frontiers in Cell and Developmental Biology

REVIEW
published: 03 February 2022
doi: 10.3389/fcell.2022.832388

The LncRNA DUXAP10 Could Function as a Promising Oncogene in Human Cancer

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Cancer is one of the most prevalent and deadliest diseases globally, with an increasing morbidity of approximately 14 million new cancer cases per year. Identifying novel diagnostic and prognostic biomarkers for cancers is important for developing cancer therapeutic strategies and lowering mortality rates. Long noncoding RNAs (lncRNAs) represent a group of noncoding RNAs of more than 200 nucleotides that have been shown to participate in the development of human cancers. The novel lncRNA DUXAP10 was newly reported to be abnormally overexpressed in several cancers and positively correlated with poor clinical characteristics of cancer patients. Multiple studies have found that DUXAP10 widely regulates vital biological functions related to the development and progression of cancers, including cell proliferation, apoptosis, invasion, migration, and stemness, through different molecular mechanisms. The aim of this review was to recapitulate current findings regarding the roles of DUXAP10 in cancers and evaluate the potential of DUXAP10 as a novel biomarker for cancer diagnosis, treatment, and prognostic assessment.

Keywords: DUXAP10, lncRNAs, cancer, function, clinical applications

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Specialty section:
This article was submitted to Cancer Cell Biology, a section of the journal Frontiers in Cell and Developmental Biology

Received: *09 December 2021*
Accepted: *18 January 2022*
Published: *03 February 2022*

Citation:
Zhao J, Xu L, Dong Z, Zhang Y, Cao J, Yao J and Xing J (2022) The LncRNA DUXAP10 Could Function as a Promising Oncogene in Human Cancer. Front. Cell Dev. Biol. 10:832388. doi: 10.3389/fcell.2022.832388

INTRODUCTION

Despite significant advances in clinical diagnostic and treatment options, many diseases still have high mortality rates, high health care costs. And poor quality of life, especially cancer (Lee et al., 2018; Moliner et al., 2019; Sidney et al., 2019; Mulder et al., 2021; Su et al., 2021). Cancer (Mohsen et al., 2014; Christensen et al., 2018; Kannan et al., 2021; Mokgautsi et al., 2021) has become one of the most common causes of death worldwide, and the identification of cancer-related targets and relevant carcinogenesis mechanisms for patients at the early stage of the disease are urgently needed (Saha et al., 2019; Jiang et al., 2020; Brennan and Smith, 2021; Hua et al., 2021; Jones et al., 2021).

Long noncoding RNAs (Zhu et al., 2013; Rathinasamy and Velmurugan, 2018; Zheng et al., 2021; Ma et al., 2022) (lncRNAs) represent a special type of non-coding RNA with more than 200 nucleotides that are not translated into proteins. The aberrant expression of lncRNAs has been frequently observed in a variety of diseases, including human malignancies (Isin and Dalay, 2015; Bhan et al., 2017; Bian et al., 2021; Homayoonfal et al., 2021; Liu and Lei, 2021). Moreover, an increasing number of studies have shown that lncRNAs are involved in the pathogenesis and development of many cancers and are associated with different clinicopathological features (Wang et al., 2021b; Dong et al., 2021; Ma et al., 2021; Zhou et al., 2021). For example,

TABLE 1 | DUXAP10 expression and clinicopathological features in cancers.

Disease type	Expression	Clinical characteristics	Refs
liver cancer	upregulation	overall survival rate and progression-free survival rate	(Zhu et al., 2018; Han et al., 2019; Sun et al., 2019)
kidney cancer	upregulation	male sex, tumor size, TNM stage, lymph node metastasis, pathologic stage, and overall survival rate	Chen et al. (2020)
lung cancer	upregulation	tumor size, pathological stage, lymph node metastasis, overall survival rate, relapse-free survival rate, and poor prognosis	(Wei et al., 2017; Lin et al., 2021)
glioma	upregulation		Wu et al. (2021)
thyroid carcinoma	upregulation		Li et al. (2020)
prostate cancer	upregulation		Wang et al. (2019a)
chronic myelogenous leukemia	upregulation	clinical stage	Yao et al. (2018)
ovarian cancer	upregulation	tumor size and FIGO stage	Zhang et al. (2018)
gastric cancer	upregulation	pathological stage, lymph node metastasis, and poor prognosis	Xu et al. (2018)
pancreatic cancer	upregulation	TNM stage, lymph node metastasis, and poor prognosis	Lian et al. (2018)
bladder cancer	upregulation		Lv et al. (2018)
colorectal cancer	upregulation	pathological stage, tumor size, lymph node metastasis, and poor prognosis	Lian et al. (2017)
esophageal squamous cell carcinoma	upregulation	TNM stage, lymph node metastasis, and survival time	Wang et al. (2018)

overexpression of the lncRNA MCM3AP-AS1 (Wang et al., 2019b) has been shown to modulate hepatocellular carcinoma (HCC) occurrence and progression and is strongly correlated with advanced tumor grade and stage, large tumor size, and poor prognosis. Additionally, a high expression level of the lncRNA AK023391 (Huang et al., 2017) was found to exert a pivotal role in gastric cancer (GC) oncogenesis and development and was significantly linked to decreased survival rates. Functionally, lncRNAs have been demonstrated to frequently participate in the regulation of multiple crucial biological processes (Gao et al., 2020; Le et al., 2021; Yi et al., 2021; Zheng et al., 2021; Zhu et al., 2021), such as cell proliferation, apoptosis, and invasion. Given the complex functions of lncRNAs in cancers, lncRNAs exhibit tremendous potential for use in tumor diagnosis, prognosis, and treatment.

Recently, the pseudogene lncRNA DUXAP10 (DUXAP10) (Booth HA, and Holland PW., 2007; Zhu et al., 2018), localized on chromosome 14q11.2, was found to be overexpressed in multiple cancers, including HCC, bladder cancer (BC), non-small-cell lung cancer (NSCLC), glioma, renal cell carcinoma (RCC), papillary thyroid carcinoma (PTC), prostate cancer (PCa), chronic myelogenous leukemia (CML), ovarian cancer (OC), pancreatic cancer (PC), GC, colorectal cancer (CRC), esophageal squamous cell carcinoma (ESCC) and oral squamous cell carcinoma (OSCC). Its aberrant expression level was predominantly in line with many poor clinical characteristics. Studies of the biological functions of DUXAP10 showed that DUXAP10 can exhibit protumor effects on regulating cell processes, such as cell proliferation, apoptosis, migration, and invasion, by targeting specific genes or through a variety of different specific pathways. Therefore, the above evidence implicates the high potential of DUXAP10 as a biomarker for cancer diagnosis prognosis and therapy.

In this review, we summarize the roles of DUXAP10 in different cancers, including dysregulated expression, related clinical characteristics, biological functions underlying molecular mechanisms, and potential clinical applications.

THE ROLE OF THE LNCRNA DUXAP10 IN DIFFERENT CANCERS

Several studies have reported that DUXAP10 is aberrantly expressed in numerous human cancers, such as HCC, BC, NSCLC, glioma, RCC, PTC, PCa, CML, OC, PC, GC, CRC, ESCC, and OSCC. In addition, it was demonstrated that a high DUXAP10 expression level was positively related to advanced clinicopathological features (**Table 1**). The diverse regulatory functions and underlying mechanisms of DUXAP10 during tumor progression are shown in **Table 2**.

We next discuss the DUXAP10 expression level, relevant clinical characteristics, and biological functions in different cancer types.

Liver Cancer

Liver cancer is one of the leading causes of cancer death worldwide (Sun et al., 2013; Zhao et al., 2015; Kido et al., 2020). Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer (Ahn et al., 2018; Xu et al., 2021). Numerous studies have recently revealed that DUXAP10 was overexpressed in HCC cell lines (including Hep3B, HepG2, SMMC7721, HuH7, MHCC-97L, MHCC-97H, HCC-LM, and SK-Hep-1 cells) and tissues (Zhu et al., 2018; Han et al., 2019; Sun et al., 2019). And its level was positively related to the severity of HCC, higher DUXAP10 expression was observed in advanced HCC patients. In addition, a high expression level of DUXAP10 was significantly correlated with poor overall survival (OS) and

TABLE 2 | Functions and mechanisms of DUXAP10 in cancers.

Disease type	Cell lines	Related mechanisms		Functions	Refs
		Molecule	Pathway		
liver cancer	Hep3B, Hep G2, SMMC7721, HuH7, MHCC-97L, MHCC-97H, HCC-LM, and SK-Hep-1	microRNA-1914, and GPR39	PI3K/AKT/mTOR pathway, and Wnt/β-catenin pathway	cell cycle, colony formation, proliferation, epithelial-mesenchymal transition, metastasis, and apoptosis	(Zhu et al., 2018; Han et al., 2019; Sun et al., 2019)
kidney cancer	786-O and A498			cell cycle, proliferation, apoptosis, migration, and invasion	Chen et al. (2020)
lung cancer	A549, H1975, SPC-A1, H1299, and BEAS-2B	Cd, Pax6, GLI1, LSD1, LATS2, and RRAD	Hedgehog pathway	cell cycle, proliferation, migration and invasion, and cancer stem cell transformation	(Wei et al., 2017; Lin et al., 2021)
glioma	HS683, U251, U373, U87, T98G LN-319 and SW1783	HuR, CD133, Oct4, and Sox12		cell stemness	Wu et al. (2021)
thyroid carcinoma	TPC-1, BCPAP, K1, and IHH-4		Akt/mTOR pathway	cell proliferation, apoptosis, invasion, and migration	Li et al. (2020)
prostate cancer	PC3, 22RV1, and DU145			cell cycle, proliferation, and metastasis	Wang et al. (2019a)
chronic myelogenous leukemia	THP-1, KG-1, and K562	PTEN		cell proliferation, apoptosis, and cell cycle	Yao et al. (2018)
ovarian cancer	HO8910 and A2780			cell proliferation	Zhang et al. (2018)
gastric cancer	BGC823, SGC7901, MGC803, AGS, HGC27, and MKN45	PRC2, LSD1, HuR, KLF2, LATS1, and β-catenin		cell proliferation, cell cycle, invasion, and migration	Xu et al. (2018)
pancreatic cancer	AsPC-1, BxPC-3, and PANC-1	EZH2, and LSD1		cell cycle, proliferation, and apoptosis	Lian et al. (2018)
bladder cancer	5,637, T24, E-j, TCCSUP, UM-UC-3, and RT4		PI3K/Akt/mTOR pathway	cell cycle, proliferation, and apoptosis	Lv et al. (2018)
colorectal cancer	HCT116, SW620, and SW480	LSD1, PTEN, and p21		cell proliferation, apoptosis, and cell cycle	Lian et al. (2017)
esophageal squamous cell carcinoma	KYSE30, KYSE510, KYSE180, and KYSE150	EZH2, and p21		cell cycle, proliferation, metastasis, and apoptosis	Wang et al. (2018)

progression-free survival (PFS) rates (Han et al., 2019). It has also been proven to exert pivotal pro-oncogenic functions in the regulation of cell cycle progression, colony formation, proliferation, epithelial-mesenchymal transition (EMT), invasion, migration, and cell apoptosis in SMMC-7721, Hep G2, Hep3B, and MHCC-97L cells.

Kidney Cancer

Renal cell carcinoma (RCC), arising from the renal epithelium (Wang et al., 2020b; Singh et al., 2020), is the most common kidney tumor (Wang et al., 2017; Chen et al., 2018). High expression of DUXAP10 was observed in 18 RCC specimens collected from the Urology Department of Peking University Shougang Hospital and 786-O and A498 cell lines in comparison with adjacent normal tissues and normal kidney epithelial cells (HKCs). Its level was positively correlated with male sex, tumor size, TNM stage, lymph node metastasis, and advanced pathologic stage. Additionally, Kaplan–Meier analysis further verified the strong link between DUXAP10 and poor overall patient survival. DUXAP10 has been proven to have pro-oncogenic functions in the regulation of cell proliferation, cell cycle transition to the S phase, cell apoptosis, cell migration, and invasion.

Lung Cancer

Lung cancer (Molina et al., 2008; Zhang et al., 2019; Chen et al., 2021b) remains the leading cause of cancer-related mortality worldwide, with approximately 1.8 million (Chen et al., 2021a; Sung et al., 2021) deaths per year. While there has been a modest improvement in lung cancer (Sławińska-Brych et al., 2021) OS in recent decades, further studies are needed to improve patients' clinical outcomes. Several studies have reported that DUXAP10 is significantly upregulated in 93 human cancer tissues obtained from The First and Second Affiliated Hospital of Nanjing Medical University, non-small-cell lung cancer (NSCLC) cell lines (A549, H1975, SPC-A1, and H1299 cells) and the chronic cadmium (Cd)-induced human bronchial epithelial BEAS-2B cell line. A high level of DUXAP10 expression in lung cancer patients was linked to not only lower OS and relapse-free survival (RFS) rates but also larger tumor sizes, advanced tumor stages, lymph node metastasis, and even poor prognosis (Wei et al., 2017; Lin et al., 2021). Moreover, *in vitro* functional assays and *in vivo* tumor models have demonstrated that DUXAP10 is mainly implicated in eliciting the transformation of Cd-exposed (Cd-T) cells to cancer stem cells (CSCs), promoting the cell cycle progression, proliferation, migration, and invasion of A549 or H1975 cells, and thus accelerating tumorigenesis and progression in lung cancer.

Glioma

Gliomas are the most common primary malignancy of the central nervous system (Briançon-Marjollet et al., 2010; Deluche et al., 2019; Shi et al., 2020a). DUXAP10 has been indicated to be highly expressed in glioma cell lines (HS683, U251, U373, U87, T98G

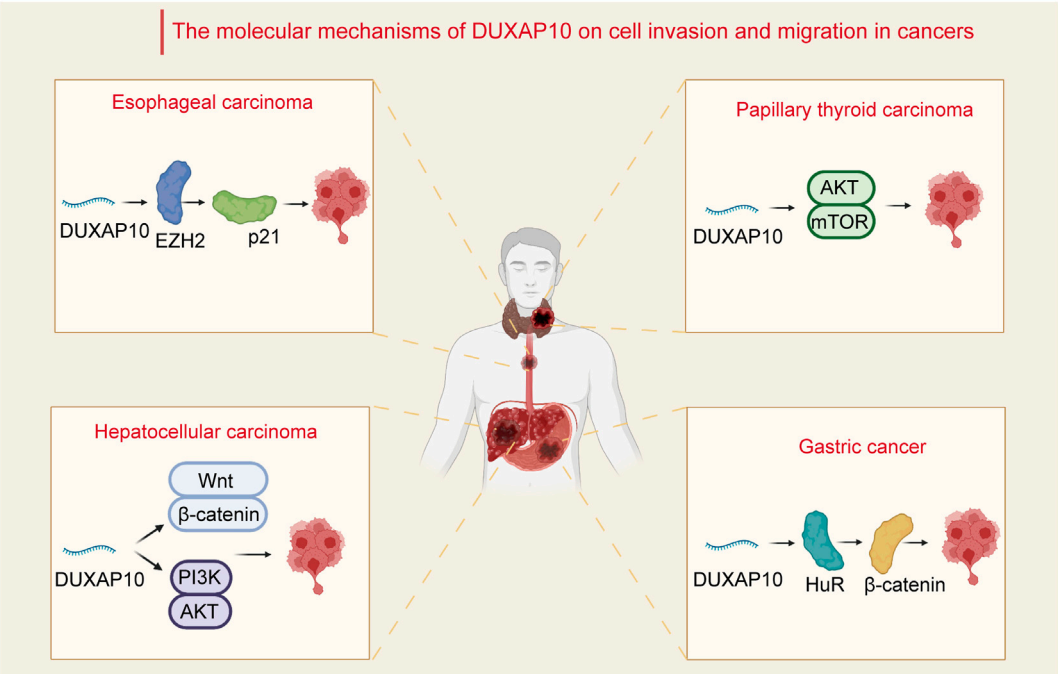

FIGURE 1 | Relevant molecular mechanisms of DUXAP10 in the process of cell invasion and migration in cancers. In hepatocellular carcinoma, DUXAP10 enhances cell invasion and migration through the Wnt/*β*-catenin and PI3K/Akt signaling pathways. In papillary thyroid carcinoma, DUXAP10 mediates the activity of the Akt/mTOR pathway to regulate cancer cell invasion and migration. In gastric cancer, DUXAP10 is involved in the regulation of invasion and migration via combination with the RNA-binding protein HuR and subsequently increases the stability of *β*-catenin. In esophageal carcinoma, DUXAP10 regulates cell metastasis by binding with EZH2 and inhibiting p21 expression.

LN-319, and SW1783 cells) and tissues gained from patients under surgery at the First Affiliated Hospital of Jinan University. Notably, it was found that DUXAP10 (Wu et al., 2021) was involved in facilitating the stem cell-like properties of glioma U251 and T98G cells by increasing the expression of Sox2, CD133, Oct4 stemness markers, the ability of tumorsphere formation, and the activity of ALDH, which closely aligns with the CSC induction mentioned in the above chronic Cd exposure study on lung cancer.

Thyroid Carcinoma

Thyroid carcinoma can be divided into four types: papillary thyroid carcinoma (PTC), follicular thyroid carcinoma, medullary thyroid carcinoma, and anaplastic thyroid carcinoma (Wen et al., 2019; Zhang et al., 2021). PTC is the most common type of thyroid carcinoma (Li et al., 2018; Hu et al., 2019; Wang et al., 2021a). DUXAP10 was first confirmed by Li et al. (2020) to be highly expressed in PTC tissues and TPC-1, BCPAP, K1, and IHH-4 cells compared with adjacent normal thyroid tissues. In addition, DUXAP10 has been demonstrated to contribute to protumorigenic effects by promoting BCPAP and K1 (Li et al., 2020) cell proliferation and invasion in addition to inhibiting cell apoptosis.

Prostate Cancer

Prostate cancer (Chang et al., 2014; Siegel et al., 2021) (PCa) is one of the most frequently diagnosed malignancies in the male genitourinary system. In PCa (Luo et al., 2019; Shang et al., 2019; Wen et al., 2020), lncRNAs have been found to play increasingly vital roles in tumorigenesis and development in recent years. Previously, X-F Wang indicated that DUXAP10 was highly expressed in PCa tissues and PC3, 22RV1, and DU145 cell lines. Downregulation of DUXAP10 was able to suppress tumor development by inactivating the processes of cell cycle progression, cell proliferation, and metastasis in PC3 and DU145 cells (Wang et al., 2019b).

Chronic Myelogenous Leukemia

DUXAP10 (Yao et al., 2018) was upregulated in chronic myelogenous leukemia (CML) THP-1, KG-1, and K562 cells, and its expression level was observed to gradually increase in response to clinical upstaging of CML (chronic phase, acceleration phase, and blast phase). Furthermore, *in vitro* functional assays showed that knockdown of DUXAP10 notably weakened cell proliferation and enhanced cell apoptosis and cell cycle arrest in K652 and KG-1 cells.

Ovarian Cancer

Ovarian cancer (OC) has the highest mortality rate among gynecological cancers (Chen et al., 2013; Gurunathan et al., 2019; Yu et al., 2019). Studies have indicated that DUXAP10 (Zhang et al., 2018) is upregulated in OC tissues and cell lines. A high expression level of DUXAP10 was remarkably connected with tumor size and the FIGO stage. More importantly,

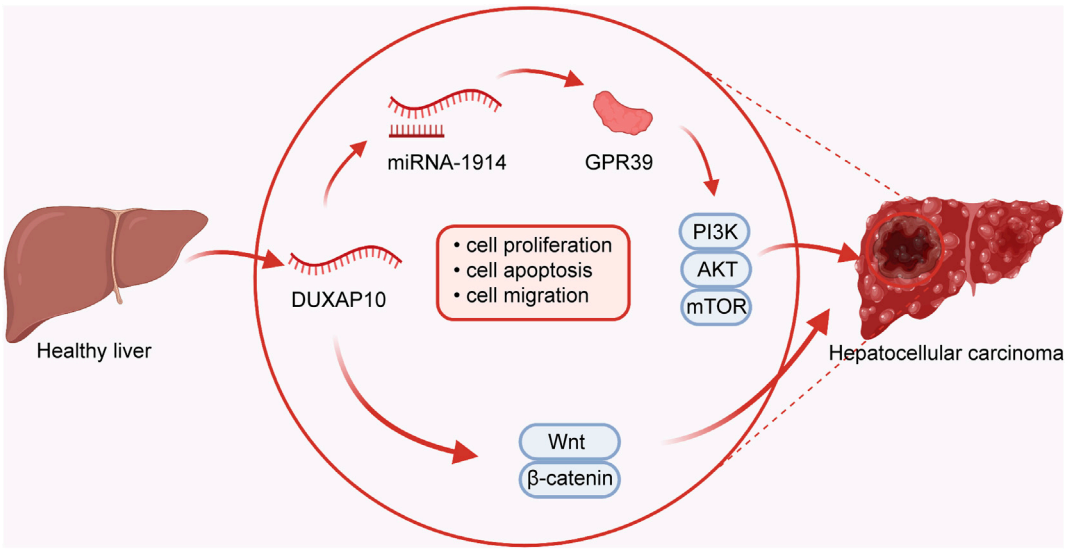

FIGURE 2 | In hepatocellular carcinoma, DUXAP10 plays an oncogenic role in regulating the processes of cell proliferation, apoptosis, and migration by combining with microRNA-1914 and further activating the GPR39-dependent PI3K/AKT/mTOR pathway or Wnt/*β*-catenin pathway.

DUXAP10 was involved in the momentous modulation of tumor progression by stimulating the proliferation of HO8910 and A2780 cells.

Gastric Cancer

Gastric cancer (GC) is the fourth most common cancer and the third most common cause of cancer-related death worldwide (Sun et al., 2017; Zhao et al., 2017; Shin et al., 2021). DUXAP10 has been recently reported to show higher expression in GC (Xu et al., 2018) tissues and cell lines (including BGC823, SGC7901, MGC803, AGS, HGC27, and MKN45 cells) and was strongly correlated with deteriorating pathological stage, lymph node metastasis and even worse prognosis. In AGS, BGC823, SGC7901, and MGC803 cell lines, DUXAP10 was found to exert cancer-promoting functions through the activation of cell proliferation, cell cycle progression, invasion, and migration. In an *in vivo* BALB/c nude mouse tumor formation study, the mice exhibited larger tumor weights and sizes, which further verified the tumorigenic ability of DUXAP10.

Pancreatic Cancer

In recent years, it has been found that DUXAP10 is excessively expressed in pancreatic (Lian et al., 2018) cancer (PC) tissues and cell lines (AsPC-1, BxPC-3, and PANC-1 cells), and a close correlation was observed between the overexpression of DUXAP10 and unfavorable clinicopathological characteristics, such as poor prognosis, aggressive TNM stage and lymph node metastasis. Functional analyses in BxPC-3 and PANC-1 cell lines provided powerful evidence that DUXAP10 accelerated cell cycle progression and proliferation and suppressed cell apoptosis. Additionally, *in vivo* xenograft tumor model experiments validated the tumor-promoting role of DUXAP10 in accelerating tumor growth and increasing tumor volumes.

Bladder Cancer

Bladder cancer (BC) is the most common cancer of the urinary tract (Gan et al., 2016; Loras et al., 2019). Lv et al. (2018) proposed for the first time that DUXAP10 was overexpressed in BC tissues and 5,637, T24, E-j, TCCSUP, UM-UC-3, and RT4 cells. Additionally, DUXAP10 contributed to cancer progression through its involvement in several cellular functions in T24 and 5,637 cells, including cell cycle progression, proliferation, and apoptosis.

Colorectal Cancer

Over the past decade, DUXAP10 was highly expressed in colorectal cancer (CRC) (Lian et al., 2017) tissues and HCT116, SW620, and SW480 cell lines. DUXAP10 was also found to be positively correlated with advanced pathological stages, larger tumor sizes, lymph node metastasis, and poor prognosis. Knocking down DUXAP10 attenuated the proliferative ability, accelerated the apoptotic process, and blocked the cell cycle progression of HCT116 and SW480 cells. Subsequently, the increased tumor volumes and weights in experimental tumor models further demonstrated the carcinogenicity of DUXAP10.

Esophageal Squamous Cell Carcinoma

Esophageal squamous cell carcinoma (ESCC) (Pan et al., 2019; Wang et al., 2020a; Li et al., 2021) is the predominant subtype of esophageal carcinoma, with a poor 5-years survival (De Angelis et al., 2014) rate of less than 21%. DUXAP10 has been found to be expressed at high levels in ESCC tissues and cells (KYSE30, KYSE510, KYSE180, and KYSE150 cells), whereas overexpression of DUXAP10 was closely correlated with short survival time, TNM stage, and lymph node metastasis. In addition, DUXAP10 essentially participates in ESCC development and progression by enhancing cell proliferation

and metastasis, accelerating cell cycle progression, and hindering cell apoptosis in KYSE30 and KYSE180 cells.

Head and Neck Squamous Cell Carcinoma

Head and neck squamous cell carcinoma (HNSCC) (Meehan et al., 2020) represents a heterogeneous mucosal malignancy derived from the oral, oropharyngeal, hypopharyngeal, and laryngeal cavities. Oral squamous cell carcinoma (Feng et al., 2017; Jia et al., 2020) (OSCC) and oropharyngeal squamous cell carcinoma (OPSCC) are the most frequent types of HNSCC, accounting for 377,713 new cases and 177,757 (Sung et al., 2021) deaths worldwide. Recent studies have also demonstrated that DUXAP10 is differentially expressed in OSCC and OPSCC tissues.

REGULATORY MECHANISMS OF THE LNCRNA DUXAP10

As a newfound oncogene, DUXAP10 has been reported to be widely involved in the mediation of several crucial biological processes, such as cell proliferation, apoptosis, and metastasis, in diverse cancer types. Here, we mainly provide a current understanding of the major biological functions and corresponding molecular mechanisms of DUXAP10 (**Figure 1**).

Cell Proliferation and Apoptosis

Cell proliferation and apoptosis are fundamental for normal cell growth and development. Abnormal cell growth is a key marker for cancer (Shi et al., 2020a; Go et al., 2021; Hu et al., 2021). It has been shown that microRNA-1914 could increase the effect of DUXAP10 on cell proliferation and apoptosis through activation of the GPR39-mediated PI3K/AKT/mTOR pathway in HCC Hep3B and MHCC-97L (Sun et al., 2019) cells (**Figure 2**). In addition, the proliferative mechanism of DUXAP10 in HCC SMMC-7721 and HepG2 (Han et al., 2019) cells was observed via the Wnt/β-catenin and PI3K/Akt signaling pathways. Likewise, one study has shown that DUXAP10 can enhance cell cycle progression and subsequent cell proliferation in NSCLC (Wei et al., 2017) A549 or H1975 cells by specifically binding to LSD1 and increasing the levels of LATS2 and RRAD. In PTC (Li et al., 2020), there was experimental evidence that DUXAP10 restrained cell apoptosis via inactivation of Caspase-3, in turn resulting in the promotion of proliferative ability in BCPAP and K1 cells. Moreover, DUXAP10 was found to facilitate cell proliferation and inhibit the apoptosis of CML (Yao et al., 2018) K652 and KG-1 cells by inhibiting PTEN expression. Functional studies in GC (Xu et al., 2018) BGC823, SGC7901, and MGC803 cells also suggest a critical regulatory role for DUXAP10 in cell proliferation by directly interacting with PRC2 and LSD1, thus repressing the expression of LATS1. Similarly, DUXAP10 has been indicated to induce PC BxPC-3 and PANC-1 cell proliferation and suppress apoptosis through combination with the RNA-binding proteins EZH2 and LSD1. Mechanistic research in T24 and 5,637 (Lv et al., 2018) BC cells has also proven that DUXAP10 regulates cell proliferation and apoptosis by modulating the PI3K/Akt/mTOR signaling pathway. In CRC (Lian et al., 2017), DUXAP10 regulates the expression of p21 and phosphatase and tensin homolog (PTEN) by binding to the histone demethylase lysine-specific demethylase 1 (LSD1), enhancing CRC cell proliferation and reducing apoptosis. As shown in KYSE30 and KYSE180 ESCC (Wang et al., 2018) cells, DUXAP10 has been similarly confirmed to modulate the processes of cell proliferation and apoptosis by negatively modulating p21 expression by interacting with zeste homolog 2 (EZH2).

Cell Invasion and Migration

Cancer metastasis remains one of the biggest challenges in cancer therapy (Gou et al., 2020; Wang et al., 2021c). Migration and invasion are prerequisites for cancer cell metastasis (Zacharias et al., 2018). The mechanisms of cell migration and invasion have been a focus of research. Current studies have revealed that DUXAP10 mainly affects the processes of tumor cell EMT, thus enhancing tumor cell migratory properties in several cancers. By modulating the Wnt/β-catenin and PI3K/Akt signaling pathways, DUXAP10 has been demonstrated to influence the invasion and migration of HCC (Han et al., 2019) SMMC-7721 and HepG2 cells through the regulation of EMT. A previous study of PTC also demonstrated that DUXAP10 was involved in increasing cell invasion and migration and regulating EMT via activation of the Akt/mTOR (Li et al., 2020) pathway. Additionally, DUXAP10 was found to play a crucial role in GC (Xu et al., 2018) cell invasiveness and migration by interacting with the RNA-binding protein HuR and subsequently stabilizing β-catenin mRNA. It was also demonstrated that in ESCC KYSE30 and KYSE180 cells, DUXAP10 regulated cell metastasis by binding with EZH2 and downregulating p21 (Wang et al., 2018) expression.

Cell Stemness

The CSC hypothesis suggests that CSCs (Tang, 2012; Eun et al., 2017) are a subpopulation of tumor cells with the characteristics of powerful self-renewal and aberrant differentiation potential. Interestingly, an emerging role of DUXAP10 in promoting the transition of CSCs has been observed, which is essential for the tumorigenicity of cancer cells.

4 A recent study using a post-chronic Cd-exposed human bronchial epithelium BEAS-2B cell model demonstrated that DUXAP10 induces CSC-like (Lin et al., 2021) properties by improving GLI1 protein stability and ultimately regulating the Hedgehog signaling pathway. In Cd-exposed transformed cells, Hedgehog signaling pathway was activated and subsequently involved in mediating CSC-like characteristics. At the same time, Pax6 was upregulated and significantly increase the duxap10 level and CSC like characteristics. It was also found that DUXAP10 promotes the stemness of glioma (Wu et al., 2021) U251 and T98G cells by binding to HuR and thus upregulating the expression of Sox12. DUXAP10 knockdown remarkably reduced the activity of ALDH and the expression of stemness markers (Sox2, CD133, Oct4) in glioma cells. Thus, these results have shown DUXAP10 had vital effects on glioma cell stemness. Promising Clinical Applications of DUXAP10.

Accumulating studies have shown that dysregulated lncRNA (Bhan et al., 2017; Gao et al., 2021; Tan et al., 2021) expression contributes to the development of tumors and can be used as a promising marker for lncRNA-based applications in cancer management. Aberrantly expressed DUXAP10 was recently revealed to be involved in a wide range of biological functions and pathological characteristics, and its vital clinical applications in several cancer types are valuable for clinical diagnosis, prognosis, and treatment management. In this section, we describe the meaningful medicinal applications of DUXAP10 in numerous tumor types.

DUXAP10 as a Diagnostic and Prognostic Biomarker

It is now widely accepted that the early diagnosis (An et al., 2021; Kannan et al., 2021) of tumors is essential for achieving a better prognosis and a lower mortality rate. Accurate diagnostic biomarkers (Ott et al., 2009; Wardle et al., 2015; Dragani et al., 2020) for detecting early-stage tumors are of great clinical significance. An increasing number of oncology studies have reported that the overexpression of DUXAP10 in diverse tumor tissues (such as NSCLC (Wei et al., 2017), glioma (Wu et al., 2021), and ESCC (Wang et al., 2018)) could be used to distinguish normal from tumor tissues, making it highly promising for the early diagnosis of tumors.

In addition, high DUXAP10 expression was closely associated with more advanced tumor stage or grade, earlier lymph node metastasis, and unfavorable OS, PFS, and RFS rates, which provides powerful evidence for the prognostic ability of DUXAP10 in various cancers, such as HCC (Zhu et al., 2018), NSCLC (Wei et al., 2017), RCC (Chen et al., 2020), OC (Zhang et al., 2018), GC (Xu et al., 2018), CRC (Lian et al., 2017), and ESCC (Wang et al., 2018). Therefore, DUXAP10 in combination with relevant clinicopathological features can function as an independent prognostic indicator in diverse cancer types.

DUXAP10 as a Treatment Target

In recent decades, several reports have shown that lncRNAs (Yin et al., 2018; Diniz et al., 2021; Homayoonfal et al., 2021) play important roles in tumor progression and could be biomarkers for clinical treatments. Increasing studies have demonstrated that DUXAP10 is involved in the tumorigenesis and development of tumors through the modulation of diverse cellular processes, comprising cell colony formation, cell cycle progression, cell proliferation, apoptosis, metastasis, and even CSC-like properties. Moreover, numerous molecular mechanism experiments have confirmed that DUXAP10 plays a tumor promoter role by regulating key target gene activity and affecting multiple important signaling pathways, making it a possible molecular factor that can be used as a therapeutic target in HCC (Han et al., 2019; Sun et al., 2019), NSCLC (Wei et al., 2017), glioma (Wu et al., 2021), RCC (Chen et al., 2020), PTC (Li et al., 2020), OC (Zhang et al., 2018), GC (Xu et al., 2018), PC (Lian et al., 2018), BC (Lv et al., 2018), CRC (Lian et al., 2017) and ESCC (Wang et al., 2018). Therefore, a further in-depth understanding of the pro-oncogenic mechanisms of DUXAP10 for cancer treatment is needed.

CONCLUSION

With the advent of novel genomic approaches as well as technological breakthroughs, an unprecedented understanding of the development of cancer has provided novel insight for establishing more effective cancer management strategies. Mounting evidence indicates that DUXAP10 is abnormally highly expressed in a variety of cancers, including HCC, lung cancer, glioma, RCC, PTC, PCa, CML, OC, GC, PC, BC, CRC, and ESCC. The higher expression of DUXAP10 in tumor tissues compared with adjacent normal tissues indicates the diagnostic potential of using DUXAP10 to successfully distinguish cancerous tissues from normal tissues. However, the detection of DUXAP10 in tissue is an invasive and complicated method, and further studies are needed to search for possible noninvasive methods for the diagnosis of cancers using DUXAP10.

In addition, DUXAP10 overexpression was positively correlated with the adverse clinicopathological features and aggressive outcomes of several cancer types, including tumor size, TNM staging, histological grading, lymph node metastasis, and survival rates. These associations revealed the potential for DUXAP10 to be used as a prognostic biomarker to predict cancer prognosis and provide guiding recommendations for the future treatment of tumors. More importantly, DUXAP10 has been found to play an oncogenic role and participate in the biological processes of cellular proliferation, apoptosis, invasion, migration, and stemness through the regulation of various target genes or signaling pathways. Thus, the molecular mechanisms of DUXAP10 involved in tumor progression should be further explored, contributing to new hopes in tumor treatment.

AUTHOR CONTRIBUTIONS

JX designed the study. LZ and ZG drafted the manuscript. LZ and MX analyzed the data. All authors read and approved the final manuscript.

FUNDING

This work was supported by Henan Medical Science and Technology Joint Building Program (LHGJ20200320).

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