Am J Transl Res 2020;12(12):7682-7692
www.ajtr.org /ISSN:1943-8141/AJTR0121135

Review Article

Promising long noncoding RNA DLX6-AS1 in malignant tumors

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Received August 26, 2020; Accepted November 11, 2020; Epub December 15, 2020; Published December 30, 2020

Abstract: Although its diagnosis and treatment have greatly improved in recent decades, cancer remains the major cause of death worldwide. Thus, there is an urgent need to find novel biomarkers and therapeutic targets to improve efficiency of diagnosis and treatment of patients with cancer. Long noncoding RNAs (lncRNAs), a new class of noncoding RNAs (ncRNAs), have been found to play a salient role in human tumorigenesis and progression. Distal-less homeobox 6 antisense RNA 1 (DLX6-AS1) is a novel lncRNA with aberrant expression in various cancers tissues and cell lines compared with nontumor tissues and normal cell lines. Importantly, DLX6-AS1 is closely associated with tumor cell proliferation, apoptosis, invasion, and migration. Patients with high DLX6-AS1 expression often had poorer prognosis than those with low expression. The oncogenicity of DLX6-AS1 mainly (indirectly or indirectly) interacts with targeting genes, and then regulates downstream genes and signaling pathways. Together with the findings of animal model studies, these data suggest that DLX6-AS1 may serve as a feasible predictor or therapeutic target in different cancers. Herein, we summarize the main findings concerning the function and molecular mechanisms of DLX6-AS1 to identify a molecular basis for future clinical application.

Keywords: DLX6-AS1, malignancy, lncRNA, molecular mechanisms, biomarker

Introduction

Several cancers can result in malignant disease marked by unregulated proliferation, migration, invasion, and apoptosis [1-3]. This represents a major public health problem, and thus, studies have focused on malignancies in a variety of cancer types, including breast cancer [4], lung cancer [5], gastric cancer [6], colorectal cancer [7], and hepatocellular carcinoma (HCC) [8]. In 2015, approximately 8.8 million deaths were caused by cancer, a global increase of 17.0% than 2014 [9]. However, treatments remain limited for advanced cancers and effective indicators are still lacking to diagnose cancer at early stages.

In recent years, with technological advances in transcriptome profiling, many noncoding RNAs (ncRNAs) were revealed to be involved in cellular biological processes, as well as several pathological processes, rather than transcriptional noise with no biological function [10-12]. Long noncoding RNAs (lncRNAs), one of the most common types of ncRNAs, are longer than 200 nucleotides but lack protein-coding capacity [13]. Several studies have found that lncRNAs regulate gene expression and that dysfunction is associated with tumorigenesis and progression of human cancers [14-17]. Therefore, researching lncRNAs may provide novel diagnostic biomarkers and therapeutic targets.

Distal-less homeobox 6 antisense RNA 1 (DLX6-AS1) was first identified as an in-trans modifier increasing the activity of the distal-less homeobox 5/6 enhancer [18]. Several studies have demonstrated that DLX6-AS1 expression is increased in tumor tissues, and is significantly associated with unfavorable outcomes in patients [19-21]. Moreover, studies in vivo and in vitro suggest that the knockdown of DLX6-AS1 suppresses tumor growth, migration, and metastasis. In this review, we summarize the current evidence of DLX6-AS1 in human can-

cers, especially its identification, functions, regulatory mechanisms, and potential clinical application.

Human studies of lncRNA DLX6-AS1

DLX6-AS1 expression in tumor tissues

Many lncRNAs have been found to be aberrantly expressed in cancer, including, PVT1 [22], HORAS5 [23], NEAT1 [24], MNX1-AS1 [25], PCA3 [26], among others. Recently, research groups have explored the expression of DLX6-AS1 in human tissues and its clinical value in various cancers. All studies consistently concluded that DLX6-AS1 is upregulated in patients with cancer. In lung cancer, DLX6-AS1 expression was elevated in lung cancer samples, compared with normal lung samples [20, 27-29]. Meanwhile, data regarding the expression levels of DLX6-AS1 were assessed in several other human cancer samples including HCC [30-32], colon cancer [33, 34], gastric cancer [35-38], breast cancer [21, 39], nasopharyngeal carcinoma (NPC) [40], osteosarcoma [41, 42], thyroid cancer [43], bladder cancer [44, 45], renal cell carcinoma [46], pancreatic cancer [47], and other cancers [48, 49] (**Table 1**).

Clinical and prognostic values of DLX6-AS1 in various cancers

Notably, Kaplan-Meier analyses indicated that patients could be stratified by DLX6-AS1 expression into low or high expression groups, and those with high expression exhibited worse clinical prognoses. In addition, univariate cox regression analysis and multivariate regression analysis demonstrated that DLX6-AS1 is an independent prognostic indictor for disease-free survival or overall survival (OS) in different cancer types.

In human epithelial ovarian cancer, overexpression of DLX6-AS1 was closely correlated to lymph node metastasis, tumor stage, and poor prognosis. Further, univariate cox regression analysis and multivariate regression analysis verified that DLX6-AS1 is an independent risk factor in patients with epithelial ovarian cancer [50]. In patients with bladder cancer, 45 samples were collected and classified according to the DLX6-AS1 expression. And the subgroup with elevated DLX6-AS1 expression had shorter OS time ($P<0.05$) and was remarkably related with the TNM stage ($P=0.006$), lymphatic metastasis ($P=0.038$), and tumor size ($P=0.033$) [22]. A similar conclusion was made in patients with gastric cancer. The findings indicated that DLX6-AS1 may be a promising biomarker because its expression was increased in late-stage gastric cancer samples compared with early-stage samples. In addition, upregulated DLX6-AS1 was correlated with distant metastasis, lymph node metastasis, advanced clinical stage, and poor prognosis [36, 38]. Furthermore, accumulating evidence has demonstrated that the level of DLX6-AS1 in NSCLC samples is positively related to TNM stage and tumor size [20, 27].

Collectively, these results imply that DLX6-AS1 is an oncogene whose expression is markedly related with tumor progression, which may be helpful to predict the prognosis in various cancers.

Expression and function of lncRNA DLX6-AS1 in different cell lines

Many studies have explored the expression of lncRNA DLX6-AS1 in different types of cell lines. These studies have found that silencing or forced overexpression of DLX6-AS1 affected cell proliferation, migration, invasion, and apoptosis in various cancers. Specifically, expression of this lncRNA affects numerous interconnected signaling pathways, including the mTOR, Wnt/β-catenin, TGF-β, and PI3K/AKT pathways. In the following sections, we summarize the role of DLX6-AS1 in various cancer cell lines.

Lung cancer

Lung cancer is now the most common malignancy and the leading cause of tumor-related death worldwide [51, 52]. LncRNAs are novel regulatory molecules in lung cancer development and progression [53-56]. A growing number of findings have shown that DLX6-AS1 affects biological processes of the tumor cell. Sun et al. revealed that DLX6-AS1 is highly expressed in NSCLC cells and its downregulation suppresses NSCLC cell clone formation, migration, and invasion through the miR-27b-3p/GSPT1 axis [20]. Consistent with these results, Huang et al. demonstrated that silencing DLX6-AS1 decreased NSCLC cell proliferation, migration, invasion, and pro-apoptosis through regulating expression of miR-144 and

Table 1. Clinical features of DLX6-AS1 in human cancers

Cancer types	Number (cancer and normal tissues)	Expression	Relationship with clinicopathologic parameters	Property	Reference
Lung cancer	51 pairs	upregulated	size of tumor, TNM stage	oncogenic	[20]
	48 pairs	upregulated	/	oncogenic	[29]
	72 pairs	upregulated	histological differentiation, TNM stage	oncogenic	[28]
Nasopharyngeal carcinoma (NPC)	72 pairs	upregulated	/	oncogenic	[40]
Hepatocellular carcinoma (HCC)	48 pairs	upregulated	/	oncogenic	[31]
	30 pairs	upregulated	/	oncogenic	[32]
	60 pairs	upregulated	tumor size, TNM stage	oncogenic	[30]
Cervical cancer (CC)	60 pairs	upregulated	/	oncogenic	[59]
Osteosarcoma	80 pairs	upregulated	clinical stage	oncogenic	[42]
Ewing's sarcoma	20 pairs	upregulated	/	oncogenic	[41]
Laryngeal cancer	43 pairs	upregulated	primary tumor, tumor stage, lymphatic metastasis, distant metastasis	oncogenic	[62]
Thyroid cancer	60 pairs	upregulated	/	oncogenic	[43]
Colorectal Cancer	76 pairs	upregulated	TNM stage, lymphatic metastasis	oncogenic	[34]
	60 pairs	upregulated	T stage, distant metastasis	oncogenic	[33]
Human epithelial ovarian cancer (EOC)	128 pairs	upregulated	FIGO stage, lymph node metastasis	oncogenic	[50]
Ovarian cancer	58 pairs	upregulated	/	oncogenic	[61]
Bladder cancer (BC)	80 pairs	upregulated	/	oncogenic	[44]
	54 pairs	upregulated	TNM stage, lymphatic node metastasis, distant metastasis	oncogenic	[45]
Triple-negative breast cancer (TNBC)	47 tumor tissues and 28 normal tissues	upregulated	/	oncogenic	[39]
Breast cancer	45 pairs	upregulated	tumor size, lymph node status	oncogenic	[21]
Neuroblastoma	36 tumor tissues and 18 normal tissues	upregulated	TNM stage	oncogenic	[48]
	70 pairs	upregulated	distant metastasis	oncogenic	[49]
Renal cell carcinoma	15 pairs	upregulated	metastasis	oncogenic	[46]
Esophageal squamous cell carcinoma (ESCC)	73 pairs	upregulated	differentiation status, lymph node metastasis, TNM stage	oncogenic	[57]
Gastric Cancer	60 pairs	upregulated	tumor size, lymph node involvement, TNM stage	oncogenic	[35]
	56 pairs	upregulated	invasion, distant metastasis	oncogenic	[36]
	62 pairs	upregulated	metastasis, TNM stage	oncogenic	[38]
Pancreatic cancer	84 pairs	upregulated	tumor size, TNM stage, lymph node metastasis	oncogenic	[47]
	60 pairs	upregulated	/	oncogenic	[64]

PRR11 genes. In addition, Zhang et al. suggested that DLX6-AS1 expression is increased in NSCLC cell lines and that DLX6-AS1 knockdown suppresses cell proliferation and migration [27].

Hepatocellular carcinoma

Studies have reported that DLX6-AS1 is elevated in HCC cell lines compared with a normal human liver cell line. Downregulated DLX6-AS1 suppresses HCC cell proliferation, migration, and invasion. Moreover, bioinformatics analysis revealed miR-203a potentially targets DLX6-AS1 3'UTR, and miR-203a targets MMP-2 during tumorigenesis [30]. Li et al. demonstrated that DLX6-AS1 could regulate miR-424-5p, and oncogene WEE1 (G2 checkpoint kinase) expression is the target of miR-422-5p and associated with DLX6-AS1 expression [32]. Furthermore, in liver cancer stem cells, silencing lncRNA DLX6-AS1 impaired the stem cell properties of liver cancer stem cells by limiting the methylation of CADM1 promoter and activating the STAT3 signaling pathway [31].

Gastric cancer

In gastric cancer cells, functional analysis had showed that highly expressed DLX6-AS1 is obviously related with the enhancement of cell proliferation, migration, invasion, EMT, and apoptotic induction. Regarding the molecular mechanism, Qian et al. verified that DLX6-AS1 knockdown inhibits aerobic glycolysis but promotes mitochondrial respiration in gastric cancer cells by targeting miR-4290 and 3-phosphoinositide-dependent protein kinase 1 [35]. Liang et al. demonstrated that DLX6-AS1 serves as a competing endogenous RNA through targeting miR-204-5P and increasing OCT1 expression [36]. Meanwhile, Wu et al. reported that DLX6-AS1 regulates gastric cancer cell progression through the DLX6-AS1/FUS/MAP4K1 axis [37].

Esophageal squamous cell carcinoma

The role and potential mechanism of DLX6-AS1 in squamous cell carcinoma has rarely been assessed. The expression of DLX6-AS1 was upregulated in esophageal squamous cell carcinoma cell lines, as shown by qRT-PCR [57]. Functional analysis revealed that inhibiting DLX6-AS1 significantly attenuates cell proliferation, migration, and invasion, yet enhances apoptosis [57, 58].

Colorectal cancer

Some research groups have reported that DLX6-AS1 is obviously increased in colorectal cancer cells relative to normal human colorectal epithelial cell lines and that silencing DLX6-AS1 can block the malignant characteristics of colorectal cancer cells. Mechanistically, Kong et al. showed that DLX6-AS1 targets miR-26a and miR-26a upregulates the expression of *EZH2* [34]. Additional evidence indicated that DLX6-AS1 promotes colorectal cancer cell malignant characteristics through the PI3K/AKT pathway [33].

Breast cancer

In breast cancer cells, the DLX6 expression was enhanced in cell lines. DLX6-AS1 knockdown increased cell apoptosis and suppressed cell proliferation and EMT. Moreover, dual luciferase reporter and RNA pull-down assays revealed that DLX6-AS1 interacts with miR-199b-5p modulating the expression of paxillin [39]. Meanwhile, another study found that DLX6-AS1 promotes breast cancer malignant characteristics through the miR-505-3p/RUNX2 axis [21].

Other cancers

In cervical cancer cells, elevated DLX6-AS1 expression is significantly related with cell proliferation, EMT, migration, and anti-apoptosis [59]. One study reported that DLX6-AS1 increases the cellular process via sponging miR-16-5p, which targets the downstream gene *ARPP19* [60]. Meanwhile, some evidence was uncovered that DLX6-AS1 is much higher in epithelial ovarian cancer cells, and downregulation of this lncRNA weakened cells' malignant characteristics via targeting miR-613 or regulating the Notch signaling pathway [50, 61].

Studies have showed a promotive role for DLX6-AS1 in nasopharyngeal carcinoma [40], osteosarcoma [42], thyroid cancer [43], bladder cancer [45], renal cell carcinoma [46], pancreatic cancer [47], and other cancers. **Table 2** summarizes the evidence concerning its expression, functional analyses, and underlying mechanism of DLX6-AS1 in diverse malignant cancers.

Table 2. Expression pattern and function of DLX6-AS1 in cell lines and animal models

Cancer types	Assessed cancer cell lines	Expression	Related genes and pathways	Biological significance	Reference
Lung cancer	CALU3, CALU6, A549, H1229	up	miR-27b-3p, GSPT1	proliferation, migration, invasion	[20]
	NSCLC A549, H1299, 95D	up	/	proliferation, migration	[27]
	H1975, A549	up	miR-144, PRR11	proliferation, migration, invasion, anti-apoptosis	[29]
	A549, H1650	up	/	/	[28]
Nasopharyngeal carcinoma (NPC)	S26, CNE-1, CNE-2, HONE-1, 5-8F	up	miR-199a-5p, HIF-1α	proliferation, migration, invasion	[40]
Hepatocellular carcinoma (HCC)	SMMC-7721, HCCLM3, Hep3B, HepG2, Huh7	up	CADM1, STAT3 signaling pathway	self-renewal, proliferation, proliferation	[31]
	MHCC97L, HCCLM3, SK-HEP-1, Hep3B, Huh7	up	miR-424-5p, WEE1	proliferation, migration, invasion	[32]
	HepG2, HCCLM3	up	miR-203a, MMP-2	proliferation, migration, invasion	[30]
Cervical cancer (CC)	SiHa, HeLa, C-33A, CaSki	up	miR-16-5p, ARPP19	proliferation, migration, EMT, anti-apoptosis	[60]
	HeLa, SiHa, C4-1, C-33a	up	FUS	proliferation, invasion	[59]
Osteosarcoma	MG63 and U2OS	up	miR-129-5p, DLK1, Wnt signaling	stemness	[42]
Ewing's sarcoma	SK-ES-1, A673, RD-ES, MSCs	up	miR-124-3p, CDK4	proliferation, anti-apoptosis	[41]
Laryngeal cancer	HEp-2, Tu-177	up	miR-26a, TRPC3 axis	proliferation, mitochondrial metabolism	[62]
Thyroid cancer	TPC-1, K1, SW579	up	UPF1	migration, invasion	[43]
Colorectal Cancer	DLD-1, HCT-116, HT-29, SW480, SW620	up	miR-26a, EZH2	proliferation, cell cycle, migration, invasion	[34]
	HCT116, HT-29, SW480	up	PI3K, AKT, mTOR pathway	proliferation, invasion, migration, apoptosis	[33]
Epithelial ovarian cancer (EOC)	IOSE80, HEY, SKOV3, OVCAR-3	up	Notch signaling pathway	proliferation, migration, invasion, cell cycle, anti-apoptosis	[50]
Ovarian cancer	A2780, SKOV3, OVCAR-3	up	miR-613	cell migration, invasion	[60]
Bladder cancer	T24, SW780	up	miR-223, HSP90B1	proliferation, invasion	[44]
	5637, J82 and T24	up	Wnt/β-catenin signaling pathway	proliferation, invasion, migration, EMT	[45]
Triple-negative breast cancer (TNBC)	HCC1599, MDA-MB-231, HCC1806, HS578 T	up	miR-199b-5p, paxillin	proliferation, EMT, anti-apoptosis	[39]
Breast cancer	MDA-MB-231, MCF-7, MDA-MB-468, T47D, BT-474	up	miR-505-3p, RUNX2	proliferation, invasion, migration, anti-apoptosis	[21]
Glioma carcinogenesis	U251, U87MG, T98G, SHG44	up	miR-197-5p, E2F1	proliferation, invasion	[63]
Neuroblastoma	NB-1643, NB-1691, SK-N-AS, IMR-32, SH-SY5Y, SK-N-SH	up	miR107, BDNF	growth, invasion, metastasis, differentiation	[48]
	SK-N-SH, SH-SY5Y, SK-N-AS, SK-N-BE	up	miR-497-5p, YAP1	proliferation, migration, invasion ability, EMT	[49]
Renal cell carcinoma	A498, ACHN, Caki-1, Caki-2, 786-O, G401	up	miR-26a, PTEN	proliferation, cell cycle, anti-apoptosis	[46]
Esophageal squamous cell carcinoma (ESCC)	Eca109, Ec9706, TE-1, TE-10, TE-11, KYSE-520	up	/	proliferation, invasion	[58]
	EC109, KYSE30	up		proliferation, anti-apoptosis, invasion	[57]
Gastric Cancer	HGC-27, MGC803, SGC7901, MKN45	up	miR-4290, PDK1	anti-apoptosis, proliferation, glucose metabolism	[35]
	MKN-7, MKN-28, MGC-803, HGC-27, MKN-45, AGS, SGC-7901	up	miR-204-5p, OCT1	proliferation, migration, invasion, EMT	[36]
	AGS, HGC-27, SGC-7901, BGC-823	up	FUS, MAP4K1	proliferation, migration, EMT	[37]
	HGC27, BGC823, SGC7901, AGS	up	/	proliferation, cell cycle, migration, invasion, EMT	[38]
Pancreatic cancer	CAPAN-1, BxPC-3, SW 1990, PANC-1	up	miR181b	proliferation, migration, invasion	[47]
	Panc-1, Bxpc-3, AsPC-1, Capan-1, CFPAC-1, MIA PaCa-2	up	miR-497-5p, FZD4, FZD6, Wnt/β-catenin	proliferation, invasion, migration, anti-apoptosis	[64]

Table 3. Assessed function of DXL6-AS1 in animal models

Cancer	Model type	Know-down DXL6-AS	Reference
Lung cancer	male BALB/c nude mice	suppressed tumor growth	[20]
	male BALB/c nude mice	suppressed tumor growth	[29]
Hepatocellular carcinoma (HCC)	NOD-SCID mice	suppressed tumor growth	[31]
	male BALB/c nude mice	suppressed tumor growth	[30]
Cervical cancer (CC)	BALB/c nude mice	suppressed tumor growth	[60]
	NOD/SCID mice	suppressed tumor growth and lung metastatic	[59]
Osteosarcoma	male BALB/c nude mice	suppressed tumor formation	[42]
Laryngeal cancer	male BALB/c nude mice	suppressed tumor growth	[62]
Thyroid cancer	NOD/SCID mice	suppressed lung metastatic	[43]
Bladder cancer	BALB/c nude mice	suppressed tumor growth	[44]
Triple-negative breast cancer (TNBC)	BALB/c nude	suppressed tumor growth	[39]
Glioma carcinogenesis	male nude mic	suppressed tumor growth	[63]
Neuroblastoma	male BALB/c athymic nude mice	suppressed tumor growth	[48]
	female nude BALB/c mice	suppressed tumor growth	[49]
Pancreatic cancer	female BABL/c athymic nude mice	suppressed tumor growth and metastasis	[47]
	BALB/c nude mice	suppressed tumor growth and metastasis	[64]

Studies of lncRNA DLX6-AS1 in animal models

Studies have explored the effects of DLX6-AS1 knockdown or overexpression in tumor-bearing nude mice. Regarding NSCLC, nude mice were injected with NSCLC cells transfected with shDLX6-AS1 or shNC. The results showed that tumors with shDLX6-AS1 obviously decreased than those with shNC ($P<0.001$). In addition, the Ki67 and GSPT1 expression of tumor tissues were lower in the shDlX6-AS1 subgroup than in the control group [20]. Regarding HCC, Sun et al. found that DLX6-AS1 knockdown mice had remarkably reduced tumor size after being subcutaneously implanted with HCC cells, including HCCLM3 cells and HepG2 cells [30]. Moreover, a signal study investigated the effect of DLX6-AS1 in laryngeal tumor-bearing mice model, silencing DLX6-AS1 promoted mitochondrial metabolism but inhibited the IRPC3 expression [62]. Researchers also concluded that DLX6-AS1 was a tumor-promoting lncRNA in breast cancer [39], glioma carcinogenesis [63], and pancreatic cancer [47, 64] using xenografted nude mice.

All evidence indicates that DLX6-AS1 facilitates disease progression but silencing DLX6-AS1 can suppress tumor growth in several cancers. **Table 3** summarizes the studies of silencing or overexpressing DLX1-AS1 in animal models.

Conclusions

As a novel class of ncRNAs, lncRNAs have attracted much attention about their crucial regulation function, such as affecting cancer cell proliferation, apoptosis, invasion, migration, and drug sensitivity [65]. LncRNA DLX6-AS1, a tumor-promoting gene, has pleiotropic effects in several cancers. Notably, the expression levels of DLX6-AS1 in tumor samples were remarkably elevated than normal samples, as assessed by qRT-PCR and immunohistochemical analysis. This observation emphasized that aberrant expression of DLX6-AS1 does not depend on the tissue type. Through further analysis of the relationship within the expression level of DLX6-AS1 and clinicopathological characters in patients with different kinds of cancers, we found that DLX6-AS1 is strongly connected with advanced TNM stage. Together with Kaplan-Meier analyses, univariate cox regression analysis, and multivariate regression analysis, we concluded that this lncRNA is an independent risk factor and may be a promising biomarker for more than a dozen human cancers, including NSCLC, HCC, nasopharyngeal carcinoma, osteosarcoma, renal cell carcinoma, and cancers of the thyroid, bladder, colon, stomach, breast, and pancreas.

Specifically, this lncRNA was increased in tumor cells. Furthermore, using gene knockdown and overexpression technology, it was demonstrated that this lncRNA participates in diverse cancer biological processes, such as metastasis, and apoptosis. In terms of molecular mechanisms, the oncogenic function of DLX6-AS1 is complicated due to its ability to regulate the target multiple genes expression and interlinking signaling pathways related with various cancers (**Figure 1**). Nude mice were subcutane-

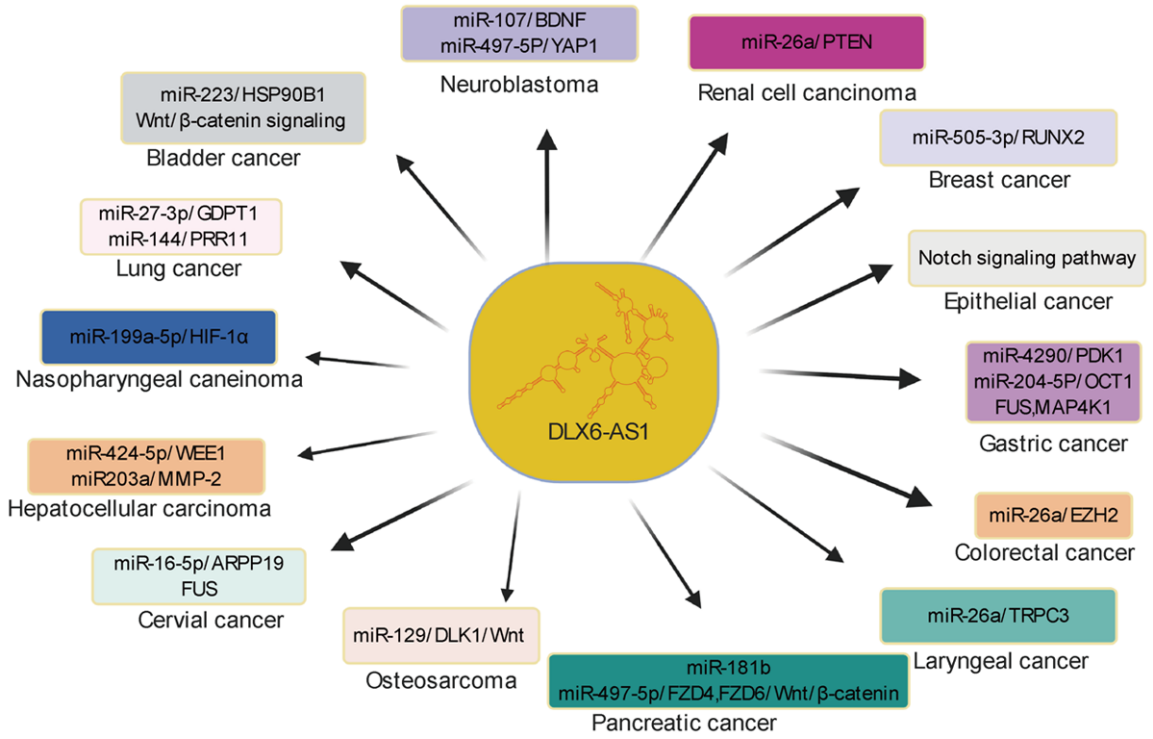

Figure 1. Schematic representation showing interaction between DLX6-AS1 and target miRNA or/and interlinking signaling pathways in various cancers.

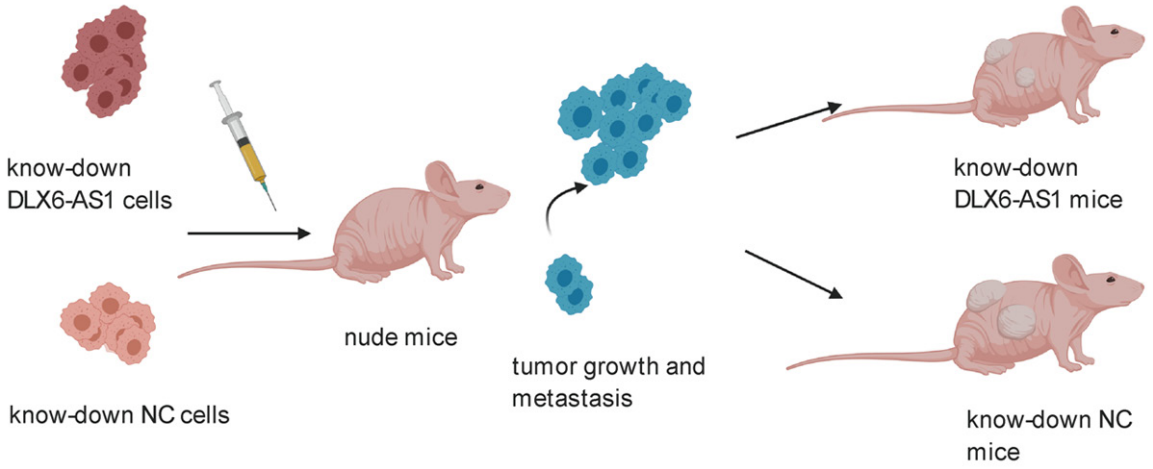

Figure 2. Knock-down DLX6-AS1 suppress the rumor growth in animal models.

ously implanted with tumor cells transfected with shDLX6-AS1, overexpressed DLX6-AS1, or shNC to assess the function of DLX6-AS1 in vivo. Taken together, current evidence indicates that DLX6-AS1 is an oncogene and interfering with this lncRNA can impair the tumor growth of several cancers (**Figure 2**).

The diversity of involved miRNAs, target genes, and signaling pathways even within one cancer type suggests the complexity of human cancer. Based on the literature presented herein, the findings uncover a critical role for DLX6-AS1 in cancers. Importantly, the central role of DXL6-AS1 is an essential shared character in almost all cancer types and indicates to the enormous possibility of DXL6-AS1 as a target in cancer therapy. Considering the complicated mechanism of DXL6-AS1 promote tumor development, targeting this gene may also induce toxic-

ity to normal human tissues. The detailed regulatory mechanisms including upstream and downstream molecules remain to be systematically researched. Extensive research concluded that the expression level of DXL6-AS1 could serve as a prognostic indicator because of its high expression in tumor tissues related with poorer prognosis and clinicopathological parameters, but the expression level of DXL6-AS1 in easily obtained human samples (for example, plasma) have not been clearly explored. Thus, ongoing efforts to explore the expression level of this lncRNA in human samples through the method of liquid biopsies and to clarify the underlying mechanisms promise that DXL6-AS1 will ultimately reach the clinic. We are optimistic that this review will contribute to better understanding of DLX6-AS1 and its relationship with a variety of cancers to act as a stepping stone for future clinical application.

Acknowledgements

This study is funded by the National Natural Science Foundation of China (81790631, 81570512 and 81672422), the National Key Research and Development Program of China (2018YFC2000500), the Natural Science Foundation of Zhejiang Province in China (LQ19H030007), Zhejiang Province Health Department Program (2021KY657), and Dr. Xue was supported by Zhejiang University Academic Award for Outstanding Doctoral Candidates (2020055).

Disclosure of conflict of interest

None.

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