17: 46, 2024.
161. Peng CW, Yue LX, Zhou YQ, Tang S, Kan C, Xia LM, Yang F and Wang SY: miR-100-3p inhibits cell proliferation and induces apoptosis in human gastric cancer through targeting to BMPR2. Cancer Cell Int 19: 354, 2019.
162. Yang G, Gong Y, Wang Q, Wang Y and Zhang X: The role of miR-100-mediated Notch pathway in apoptosis of gastric tumor cells. Cell Signal 27: 1087-1101, 2015.
163. Huang C, Qin X, Zhao N, Jin H, Zhang S and Yang H: MicroRNA-100 functions as a tumor suppressor in cervical cancer via downregulating the SATB1 expression and regulating AKT/mTOR signaling pathway and epithelial-to-mesenchymal transition. Oncol Lett 20: 1336-1344, 2020.
164. Morgos DT, Stefani C, Miricescu D, Greabu M, Stanciu S, Nica S, Stanescu-Spinu II, Balan DG, Balcangiu-Stroescu AE, Coculescu EC, *et al*: Targeting PI3K/AKT/mTOR and MAPK signaling pathways in gastric cancer. Int J Mol Sci 25: 1848, 2024.
165. Qin C, Huang RY and Wang ZX: Potential role of miR-100 in cancer diagnosis, prognosis, and therapy. Tumour Biol 36: 1403-1409, 2015.
166. Wei X, Feng Y, Fu Y, Liu F, Chen Q, Zhang W, Zhao Y, Huang X, Chen Y, Li Q and Zhang Q: miR-100-5p is upregulated in multiple myeloma and involves in the pathogenesis of multiple myeloma through targeting MTMR3. Hematology 28: 2196857, 2023.
167. Eniafe J and Jiang S: MicroRNA-99 family in cancer and immunity. Wiley Interdiscip Rev RNA 12: e1635, 2021.
168. Gu L, Li H, Chen L, Ma X, Gao Y, Li X, Zhang Y, Fan Y and Zhang X: MicroRNAs as prognostic molecular signatures in renal cell carcinoma: A systematic review and meta-analysis. Oncotarget 6: 32545-32560, 2015.
169. Ghafouri-Fard S, Glassy MC, Abak A, Hussen BM, Niazi V, and Taheri M: The interaction between miRNAs/lncRNAs and Notch pathway in human disorders. Biomed Pharmacother 138: 111496, 2021.
170. Servín-González LS, Granados-López AJ and López JA: Families of microRNAs expressed in clusters regulate cell signaling in cervical cancer. Int J Mol Sci 16: 12773-12790, 2015.
171. Shemesh R, Laufer-Geva S, Gorzalczany Y, Anoze A, Sagi-Eisenberg R, Peled N and Roisman LC: The interaction of mast cells with membranes from lung cancer cells induces the release of extracellular vesicles with a unique miRNA signature. Sci Rep 13: 21544, 2023.
172. Jamali L, Tofigh R, Tutunchi S, Panahi G, Borhani F, Akhavan S, Nourmohammadi P, Ghaderian SMH, Rasouli M and Mirzaei H: Circulating microRNAs as diagnostic and therapeutic biomarkers in gastric and esophageal cancers. J Cell Physiol 233: 8538-8550, 2018.
173. Farasati Far B, Vakili K, Fathi M, Yaghoobpoor S, Bhia M and Naimi-Jamal MR: The role of microRNA-21 (miR-21) in pathogenesis, diagnosis, and prognosis of gastrointestinal cancers: A review. Life Sci 316: 121340, 2023.
174. Grimaldi AM, Nuzzo S, Condorelli G, Salvatore M and Incoronato M: Prognostic and clinicopathological significance of miR-155 in breast cancer: A systematic review. Int J Mol Sci 21: 5834, 2020.
175. Seyhan AA: Trials and tribulations of microRNA therapeutics. Int J Mol Sci 25: 1469, 2024.
176. Qian H, Maghsoudloo M, Kaboli PJ, Babaeizad A, Cui Y, Fu J, Wang Q and Imani S: Decoding the promise and challenges of miRNA-based cancer therapies: An essential update on miR-21, miR-34, and miR-155. Int J Med Sci 21: 2781-2798, 2024.