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A New Insight of MicroRNA-96 In Human Malignant Disorders and Drug Resistance

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ABSTRACT

miRNA-96 is a short non-coding RNA molecule which plays an essential function in the regulation of post-transcriptional gene, and play a role in the development of a number of illnesses, such as cancer, depending on the cellular setting, it may function as a tumor suppressor or an oncogene. According to a recent research, miRNA-96 levels has been decreased in gastric cancer, breast cancer, pancreatic cancer, renal cancer and cervical cancer. However, the levels of miRNA-96 in several kinds of cancers are increased, including colorectal, lung, prostate, glioma, osteosarcoma, and hepatocellular carcinoma. The current review aims to offer a summary of miRNA-96's role in the advancement of cancer illnesses and with an emphasis on dysregulated signaling pathways. Based on in vivo, in vitro, and human research, we also go over the function of this miRNA-96 as a cancer biomarker of prognosis and emphasize how it contributes to drug resistance.

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1. Introduction

Short non-coding RNA molecules known as microRNAs (miRNAs) via influencing the stability and translation of produced mRNAs, play crucial roles in the regulation of gene expression post-transcriptionally (Hussen et al., 2023). They are generally 18–25 nucleotides in length (Kanwal, Al Samarrai, Al-Zaidi, Mirzaei, & Heidari, 2023). RNA polymerase II produces pri-miRNAs that are polyadenylated and cap-coated (Hussen et al., 2023). Specific genes in the genome, called miRNA genes, are used to produce miRNAs (Samad & Kamaroddin, 2023). These genes may be found in the genome's coding or non-coding sections (Gullotta, Korte, & Marquardt, 2023). MicroRNA-96 (miRNA-96) has attracted the most attention among miRNAs because of its role in a number of clinical processes and its influence on how drugs respond (Radhi, Matti, & Hamzah, 2023; Taheri et al., 2022). Numerous human ailments, including cancer, neurological issues, and cardiovascular conditions have been linked to miRNA-96 (Suzuki, 2023). MiRNA-96 in cancer play as an oncogenic miRNA, increasing invasion, metastasis, and tumor growth (Zhang et al., 2015). Its dysregulation is connected to medication resistance and is associated with poor prognoses, making it a viable therapeutic target (Elrebehy et al., 2022).

The aim of this review is to provide a comprehensive overview of the recently acquired knowledge on the function of miRNA-96 in human diseases and treatment resistance in this review. It will discuss the unique functions of miRNA-96 in various diseases, its regulatory mechanisms, and how it affects the effectiveness of treatments. Additionally, it will look into the potential of miRNA-96 as a diagnostic biomarker and potential therapeutic target.

1.1 Search methodology:

Searched PubMed, one of the best-known libraries of scientific literature, using the primary keywords (Cancer, MicroRNA-96, Biomarker, Drug resistance). Review research on miRNA-96 in relation to drug resistance and tumor illnesses included the actual samples in line with its specifications.

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2. Biogenesis of miRNA

Mature miRNA molecules are produced as a result of a series of stages in the biogenesis of miRNAs (Mencia, Gonzalo, Tossolini, & Manavella, 2023). RNA pol II or III transcribes the genes of miRNA to create primary microRNA transcripts (pri-miRNAs) (Cambiagno et al., 2021). These pri-miRNAs can be found in non-coding areas of the genome, introns of protein-coding genes, or even within their own specific miRNA genes (Park et al., 2022). As shown in (figure1), the pri-miRNA transcripts are first translated into hairpin-shaped precursor miRNAs (pre-miRNAs) in the nucleus by a protein called Drosha and its cofactor DGCR8 (DiGeorge syndrome critical region 8) (Mirzaei, Rahimian, Mirzaei, Nahand, & Hamblin, 2022). Drosha recognizes and cleaves the pri-miRNA near its base to release the pre-miRNA stem-loop structure (Hussen et al., 2021; Jones, Walbrun, Falleroni, Rief, & Sattler, 2022). The protein Exportin-5 (XPO5) transports pre-miRNAs to the cytoplasm from the nucleus. XPO5 enhances pre-miRNA trafficking via the nuclear pore complex by identifying its structure (Campos-Melo, Hawley, McLellan, & Strong, 2022). The exported pre-miRNA is identified in the cytoplasm by the RNase III enzyme known as Dicer, which then cleaves it close to the base of the hairpin structure (Rani & Sengar, 2022). A short RNA duplex made composed of the mature miRNA sequence and its complementary strand, also called the miRNA or passenger strand, is released as a result of this breakage (Letafati et al., 2022). The RNA-induced silencing complex (RISC), which is made up of Argonaute proteins, is subsequently loaded with the RNA duplex (Bhagtaney & Sundarrajan, 2023). The guide strand of the duplex is chosen to be the mature miRNA within the RISC, while the passenger strand is normally destroyed (Ergin & Çetinkaya, 2022). The complex is directed to target messenger RNA (mRNA) molecules by the mature miRNA, which is linked to the RISC. Through complementary base pairing, the miRNA predominantly binds to the target mRNA's 3' untranslated region (UTR) (Han & Mendell, 2022). The outcome of this interaction could be translational suppression, mRNA destruction, or both, depending on how complementary the miRNA and its target are to one another. However, Numerous miRNAs have been discovered in various species, and continuing research is still revealing more about their precise roles and modes of activity.

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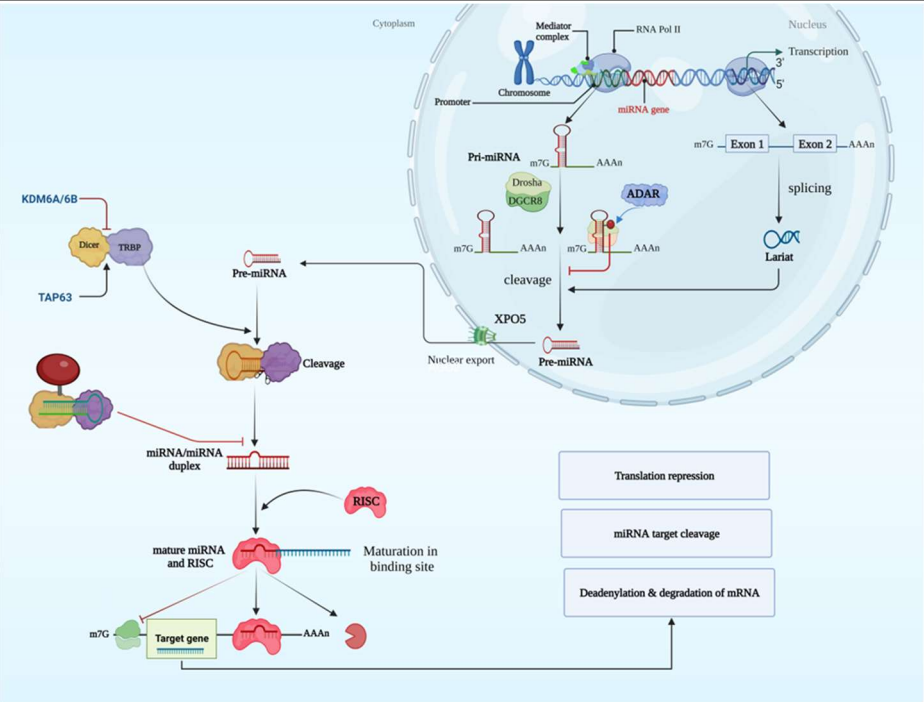

Figure (1): The illustration shows the mechanism of miRNA biogenesis.

3. Malignant conditions

Cancer affects several miRNAs, and according to the situation, they may act as oncogenes or tumor suppressors (Ghafouri-Fard et al., 2021; Hussen, Salihi, et al., 2022). Previous researches have highlighted the miRNA-96 function in the progression of cancer in cancer cell lines, cancer-causing animal models, and cancer clinical samples. In the sections that follow, it will describe the miRNA-96's role in the development of cancer using these three datasets.

3.1 Cancer and miRNA-96 expression

In some tumor cell lines, the level of miRNA-96 is frequently increased, while in some tumor cell lines, it can also be decreasing the level (Table 1). For instance, in lung cancer, Chu et al. revealed that LIM-domain binding protein 2 was downregulated by miRNA-96-5p, which prevented lung cancer H1299 cells from proliferating, invasiveness, and metastasizing (Chu et al., 2023). Similarly, Zhang et al. Findings show that miR-96 is more expressed in breast cancer tissues and cell lines and can

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directly influence the expression of RECK to increase cellular proliferation, migration, and invasion, suggesting that miR-96 may be a potential drug target for breast cancer (Zhang et al., 2014). Likewise, in colorectal cancer, microRNA-96 targets the tumor proteins fork head box protein O1 (FOXO1) and FOXO3a, that stimulates the growth of cancer cells (Gao & Wang, 2015). Furthermore, one cause of the redaction resistance of rectal cancer cells may be decreased level of expression of the GPC3 gene, which is directly regulated by miRNA-96-5p (Wu et al., 2021). This impact may be connected to alterations in the activity of the Wnt/-catenin signal transduction pathway. In addition, in gastric adenocarcinoma, Zhou et al. suggested that downregulated miR-96-5p may increase ZDHHC5 expression in MGC-803 cells, which in turn may cause cell death (Zhou, Wu, & Bi, 2019). It's crucial to remember that miRNA-96 dysregulation can change between different cancers and patient clinical samples. To fully comprehend the mechanics and clinical ramifications of miRNA-96 dysregulation in cancer, more investigation is required.

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Table (1): miRNA-96 dysregulation in different cancers.

Cancer type	Micro-RNAs	Compared to normal cell lines, levels in cancer cell lines	Interactions	Downstream target of micro-RNA	Effect of up-regulation of miRNA-96 on its target	Cell lines	Associated manifestations of miRNA-96 dysregulation	Ref.
Lung Cancer	miRNA-96-5p	Upregulated	LDB2, ERK1/2 signaling pathway	LDB2	Inhibition	A549, SPAC1, H1650, H1299, H1975, BEAS-2B	↑ miRNA-96, ↓ LDB2: ↑ proliferation, invasion, and metastasis	(Chu et al., 2023)
	miRNA-96	Upregulated	SAMD9	SAMD9	Inhibition	H23, H358	↑ miRNA-96, ↓ SAMD9: ↑ cisplatin chemoresistance	(Wu et al., 2016)
Breast Cancer	miRNA-96-5p	Upregulated	FOXO3	FOXO3	Inhibition	MCF-7, T47D	↑ miRNA-96-5p, ↓ FOXO3: ↑ cell proliferation	(Yin et al., 2020)
	miRNA-96-5p	Upregulated	FOXO1	FOXO1	Inhibition	MCF-7, BT-549, MDA-MB-231, HS 578T, T47D, MCF-10A, ZR-75-1	↑ miRNA-96-5p, ↓ FOXO1: ↑ proliferation, migration and invasion, ↓ autophagy, and induce apoptosis	(Shi et al., 2017)

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	miRNA-96	Upregulated	MTSS1	MTSS1	Inhibition	MDA-MB-231, MCF-7	↑ miR-96, ↓ MTSS1: ↑ metastasis	(Xie, Sun, Chen, & Cao, 2018)
	miRNA-96	Upregulated	RECK	RECK	Inhibition	MDA-MB-231, MCF-10A, MCF-7, MDA-MB-435, MDA-MB-468, T-74D, MDA-MB-453	↑ miRNA-96, ↓ RECK: ↑ proliferation and invasion	(Zhang et al., 2014)
	miRNA-96	Upregulated	PTPN9	PTPN9	Inhibition	MDA-MB-468, 293 T, MCF-7	↑ miRNA-96, ↓ PTPN9: ↑ proliferation, metastasis	(Hong et al., 2016a)
Colorectal Cancer	miRNA-96	Upregulated	TP53INP1, FOXO1, FOXO3a	TP53INP1, FOXO1, FOXO3a	Inhibition	SW480, SW620	↑ miRNA-96, ↓ TP53INP1, FOXO1, FOXO3a: ↑ proliferation	(Gao & Wang, 2015)

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	miRNA-96	Upregulated	XIAP, p53 , UBE2N	XIAP, p53 , UBE2N	Inhibition	HT-29, DLD-1, HCT-116	↑ miRNA-96, ↓ XIAP, p53 , UBE2N: ↑apoptosis, ↓ growth	(Kim, Kim, Yoon, Lee, & Kuh, 2015)
Rectal cancer	miRNA-96-5p	Upregulated	GPC3, Wnt/β-catenin pathway	GPC3	Inhibition	HRC-99, RCM-1, HR-8348, SW837, SW1463	↑ miRNA-96-5p, ↓ FOXO1, ↑Wnt/β-Catenin: ↑ Irradiation Resistance	(Wu et al., 2021)
Hepatocellular carcinoma	miRNA-96	Upregulated	GPM6A	GPM6A	Inhibition	Huh-7	↑ miRNA-96, ↓ GPM6A: ↑ HCC progression	(Li et al., 2022)
Gastric Cancer	miRNA-96-5p	Downregulated	ZDHHC5	ZDHHC5	Inhibition	MGC-803	↓ miRNA-96-5p, ↑ ZDHHC5: ↑ apoptosis	(Zhou et al., 2019)
Pancreatic Cancer	miRNA-96	Downregulated	KRAS/Akt signaling pathway	KRAS	Inhibition	MIA PaCa-2, PANC-1, BxPC-3, HeLa	↑ miRNA-96, ↓ KRAS: ↓ tumor development, cell invasion and migration	(Yu et al., 2010)

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Bladder carcinomas	hsa-miRNA-96	Upregulated	IRS1, MAP4K1	IRS1, MAP4K1	Inhibition	T24, 5637	↑ miRNA-96, ↓ IRS1, MAP4K1:	(Yi Wang et al., 2012)
Cervical Cancer	miRNA-96	Upregulated	FOXO1	FOXO1	Inhibition	C41, C33A, HeLa, CaSki, MS751, SiHa, HT-3	↑ miRNA-96, ↓ FOXO1: ↑ cell proliferation	(Yang et al., 2020)
	miRNA-96	Upregulated	PTPN9	PTPN9	Inhibition	HeLa	↑ miRNA-96, ↓ PTPN9: ↑ cellular proliferation and tumorigenicity	(Ma, Shi, Peng, Qin, & Hui, 2018)
	miRNA-96-5p	Upregulated	SFRP4	SFRP4	Inhibition	HaCaT, Hela, SiHa, Me180, Ms751	↑ miRNA-96, ↓ SFRP4: ↑ cell viability, migration, and invasion	(Zhang, Chen, & Shao, 2020)
Prostate Cancer	miRNA-96	Upregulated	EGFR Signaling, ETV	ETV	Inhibition	PC3, RasB1	↑ miRNA-96, ↑ EGFR Signaling, ↓ ETV: ↓ tumor progression	(Tsai et al., 2017)

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Ovarian cancer	miRNA-96	Upregulated	FOXO3a	FOXO3a	Inhibition	SKOV3, CAOV3, PEO1, A2780, 3AO, OVCAR3, HOSEPiCs	↑ miRNA-96, ↓ FOXO3a: ↑ OC progression	(Yang, Zhang, & Bi, 2020)
Glioma	miRNA-96		MEG3, MTSS1	MEG3	Inhibition	GSC11, M059J, D54	↓MEG3, ↑miRNA-96, ↓ MTSS1: ↑ proliferation, migration and invasion	(Zhang & Guo, 2019)
Osteosarcoma	miRNA-96	Downregulated	EZRIN	EZRIN	Inhibition	MG-63	↑miRNA-96, ↓ EZRIN: ↓ proliferation, metastasis, tumor formation ability, ↑apoptosis	(Yao, Pei, Zhang, & Xie, 2018)
Papillary thyroid carcinoma	mRNA-96	Upregulated	AKT/FOXO1/ Bim pathway	FOXO1	Inhibition	TPC1, K1	↑ miRNA-96-5p, ↑AKT/FOXO1/Bim pathway ↓ FOXF2: ↑ proliferation, ↓ apoptosis	(Song et al., 2015)

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OSCC	miRNA-96-5p	Upregulated	FOXF2	FOXF2	Inhibition	SCC1, NHOK, SCC4, HSC-2, Tca8113, Cal-27	↑ miRNA-96-5p, ↓ FOXF2: ↑	(Wang, Ma, Li, & Wang, 2020)
Osteosarcoma	miRNA-96-5p	Downregulated by (LncRNA NDRG1)	PI3K/AKT pathway	-	-	MG63, U2OS, HOS, 143B, hFOB 1.19	↑ LncRNA NDRG1, ↓ miR-96-5p, ↑ PI3K/AKT: osteosarcoma progression	(Wang et al., 2022)

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3.2 Animal studies

miRNA-96 induces development and survival of tumor cells, according to extensive in vivo and in vitro experiments as shown in (Table 2). For example, Pillar et al. proved which miR-96 directly controls LCP1, which is crucial for regulating breast cancer cell motility (Pillar, Polsky, & Shomron, 2019). They showed that, in comparison to ABCE1 or LCP1 alone, downregulating LCP1 and ABCE1 combined further lowers cell motility and proliferation in vitro and general survival in vivo (Pillar et al., 2019). Similarly, AIMP3 a new tumor suppressor, drastically reduced NSCLC cell growth and metastasis in both vitro and vivo in a p53-dependent manner (Ding et al., 2021). Ding et al. discovered that miR-96-5p, which was decreased the level in both clinical tumor tissues and cancer cell lines, had AIMP3 as a direct target (Ding et al., 2021). They showed that the miR-96-5p-AIMP3-p53 axis was crucial in NSCLC, and their findings should suggest a new target and approach for clinical NSCLC treatment. In addition, in untreated BGC-823 cells, the miR-96-5p was considerably increased, while in cells that had received SAN, it was significantly downregulated (Dong et al., 2019b). In xenotransplanted tumors treated with SAN, pMEK4 and pINK1 proteins in the MAPK/JNK signaling pathway were likewise increased, as well as the target gene MAP4K4's mRNA and protein expression (Dong et al., 2019b). These suggest that SAN might prevent BGC-823 cells from proliferating by suppressing the production of miR-96-5p, which would then activate the MAPK/JNK signaling pathway.

Table (2): The role of miRNA-96 in cancer considering research in animal models.

Tumor type	**miRNAs**	**Animal model**	**Modification techniques and engrafted cells**	**Associated phenotypes with dysregulation of miRNA-96**	**Ref.**
NSCLC	miRNA-96	BALB/c mice	Tail vein injection of 104 4T1 cells co-transfected with hsa-miR-96 and LCP1 WT	lymph node micro-metastases and tumor severity	(Pillar et al., 2019)

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	miRNA-96-5p	BALB/c-nu/nu nude mice	Subcutaneous injection of A549 cells with transfected AIMP3	-	(Ding et al., 2021)
Gastric cancer	miRNA-96-5p	BALB/c-nude mice	Subcutaneous injection of 6 BGC-823 cells with transfected SAN	-	(Dong et al., 2019a)
Non-alcoholic fatty liver disease	miRNA-96-5p	SD rats	Tail vein injection of BM-MSCs cells transfected with PKH26	↑ miR-96-5p, ↓caspase-2: ↑ NASH development	(El-Derany & AbdelHamid, 2021)

3.3 Studies in clinical samples

The dysregulation of miRNA-96 has been observed in a variety of clinical specimens, indicating that it may have an impact on a number of diseases. For instance, in HCC, Gharib et al. highlighted the ability relevance of serum miRNA-96 as diagnostic HCC biomarkers by showing a strong correlation between high serum levels of miRNA-96-5p and significant tumor growth and metastasis (Gharib et al., 2022a). Likewise, He et al. findings showed that miR-96-5p was overexpressed in both stomach cancer cell lines and patient plasma samples. Additionally, tissue samples from individuals with stomach cancer had lower FOXO3 protein levels (X. He & Zou, 2020). Additionally, miR-96-5p promoted the growth of stomach cancer cells by specifically targeting FOXO3 (X. He & Zou, 2020). As a result, they draw the conclusion that miRNA-96-5p may accelerate the development of stomach cancer by specifically targeting FOXO3 mRNA and suppressing the expression of FOXO3 protein, which adds fresh information about the disease's molecular basis. Furthermore, in comparison to CIN tissues and normal cervical tissues, cervical cancer tissues had a greater expression

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level of miRNA-96 (Gong, 2018). The expression level of miRNA-96 in cervical cancer tissues was importantly associated with histological grade, FIGO stage, and lymph node metastasis (Gong, 2018).

Table (3): Dysregulation of miR-96 in clinical specimens.

Tumor/ disorder type	**Samples**	**miRNA type and expression (Tumor vs. Normal)**	**Targets/ signaling pathways**	**Kaplan-Meier and Cox regression analyses (Impact of miRNA-93 dysregulation)**	**Association of miRNA-96 expression with clinicopathologic characteristics**	**Ref.**
HCC	55 HCC patients + 55 liver cirrhotic patients + 55 control	miRNA-96-5p (Upregulated)		-	-	(Gharib et al., 2022b)
	14 pairs of HCC tissue	miRNA-96 (Upregulated)	GPM6A	Upregulation is associated with poor prognosis	-	(Li et al., 2022)
GC	70 GC patients + 70 healthy controls	miRNA-96-5p (Upregulated)	FOXO3	-	-	(He & Zou, 2020)
	410 GAC samples + 42 healthy controls	miRNA-96-5p (Upregulated)	ZDHHC5	-	-	(Wang, Liu, & Meng, 2020)
	53 GC samples	miRNA-96-5p (Upregulated)	FoxQ1	-	-	(Yang et al., 2019)
Oral squamous cell carcinoma	30 pairs of OSCC tissue	miRNA-96-5p (Upregulated)	FOXF2	-	-	(Wang et al., 2020)

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Colorectal cancer	20 CRC pairs sample	miRNA-96 (Upregulated)	TP53INP1, FOXO1, FOXO3a	-	-	(Gao & Wang, 2015)
	26 CRC pairs sample	miRNA-96-5p (Upregulated)	-	-	-	(P. Y. He et al., 2019)
	110 CRC pairs sample	miRNA-96	PI3K pathway, mTOR pathway	Upregulation is significantly associated with OS	-	(Chen et al., 2022)
Breast cancer	155 BC pairs sample	miR-96-5p (Downregulated)	CTNND1, Wnt/β-catenin signaling	Downregulation is associated with patients' survival	TNM staging and distant metastasis	(Gao et al., 2020)
Cervical cancer	122 CC tissues + 96 CIN tissues + 84 normal tissues	miRNA-96 (Upregulated)	-	Upregulation is associated with overall survival	Histological grade, FIGO stage, lymph node metastasis	(Gong, 2018)
	60 CC pairs sample	miRNA-96-5p (Upregulated)	SFRP4	-	Clinical stages and LN metastasis	(Zhang et al., 2020)
Renal cell carcinoma	11 tumor samples (2 normal sensitive, 3 normal resistant, 3 tumors sensitive, and 3 tumor-resistant samples)	miRNA-96-5p (upregulated)		Upregulation is associated with sunitinib resistance in CCRCC and poor prognosis	-	(Park et al., 2022)

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4. MiRNA-96 and drug resistance

Drug resistance is a major problem while treating cancer patients. Multiple strategies exist for cancer cells to manifest therapy resistance (Hussen, Abdullah, et al., 2022). For instance, Wu et al. demonstrate that miRNA-96 targets LMO7 to accelerate the development of lung cancer (H. Wu et al., 2017). LMO7 overexpression reverted the miRNA-96promoting impact, and LMO7 expression was inversely linked with lung cancer grades. Exosomal miRNA-96 has been found as a blood biomarker of malignant lung cancer (H. Wu et al., 2017). Similarly, as a molecular sponge for miRNA-96 in AML cells, MALAT1 reduced miRNA-96 expression (Hu, Chen, Wang, & Zhao, 2019). The effects of MALAT1 knockdown on the spread, apoptosis, and ara-C sensitivity in AML cells were eliminated by miRNA-96 downregulation (Hu et al., 2019). As a result of upregulating miRNA-96, MALAT1 knockdown reduced spread, boosted apoptosis, and improved ara-C sensitivity in AML cells, offering fresh insights into the crucial function of MALAT1 as a miRNA sponge in AML (Hu et al., 2019). Likewise, Wu et al. findings show that miR-96 targets SAMD9 and decreased the level in NSCLC, which reduces cisplatin's ability to cause apoptosis and promotes the development of cisplatin resistance in NSCLC cells (L. Wu et al., 2016). The results of this study contribute new knowledge about the roles that miR-96 and SAMD9 play in cancer as well as about the molecular processes that underlie chemoresistance in NSCLC (L. Wu et al., 2016). Furthermore, in another study by Wang and his colleges revealed that by suppressing RAD51 and REV1, miR-96 controls DNA repair and chemosensitivity, results in the promotion of cellular sensitivity to cisplatin and PARP inhibition (Y. Wang, Huang, Calses, Kemp, & Taniguchi, 2012). As a potential treatment, miR-96 may boost the effectiveness of chemotherapy by making cancer cells more sensitive to DNA damage.

5. Discussion

The intriguing molecule miR-96 has important implications for human illnesses and medication resistance (Min, Son, Yang, & Lee, 2019). By binding to mRNA and inhibiting its translation or boosting its destruction, and it is essential for post-transcriptional gene control. Cellular processes like cell spread, apoptosis,

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differentiation, and development can all be influenced by miR-96's capacity to enhance gene expression (Bagban et al., 2022).

Researches have shown that miR-96 can act as an oncogene or a cancer suppressor depending on the cellular context and target genes involved (Moazzeni, Najafi, & Khani, 2017). Dysregulation of miR-96 expression has been observed in various cancers, such as breast (Hong et al., 2016b; Xie et al., 2018), lung (H. Guo et al., 2014), prostate (Fendler et al., 2013; Haflidadóttir et al., 2013), and colorectal cancer (Ress et al., 2015). It has been linked to cancer growth, metastasis (Wei et al., 2019), and angiogenesis (Z. Guo et al., 2020), indicating its ability as a diagnostic marker and drug target in cancer. Furthermore, drug resistance has been linked to miR-96, which makes it difficult to treat a number of disorders, including cancer (H. Wu et al., 2017). Studies have demonstrated that altered miRNA-96 expression can influence how responsive cancer cells are to chemotherapeutic treatments by changing the expression of drug targets or components of signaling pathways involved in drug responsiveness (Ge et al., 2020).

The significance of miR-96 in human illnesses and treatment resistance is now being more understood, opening up promising new research directions. Finding the precise target genes and signaling pathways that miR-96 controls in various illness situations may be the main goal of future research. Furthermore, investigating miR-96's potential as a diagnostic biomarker and drug target might result in the creation of customized medicine techniques.

6. Conclusion

In conclusion, novel information about miRNA-96's function in human cancers and treatment resistance has emerged in recent studies. MiR-96 dysregulation has been implicated in different malignant disorders, including lung cancer, breast cancer, colorectal cancer, hepatocellular cancer, renal cancer and other cancers. Additionally, miR-96 can work as an oncogene or a tumor suppressor, impacting tumor growth and progression. In both chemotherapy and targeted therapies, miRNA-96 has also been linked to drug resistance. It can alter the expression of genes include in DNA repair, apoptosis, drug efflux, and drug uptake, affecting how responsive cancer cells are to therapy. In order to pinpoint particular downstream targets, understand the precise

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molecular mechanisms underlying miRNA-96's actions, and create techniques to control its expression or activity, more research is required. These developments could result in brand-new therapeutic approaches and diagnostic instruments to treat human illnesses and get around drug resistance.

Abbreviation

3' UTR	3' untranslated region
AIMP3	Aminoacyl-tRNA synthetase-interacting multifunctional protein-3
Akt	Gene: Protein kinase B or Akt (PKB/Akt)
EGFR	Gene: estimated glomerular filtration rate
ERK1/2	Gene: Extracellular signal-regulated protein kinases 1 and 2
EZRIN	It is proteins known as ERM (Ezrin–Radixin–Moesin)
FOXF2	Gene: Forkhead box protein F2
FOXO1	Gene: Forkhead box protein O1
FOXO3	Gene: Forkhead box protein O3
FOXO3a	Gene: Forkhead box protein O3a (a variant of FOXO3)
FoxQ1	Gene: Forkhead box protein Q1
GPC3	Gene: Glypican-3
GPM6A	Gene: Glycoprotein M6A
HCC	Hepatocellular carcinoma
IRS1	Gene: Insulin receptor substrate 1

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KRAS	Gene: Kirsten rat sarcoma viral oncogene homolog
LDB2	Gene: LIM domain binding 2
MALAT1	Gene: Metastasis Associated Lung Adenocarcinoma Transcript 1
MAP4K1	Gene: Mitogen-Activated Protein Kinase 1
MEG3	Gene: maternally expressed 3
miRNA	Micro-ribonucleic acid
mRNA	messenger ribonucleic acid
MTSS1	Gene: Metastasis suppressor protein 1
NSCLC	Non-small cell lung cancer
PI3K	phosphoinositide 3-kinases
pINK1	PTEN-Induced Putative Kinase Protein 1
pri-miRNA	primary miRNAs
PTPN9	Gene: Protein tyrosine phosphatase non-receptor type 9
RAD51	Gene: RAD51 Recombinase
RECK	Reversion-inducing-cysteine-rich protein with kazal motifs
REV1	DNA Directed Polymerase
SAMD9	Gene: sterile alpha motif domain containing 9
SAN	sinoatrial node
SFRP4	Gene: Secreted frizzled-related protein 4
TP53INP1	Gene: Tumor protein p53-inducible nuclear protein 1

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UBE2N	Gene: Ubiquitin-conjugating enzyme E2 N
XIAP	Gene: X-linked inhibitor of apoptosis protein p53
XPO5	Gene: Exportin-5
ZDHHC5	Gene: Zinc finger DHHC-type containing 5

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تێڕوانینێکی نوێ بۆ microRNA-96 لە تێکچوونە شێرپەنجەییەکانی مرۆڤ و بەرگری دژی دەرمان

پـوختـه:

miRNA-96 گەردیکی کورتی RNA ناکۆدکەر کە رۆڵێکی سەرەکی دەگێڕێت لە ڕێکخستنی جینی دوای لەبەرگرتنەوە، و ڕۆڵی هەیە لە گەشەکردنی ژمارەیەک نەخۆشی، وەک شێرپەنجە، بەپێی دۆخی خانەکە، لەوانەیە وەکو سەرکوتکەری وەرەم یان ئۆنکۆجین کاربکات. بەپێی توێژینەوەکانی ئەم دواییە، ئاستی miRNA-96 کەمی کردەوە لە شێرپەنجەی گەدە، شێرپەنجەی مەمک، شێرپەنجەی پەنکریاس، شێرپەنجەی ، شێرپەنجەی گورچیلە و شێرپەنجەی ملی منداڵداندا. بەڵام miRNA-96 لە چەند جۆرێکی تری شێرپەنجەدا ئاستی زیاد دەکات، لەوانە کۆڵۆن و ڕیخۆڵە، سییەکان، پرۆستات، مێشك، شێرپەنجەی ئێسك و شێرپەنجەی خانەکانی جگەر. لەم توێژینەوەیەیدا پێداچونەوەمان کردوە بۆ پوختەیەک لە ڕۆڵی miRNA-96 لە پێشخستنی نەخۆشییە شێرپەنجەییەکان و جەختکردنەوە لەسەر ئەو میکانیزمانەی کە بۆتە هۆی دروستبوونی شێرپەنجەکان. پشتبەستمان بە

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لێکۆڵینەوەکان لەسەر نمونەی زیندووی مرۆڤ و ئاژەڵ و خانەی چاندراو بەستووە، هەروەها ئێمە جەختمان کردۆتەوە سەر ئەرکی ئەم miRNA-96 وەکو نیشانەیەکی پێشبینیکردنی شێرپەنجە و جەخت لەوە دەکەینەوە کە چۆن بەشداری دەکات لە بەرگریکردن لە دژی دەرمان.

نظرة ثاقبة جديدة لـ microRNA-96 في الاضطرابات الخبيثة البشرية ومقاومة الأدوية

الملخص:

MİRNA-96هو جزيء قصير من الحمض النووي الريبي غير المشفر يلعب دور وظيفة أساسية في تنظيم الجين بعد النسخ ، و تلعب دورًا في تطوير عدد من الأمراض ، مثل السرطان ، اعتمادًا على الإعداد الخلوي ، قد يعمل كورم القامع أو الجين الورمي. وفقا لبحث حديث ، miRNA-96تقل مستوى اصابة في سرطان المعدة وسرطان الثدي ، سرطان البنكرياس وسرطان وسرطان الكلى وسرطان عنق الرحم. ومع ذلك ، تزيد مستوى اصابة MİRNA-96 في عدة أنواع من السرطانات ، بما في ذلك القولون والمستقيم ، والرئة ، والبروستات، والورم الدبقي ،و سرطان العظام ، و سرطانة الخلايا الكبدية. تهدف المراجعة الحالية إلى تقديم ملخص لدور miRNA-96في النهوض بأمراض السرطان ومع التركيز على مسارات الإشارات غير المنظمة. تركز على الأبحاث في الجسم الحي وفي المختبر والبشر ، نراجع أيضًا وظيفة miRNA -96كعلامة بيولوجية للسرطان للتشخيص والتأكيد و كيفية مساهمة في مقاومة الأدوية.