Pathology - Research and Practice 251 (2023) 154897

Contents lists available at ScienceDirect

Pathology - Research and Practice

journal homepage: www.elsevier.com/locate/prp

Review

LncRNA SNHG12: A budding star in human diseases

Soudeh Ghafouri-Fard [a], Hamed Shoorei [b,c], Bashdar Mahmud Hussen [d], Snur Rasool Abdullah [e], Yadollah Poornajaf [f], Mohammad Taheri [g,h,*], Majid Samsami [i,**]

[a] Department of Medical Genetics, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[b] Clinical Research Development Unit of Tabriz Valiasr Hospital, Tabriz University of Medical Sciences, Tabriz, Iran
[c] Department of Anatomical Sciences, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran
[d] Department of Pharmacognosy, College of Pharmacy, Hawler Medical University, Kurdistan Region, Iraq
[e] Medical Laboratory Science, Lebanese French University, Erbil, Kurdistan Region, Iraq
[f] Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran
[g] Institute of human genetics, Jena university Hospital, Jena, Germany
[h] Urology and Nephrology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[i] Cancer Research Center, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Keywords:
SNHG12
LncRNA
Cancer
Biomarker
Expression

ABSTRACT

Small nucleolar RNA host gene 12 (SNHG12) is a long non-coding RNA (lncRNA) that contributes in a variety of human pathologies. This lncRNAs acts as molecular sponge for various miRNAs, namely miR-200c-5p, miR-129–5p, miR-30a-3p, miR-195, miR-133b, miR-199a/b-5p, miR-320b, miR-16, miR-15a, miR-218–5p, miR-320 and a number of other miRNAs. Through this mechanism, SNHG12 can affect activity of HIF-1α, Wnt/β-catenin, VEGF, PI3K/AKT/mTOR, PTEN, NF-κB and ERK-1/2 signaling. SNHG12 can affect pathogenesis of several disorders, including those arising from genitourinary, gastrointestinal, pulmonary, central nervous and cardiovascular systems. These effects have been best characterized in the context of cancer where it can be used as a possible diagnostic and prognostic marker. In order to summarize the role of this lncRNA in human disorders, particularly cancer and highlight its potential application in biomedical studies, we designed the current review. We also emphasized on its diagnostic and prognostic roles.

1. Introduction

Small nucleolar host gene 12 (SNHG12), alternatively named as ASLNC04080, C1orf79, LINC00100 and PNAS-123, is a long non-coding RNA (lncRNA) located on chromosome 1. SNORA66, SNORA61, SNORA16A, and SNORD99 are four small nucleolar RNAs being encoded by SNHG12 spliced introns [23]. In addition to several transcripts with retained introns, SNHG12 lncRNA has 9 transcripts with sizes ranging from 1871 bp (SNHG12–213) to 480 bp (SNHG12–219).

SNHG12 can affect pathogenesis of several disorders, including those arising from genitourinary, gastrointestinal, pulmonary, central nervous and cardiovascular systems. These effects have been best described in the context of cancer where it can be used as a possible diagnostic and prognostic marker. Moreover, dysregulation of SNHG12 has been associated with enhancement of cell viability, proliferation and metastatic ability of tumor cells. In order to provide a summary of the role of this lncRNA in human disorders, particularly cancer and highlight its potential application in biomedical studies, we designed the current review. We also gathered information on its diagnostic and prognostic roles.

Abbreviations: PMVECs, Pulmonary Microvascular Endothelial Cells; PBMCs, Peripheral Blood Mononuclear Cells; VSMCs, Vascular Smooth Muscle Cells; HUVECs, Human Umbilical Vein Endothelial Cells; HIEC, Human Intestinal Epithelial Cell Line; MSCs, Mesenchymal Stem Cells; BMECs, Brain Microvascular Endothelial Cells; HF, Human Fibroblast; EC, Endothelial Cell; ICE, Immortalized Cervical Epithelial; ESC, Endometrial Stromal Cell; HMEC-1, Human Microvascular EC Line-1; HPMCs, Human Peritoneal Mesothelial Cells; KLF2, Kruppel-Like Factor 2; CUL4B, Cullin 4B; DXR, Doxorubicin; DDP, Cisplatin; EMT, Epithelial-Mesenchymal Transition; WWP1, WW Domain-Containing E3 Ubiquitin Protein Ligase 1; CCNE1, Cyclin-E1; TDP43, TAR-DNA Binding Protein 43; COL11A1, Collagen Type XI α1 Chain; IGF2BP2, Insulin-Like Growth Factor 2 mRNA-Binding Protein 2; MMT, Mesothelial–Mesenchymal Transition.

* Corresponding author at: Institute of human genetics, Jena university Hospital, Jena, Germany.
** Corresponding author.
E-mail addresses: Mohammad.taheri@uni-jena.de (M. Taheri), samsamimd@gmail.com (M. Samsami).

https://doi.org/10.1016/j.prp.2023.154897
Received 11 August 2023; Received in revised form 8 October 2023; Accepted 14 October 2023
Available online 16 October 2023

Table 1
SNHG12 in genitourinary system.

Diseases	SNHG12 Expression	Model of Study	Cell Line	Targets & Pathways	Observation	Ref
Renal Cell Carcinoma (RCC)	Up	Human, BALB/c nude mice	786-O, ACHN, A498, OSRC-2, Caki-1, HK-2	CDCA3	SNHG12 by upregulating CDCA3 could promote tumor progression in RCC.	[30]
RCC	Up	Human, TCGA databases	A498, 786 O, Caki-1, Caki-2, ACHN, HK-2, 293 T	miR-200c-5p, COL11A1	SNHG12 via modulating the miR-200c-5p/COL11A1 axis could enhance RCC progression.	[48]
RCC	Up	Human, BALB/c-nude mice	293 T, HK-2, A498, 786–0, 769-p, Caki-1, Caki-2, ACHN	HIF-1α, PARP, Caspase-3	Overexpression of SNHG12 via modulating HIF-1α could regulate the invasion of RCC cells.	[6]
RCC	Up	TCGA and GEO databases, cohort study, BALB/c nude mice	HUVECs, A498, 786-O, Caki-1, and 769-P, HK-2	KMT2B, CEP55, MMP-2/9, VEGF	KMT2B via upregulating SNHG12 could enhance the growth of RCC.	[11]
Clear Cell Renal Cell Carcinoma (ccRCC)	Up	TCGA and ICGC databases	786-O, CAKI-1, ACHN, 769-P, HK2	miR-129–5p, MDM4, p21/53	SNHG12 via affecting expression of MDM4 by sponging miR-129–5p could regulate ccRCC.	[45]
ccRCC	Up	Human, BALB/c nude mice	OSRC-2, 769-P	miR-30a-3p, RUNX2, IGF-IR, WNT2	SNHG12 via sponging miR-30a-3 could enhance the carcinogenesis of human renal cell cancer.	[2]
Bladder cancer (BC)	Up	GEO and TCGA databases	UMUC3, SW780	DUXAP8	SNHG12 is among dysregulated lncRNAs in BC that could be considered as potential diagnostic markers.	[19]
Prostate Cancer (PC)	Up	Human, nude mice	PC3, DU145, RWPE1	miR-195, c-Myc, Cyclin-D1, Wnt/β-catenin	SNHG12 via sponging miR-195 and activating the Wnt/β-catenin signaling could enhance cell proliferation in PC.	[35]
PC	Up	Human, TCGA, PRAD, and HCMDB databases	C4–2, PC-3, RWPE-1, LNCaP, DU 145, 22Rv1	miR-133b	SNHG12 via sponging miR-133b could indicate the prognosis of PC and accelerate tumorigenesis.	[8]
PC	Up	Human, nude mice,	WPMY-1, LNCAP, DU145, PC-3	VEGF, Bax, Bcl-2, Caspase-3	SNHG12 via targeting AKT could increase prostate tumor occurrence and progression.	[7]
PC	Up	Human	22RV1, Du145, LNCaP, RWPE1, MDaPCa2b	miR-195, CCNE1, Caspase-3/9, LC-I/II, Beclin-1, p62, PI3K, AKT, mTOR, PTEN	Dysregulation of SNHG12 via regulating the miR-195/CCNE1 axis could alter viability, apoptosis, and autophagy of PC cells.	[42]

1.1. SNHG12 in genitourinary system

Expression and function of SNHG12 in genitourinary system has been assessed in renal cell carcinoma, bladder cancer and prostate cancer (Table 1). SNHG12 has been found to be over-expressed in renal cell carcinoma tissues in association with poor clinical outcome. Moreover, it has been found to be up-regulated in sunitinib-resistant renal cell carcinoma cells. This lncRNA has a role in enhancement of proliferation, migratory potential, invasive properties and resistance to sunitinib through modulation of CDCA3 expression. From a mechanical point of view, SNHG12 has the ability to bind with SP1 and prevent the ubiquitylation-dependent proteolysis of this protein. Stabilized SP1 in turn increases expression of CDCA3 through binding with its promoter. *In vivo* assays have demonstrated that SNHG12 increases tumor growth, while its silencing reduces resistance to sunitinib. Therefore, SNHG12/SP1/CDCA3 axis represents an important mechanism in progression and sunitinib resistance of renal cell carcinoma [30]. miR-200c-5p/-COL11A1 [48] and miR-129–5p/MDM4 [25] are other routes through which SNHG12 promotes progression of renal cell carcinoma. Beisdes, SNHG12 can regulate viability and invasive properties of renal cell carcinoma cells via regulation of HIF1α [6].

Assessment of high throughput transcriptomic data in bladder cancer tissues has revealed dysregulation of lots of lncRNAs in association with genomic variations, comprising both deletions and amplifications. Notably, SNHG12 has been among dysregulated lncRNAs that have been related to clinical outcome of these patients. Moreover, the oncogenic role of SNHG12 in bladder cancer cells has been validated through siRNA assays [19].

In prostate cancer eclls, SNHG12 has been found to promote proliferation ability of cells and activate Wnt/β-catenin signals via adsorbing miR-195 [35]. Another study in prostate cancer patients has revealed that SNHG12 has the potential to predict prognosis of these patients. Based on the bioinformatic analyses, SNHG12 has been closely correlated to the progression of prostate cancer and can target miR-133b (Fig. 1). The biological effects of SNHG12 have been mediated through sponging miR-133b [8].

1.2. SNHG12 in gastrointestinal system

The role of SNHG12 in the carcinogenesis has been assessed in esophageal cancer, intrahepatic cholangiocarcinoma, hepatocellular carcinoma, pancreatic cancer, colorectal cancer and gastric cancer (Table 2). A single study has demonstrated down-regulation of SNHG12 in human esophageal carcinoma tissues compared to control samples in association with T stage, N stage, and TNM stage. Notably, down-regulation of SNHG12 expression in these cancerous tissues has been correlated with poor prognosis. Mechanistically, SNHG12 silencing has enhanced proliferation, colony forming ability, migratory potential, and invasion of esophageal cancer cells as confirmed both in vitro and in vivo. These effects are mediated through miR-195–5p/BCL9 axis [27]. Other studies in gastrointestinal tumors have reported an oncogenic role for SNHG12. Even in the context of esophageal cancer, SNHG12 has

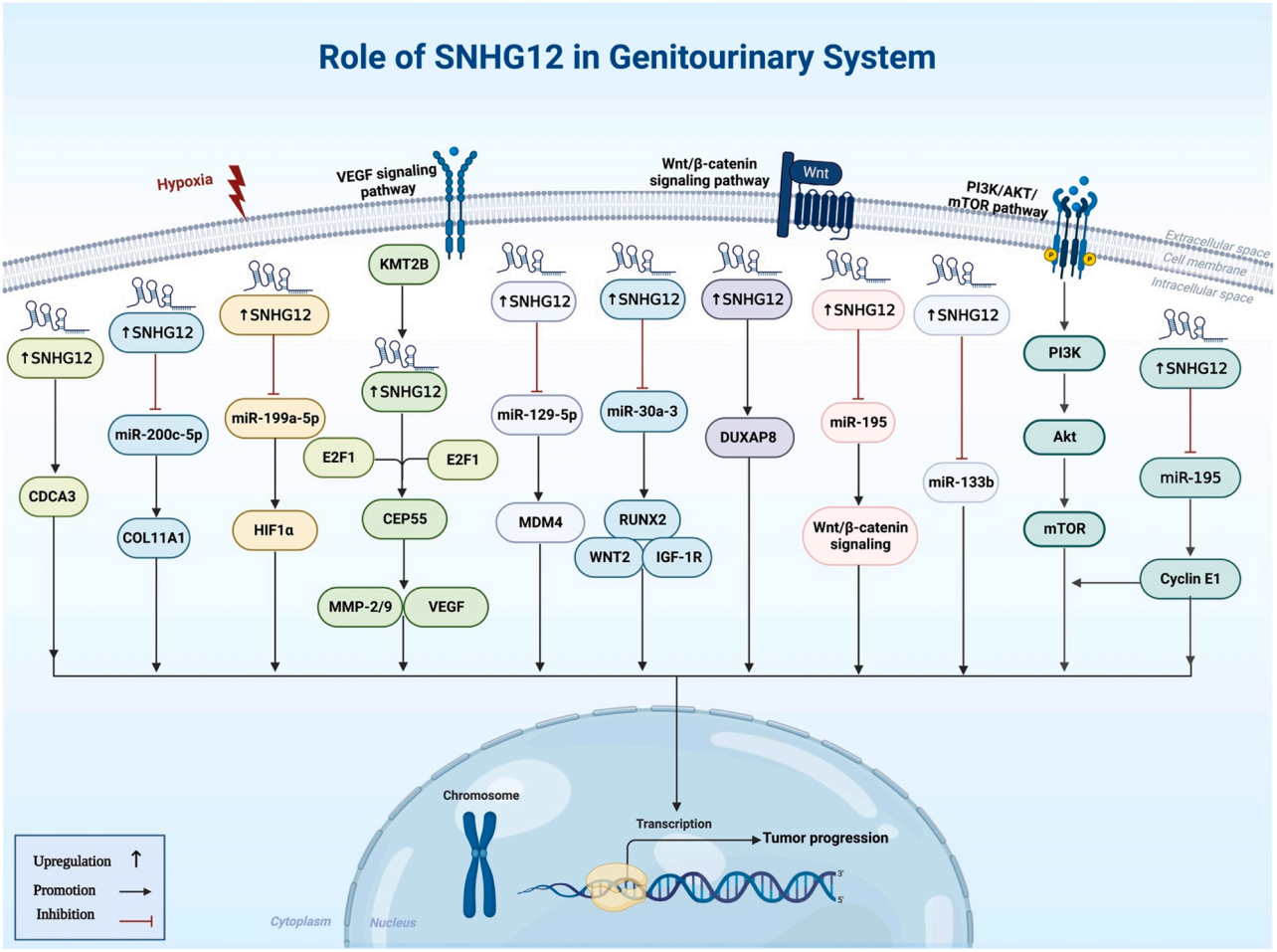

Fig. 1. Illustrates the signaling pathways give insight on the function of lncRNA SNHG12, which can stimulate the development of cancer cells in genitourinary system.

been shown to induce proliferation, migration, epithelial–mesenchymal transition (EMT), and stemness through regulation of expressions of BMI1 and CTNNB1 at post-transcriptional level [44]. Another study in intrahepatic cholangiocarcinoma cells has shown up-regulation of SNHG12 and Klotho. On the other hand, miR-199a-5p expression has been found to be decreased in these cells. Functional and in vivo studies have shown that SNHG12 affects proliferation and metastasis in this kind of cancer via modulation of miR-199a-5p/Klotho axis [44]. Activation of PI3K/AKT pathway [57], adsorption of miR-16 [60] and miR-320 [54], enhancement of stability of YWHAZ through binding with HuR and modulation of AKT/GSK-3β pathway [59], activation of miR-218–5p/YWHAZ axis [58] and induction of MAPK/ERK pathway [53] are possible routes mediating the oncogenic effects of SNHG12 in gastric cancer.

1.3. SNHG12 in female disorders

SNHG12 has been shown to induce oncogenic effects in cervical, ovarian, endometrial and breast cancers (Table 3). This lncRNA has been found to be over-expressed in human cervical cancer tissues compared with corresponding nearby normal tissues. Besides, up-regulation of SNHG12 levels in tumor tissues has been correlated with vascular involvement, lymph node metastases, advanced FIGO stage and poor clinical outcome. SNHG12 silencing could attenuate proliferation, migration and invasiveness of cervical cancer cells and inhibit tumor growth in animal models. Mechanistically, SNHG12 functions as an endogenous sponge for miR-424–5p [9]. Moreover, the sponging effect of SNHG12 on miR-125b leads to over-expression of STAT3 and enhancement of progression of cervical cancer progression (Fig. 2) [20]. Another study in cervical cancer cells has shown that expression of SNHG12 is modulated by E6 and E7 of HPV type 16 through affecting expression of transcription factor c-Myc. SNHG12 has been demonstrated to influence EMT via modulation of ERK/Slug/E-cadherin pathway [21]. Moreover, SNHG12 can accelerate progression of ovarian cancer through modulation of miR-129/SOX4 axis [36]. Most notably, SNHG12 has a prominent role in the modulation of tumor microenvironment in favor of progression of ovarian cancer though interacting with M2 macrophages [33]. In endometrial cancer, SNHG12

Table 2
SNHG12 in gastrointestinal system.

Diseases	SNHG12 Expression	Model of Study	Cell Line	Targets & Pathways	Observation	Ref
Esophageal Squamous Cell Cancer (ESCC)	Down	Human, GEPIA database, BALB/c nude mice	KYSE140, Het-1A, KYSE510, Eca9706, Ec109,	miR-195–5p, BCL9	SNHG12 via regulation of the miR-195–5p/BCL9 axis could suppress ESCC progression.	[27]
ESCC	Up	Human, BALB/c nude mice	EC9706, EC109, KYSE150/410/450	BMI1, CTNNB1, E/N-cadherin, Vimentin, IGF2BP2	SNHG12 via post-transcriptional regulation of BMI1 and CTNNB1 could induce proliferation, migration, EMT, and stemness of ESCC cells.	[44]
Intrahepatic Cholangiocarcinoma (ICC)	Up	TCGA database, BALB/c nude mice	BEC, CCLP1, TFK-1, HuCCT1, RBE	Klotho, miR-199a-5p	SNHG12 via regulating the Klotho/miR-199a-5p axis could enhance the migration and invasion of ICC cells.	[51]
Hepatocellular Carcinoma (HCC)	Up	Human	SK-Hep1	miR-199a/b-5p, NF-κB, ERK-1/2	SNHG12 via targeting miR-199a/b-5p could enhance tumorigenesis and metastasis in HCC.	[22]
Pancreatic Cancer (PC)	Up	Human	HPDE6, BXPC3, CAPAN1, PANC1, SW1990,	miR-320b, E/N-cadherin, Vimentin	SNHG12 via absorbing miR-320b could contribute to proliferation, invasion, and EMT of PC cells.	[4]
Gastric Cancer (GC)	Up	Human	SGC-7901, BGC-823, GES-1	miR-199a/b-5p	SNHG12 via targeting miR-199a/b-5p could regulate the proliferation of GC cell BGC-823.	[50]
GC	Up	Human, TCGA and GEO databases, BALB/c nude mice	GES-1, SGC-7901, HGC-27, BGC-823, MGC-803, AGS	MEK1/2, ERK1/2, Cyclin-D1, Caspase-9, MMP-2, PI3K/AKT	SNHG12 via activating the PI3K/AKT pathway could promote GC.	[57]
GC	Up	Human	AGS, HGC27, BGC823, GES-1, SGC7901	miR-16	Knockdown of SNHG12 via upregulating miR-16 could suppress migration and invasion of GC cells.	[60]
GC	Up	Human, BALB/c nude mice	MGC-803, AGS, HGC-27, MKN-28, MKN-45, GES-1, SGC-7901, BGC-823,	AKT, GSK-3β, HuR, YWHAZ, ELAVL1	SNHG12 via targeting the AKT/GSK-3β pathway by binding to HuR and stabilizing YWHAZ could enhance GC proliferation and invasion.	[59]
GC	Up	Human, BABL/c nude mice	AGS, MGC-803, SGC-7901, GES-1, HS-746 T, 293 T	YY1, miR-218–5p, YWHAZ, Snail, Vimentin, CTNB1, E/N-cadherin	YY1 via modulating SNHG12 by activating the miR-218–5p/YWHAZ axis could promote GC metastasis.	[58]
GC	Up	Human	SGC7901, AGS, NCI-N87, GES-1	miR-320, CRKL, AKT, ERK	SNHG12 via acting as a molecular sponge of miR-320 could regulate GC progression.	[54]
GC	Up	Human, GEO database, BALB/c mice, nu/ nu mice	HPMCs, MMT, GES-1, HGC-27, NCI-N87, SNU-1, SNU5, 293 T	E2F7, miR-129–5p, Caspase-3, ZO-1, Vimentin, MAPK/ERK	GC cell-derived extracellular vesicles via SNHG12 by elevating E2F7 expression and activating the MAPK/ERK pathway could promote peritoneal metastasis.	[53]
Colon cancer (CC)	Up	Human, BALB/c nude mice	LoVo, HCT116, SW480, HT29, HIEC	miR-15a, PDK4, Caspase-3/9, HIF-1α, VEGFA	SNHG12 via regulating the miR-15a/PDK4 axis could enhance the development and progression of CC.	[16]
Colorectal Carcinoma (CRC)	Up	Human, BALB/c nude mice	SW480, LOVO, HCT116, HT29, HCoEpiC	CDK4, CDK6, CCND1, Caspase-3, AKT	SNHG12 could enhance cell growth and inhibit cell apoptosis in CRC cells.	[40]
CRC	Up	Human	NCM460, HT-29, SW480, SW620, LoVo	miR-16	SNHG12 via sponging miR-16 could increase proliferation and invasion of CRC cells.	[31]

acts as a sponge for miR-4429 [3] and activation of Notch signaling pathway [2]. SNHG12 can also promote breast carcinogenesis through sponging miR-451a [10].

SNHG12 is also involved in the pathogenesis of preeclampsia, since it can promote proliferation, migration, and invasion of trophoblast cells through regulation of EMT process and cell cycle [62].

1.4. SNHG12 in pulmonary disorders

SNHG12 has been shown to be up-regulated in non-small cell lung cancer cells and tissues (Table 4). This lncRNA has an essential role in EMT in this type of cancer, since its silencing inhibits tumor metastasis and EMAT through modulation of Slug/ZEB2 signals. This lncRNA acts as a sponge for miR-218 [43] and miR-101–3p [46] in these cells. Moreover, SNHG12 facilitates immune escape via modulation of HuR/PD-L1/USP8 axis (Fig. 3) [18]. Most notably, SNHG12-containing exsosmes secreted from carcinoma-associated fibroblasts have been found to promote resistance to cisplatin in lung cancer cells [39]. SNHG12 has also been shown to decrease lung cell damage and acute lung injury-induced production of inflammatory cytokines. Mechanistically, SNHG12 interacts with miR-140–3p to affect expresion of its target gene fndc5 [56].

Table 3
SNHG12 in female disorders.

Diseases	SNHG12 Expression	Model of Study	Cell Line	Targets & Pathways	Observation	Ref
Cervical Cancer (CC)	Up	Human	C33A, ME-180, CaSki, HeLa, SiHa	miR-424–5p	Upregulation of SNHG12 via sponging miR-424–5p could contribute to cell invasion in CC.	[9]
CC	Up	-	HeLa, SiHa, Caski, C4–1, C33A, 293 T	miR-125b, STAT3	SNHG12 via modulating the miR-125b/STAT3 axis could increase the progression of CC.	[20]
Cervical Squamous Cell Carcinoma (CSCC)	Up	Human, BALB/c nude mice	CaSki, SiHa	ERK1/2, Slug, Caspase-3, E-Cadherin, c-Myc	SNHG12 could enhance CC progression via ERK/Slug pathway.	[21]
Ovarian Cancer (OC)	Up	Human	IOSE80, SKOV3, OVCAR3, A2780	miR-129, SOX4	SNHG12 via sponging miR-129 and up-regulating SOX4 could accelerate the progression of OC.	[36]
OC	Up	Human, NOD/SCID nude mice	293 T, SKOV3, THP-1	miR-21, IL-6, PD-L1, NF-κB1, TSG101	SNHG12 via interacting with M2 macrophages could enhance the immune escape of OC cells.	[33]
OC	Up	TCGA and internal databases	IGROV1, Ovc316, OVCAR3/4/5/8, IGROV1-R1, OVCAR3-R1/R2, OVCAR5-R1; Carboplatin (10 μM, 50 μM)	-	SNHG12 via epigenetic mechanisms could be considered as a mediator of carboplatin resistance in OC.	[1]
Endometrial Cancer (EC)	Up	-	Ishikawa, KLE, RL95–2, AN3 CA, ESC	miR-4429, MMP-2/9	SNHG12 via targeting miR-4429 could regulate cell proliferation, invasion, and migration of EC.	[3]
EC	Up		Ishikawa, KLE, RL95–2, ESC	ZIC2, Notch1, PCNA, MMP-2/9, HES-1	ZIC2 via upregulating SNHG12 by activating the Notch pathway could promote EC cell proliferation and migration.	[2]
Triple-Negative Breast Cancer (TNBC)	Up	Human	MDA-MB-231, BT-549	c-Myc, MMP-13, KRAS, SLUG, E-cadherin, FOXO1, Noth1	c-Myc via upregulating SNHG12 could regulate cell proliferation, apoptosis, and migration of TNBC.	[41]
Breast Cancer (BCa)	Up	Human, BALB/c nude mice	MCF-10A, MCF-7, BT-549, SK-BR-3, MDA-MB-231	miR-451a, AKT, mTOR	Knockdown of SNHG12 via sponging miR-451a could suppress cell proliferation, migration, and invasion in BCa.	[10]
Preeclampsia	Down	Human	HTR-8/SVneo	MMP-2/9, β-catenin, E-cadherin, Vimentin, CDK-2, p21, Cyclin-D1	SNHG12 via regulating EMT and cell cycle could enhance proliferation, migration, and invasion of trophoblast cells.	[62]

1.5. SNHG12 in CNS disorders

Expression of SNHG12 is elevated in glioblastoma, spinal cord injury and cerebral ischemia/reperfusion (I/R) injury (Table 5). In glioblastoma cells, SNHG12 through sponging miR-129–5p and targeting the MAPK1/E2F7 axis could activate MAPK/ERK pathway, inhibit cell apoptosis and induce temozolomide resistance [32]. Mechanistically, its expression is activated by abnormal DNA demethylation [32]. Consistent with this finding, suppression of TDP43-mediated SNHG12/miR-195/SOX5 feedback loop has been shown to impede progression of glioma [29].

In the context of cerebral I/R injury, it has been shown that SNHG12 induces autophagy and exert protective effects against neron loss [52]. On the other hand, another study has indicated that SNHG12 silencing enhances the effectiveness of mesenchymal stem cells in relieving I/R injury through the PI3K/AKT/mTOR signaling pathway [31].

Finally, SNHG12 not only amends brain microvascular endothelial cell damage through targeting miR-199a [24], but also suppresses oxygen-glucose deprivation-associated apoptosis of neurons through modulating miR-181a-5p/NEGR1 route [49].

1.6. SNHG12 in cardiovascular disorders

SNHG12 has a possible role in the pathophysiology of atherosclerosis, hypertension and peripheral artery disease (Table 6). It can regulate miR-199a-5p/HIF-1α axis to enhance proliferation and migration of vascular smooth muscle cells [38]. On the other hand, it has a role in the DNA damage response and vascular senescence [17]. This lncRNA is over-expressed in the vascular endothelial cells and is down-regulated in the process of progression of atherosclerosis. SNHG12 silencing has enhanced development of atherosclerotic lesions through increasing DNA damage and senescence in the vascular endothelial cells. On the contrary, intravenous transfer of SNHG12 has sheltered the tunica intima from DNA damage and atherosclerosis. Mechanistically, SNHG12 interacts with DNA-dependent protein kinase [17]. Sun et al. observed that ox-LDL treatment of both the animal model and VSMCs led to a considerable upregulation of SNHG12 expression. Overexpression of SNHG12 promoted VSMC proliferation and migration while knockdown of SNHG12 inhibited these processes [38]. They proved that miR-199a-5p was an SNHG12 target and that HIF-1 could be indirectly and favorably controlled by SNHG12 (Fig. 4). Furthermore, Angiogenic EC response to ischemia is mostly mediated by SNHG12, which plays a crucial role in this process. For example, Analysis of RNA-Seq data from SNHG12-deficient ECs revealed changes to angiogenesis signaling pathways and a significant impact on cell cycle, which is often controlled by IMP3. Injection of gapmeRs inhibited SNHG12 expression, which led to a decrease in angiogenesis in FAL animals and was more apparent in an insulin-resistant animal model [15].

1.7. SNHG12 in other disorders

SNHG12 has also been shown to be up-regulated in nasal-type natural killer/T-cell lymphoma, diffuse large B-cell lymphoma, melanoma, papillary thyroid carcinoma, laryngeal squamous cell carcinoma and

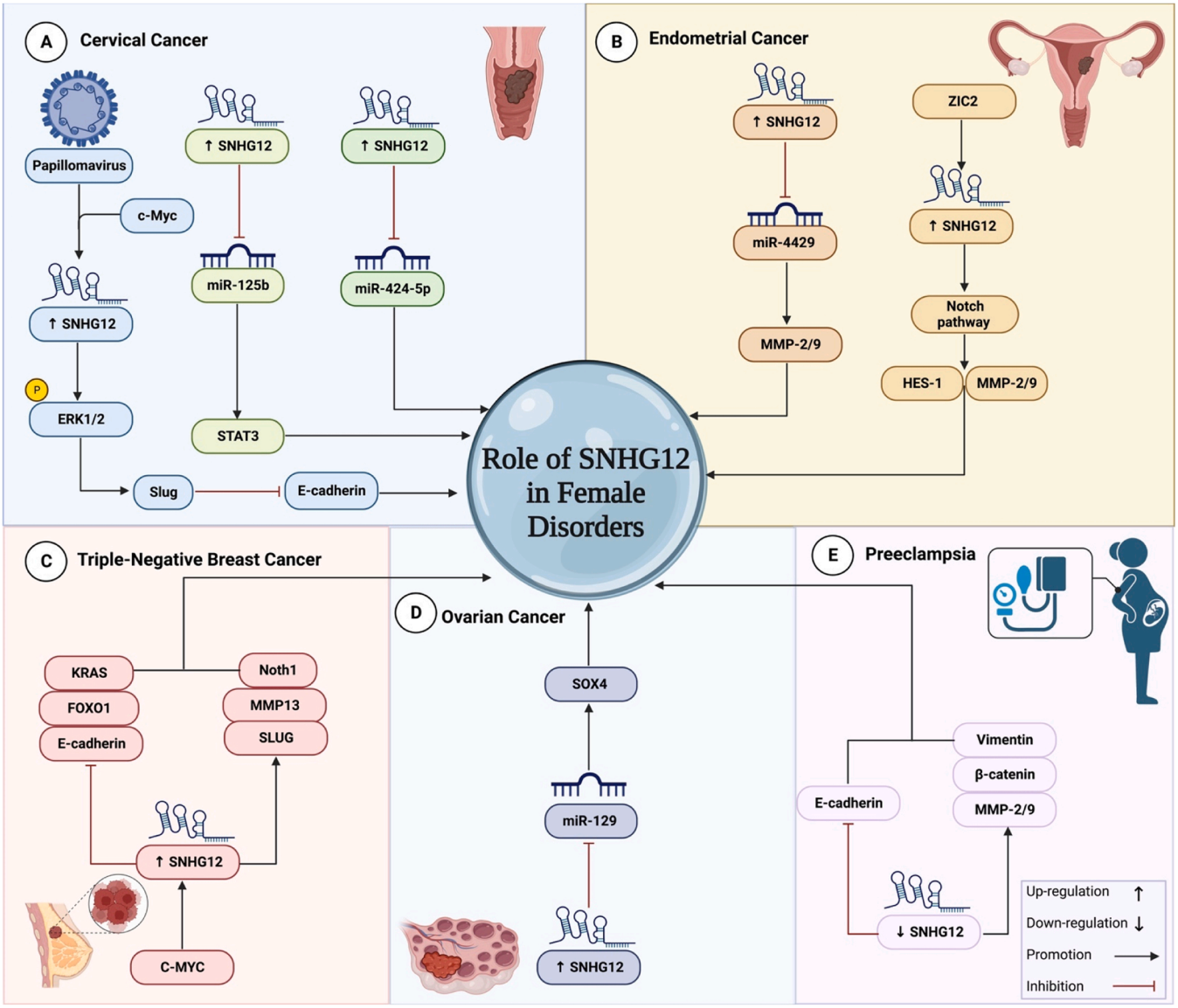

Fig. 2. Illustration highlights the key roles of lncRNA SNHG12 in female disorders. (A) SNHG12 in cervical cancer; HPV E6/E7 upregulates SNHG12 expression through the cMyc transcription factor. Increased ERK1/2 phosphorylation then facilitated in the production of Slug, a transcriptional regulator of E-cadherin. (B) SNHG12 in endometrial cancer is upregulated and miR4429 is silenced, the expression of MMP2 and MMP9 is increased, which in turn promotes the growth of endometrial cancer. (C) The oncogene role of SNHG12 in TNBC. KRAS, E-cadherin, and FOXO1 showed negatively connected with SNHG12 expression, while MMP-13, SLUG, and Notch 1 expression appeared positively associated. (D) Increased rates of ovarian cancer progression have been linked to upregulated SNHG12 (due to miR-129 sponging) and SOX4. (E) Increased trophoblast cell proliferation triggered by inhibition of SNHG12. MMP-2/9, β-catenin, and vimentin expression all have been positively connected with SNHG12, but E-cadherin expression was inversely correlated.

Table 4
SNHG12 in pulmonary disorders.

Diseases	SNHG12 Expression	Model of Study	Cell Line	Targets & Pathways	Observation	Ref
Non-small cell lung carcinoma (NSCLC)	Up	Human	A549, H1299	Slug, ZEB2, miR-218, Caspase-3/9, MMP-9, E-cadherin, Vimentin	Knockdown of SNHG12 via the Slug/ZEB2 axis by targeting miR-218 in NSCLC could suppress tumor metastasis and EMT.	[43]
NSCLC	Up	Human, GEPIA databases, C57BL/6 mice	A549, SW1573, H1975, BEAS-2B, H1299, PBMCs	HuR, PD-L1, USP8, LDH, TNF-α, IFN-γ, IL-10, TGF-β	SNHG12 via targeting the HuR/PD-L1/USP8 axis could regulate the immune escape of NSCLC.	[18]
NSCLC	Up	Human	A549, H1299	miR-101–3p, CUL4B, E/N-cadherin, Vimentin, PI3K/AKT	SNHG12 via regulating the miR-101–3p/CUL4B axis could mediate proliferation, migration, and invasion of NSCLC.	[46]
NSCLC	Up	Human, BALB/c nude mice	primary fibroblast, A549, BEAS2B, HCC44; DDP (0–10 μg/mL) for 48	α-SMA, FAP, HuR, Vimentin, XIAP	SNHG12 in extracellular vesicles derived from carcinoma-associated fibroblasts could enhance DDP resistance in NSCLC.	[39]
Acute Lung Injury	Down	BALB/c mice	PMVECs	miR-140–3p, fndc5, IL-1β, TNF-α, IL-6	Inhibition of SNHG12 via suppressing the miR-140–3p/fndc5 axis could protect the endothelium from LPS-induced inflammation.	[56]

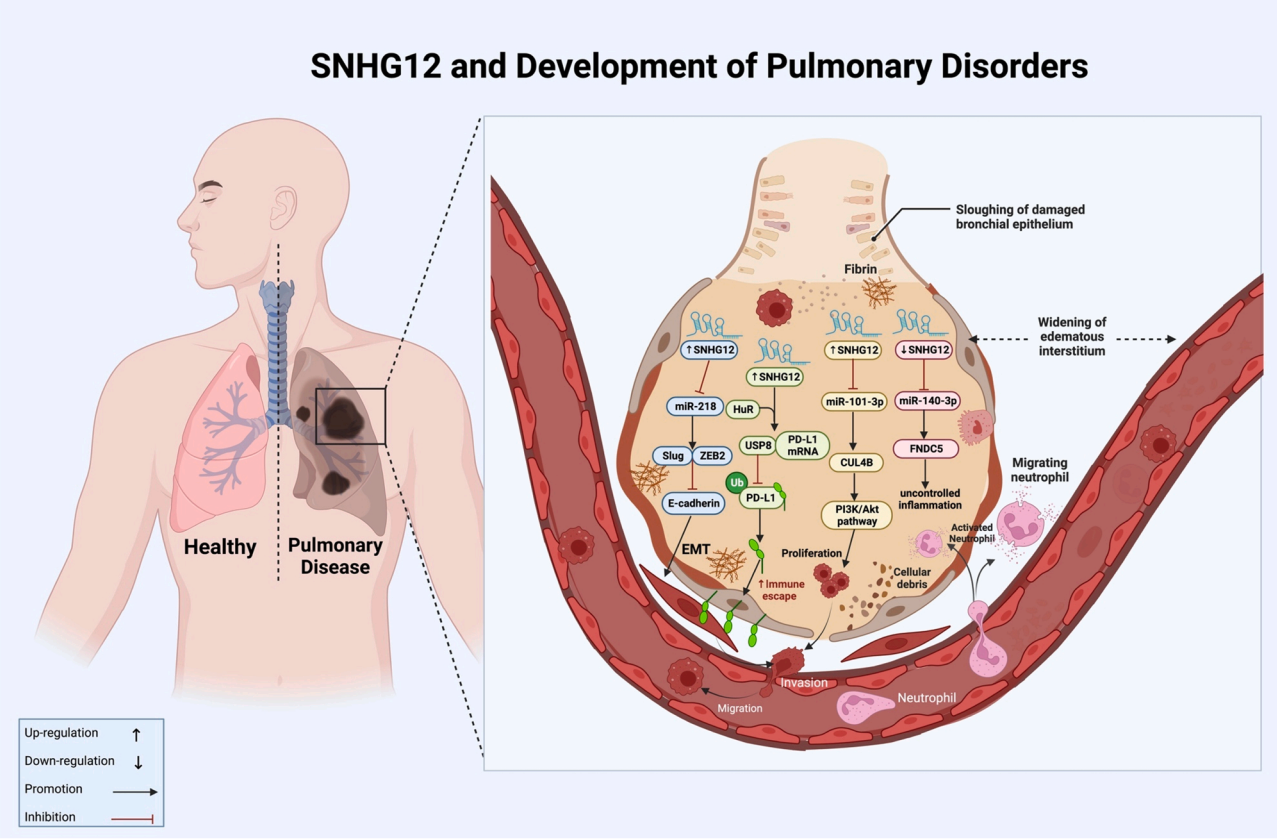

Fig. 3. Illustrates the functional mechanisms of SNHG12 in pulmonary disease.

osteosarcoma (Table 7). Moreover, this lncRNA has been shown to be an lncRNA that is associated with liver regeneration. SNHG12 expression is upregulated following partial hepatectomy. Moreover, its expression has been elevated in normal liver cells following treatment with hepatocyte growth factor. This lncRNA can enhance hepatocytes proliferation in vitro and in vivo. Up-regulation of SNHG12 has enhanced activity of Wnt/β-catenin pathway in hepatocytes [65].

2. Discussion

SNHG12 has been shown to harbor several miRNAs binding sites, thus acting as a sponge for a variety of miRNAs and modulating expression of their downstream targets. miR-200c-5p, miR-129–5p, miR-30a-3p, miR-195, miR-133b, miR-199a/b-5p, miR-320b, miR-16, miR-15a, miR-218–5p and miR-320 are examples of miRNAs being

Table 5
SNHG12 in CNS disorders.

Diseases	SNHG12 Expression	Model of Study	Cell Line	Targets & Pathways	Observation	Ref
Glioblastoma (GBM)	Up	Human, BALB/c nude mice, GEO database	Pri GBM, Rec GBM, N3S, N3T3rd, U251, U251T3rd, 293 T, N3; TMZ (200 μM) for 48 h	SP1, miR-129–5p, MAPK1, E2F7, Cyclin-D1, CDK4/6, p-Rb	SNHG12 by sponging miR-129–5p, targeting the MAPK1/E2F7 axis, and activating the MAPK/ERK pathway could inhibit cell apoptosis in GBM. SNHG12 could be activated by abnormal DNA demethylation.	[32]
GBM	-	Human, nude Mice	U87, U251, 293 T	TDP43, miR-195, SOX5, Gelsolin	Inhibition of TDP43 via affecting the SNHG12/miR-195/SOX5 feedback loop could impede progression of GBM.	[29]
Glioma	Up	Human	HF, U87, LN229, U373, U251	HuR	SNHG12 via binding to HuR could increase the proliferation and migration of glioma cells.	[24]
Spinal Cord Injury	Up	SD rats	DRGs, PC12, 293 T	KLF2, miR-494–3p, RAD23B, IL–6, TNF–α, IL-1β	The KLF2/SNHG12/miR-494–3p/RAD23B axis could spare nerve injury-induced neuropathic pain.	[55]
Cerebral I/R Injury	Up	Mice	-	LC3B I/II, Beclin-1, p62	SNHG12 as an autophagy inducer could exert neuroprotective effects against cerebral I/R injury.	[52]
Ischemic Stroke	Up	SD rats	MSCs, BMECs	PI3K, AKT, mTOR, LC3B, p62, Caspase-3	Silencing SNHG12 via targeting the PI3K/AKT/mTOR pathway could enhance the effectiveness of MSCs.	[31]
Ischemic Stroke	Up	-	BMECs	miR-199a, E-selectin, MCP-1, IL-6, VEGFA	SNHG12 via targeting miR-199a could ameliorate brain microvascular endothelial cell injury.	[24]
Stroke	Down	Human	SH-SY5Y	miR-181a-5p, NEGR1, Bax, Bcl-2, Caspase-3	SNHG12 via targeting the miR-181a-5p/NEGR1 axis could inhibit oxygen-glucose deprivation-induced neuronal apoptosis.	[49]
Neurotoxicity	Down	-	SH-SY5Y	miR-497–5p, NLRX1, LDH, SOD, MDA, GSH-Px, BDNF	SNHG12 could ameliorate neurotoxicity via sponging miR-497–5p and upregulating NLRX1.	[37]

Table 6
SNHG12 in cardiovascular disorders.

Diseases	SNHG12 Expression	Model of Study	Cell Line	Targets & Pathways	Observation	Ref
Atherosclerosis	Up	C57BL/6 mice, ApoE− /− mice	VSMCs	miR-199a-5p, HIF-1α	SNHG12 via regulating the miR-199a-5p/HIF-1α axis could enhance vascular smooth muscle cell proliferation and migration.	[38]
Atherosclerosis	Down	Human, Ldlr− /− mice, C57Bl/6 mice, ApoE− /− mice, Pig	PBMCs, HUVECs, VSMCs	DNA-PK, ATM, ATR, Ku70/80, p16/21/53, USF-2, γH2AX	SNHG12 via integrating DNA-PK could mediate DNA damage response and vascular senescence.	[17]
Hypertension	Down	C57BL/6 mice	ECs, HUVECs, HMEC-1	miR-25–3p, SIRT6, P16/21, VE-cadherin	SNHG12 via regulating the miR-25–3p/SIRT6 axis could alleviate hypertensive vascular endothelial injury.	[34]
Peripheral Artery Disease	-	db/db mice, BALB/c mice, C57BL/6 mice	HUVECs, ECs	DNAPK, DHX9, DDX3Y, IGF2BP3,	Deficiency of SNHG12 via altering the endothelial cell cycle pathway could impair ischemic limb neovascularization.	[15]

sponged by SNHG12. Through this mechanism, SNHG12 can affect activity of HIF-1α, Wnt/β-catenin, VEGF, PI3K/AKT/mTOR, PTEN, NF-κB and ERK-1/2 signaling [12–14].

The sponging effect of SNHG12 on miR-195 has been verified in prostate cancer, esophageal cancer, glioblastoma, diffuse large B-cell lymphoma and osteosarcoma representing this miRNA as a possible ubiquitous target for SNHG12. Thus, therapies targeting SNHG12/miR-195 can be beneficial in wide array of malignancies. Most notably, this axis is a shared axis for mediation of both oncogenic and tumor suppressor role of SNHG12.

Similarly, miR-199 has been found to be targeted by SNHG12 in intrahepatic cholangiocarcinoma, hepatocellular carcinoma, gastric cancer, melanoma, ischemic stroke and atherosclerosis, showing SNHG12/miR-199 axis as a mechanism in the development of both malignant and non-malignant conditions.

Except from a single study in esophageal cancer [27], all conducted studies have reported an oncogenic role for SNHG12. This effect of SNHG12 has been verified in animal models as well as expression studies in clinical samples that revealed association between up-regulation of SNHG12 and poor patients' prognosis. Besides, SNHG12 has been reported to enhance EMT in esophageal, lung and pancreatic cancers.

Since SNHG12 can modulate response of cancer cells to different anti-cancer agents such as cisplatin, sunitinib, doxorubicin, temozolomide and carboplatin, SNHG12-targeting therapies are regarded as important tools for defeating chemoresistance in cancers. In spite of the presence of extensive evidence on the efficacy of SNHG12 targeting strategies in suppression of tumor growth in animal models of cancers, there is no evidence from clinical studies in this regard which is partly due to safety issues for introduction of these kinds of therapies into human cells.

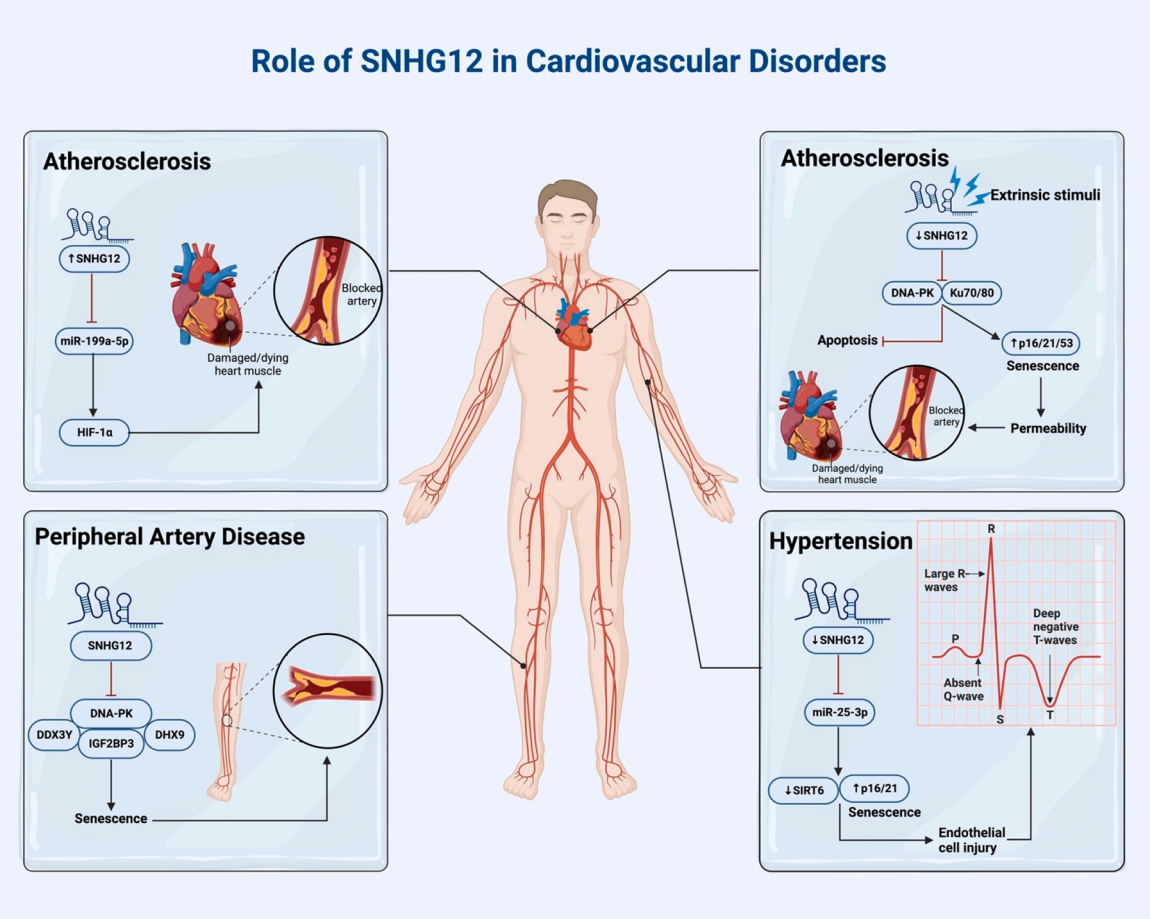

Fig. 4. Potential involvement of SNHG12 in atherosclerosis, hypertension, and peripheral arterial disease.

Table 7
SNHG12 in other disorders.

Diseases	SNHG12 Expression	Model of Study	Cell Line	Targets & Pathways	Observation	Ref
Nasal-Type Natural Killer/T-Cell Lymphoma (NKTCL)	Up	Human	YTS, SNK-6, SNK-1, SNT-8; CDDP (5 μg/mL) for 48 h	c-Myc, P-gp	c-Myc via upregulating SNHG12 could regulate proliferation and drug sensitivity in NKTCL.	[64]
Diffuse Large B-Cell Lymphoma (DLBCL)	Up	Human, BALB/c nude mice	OCI-LY7, OCI-LY3, IM-9I	miR-195, LDH	SNHG12 via sponging miR-195 could indicate prognosis and accelerate tumorigenesis of DLBCL.	[5]
Melanoma	Up	-	A2058, SK-MEL-28, CHL-1, A375, HEMa-LP	miR-199b, ETS1, PXN, JAG1, DDR1	SNHG12 via targeting miR-199b could increase the malignant progression of melanoma.	[47]
Papillary Thyroid Carcinoma (PTC)	Up	Human, GEO and TCGA, and GEPIA databases	-	-	Upregulation of SNHG12 could be considered as a diagnostic marker of PTC.	[28]
Laryngeal Squamous Cell Carcinoma (LSCC)	Up	Human	AMC-HN-8	miR-129–5p, WWP1	SNHG12 via sponging miR-129–5p and potentiating WWP1 expression could increase proliferation and invasion of LSCC.	[26]
Osteosarcoma (OS)	Up	Human	143B, U2OS, MG63, HOS, hFOB	miR-195–5p, CDK4/6, CCND1, Notch-2	SNHG12 via upregulating the Notch2 by sponging miR-195–5p could enhance tumorigenesis and metastasis in OS.	[63]
OS	-	Human	MG-63, U2OS; DXR (0.125, 0.250, 0.500, 1.000, 2.000, 4.000 μg/mL) DXR HOS, SAOS-2, hFOB, MG-63/DXR; DXR (2.000, 4.000, 8.000, 16.000, 32.000 and 64.000 μg/mL)	miR-320a, MCL1	SNHG12 via targeting the miR-320a/MCL1 axis could mediate DXR resistance of OS.	[61]
-	Up	BALB/c mice	NCTC 1469, BNL CL.2	Wnt/β-catenin	Partial hepatectomy via upregulating SNHG12 could enhance hepatocyte proliferation and liver regeneration.	[65]

3. Conclusion

SNHG12 has diverse roles in the physiological processes. Abnormal regulation of this lncRNA leads to diverse pathologies, especially malignancies. SNHG12 can serve as a biomarker for detection of these conditions.

Ethics approval and consent to participant

Not applicable.

Consent of publication

Not applicable.

Funding

Not applicable.

CRediT authorship contribution statement

SGF and AB wrote the draft and revised it. MT and MS designed and supervised the study. YP, BMH, SRA and HS collected the data and designed the figures and tables. All the authors read the submitted version and approved it.

Declaration of Competing Interest

The authors declare they have no conflict of interest.

Acknowledgement

The authors would like to thank the clinical Research Development Unit (CRDU) of Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran for their support, cooperation and assistance throughout the period of study.

References

[1] C. Abildgaard, L.M. Do Canto, C.A. Rainho, F.A. Marchi, N. Calanca, M. Waldstrøm, K.D. Steffensen, S.R. Rogatto, The long non-coding RNA SNHG12 as a mediator of carboplatin resistance in ovarian cancer via epigenetic mechanisms, Cancers 14 (2022) (1664).
[2] P. Cai, G. Li, M. Wu, B. Zhang, H. Bai, ZIC2 upregulates lncRNA SNHG12 expression to promote endometrial cancer cell proliferation and migration by activating the Notch signaling pathway, Mol. Med. Rep. 24 (2021) 1–9.
[3] P. Cai, M. Wu, B. Zhang, S. Wu, H. Wei, L. Wei, Long non-coding RNA SNHG12 regulates cell proliferation, invasion and migration in endometrial cancer by targeting miR-4429, Mol. Med. Rep. 22 (2020) 2842–2850.
[4] W. Cao, G. Zhou, LncRNA SNHG12 contributes proliferation, invasion and epithelial–mesenchymal transition of pancreatic cancer cells by absorbing miRNA-320b, Biosci. Rep. 40 (2020).
[5] L.-Y. Chen, X.-M. Zhang, B.-Q. Han, H.-B. Dai, Long noncoding RNA SNHG12 indicates the prognosis and accelerates tumorigenesis of diffuse large B-cell lymphoma through sponging microR-195, OncoTargets Ther. 13 (2020) 5563.
[6] Q. Chen, W. Zhou, S.-q Du, D.-x Gong, J. Li, J.-b Bi, Z.-h Li, Z. Zhang, Z.-l Li, X.-k Liu, Overexpression of SNHG12 regulates the viability and invasion of renal cell carcinoma cells through modulation of HIF1α, Cancer Cell Int. 19 (2019) 1–12.
[7] Z. Chen, T. Qi, X.-p Qin, J. Wang, Z.-s Huang, X.-y Hu, G. Chen, L.-j Qu, Y.-m Zhuo, Long noncoding RNA SNHG12 promotes prostate tumor occurrence and progression via AKT regulation, BioMed. Res. Int. 2020 (2020).
[8] G. Cheng, Z. Song, Y. Liu, H. Xiao, H. Ruan, Q. Cao, K. Wang, W. Xiao, Z. Xiong, D. Liu, Long noncoding RNA SNHG12 indicates the prognosis of prostate cancer and accelerates tumorigenesis via sponging miR-133b, J. Cell. Physiol. 235 (2020) 1235–1246.
[9] J. Dong, Q. Wang, L. Li, Z. Xiao-Jin, Upregulation of long non-coding RNA small nucleolar RNA host gene 12 contributes to cell growth and invasion in cervical cancer by acting as a sponge for MiR-424-5p, Cell. Physiol. Biochem. 45 (2018) 2086–2094.
[10] Y. Dong, G. Wang, Knockdown of lncRNA SNHG12 suppresses cell proliferation, migration and invasion in breast cancer by sponging miR-451a, Int. J. Clin. Exp. Pathol. 13 (2020) 393.
[11] J.-f Feng, J. Wang, G. Xie, Y.-d Wang, X.-h Li, W.-y Yang, Y.-w Yang, B. Zhang, KMT2B promotes the growth of renal cell carcinoma via upregulation of SNHG12 expression and promotion of CEP55 transcription, Cancer Cell Int. 22 (2022) 1–13.
[12] S. Ghafouri-Fard, A. Abak, F. Fattahi, B.M. Hussen, Z. Bahroudi, H. Shoorei, M. Taheri, The interaction between miRNAs/lncRNAs and nuclear factor-κB (NF-κB) in human disorders, Biomed. Pharmacother. 138 (2021), 111519.
[13] S. Ghafouri-Fard, M.C. Glassy, A. Abak, B.M. Hussen, V. Niazi, M. Taheri, The interaction between miRNAs/lncRNAs and Notch pathway in human disorders, Biomed. Pharmacother. 138 (2021), 111496.
[14] S. Ghafouri-Fard, H. Shoorei, M. Mohaqiq, J. Majidpoor, M.A. Moosavi, M. Taheri, Exploring the role of non-coding RNAs in autophagy, Autophagy 18 (2022) 949–970.
[15] D.A. Gross, H.S. Cheng, R. Zhuang, M.G. McCoy, D. Pérez-Cremades, Z. Salyers, A. Wara, S. Haemmig, T.E. Ryan, M.W. Feinberg, Deficiency of lncRNA SNHG12 impairs ischemic limb neovascularization by altering an endothelial cell cycle pathway, JCI Insight 7 (2022).
[16] K. Guo, Y. Zhang, L. Liu, H. Meng, LncRNA SNHG12 promotes the development and progression of colon cancer by regulating the miR-15a/PDK4 axis, Am. J. Transl. Res. 13 (2021) 10233.
[17] S. Haemmig, D. Yang, X. Sun, D. Das, S. Ghaffari, R. Molinaro, L. Chen, Y. Deng, D. Freeman, N. Moullan, Long noncoding RNA SNHG12 integrates a DNA-PK–mediated DNA damage response and vascular senescence, Sci. Transl. Med. 12 (2020), eaaw1868.
[18] Y. Huang, L. Xia, X. Tan, J. Zhang, W. Zeng, B. Tan, X. Yu, W. Fang, Z. Yang, Molecular mechanism of lncRNA SNHG12 in immune escape of non-small cell lung cancer through the HuR/PD-L1/USP8 axis, Cell. Mol. Biol. Lett. 27 (2022) 1–23.
[19] B. Jiang, S. Hailong, J. Yuan, H. Zhao, W. Xia, Z. Zha, W. Bin, Z. Liu, Identification of oncogenic long noncoding RNA SNHG12 and DUXAP8 in human bladder cancer through a comprehensive profiling analysis, Biomed. Pharmacother. 108 (2018) 500–507.
[20] X.J. Jin, X.J. Chen, Z.F. Zhang, W.S. Hu, R.Y. Ou, S. Li, J.S. Xue, L.L. Chen, Y. Hu, H. Zhu, Long noncoding RNA SNHG12 promotes the progression of cervical cancer via modulating miR-125b/STAT3 axis, J. Cell. Physiol. 234 (2019) 6624–6632.
[21] S.Y. Lai, H.M. Guan, J. Liu, L.J. Huang, X.L. Hu, Y.H. Chen, Y.H. Wu, Y. Wang, Q. Yang, J.Y. Zhou, Long noncoding RNA SNHG12 modulated by human papillomavirus 16 E6/E7 promotes cervical cancer progression via ERK/Slug pathway, J. Cell. Physiol. 235 (2020) 7911–7922.
[22] T. Lan, W. Ma, Z. Hong, L. Wu, X. Chen, Y. Yuan, Long non-coding RNA small nucleolar RNA host gene 12 (SNHG12) promotes tumorigenesis and metastasis by targeting miR-199a/b-5p in hepatocellular carcinoma, J. Exp. Clin. Cancer Res. 36 (2017) 1–10.
[23] T. Lan, W. Ma, Z. Hong, L. Wu, X. Chen, Y. Yuan, Long non-coding RNA small nucleolar RNA host gene 12 (SNHG12) promotes tumorigenesis and metastasis by targeting miR-199a/b-5p in hepatocellular carcinoma, J. Exp. Clin. Cancer Res. CR 36 (2017) 11.
[24] W. Lei, Z.-L. Wang, H.-J. Feng, X.-D. Lin, C.-Z. Li, D. Fan, Long non-coding RNA SNHG12promotes the proliferation and migration of glioma cells by binding to HuR, Int. J. Oncol. 53 (2018) 1374–1384.
[25] H. Li, Z. Cui, X. Lv, J. Li, M. Gao, Z. Yang, Y. Bi, Z. Zhang, S. Wang, S. Li, Long non-coding RNA HOTAIR function as a competing endogenous RNA for miR-149-5p to promote the cell growth, migration, and invasion in non-small cell lung cancer, Front. Oncol. 10 (2020), 528520.
[26] J. Li, S. Sun, W. Chen, K. Yuan, Small nucleolar RNA host gene 12 (SNHG12) promotes proliferation and invasion of laryngeal cancer cells via sponging miR-129-5p and potentiating WW domain-containing E3 ubiquitin protein ligase 1 (WWP1) expression, Med. Sci. Monit. Int. Med. J. Exp. Clin. Res. 25 (2019) 5552.
[27] M. Liang, Z. Pan, F. Yu, C. Chen, Long noncoding RNA SNHG12 suppresses esophageal squamous cell carcinoma progression through competing endogenous RNA networks, Clin. Transl. Oncol. 22 (2020) 1786–1795.
[28] J. Liu, X. Tang, J. Lv, X. Peng, K. Zhang, C. Li, J. Liu, G. Wang, Z. Li, LncRNAs SNHG12 and LINC00152 were associated with progression of patients with papillary thyroid carcinoma, Future Oncol. 15 (2019) 4167–4179.
[29] X. Liu, J. Zheng, Y. Xue, C. Qu, J. Chen, Z. Wang, Z. Li, L. Zhang, Y. Liu, Inhibition of TDP43-mediated SNHG12-miR-195-SOX5 feedback loop impeded malignant biological behaviors of glioma cells, Mol. Ther. -Nucleic Acids 10 (2018) 142–158.
[30] Y. Liu, G. Cheng, Z. Huang, L. Bao, J. Liu, C. Wang, Z. Xiong, L. Zhou, T. Xu, D. Liu, Long noncoding RNA SNHG12 promotes tumour progression and sunitinib resistance by upregulating CDCA3 in renal cell carcinoma, Cell Death Dis. 11 (2020) 1–17.
[31] Y. Liu, J. Zhou, S. Wang, Y. Song, J. Zhou, F. Ren, Long non-coding RNA SNHG12 promotes proliferation and invasion of colorectal cancer cells by acting as a molecular sponge of microRNA-16, Exp. Ther. Med. 18 (2019) 1212–1220.
[32] C. Lu, Y. Wei, X. Wang, Z. Zhang, J. Yin, W. Li, L. Chen, X. Lyu, Z. Shi, W. Yan, DNA-methylation-mediated activating of lncRNA SNHG12 promotes temozolomide resistance in glioblastoma, Mol. Cancer 19 (2020) 1–19.
[33] M. Qian, W. Ling, Z. Ruan, Long non-coding RNA SNHG12 promotes immune escape of ovarian cancer cells through their crosstalk with M2 macrophages, Aging (Albany NY) 12 (2020) 17122.
[34] W. Qian, Zq Zheng, Jg Nie, Lj Liu, Xz Meng, H. Sun, Fm Xiao, T. Kang, LncRNA SNHG12 alleviates hypertensive vascular endothelial injury through miR-25–3p/SIRT6 pathway, J. Leukoc. Biol. 110 (2021) 651–661.
[35] J. Song, X. Wu, R. Ma, L. Miao, L. Xiong, W. Zhao, Long noncoding RNA SNHG12 promotes cell proliferation and activates Wnt/β-catenin signaling in prostate cancer through sponging microRNA-195, J. Cell. Biochem. 120 (2019) 13066–13075.

[36] D. Sun, X. Fan, LncRNA SNHG12 accelerates the progression of ovarian cancer via absorbing miRNA-129 to upregulate SOX4, Eur. Rev. Med Pharm. Sci. 23 (2019) 2345–2352.
[37] L. Sun, R. Yuan, LncRNA SNHG12 ameliorates bupivacaine-induced neurotoxicity by sponging miR-497–5p to upregulate NLRX1, Hum. Exp. Toxicol. 41 (2022), 09603271221089001.
[38] Y. Sun, J.T. Zhao, B.J. Chi, K.F. Wang, Long noncoding RNA SNHG12 promotes vascular smooth muscle cell proliferation and migration via regulating miR-199a-5p/HIF-1α, Cell Biol. Int 44 (2020) 1714–1726.
[39] D. Tan, G. Li, P. Zhang, C. Peng, B. He, LncRNA SNHG12 in extracellular vesicles derived from carcinoma-associated fibroblasts promotes cisplatin resistance in non-small cell lung cancer cells, Bioengineered 13 (2022) 1838–1857.
[40] J. Wang, C. Xu, H. Wu, S. Shen, LncRNA SNHG12 promotes cell growth and inhibits cell apoptosis in colorectal cancer cells, Braz. J. Med. Biol. Res. 50 (2017).
[41] O. Wang, F. Yang, Y. Liu, L. Lv, R. Ma, C. Chen, J. Wang, Q. Tan, Y. Cheng, E. Xia, C-MYC-induced upregulation of lncRNA SNHG12 regulates cell proliferation, apoptosis and migration in triple-negative breast cancer, Am. J. Transl. Res. 9 (2017) 533.
[42] X. Wang, C. He, Z. Yang, S. Li, L. Qiao, L. Fang, Dysregulation of long non-coding RNA SNHG12 alters the viability, apoptosis, and autophagy of prostate cancer cells by regulating miR-195/CCNE1 axis, Int. J. Clin. Exp. Pathol. 12 (2019) 1272.
[43] Y. Wang, S. Liang, Y. Yu, Y. Shi, H. Zheng, Knockdown of SNHG12 suppresses tumor metastasis and epithelial-mesenchymal transition via the Slug/ZEB2 signaling pathway by targeting miR-218 in NSCLC, Oncol. Lett. 17 (2019) 2356–2364.
[44] D. Wu, X. He, W. Wang, X. Hu, K. Wang, M. Wang, Long noncoding RNA SNHG12 induces proliferation, migration, epithelial–mesenchymal transition, and stemness of esophageal squamous cell carcinoma cells via post-transcriptional regulation of BMI1 and CTNNB1, Mol. Oncol. 14 (2020) 2332–2351.
[45] Z. Wu, D. Chen, K. Wang, C. Cao, X. Xu, Long non-coding RNA SNHG12 functions as a competing endogenous RNA to regulate MDM4 expression by sponging miR-129-5p in clear cell renal cell carcinoma, Front. Oncol. 9 (2019).
[46] F.W. Xie, J.C. Liu, LncRNA SNHG12 regulates the miR-101–3p/CUL4B axis to mediate the proliferation, migration and invasion of non-small cell lung cancer, Kaohsiung J. Med. Sci. 37 (2021) 664–674.
[47] Y. Xie, G. Chen, LncRNA SNHG12 promotes the malignant progression of melanoma by targeting miR-199b, Ann. Transl. Med. 10 (2022).
[48] C. Xu, H. Liang, J. Zhou, Y. Wang, S. Liu, X. Wang, L. Su, X. Kang, lncRNA small nucleolar RNA host gene 12 promotes renal cell carcinoma progression by modulating the miR-200c-5p/collagen type XI α1 chain pathway, Mol. Med. Rep. 22 (2020) 3677–3686.
[49] Y. Yan, L. Chen, J. Zhou, L. Xie, SNHG12 inhibits oxygen-glucose deprivation-induced neuronal apoptosis via the miR-181a-5p/NEGR1 axis, Mol. Med. Rep. 22 (2020) 3886–3894.
[50] B. Yang, W. Cai, B. Chen, LncRNA SNHG12 regulated the proliferation of gastric carcinoma cell BGC-823 by targeting microRNA-199a/b-5p, Eur. Rev. Med. Pharm. Sci. 22 (2018) 1297–1306.
[51] H.-G. Yang, T.-p Wang, S.-a Hu, C.-z Hu, C.-h Jiang, Q. He, Long non-coding RNA SNHG12, a new therapeutic target, regulates miR-199a-5p/Klotho to promote the growth and metastasis of intrahepatic cholangiocarcinoma cells, Front. Med. 8 (2021) 878.
[52] X. Yao, R. Yao, F. Huang, J. Yi, LncRNA SNHG12 as a potent autophagy inducer exerts neuroprotective effects against cerebral ischemia/reperfusion injury, Biochem. Biophys. Res. Commun. 514 (2019) 490–496.
[53] F. Zhang, C. Guo, X. Cao, Y. Yan, J. Zhang, S. Lv, Gastric cancer cell-derived extracellular vesicles elevate E2F7 expression and activate the MAPK/ERK signaling to promote peritoneal metastasis through the delivery of SNHG12, Cell Death Discov. 8 (2022) 1–11.
[54] H. Zhang, W. Lu, LncRNA SNHG12 regulates gastric cancer progression by acting as a molecular sponge of miR-320, Mol. Med. Rep. 17 (2018) 2743–2749.
[55] J. Zhang, H. Zhao, A. Zhang, C. Zhao, Z. Mei, H. Yao, Z. Fan, D. Liang, Identifying a novel KLF2/lncRNA SNHG12/miR-494-3p/RAD23B axis in Spare Nerve Injury-induced neuropathic pain, Cell Death Discov. 8 (2022) 1–10.
[56] L. Zhang, B. Li, D. Zhang, Y. Zhao, Q. Yu, lncRNA SNHG12 inhibition based on microsystem cell imaging technology protects the endothelium from LPS-induced inflammation by inhibiting the expression of miR-140-3p target gene fndc5, Contrast Media Mol. Imaging 2022 (2022).
[57] R. Zhang, Y. Liu, H. Liu, W. Chen, H.-N. Fan, J. Zhang, J.-S. Zhu, The long non-coding RNA SNHG12 promotes gastric cancer by activating the phosphatidylinositol 3-kinase/AKT pathway, Aging 11 (2019) 10902.
[58] T. Zhang, M.K. Beeharry, Z. Wang, Z. Zhu, J. Li, C. Li, YY1-modulated long non-coding RNA SNHG12 promotes gastric cancer metastasis by activating the miR-218-5p/YWHAZ axis, Int. J. Biol. Sci. 17 (2021) 1629.
[59] T. Zhang, M.K. Beeharry, Y. Zheng, Z. Wang, J. Li, Z. Zhu, C. Li, Long noncoding RNA SNHG12 promotes gastric cancer proliferation by binding to HuR and stabilizing YWHAZ expression through the AKT/GSK-3β pathway, Front. Oncol. 2100 (2021).
[60] G. Zhao, S. Wang, X. Liang, C. Wang, B. Peng, Oncogenic role of long non-coding RNA SNHG12 in gastric cancer cells by targeting miR-16, Exp. Ther. Med. 18 (2019) 199–208.
[61] B. Zhou, L. Li, Y. Li, H. Sun, C. Zeng, Long noncoding RNA SNHG12 mediates doxorubicin resistance of osteosarcoma via miR-320a/MCL1 axis, Biomed. Pharmacother. 106 (2018) 850–857.
[62] F. Zhou, Y. Sun, Z. Chi, Q. Gao, H. Wang, Long noncoding RNA SNHG12 promotes the proliferation, migration, and invasion of trophoblast cells by regulating the epithelial–mesenchymal transition and cell cycle, J. Int. Med. Res. 48 (2020), 0300060520922339.
[63] S. Zhou, L. Yu, M. Xiong, G. Dai, LncRNA SNHG12 promotes tumorigenesis and metastasis in osteosarcoma by upregulating Notch2 by sponging miR-195-5p, Biochem. Biophys. Res. Commun. 495 (2018) 1822–1832.
[64] L. Zhu, X. Zhang, X. Fu, Z. Li, Z. Sun, J. Wu, X. Wang, F. Wang, X. Li, S. Niu, c-Myc mediated upregulation of long noncoding RNA SNHG12 regulates proliferation and drug sensitivity in natural killer/T-cell lymphoma, J. Cell. Biochem. 120 (2019) 12628–12637.
[65] Y. Zhu, Z. Qiu, Y. Zhang, B. Li, X. Jiang, Partial hepatectomy-induced upregulation of SNHG12 promotes hepatocyte proliferation and liver regeneration, Mol. Med. Rep. 21 (2020) 1089–1096.