SNHG16: A Novel Long-Non Coding RNA in Human Cancers

Abstract: Long noncoding RNAs (lncRNAs) have recently been considered as central regulators in diverse biological processes controlling tumorigenesis. Small nucleolar RNA host gene 16 (SNHG16) is an important tumor-associated lncRNA mainly involved in tumorigenesis and progression by competing with endogenous RNA (ceRNA) which sponges tumor-suppressive microRNA (miRNA), and by its recruitment mechanism. SNHG16 is overexpressed in tumor tissues and cell lines of different kinds of cancers, and its presence is associated with a poor clinical prognosis. Reviewing all publications about SNHG16 revealed that it plays a key role in the different hallmarks that define human cancer, including promoting proliferation, activating migration and invasion, inhibiting apoptosis, affecting lipid metabolism and chemoresistance. This review highlights the role that the aberrant expression of SNHG16 plays in the development and progression of cancer, and suggests that SNHG16 may function as a potential biomarker and therapeutic target for human cancers.

Keywords: long noncoding RNA, biomarker, cancer, SNHG16

Plain Language Summary

Studies have shown that the long non-coding RNA SNHG16 plays a functional role in various human cancers and is closely associated with tumor growth, metastasis and poor prognoses. SNHG16 is upregulated in hepatocellular carcinoma, osteoblastoma, lung cancer, colorectal cancer, glioma, ovarian cancer, bladder cancer, breast cancer, gastric cancer, retinoblastoma, cervical cancer, and thyroid cancer.

SNHG16 is overexpressed in several types of cancer and is implicated in multiple different hallmarks that define human cancer.

In order to have a deeper comprehension of this novel biomarker for prognosis and therapy in cancers, more studies are need for further analysis.

Introduction

Cancer is a group of malignant diseases in which cell growth, migration, and invasion are uncontrolled. The high mortality and disability rates associated with cancer are a cause of distress and burden on patients and society as a whole.1 Surgical treatment, chemotherapy, and radiation therapy are currently the main treatments for cancer. However, the therapeutic effects of these primary treatments remain limited.2 Therefore, early diagnostic markers and new treatments are urgently needed.

About 70–90% of the human genome is transcribed into RNA, but only 2% of the total RNA is translated into protein. The remaining RNA that is not translated into

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A noncoding RNA (ncRNA) is 200 nucleotides in length or shorter, and is categorized as a short ncRNA, whereas an ncRNA longer than 200 nucleotides is considered a long ncRNA (lncRNA). However, studies have shown that lncRNAs can directly inhibit the expression of p21 by competing with miRNAs in cancer. In addition, overexpression of SNHG16 promotes tumor development by acting as a ceRNA to regulate mRNA by sponging corresponding miRNAs in multiple cancers. Argonaute-crosslinking and immunoprecipitation (AGO-CLIP) analysis led to the hypothesis that SNHG16 heavily binds to AGO. It has 27 AGO/miRNA target sites along its length and may act as a ceRNA for miRNA in cancer. This phenomenon can be alleviated. In this manner, lncRNAs can have tumor-promoting or -inhibiting abilities. The ceRNA model is a very important biological pathway and, through this pathway, lncRNAs can participate in the entire process of tumorigenesis. It is evident from previous literature that SNHG16 acts as a ceRNA to regulate mRNA by sponging corresponding miRNAs in multiple cancers.

SNHG16 is encoded by a 7571-bp region at chromosome 17q25.1, has recently been recognized as a cancer-related lncRNA. The SNHG16 was initially discovered in neuroblastoma. The dysregulation of SNHG16 has been detected in various types of cancer, including colorectal cancer (CRC), hepatocellular carcinoma (HCC), osteosarcoma, and glioma. Recent studies have demonstrated that SNHG16 expression is upregulated in multiple types of tumors. Furthermore, downregulation of SNHG16 in cancer cells inhibits cell proliferation, invasion, and migration; induces apoptosis; and results in decreased N-cadherin and increased E-cadherin, suggesting that SNHG16 also acts as an oncogetic lncRNA in cancer.

Understanding the role of SNHG16 may provide a new perspective to study the mechanisms of cancer development. This paper reviews current studies on the expression, function, mechanism, and clinical significance on tumor development of SNHG16 and highlights its impact on the hallmarks of cancer.

**Mechanisms of SNHG16 in Human Cancers**

Further evidence shows that SNHG16 promotes tumor development by acting as a competitive endogenous RNA (ceRNA). The ceRNA hypothesis states that various RNA species, including miRNAs encoding proteins and RNAs without protein-encoding capabilities (eg, pseudogenes, lncRNA, and circular RNA), share miRNA binding sites, allowing for competitive binding to common miRNAs with pro- or anti-cancer effects. Thus, the inhibition of miRNAs on other targets can be alleviated. In this manner, lncRNAs can have tumor-promoting or -inhibiting abilities. The ceRNA model is a very important biological pathway and, through this pathway, lncRNAs can participate in the entire process of tumorigenesis. It is evident from previous literature that SNHG16 acts as a ceRNA to regulate mRNA by sponging corresponding miRNAs in multiple cancers.

**Overexpression of SNHG16 and Clinical Significance in Cancer**

It has been shown that SNHG16 expression is significantly upregulated in tumor tissues and cell lines, such as hepatocellular carcinoma (HCC), lung cancer (LC), colorectal cancer (CRC) and glioma. In addition, overexpression of SNHG16 indicates poor prognosis and is usually correlated with tumor size, lymph node metastasis, tumor grade, disease-free survival, and overall survival (OS). For example, to gain more in-depth knowledge of tumor biology, nine co-expression modules were identified in the Cancer Genome Atlas database after screening and analysis. These modules identified four important...
In normal cells, the regulation of proliferation is strictly controlled. The production and signal transmission of growth-promoting factors must be fully controlled, and checkpoints must be set up at each node of cell division to ensure tissue homeostasis (cell number, tissue structure, and function). In cancer cells, this balance is disrupted. SNHG16 has been shown to sustain proliferation of cancer cells in different types of cancers.

Many related mechanisms have been reported. SNHG16 is negatively correlated with known miRNAs that act as tumor suppressors. In HCC, Xie et al revealed that SNHG16 was correlated with TNM stage, lymph node metastasis, and shorter survival.

In addition to sequencing in tumor tissues, IncRNAs levels can also be measured in exosomes. Exosomes, which are microvesicles (70–120 nm) derived from endosomes secreted by many cell types, can participate in intercellular communication by transferring intracellular substances (such as proteins, lipids, and nucleic acids, including IncRNA). Certain IncRNAs within exosomes secreted by tumor cells have been described as candidate biomarkers to predict prognosis.

These findings indicate that SNHG16 may serve as a potential biomarker for human cancer diagnosis, prognosis, and effective treatment.

Implication of SNHG16 in the Hallmarks of Cancer

Promoting Proliferation

Proliferation is considered to be the most basic feature of cancer cells. In normal cells, the regulation of proliferation is strictly controlled. The production and signal transmission of growth-promoting factors must be fully controlled, and checkpoints must be set up at each node of cell division to ensure tissue homeostasis (cell number, tissue structure, and function). In cancer cells, this balance is disrupted. SNHG16 has been shown to sustain proliferation of cancer cells in different types of cancers.

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<th>Phenotypes Affected</th>
<th>Role</th>
<th>References</th>
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(Continued)
that knockdown of SNHG16 inhibited cell proliferation of HCC cells by inhibiting the expression of proliferation protein Ki67 and miR195 acted as a direct target of SNHG16.\textsuperscript{22} Li et al found that the SNHG16/miR-302a-3p/fibroblast growth factor 19 (FGF19) axis was an important pathway in promoting proliferation of HCC cells.\textsuperscript{21} Lin et al found that SNHG16 modulates signal transducer and activator of transcription 3 (STAT3) expression by competitively binding miR-4500.\textsuperscript{20} In addition, Knockdown of SNHG16 hinders osteosarcoma cell proliferation. However, in osteosarcoma, mechanistic investigations revealed that SNHG16 could act as a sponge for miR-98-5p, miR-1301, miR-16, miR-340, and miR-205.\textsuperscript{16,36–39} Inhibition of miR-98-5p and miR205 increases zinc finger E-box binding homeobox 1 (ZEB1), E2F transcription factor 5 (E2F5), and STAT3 expression to promote tumorigenesis.\textsuperscript{36,37} Li et al reported that SNHG16 was revealed to bind with miR-200a-3p, leading to the proliferation of CRC cells.\textsuperscript{31} Zhou et al found that SNHG16 regulated proliferation and invasion

<table>
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<th>Phenotypes Affected</th>
<th>Role</th>
<th>References</th>
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<td>T24</td>
<td>Bcl, Bax, capase3, E-cadherin, N-cadherin, Wnt1, c-myc, P2TkipI</td>
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<td>Up</td>
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<td>T24, BIU67</td>
<td>P2I</td>
<td>Proliferation, migration, invasion, apoptosis, cell cycle</td>
<td>Oncogenic</td>
<td>[56]</td>
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<td>miR-98, E2F5</td>
<td>Migration</td>
<td>Oncogenic</td>
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<td>Proliferation, colony formation</td>
<td>Oncogenic</td>
<td>[48]</td>
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<td>BGC-823, SGC-7901</td>
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<td>Apoptosis</td>
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<td>MGC-803</td>
<td>JAK2, p-STAT3, miR-135a</td>
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<td>Up</td>
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<td>miR-218-5p, HMGB1</td>
<td>Migration, invasion</td>
<td>Oncogenic</td>
<td>[41]</td>
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<td>Lymphoma</td>
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<td>48</td>
<td>OCL-LY7</td>
<td>miR-497-5p, P1M1</td>
<td>Proliferation, migration, apoptosis, cell cycle</td>
<td>Oncogenic</td>
<td>[50]</td>
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</table>

Table 1 (Continued).
of glioma cells through the miR-373/epidermal growth factor receptor (EGFR) axis by the phosphatidylinositol 3-kinase (PI3K) -protein kinase B (AKT) pathway. Xu et al explored the molecular mechanism and revealed that SNHG16 acts as a miR-140-5p sponge in RB carcinogenesis. In addition, suppressing SNHG16 can slow tumor growth in vivo.

Moreover, SNHG16 can also promote cancer cell proliferation by activating cell cycle progression through G1/S transition. Knockdown of SNHG16 in osteosarcoma results in the inhibition of cell proliferation in vitro by the induction of a G0/G1 arrest. Zhu et al revealed that silencing of SNHG16 inhibited proliferation, migration, and invasion, in addition to causing cell cycle arrest. SNHG16 acts by repressing miR-497-5p, blocking its repression of interacting with Moloney murine leukaemia virus 1 in diffuse large B-cell lymphoma (DLBCL). SNHG16 can also stimulate cell cycle progression through repressing p21 by recruiting enhancer of zeste homolog 2 (EZH2) to its promoter region. p21 belongs to a family of cyclin-dependent kinases (CDK) inhibitors and has been reported to be able to block cell cycle progression at the G0/G1 checkpoint. p21 can therefore act as a tumor suppressor in bladder cancer.

These results show the significance of SNHG16 in the molecular etiology of proliferation of cancer cells and suggest the potential application of SNHG16 as an essential diagnostic marker.

### Activating Migration and Invasion

Metastasis is the main cause of cancer treatment failure and death. Its molecular mechanism is complex, involving multistep, multistage, multigene changes. At the initial stage of cancer formation, epithelial cells are transformed into cells with a mesenchymal phenotype through specific signaling pathways. The main characteristics of this transformation are decreased expression of cell adhesion

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**Table 2 Clinical Significance of SNHG16 in Diverse Cancers**

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Overexpression of SNHG16 and Clinical Features</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-small cell cancer</td>
<td>Tumor size, TNM stage, lymph node metastasis, shorter DFS and OS</td>
<td>[32]</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>TNM stage, metastasis</td>
<td>[29]</td>
</tr>
<tr>
<td></td>
<td>Tumor size, TNM stage, ALT (U/L)</td>
<td>[14]</td>
</tr>
<tr>
<td></td>
<td>Shorter DFS and OS, multiple tumors, macro vascular invasion</td>
<td>[26]</td>
</tr>
<tr>
<td></td>
<td>Shorter DFS and OS</td>
<td>[28]</td>
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<tr>
<td></td>
<td>Lymph node involvement, TNM stage</td>
<td>[27]</td>
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<td></td>
<td>Tumor size, TNM stage, vascular invasion</td>
<td>[25]</td>
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<tr>
<td></td>
<td>Tumor size, TNM stage, metastasis, portal vein tumor thrombus (PVT)</td>
<td>[30]</td>
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<tr>
<td>Cervical cancer</td>
<td>Tumor size, FIGO stage, lymph node metastasis, poor differentiation</td>
<td>[34,35]</td>
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<tr>
<td>Osteosarcoma</td>
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<td>[39]</td>
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<tr>
<td></td>
<td>Tumor size, TNM stage, distance, metastasis, shorter OS</td>
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<tr>
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<td>Gastric cancer</td>
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<td>Pancreatic cancer</td>
<td>Tumor size, TNM stage, lymph node metastasis, differentiation</td>
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</table>
molecules (such as E-cadherin), vimentin, rather than cytokeratin, as the main cytoskeletal protein, and the cells taking on the morphological characteristics of mesenchymal cells.53 This phenotypic plasticity, named epithelial-to-mesenchymal transition (EMT), causes epithelial cells to lose cell polarity, lose the connection with basement membrane and other epithelial phenotypes, and gain higher migration and invasion ability.52

Several studies have shown that the overexpression of SNHG16 can promote EMT and migration, thus promoting the invasion of cancer cells. Lin et al showed that inhibition of SNHG16 in HCC reverses EMT and represses cell migration and invasion in vitro.20 Peng et al reported metalloproteinases 3 (TIMP3) can be downregulated by elevated SNHG16 and miR-17-5p, promoting proliferation, migration, invasion, and EMT in bladder cancer cells.54 Previous studies have shown that activating the Wnt/β-catenin pathway affected cell metastasis and induced EMT in cancers. Feng et al found that suppressing SNHG16 can inhibit proliferation, migration, invasion, and EMT and promote apoptosis in bladder cancer cells. They further stated that SNHG16 could sponge miR-98 and target STAT3 through the Wnt/β-catenin pathway to act as an oncogene in bladder cancer.55 And SNHG16 acts as a ceRNA in colorectal cancer cells to suppress miR-200a-3p and increase the expression of ZEB1 and, thereby, promote the expression of EMT-related genes, such as cadherins and vimentin, and promote cell migration and invasion. Similarly, Zhu et al revealed that silencing SNHG16 inhibits cell migration and invasion, and EMT in vitro, indicating that SNHG16 is involved in the tumorigenesis of cervical cancer (CC). Although the oncogenic function of SNHG16 in CC is not completely known, it is known to act in a miR-216-5p-dependent manner and positively regulate the miR-216-5p target ZEB1 in CC cells.34,35

In addition, SNHG16 can also regulate migration and invasion by sponging miRNA through transcriptional activation of mRNA. Chen et al reported SNHG16 might function as a ceRNA for miR-186 to regulate rho-associated coiled-coil-containing protein kinase 1 (ROCK1) expression, which plays important roles in regulating cell polarity and migration in HCC.15 Su et al have found that SNHG16 directly bind to miR-340 to promote OS cells migration and invasion.16 Additionally, Wang et al found that SNHG16 promotes B Cell Lymphoma 9 (BCL9) expression by splicing miR-1301 to facilitate the migration and invasion of osteosarcoma cells.38 Cai et al revealed that SNHG16 competitively binding miR-98 with E2F5 may promote breast cancer metastasis in an miR-98-dependent manner.56 Interestingly, in this model, SNHG16 transcript levels were significantly positively associated with E2F5 mRNA levels, indicating an activation loop of that metastasis process.56 A similar situation was posited in another study. Wang et al found that knockdown of SNHG16 suppressed gastric cancer cell migration and invasion in vitro. Further, mechanistic investigation revealed that SNHG16 could mediate Janus kinase 2 (JAK2) and STAT3 expression as a ceRNA of miR-135a. Additionally, STAT3 can affect the expression of SNHG16.57 Another study found that miR-628 is regulated by SNHG16 and its target Neuropilin-1 (NRP1) can promote tumor metastasis.58 SNHG16 was shown to promote cell invasion and migration in pancreatic cancer cells via mediating high mobility group box 1 (HMGB1) (a known oncogene in PC) expression through sponging miR-218-5p.45 Wen et al found that knockdown of SNHG16 inhibits migration and invasion of TPC-1 cells via regulating miR-497.42 Interestingly, Vahid found a correlation between SNHG16 expression and the vitamin D receptor (VDR), which supports the hypothesis of an interactive network between SNHG16, VDR, and miR-98 in the context of cancer.59 SNHG16 is expected to become a novel molecular marker for diagnosis, prognosis, and treatment of BC.

Moreover, matrix metalloproteinases (MMPs) are highly expressed in tumor tissues. MMPs cause degradation of protein components in the extracellular matrix and increased tumor invasion and metastatic risk. Xie et al found SNHG16 significant increase in expression of MMP-2 and MMP-9 through a novel SNHG16-miR-195 axis in HCC cells. SNHG16 was shown to induce OC cell migration and invasion through the upregulation of P-AKT and MMP-9, indicating its potential in promoting tumor progression by regulating the PI3K/AKT pathway and MMPs.60

**Inhibiting Apoptosis**

Apoptosis is a natural, multistep process that plays an important role in development and homeostasis.61 Cancer cells exhibit enhanced tolerance to both environmental and genomic stresses, resulting in resistance to apoptosis and tumor progression.62 The B-cell lymphoma protein 2 (Bcl-2) family proteins, PI3K-AKT pathway, and nuclear factor κB (NF-κB) signaling are vital regulators of apoptosis.63,64 It has been shown that overexpressed SNHG16 directly interacted with miR-4518 and promoted protein arginine methyltransferase 5 to inhibit apoptosis in glioma cells. Furthermore,
downregulation of SNHG16 could lead to the repression of anti-apoptotic Bcl-2 family members and PI3K/Akt signaling.\textsuperscript{40} Additionally, Zhou et al revealed that SNHG16 suppressed the expression of p21, caspase 3, and caspase 9, while promoting cyclin D1 and cyclin B1 expression, to inhibit apoptosis in glioma cells.\textsuperscript{65} Silencing SNHG16 increases caspase 3/7 to promote apoptosis in osteosarcoma cells.\textsuperscript{16} NF-\(\kappa\)B is a eukaryotic transcription factor that can cause abnormal expression of tumor necrosis factors and promote carcinogenesis and apoptosis. Zhang et al found that SNHG16 may act as an endogenous sponge of miR-17-5p to upregulate its target p62 and activate the mammalian target of rapamycin (mTOR) pathway to promote metabolism and proliferation in HCC cells, as well as activating PI3K/Akt and NF-\(\kappa\)B signaling to resist apoptosis.\textsuperscript{19} Christensen et al. reported SNHG16 overexpression is an early event in CRC, which is regulated by the Wnt pathway and c-Myc. They also found that knockdown of SNHG16 can reduce cell viability and induce apoptotic death.\textsuperscript{14} Another study found that miR-628 is regulated by SNHG16 and the expression of miR-628-3p is down in GC tissues and GC cell lines, and its target NRP1 can inhibit cell apoptosis.\textsuperscript{58}

**Affecting Lipid Metabolism**

Lipid biosynthesis has been frequently observed in tumor tissues.\textsuperscript{66} Enhanced lipid synthesis is required for the metabolic reprogramming of cancer cells and tumor development.\textsuperscript{56} Christensen et al. found that SNHG16 is enriched in the cytoplasm of CRC cell lines and associated with ribosomes, which may lend a better understanding of its function and means of action.\textsuperscript{14} Overexpression of SNHG16 is positively correlated to the expression of Wnt-regulated transcription factors, including achaete-scute complex homolog 2 (ASCL2) and c-Myc. Moreover, knockdown of SNHG16 predominantly affects genes involved in lipid metabolism. Interestingly, these genes contain a common sequence motif, suggesting that a broad spectrum of lncRNA-miRNA targets may converge on a few co-target genes.\textsuperscript{14}

**Inhibiting Inflammation**

There are few data available about the link between SNHG16 and cancer inflammation. NF-\(\kappa\)B is a eukaryotic transcription factor that helps regulate the immune and inflammatory response, cell proliferation, apoptosis, tumor growth, and differentiation. NF-\(\kappa\)B signal transduction can cause the abnormal expression of tumor necrosis factors (TNF) and promote tumorigenesis and apoptosis. Zhang et al. found that SNHG16 may act as an endogenous sponge of miR-17-5p to upregulate its target p62 and activate the mTOR pathway to promote metabolism and proliferation in HCC cells, as well as activating the NF-\(\kappa\)B pathway to aggravate inflammation.\textsuperscript{19}

**Chemoresistance and Vasculogenic Mimicry**

There are evidences that SNHG16 is involved in drug resistance. Ye et al. and Guo et al both found that knocking down SNHG16 increased sensitivity to sorafenib in HCC cells via acting as an endogenous sponge for miR-140-5p, which indicates that SNHG16 might be a promising therapeutic target to boost the effectiveness of chemotherapy for HCC patients.\textsuperscript{18,23} Osteosarcoma is a rare cancerous bone tumor characterized by high metastasis, rapid progression, and poor prognosis.\textsuperscript{67} In the past few decades, there has been great progress in the diagnosis and treatment of osteosarcoma, but the OS is still unsatisfactory.\textsuperscript{68} The molecular mechanisms underlying the development and progression of osteosarcoma remain unclear, and multidrug resistance severely limits the development and use of neoadjuvant chemotherapy.\textsuperscript{69} Therefore, it is particularly urgent to find feasible molecular therapeutic targets for osteosarcoma. Interestingly, increases in autophagy-related genes (such as ATG4B) via downregulation of miR-16 can reduce cell apoptosis by inducing cell autophagy, which leads to chemoresistance.\textsuperscript{39} This finding may signify novel therapeutic directions in osteosarcoma.

In addition, glioma is one of the most common and aggressive malignant primary brain tumors, with a 5-year survival rate of less than 10% and a median survival period of only 14 months.\textsuperscript{70} Glioma is poorly understood, and the dismal clinical outcome makes the study of molecular mechanisms in glioma urgent.\textsuperscript{71} The anti-angiogenic treatment of malignant glioma cells is an effective method to treat high-grade gliomas. However, the effect is limited in glioma due to the presence of vasculogenic mimicry (VM).\textsuperscript{72} Wang reported that knockdown of SNHG16 can promote the expression of miR-212-3p and inhibit VM to sensitize glioma to anti-angiogenic treatment, which provides deeper comprehension and a novel direction for the treatment of glioma.\textsuperscript{72} The results indicate that SNHG16 plays a key role in glioma and it can be a novel therapeutic target.

**Conclusion and Future Perspectives**

A growing number of studies have shown that dysregulated lncRNAs are potential oncogenes or tumor
suppressors that play important roles in tumorigenesis and tumor progression. LncRNAs can be used as biological markers and therapeutic targets for tumors and have broad applications in the diagnosis and treatment of tumors. 

*SNHG16* is a newly discovered lncRNA, and it has been shown to be upregulated in many tumor types and associated with tumor stage, lymph node metastasis, and tumor size, indicators of poor prognosis. *SNHG16* binds to endogenous miRNAs, resulting in abnormal expression of downstream target genes or dysregulation of classical signaling pathways (Table 1, Figure 1). The studies discussed here highlight that the study of *SNHG16* is of great significance for further study of the mechanism of tumor development and progression, and *SNHG16* may be considered as a new diagnostic/prognostic biomarker and a therapeutic target for cancer. Although the role of *SNHG16* in cancer has been studied, there are still many areas that need further research. For example, there are few studies on thyroid cancer, breast cancer and retinoblastoma, and the understanding of the molecular mechanisms by which it drive carcinogenesis is not deep enough, instead focusing on in vitro experiments. Further research should be focused on investigating the precise molecular regulatory mechanisms of *SNHG16*, and a larger cohort of tumor samples should also be included to facilitate the clinical application of *SNHG16* as early as possible.

**Abbreviations**

BC, breast cancer; CC, cervical cancer; ceRNA, competitive endogenous RNA; CRC, colorectal cancer; DLBCL, diffuse large B-cell lymphoma; EMT, epithelial-mesenchymal transition; GC, gastric cancer; HCC, hepatocellular carcinoma; lncRNA, long noncoding RNA; MMP, matrix metalloproteinase; ncRNA, noncoding RNA; NSCLC, non-small cell lung cancer; OC, ovarian cancer; OS, overall survival; PC, pancreatic cancer; PI3K, phosphatidylinositol 3-kinase; PTC, papillary thyroid carcinoma; RB, retinoblastoma; *SNHG16*, small nucleolar RNA host gene 16; STAT3, Signal Transducers and Activators of Transcription 3; TNM, tumor, node, metastasis; VDR, vitamin D receptor; VM, vasculogenic mimicry; ZEB1, zinc finger E-box binding protein 1.

**Acknowledgment**

All the authors thank the library of Beijing Tongren Hospital for assistance with literature search.
Author Contributions
All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Funding
The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Disclosure
The authors report no conflicts of interest in this work.

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