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Review

A review on the role of SNHG8 in human disorders

Soudeh Ghafouri-Fard [a], Atefeh Harsij [b], Bashdar Mahmud Hussen [c], Mohammad Taheri [d,e,*], Seyed Abdulmajid Ayatollahi [f,**]

[a] Department of Medical Genetics, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[b] Men's Health and Reproductive Health Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[c] Department of Clinical Analysis, College of Pharmacy, Hawler Medical University, Kurdistan, Erbil, Iraq
[d] Institute of Human Genetics, Jena University Hospital, Jena, Germany
[e] Urology and Nephrology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[f] Phytochemistry Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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ABSTRACT

Small nucleolar RNA host gene 8 (SNHG8) is a long non-coding RNA that has physiological roles in epithelial and muscle satellite cells. This lncRNA has been reported to be over-expressed in a variety of cancer cell lines. Its silencing has attenuated tumor growth in animal models of cancers. SNHG8 can be served as a molecular sponge for some miRNAs to regulate their target genes. miR-634/ZBTB20, miR-335–5p/PYGO2, miR588/ATG7, miR-152/c-MET, miR-1270/BACH1, miR-491/PDGFRA, miR-512–5p/TRIM28, miR-149–5p/PPM1F, miR-542–3p/CCND1/CDK6, miR-656–3p/SERBP1, miR-656–3p/SATB1, miR-1270/S100A11 and miR-384/HOXB7 are examples of molecular axes being regulated by SNHG8 in the context of cancer. Moreover, it can affect pathogenesis of atherosclerosis, chronic cerebral ischemia, acute gouty arthritis, ischemic stroke and myocardial infarction through modulation of a number of molecular axes such as SNHG8/miR-384/Hoxa13/FAM3A and miR-335/RASA1 as well as NF-κB signaling pathway. The current review aims at summarization of the role of SNHG8 in diverse human disorders.

1. Introduction

Long non-coding RNAs (lncRNAs) represent an important group of non-coding transcripts with several similar features with mRNAs, yet the vast majority of these transcripts do not produce functional polypeptides [10,12,27]. Instead, the RNA itself exerts regulatory effects on protein-coding genes [13,38]. LncRNAs can affect expression of genes via epigenetic mechanisms. They can also modulate gene expression at transcriptional, post-transcriptional and translational stages of gene expression [7,18]. They have tissue- and condition-specific signatures that imply that these transcripts can be used are potential biomarkers. Moreover, these types of expression pattern offer a basis to target them in the clinical settings [30].

Small nucleolar RNA host genes (SNHGs) are a group of lncRNAs with diverse biological roles [11]. They contribute to the pathoetiology of several disorders, especially cancer. *SNHG8* is a member of this group of transcripts. This RNA gene is located on chr4:118,278,631–118,285,316 (GRCh38/hg38), plus strand and has 6686 bases. Alternatively named as LINC00060, it has at least 15 transcripts being produced by alternative splicing mechanisms. The largest transcript (SNHG8–207) has 6166 bp length.

SNHG8 has important functions in the physiology of epithelial cells and muscle satellite cells. This lncRNA has been found to be closely related with epithelial-mesenchymal transition (EMT)-associated genes signature [3]. Moreover, its expression has been decreased by ZEB1 in the course of EMT progression. From a functional point of view, SNHG8 silencing has induced EMT in epithelial cells via destabilizing CDH1 transcripts via a mechanism which relies on a shared 17-nucleotide sequence by SNHG8 and CDH1 [3].

Another experiment aimed at screening of epithelial cell-enriched lncRNAs has reported SNHG8 as a chromatin-localized lncRNA with robust interaction and phase separation with histone H1 variants. Notably, SNHG8 has more powerful capacity to bind H1s compared with linker DNA. As a consequent, loss of SNHG8 has been shown to increase the quantity of H1s that bind to chromatin, induce chromatin condensation, and stimulate an epithelial differentiation-related gene signature

* Corresponding author at: Institute of Human Genetics, Jena University Hospital, Jena, Germany.
** Corresponding author.
E-mail addresses: mohammad.taheri@uni-jena.de (M. Taheri), majid_ayatollahi@yahoo.com (S.A. Ayatollahi).

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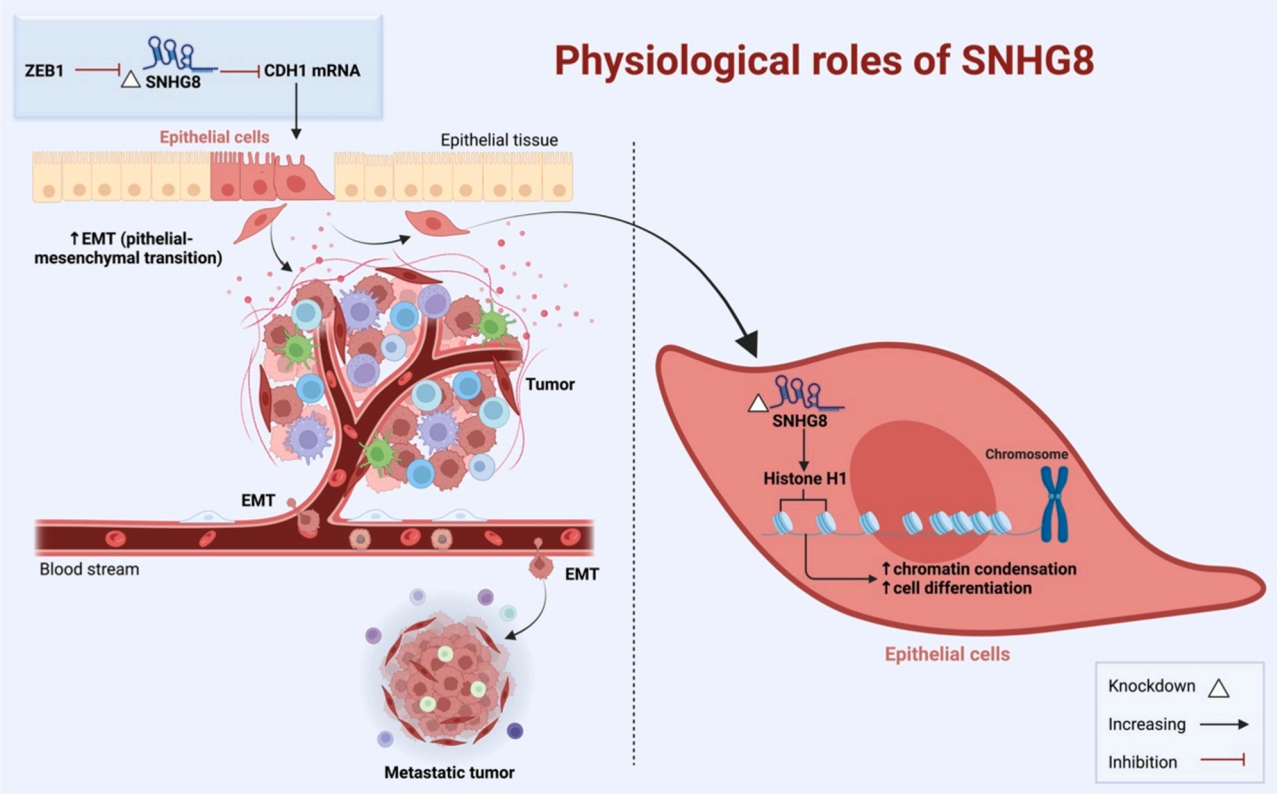

Fig. 1. SNHG8 affects epithelial cell physiology. This lncRNA is linked to EMT-associated genes such as CDH1. SNHG8 interacts with histone H1 in chromatin. Loss of SNHG8 increases chromatin-binding H1, induces chromatin condensation, and stimulates epithelial differentiation.

Table 1
Physiological roles of SNHG8.

Study type	Cell type	Regulator of SNHG8	Target of SNHG8	Function	References
Cell line study (MCF10A, MCF7, HT29, HEK-293 T cell lines)	Epithelial cells	ZEB1 (Zinc finger E-box-binding homeobox1)	*CDH1*mRNA	ΔSNHG8: ↑EMT (epithelial-mesenchymal transition)	[3]
Cell line study (MCF10A, RWPE-1, HEK-293 T cell lines)	Epithelial cells	_	Histone H1	ΔSNHG8: ↑chromatin condensation, ↑cell differentiation	[15]
Animal study (C57BL/6 mice)	Muscle Satellite cells	FoxM1 (Forkhead Box M1)	Ribosomal protein gene transcription	ΔSNHG8: ↓proliferation	[4]

(Fig. 1). Taken together, high abundance of SNHG8 in epithelial cells preserves histone H1 variants out of nucleosomes and its loss is associated with epithelial cell differentiation [15].

Besides, Snhg8 has also been reported to be a target of FoxM1 in the regulation of proliferation and survival of muscle satellite cells. Snhg8 could sustain proliferation of these cells through enhancement of transcription of ribosomal proteins [4]. Table 1 summarizes the physiological roles of SNHG8.

2. SNHG8 in cancers

2.1. Cell line studies

SNHG8 expression has been upregulated in breast cancer cell lines. SNHG8 silencing has significantly reserved migration and invasion of these cells, and stimulated their apoptosis. SNHG8 has been found to serve as an inhibitor of miR-634 to enhance expression of ZBTB20. Taken together, SNHG8/miR-634/ZBTB20 axis has been shown to contribute to the pathogenesis of breast cancers (Fig. 2) [8,41]. Moreover, SNHG8 expression has been found to be up-regulated in triple negative breast cancer cells where it has promoted their proliferation, migratory potential and EMT process. These effects are mediated through sequestering miR-335–5p to release PYGO2 from its suppressive effects [25].

SNHG8 expression has also been elevated in colorectal cancer cell lines. SNHG8 could facilitate proliferation and autophagy in these cell lines through modulation of expression of ATG7. More importantly, the effects of SNHG8 on autophagy in these cells have been shown to depend on the miR-588/ATG7 axis [3]. Moreover, direct sponging effect of SNHG8 on miR-663 has an important role in the oncogenic function of this lncRNA in colorectal cancer cells [40].

In cervical cancer cells, SNHG8 could accelerate proliferation and block apoptotic pathways via recruiting EZH2 to silence expression of RECK through epigenetic mechanisms [26]. In the endometrial carcinoma cell line AN3CA, SNHG8 silencing has decreased cell viability, while SNHG8 overexpression has enhanced the activity of cells. SNHG8

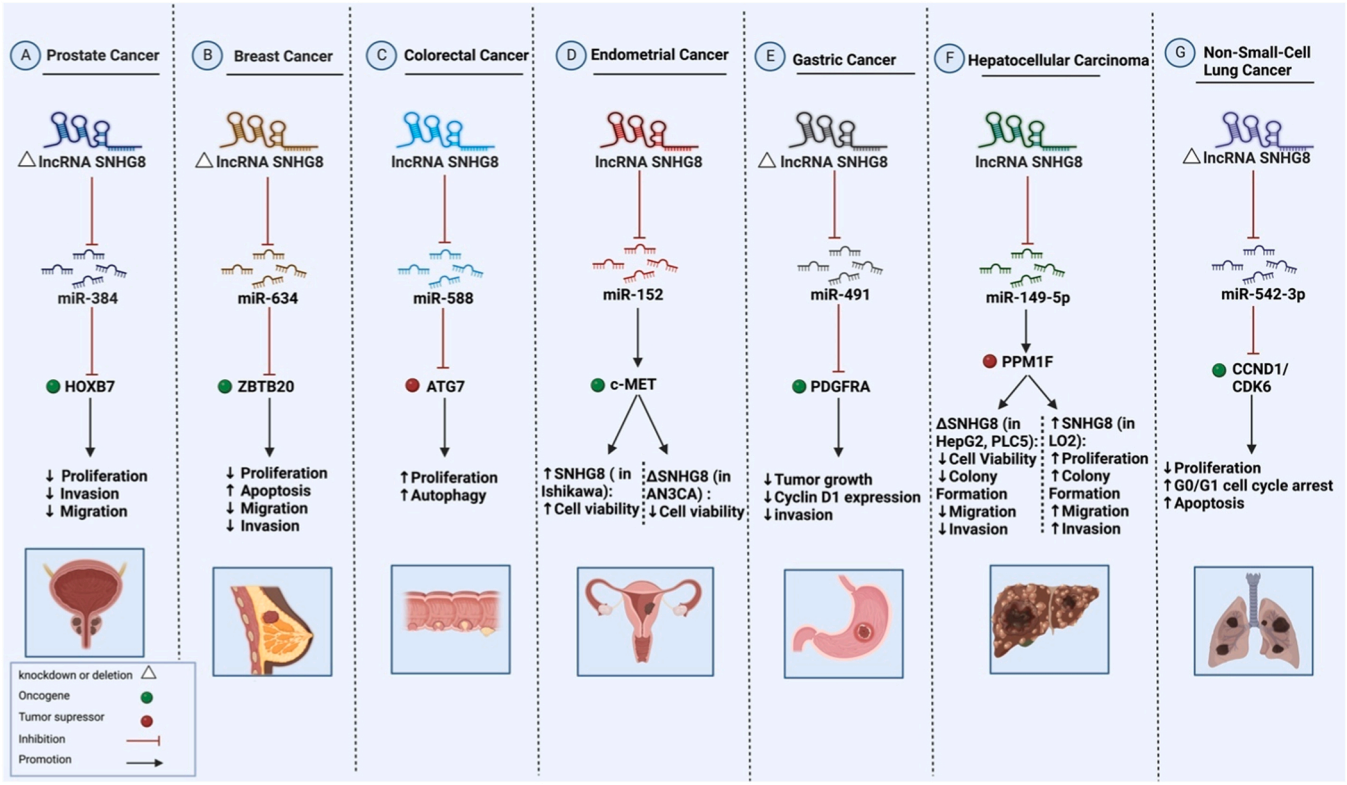

Fig. 2. Expression and function of SNHG8 lncRNA in various malignancies based on cell line studies.

has been shown to sponge miR-152 and increase expression of its target c-MET [35]. Table 2 summarizes the effect of SNHG8 over-expression or silencing in different cancer cell lines.

3. Animal studies

The impact of SNHG8 silencing on tumor growth has been assessed in xenograft models of esophageal [33], gastric [42], liver [6], lung [2], nasopharyngeal [32], bone [14] and ovarian [34] cancers. These studies have consistently pointed to the oncogenic effects of SNHG8, since its silencing has reduced tumor growth (Fig. 3) (Table 3). Moreover, in gastric cancer models, SNHG8 silencing has significantly enhanced chemosensitivity through inhibition of DNA damage repair [42].

4. Studies in human samples

Over-expression of SHNG8 has been reported in a wide array of clinical samples obtained from different cancerous tissues (Table 4). In colorectal cancer, over-expression of SNHG8 has been associated with poor clinical outcome and higher rate of metastasis [40]. In endometrial cancer, up-regulation of SNHG8 not only has been associated with shorter survival time, but also with lymph node involvement, FIGO stage and histological grade [35]. In EBV-associated gastric cancer, up-regulation of SNHG8 has been found to indicate poor overall survival, in association with larger tumor size and vascular tumor thrombus [44]. In hepatocellular carcinoma, over-expression of SNHG8 has been associated with recurrence of tumor but not overall survival of patients [6]. Although SNHG8 expression and T stage have been independent predictive factors for tumor recurrence, authors have been reported no relationship between SNHG8 up-regulation and assessed clinicopathological features [6].

5. Non-malignant disorders

5.1. Cell line studies

The importance of SNHG8 in the pathogenesis of atherosclerosis, chronic cerebral ischemia, acute gouty arthritis, ischemic stroke and myocardial infarction has been assessed in different cell lines (Table 5). To unravel the underlying mechanism of SNHG8 participation in the pathogenesis of atherosclerosis, SNHG8 expression has been suppressed in vascular smooth muscle cells. This intervention has led to inhibition of proliferation and migration of these cells. Mechanistically, SNHG8 has been shown to promote proliferation and migration of these cells via sequestering miR-224–3p [5].

Up-regulation of Snhg8 has suppressed chronic ischemia-induced apoptosis of HT22 cells. Mechanistically, Snhg8 has been shown to bind with miR-384 through a sequence-specific manner to repress its expression. Most notably, a reciprocal repression mechanism has been detected between Snhg8 and miR-384. Up-regulation of miR-384 could impair expression of Hoxa13 through binding with its 3′UTR. Hoxa13 could bind with FAM3A promoter and enhance its promoter activity, thus regulating apoptosis of neurons [21].

Another experiment in a human monocytic cell line has shown that SNHG8 sponges miR-542–3p, a miRNA that targets AP3D1 3′ UTR. This experiment has verified that the role of SNHG8 in acceleration of acute gouty arthritis is mediated through up-regulation of AP3D1 [9].

SNHG8 is also involved in the pathoetiology of ischemic stroke, since it can attenuate microglial inflammatory responses and blood-brain barrier injury via regulation of SIRT1/NF-κB signals through a miR-425–5p manner [31]. Moreover, activity of microglia and permeability of blood-brain barrier in this context can be regulated through the ponging effect of SNHG8 on miR-449c-5p and subsequent regulation of

Table 2
Expression and function of SNHG8 in various malignancies based on cell line studies (TCL: tumor cell line, NCL: normal cell line, Δ: knockdown or deletion, EMT: epithelial-mesenchymal transition, NR: not reported).

Tumor type	Cell line	Expression	Targets/Regulators and Signaling Pathways	Function	References
Breast Cancer	TCLs: MCF7, Hs-578 T, ZR-75–30, HCC1973 NCL: MCF-10A	High (TCL vs. NCL)	miR-634/ZBTB20	ΔSNHG8: ↓ Proliferation ↑Apoptosis ↓ Migration ↓ Invasion	[8,41]
Triple-Negative Breast Cancer	TCLs: MDA-MB-231, MDA-MB-436, BT-549, HCC1937 NCLs: MCF-10A, HEK-293 T	High (TCL vs. NCL)	miR-335–5p/PYGO2	ΔSNHG8: ↓proliferation, ↓colony formation ↓ Migration ↓EMT process	[25]
Colorectal Cancer	TCLs: HT29, HCT8, HCT116, SW480 NCL: FHC	High (TCL vs. NCL)	miR588/ATG7	↑SNHG8: ↑proliferation ↑Autophagy	[3]
	TCLs: SW480, SW620, LOVO, HCT116, HT29 NCL: HCoEpiC	High (TCL vs. NCL)	miR-663	ΔSNHG8: ↓proliferation, ↓colony formation ability ↓ Migration ↓ Invasion	[40]
HPV-induced Cervical Cancer	HeLa (HPV18 +), MS751 (HPV45 +) SiHa and CaKi (HPV16 +) C33A(HPV-)	High (In HPV+ cell lines)	EZH2/RECK	ΔSNHG8: ↓Tumor growth ↑Apoptosis ↓ Migration	[26]
Endometrial Cancer	TCLs: Ishikawa, HEC1-A, HEC1-B, AN3CA, RL95–2	Highest in AN3CA Lowest in Ishikawa	miR-152/c-MET	↑SNHG8 (in Ishikawa): ↑Cell viability ΔSNHG8 (in AN3CA): ↓Cell viability	[35]
Esophageal Cancer	TCLs: KYSE30, EC9706, TE-1 NCL: Het-1A	High (TCL vs. NCL)	miR-1270/BACH1	ΔSNHG8: ↓Proliferation ↑Apoptosis	[33]
Gastric Cancer	TCLs: MGC-803, AGS, SGC-7901, MKN-45 NCL: GES-1	High (TCL vs. NCL)	miR-491/PDGFRA	ΔSNHG8: ↓Tumor growth ↓Cyclin D1 expression ↓invasion	[37]
	TCLs: MKN45, AGS, SGC7901, GES1 GC/CDDP cell lines (treated with cisplatin)	High (GC/CDDP cell lines vs. GC cell lines)	hnRNPA1-TROY	ΔSNHG8: ↑Apoptosis ↑ chemotherapy sensitivity ↓DNA repair	[42]
Epstein-Barr Virus-Associated Gastric Cancer (EBVaGC)	TCLs: AGX-BX1(EBVaGC cell line) MKN-28 (GC cell line) NCL: GES-1	High (in EBVaGC cell line)	BHRF1 (regulator of SNHG8) miR-512–5p/TRIM28	↑SNHG8: ↑proliferation, ↑colony formation, ↑G2/M cell cycle rrest,↑migration, ↑invasion	[44]
	TCLs: GT38, GT39 (EBVaGC cell line) AGS, SGC7901 (EBVnGC cell line) NCL: GES-1	High (in EBVaGC cell lines)	NR	ΔSNHG8: ↓proliferation, ↓colony formation ability ↑Apoptosis ↑G0/G1 cell cycle arrest	[22]
Hepatocellular Carcinoma	TCLs: LO2, Huh6, Huh7, SK-hep1, HepG2, PLC5	High (in HepG2 and PLC5) Low (in LO2)	miR-149–5p/PPM1F	ΔSNHG8 (in HepG2, PLC5): ↓cell viability, ↓colony formation ↓migration, ↓invasion ↑SNHG8 (in LO2): ↑proliferation, ↑colony formation ↑migration, ↑invasion	[6]
Diffuse Large B-Cell Lymphoma	TCLs: OCI-Ly10, OCI-Ly7, OCI-Ly3, U2932 NCL: GM12878	High (TCL vs. NCL)	miR-335–5p	ΔSNHG8: ↓proliferation, ↓colony formation ↑Apoptosis	[19]
Non-Small-Cell Lung Cancer	TCLs: A549, H23, SPC-A1, NCI-H292 NCL: 16HBE	High (TCL vs. NCL)	miR-542–3p/CCND1/CDK6 Caspase-3	ΔSNHG8: ↓Proliferation ↑G0/G1 cell cycle arrest ↑Apoptosis	[2]
Melanoma	TCLs: A375, A875, M14, SK-MEL-5 NCL: HEMa-LP	High (TCL vs. NCL)	miR-656–3p/SERBP1	ΔSNHG8: ↓ Cell viability ↓ Colony formation ↓ Proliferation ↓ Invasion ↓ Migration	[28]
Nasopharyngeal Carcinoma	TCLs: CNE-1, CNE-2 NCL: NP69	High (TCL vs. NCL)	miR-656–3p/SATB1	ΔSNHG8: ↓proliferation, ↓colony formation, ↓ Invasion, ↓ Migration ↑SNHG8: ↑proliferation, ↑colony formation, ↑migration, ↑invasion	[32]

(*continued on next page*)

Table 2 (*continued*)

Tumor type	Cell line	Expression	Targets/Regulators and Signaling Pathways	Function	References
Osteosarcoma	TCLs: SaOS2, U2OS, MG63, HOS NCL: hFOB 1.19	High (TCL vs. NCL)	miR-876–5p	ΔSNHG8: ↓Tumor growth ↓ Migration	[14]
Ovarian Cancer	TCLs: SKOV3, HO8910, OVCAR3, A2780 NCLs: IOSE, HOSE 11–12	High (TCL vs. NCL)	miR-1270/S100A11	↑SNHG8: ↑proliferation, ↑migration, ↑invasion ΔSNHG8: ↓proliferation, ↓ Invasion, ↓ Migration	[34]
	TCLs: SKOV3, ES2, CaOV3, HG-SOC NCL: FTE187	High (TCL vs. NCL)	CAPRIN1/CTNNB1, Axin1 Wnt/β-catenin pathway	ΔSNHG8: ↓proliferation, ↑apoptosis ↓migration, ↓EMT process ↓sphere formation ability, ↓stemness	[24]
Pancreatic Adenocarcinoma	TCLs: AsPC-1, BxPC-3, CFPC-1, PANC-1, Hs766T NCL: HPC-Y5	High (TCL vs. NCL)	NR	ΔSNHG8: ↓ Cell viability ↑ G0/G1 cell cycle arrest ↑ Apoptosis ↑ Gemcitabine sensitivity	[29]
Prostate Cancer	TCLs: LNCaP, PC3, DU145, VCap, 22RV1 NCL: RWPE1	High (TCL vs. NCL)	miR-384/HOXB7	ΔSNHG8: ↓proliferation ↓ Invasion ↓ Migration	[1]

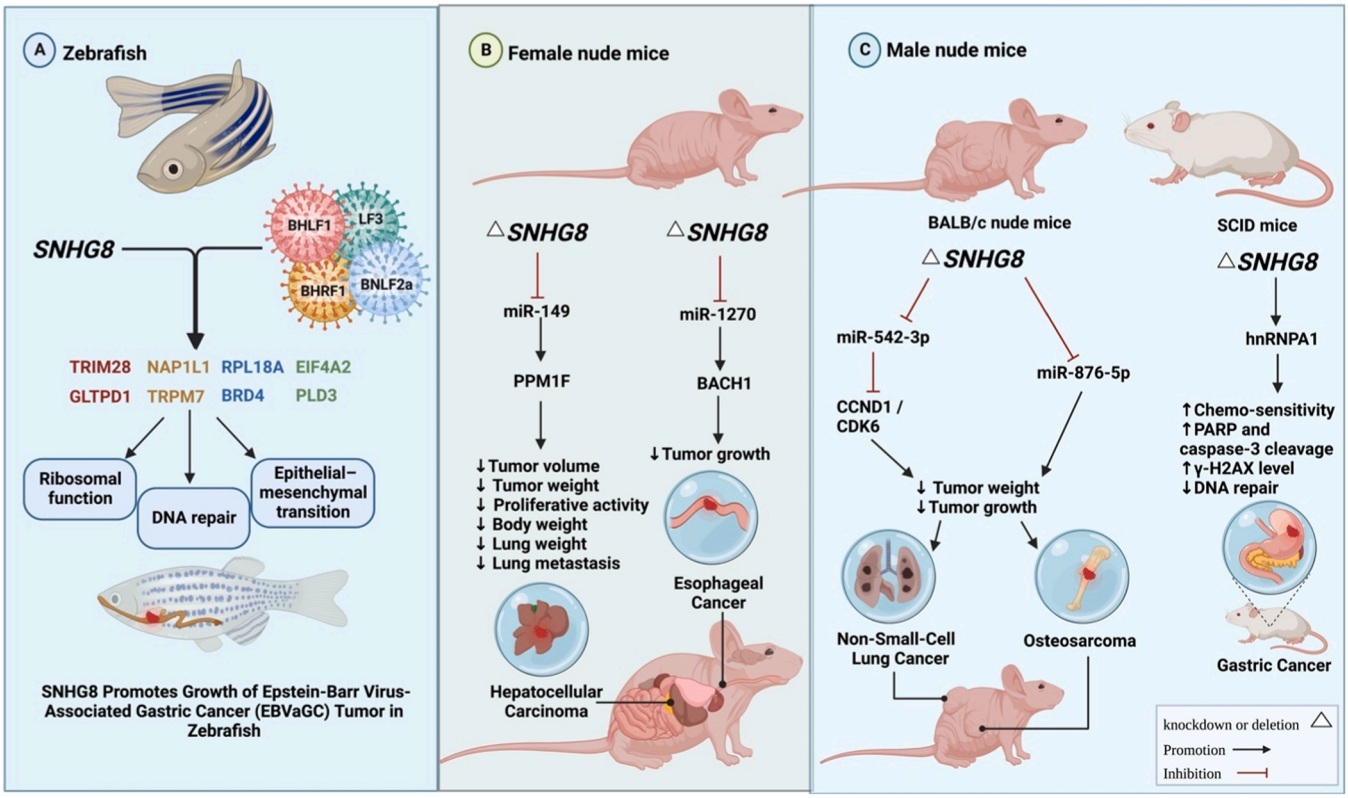

Fig. 3. The significance of SNHG8 in the development of tumors is based on research conducted on animals.

the SIRT1/FoxO1 signaling [36]. Table 5 summarizes the identified mechanisms for involvement of SNHG8 in the pathophysiology of non-malignant conditions.

6. Animal studies

Animal studies have shown that up-regulation of Snhg8 in combination with miR-384 silencing can reduce apoptosis of neurons, demonstrating the role of Snhg8/miR-384/Hoxa13/FAM3A pathway in the modulation of neuronal apoptosis triggered by chronic cerebral ischemia [21].

Experiment in an animal model of monosodium urate monohydrate (MSU)-induced acute gouty arthritis have shown up-regulation of SNHG8 following MSU treatment. Notably, SNHG8 silencing has reduced the MSU-induced paw swelling. Moreover, SNHG8 ablation has led to reduction of proinflammatory factors in animals [9].

Finally, independent studies in animal models of ischemic stroke have reported a protective role for SNHG8 in this condition [31,36].

Table 3
The role of SNHG8 in tumorigenesis based on animal experiments (Δ: knockdown or deletion, SCID: severe combined immunodeficiency).

Tumor type	Animal models	Pathways	Results	References
Esophageal Cancer	Nude female mice	-	ΔSNHG8: ↓Tumor growth	[33]
Gastric Cancer	SCID mice	miR-491/PDGFRA	ΔSNHG8: ↑Chemo-sensitivity ↑PARP and caspase-3 cleavage ↑γ-H2AX level ↓DNA repair	[42]
Epstein-Barr Virus-Associated Gastric Cancer (EBVaGC)	Zebrafish	-	ΔSNHG8: ↓Tumor growth	[44]
	Male BALB/c nude mice	-	ΔSNHG8: ↓ Tumor weight, ↓Tumor growth	[22]
Hepatocellular Carcinoma	Female immune-deficient nude mice (BALB/c-nu)	miR-149–5p/PPM1F	ΔSNHG8: ↓Tumor volume, ↓ Tumor weight, ↓Proliferative activity ↓ Body weight, ↓ Lung weight, ↓ Lung metastasis	[6]
Non-Small-Cell Lung Cancer	Male BALB/c nude mice	miR-542–3p/CCND1/CDK6	ΔSNHG8: ↓ Tumor weight, ↓Tumor growth	[2]
Nasopharyngeal Carcinoma	Male BALB/c nude mice	miR-656–3p/SATB1	ΔSNHG8: ↓Tumor volume, ↓ Tumor weight, ↓Tumor growth	[32]
Osteosarcoma	Male athymic BALB/c nude mice	-	ΔSNHG8: ↓ Tumor weight, ↓Tumor growth	[14]
Ovarian Cancer	BALB/c nude mice	miR-1270/S100A11	ΔSNHG8: ↓ Tumor weight, ↓Tumor volume	[34]

Table 6 shows the effect of SNHG8 in animal models of non-malignant diseases.

7. Human studies

Expression levels of SNHG8 have been found to be higher in patients with atherosclerosis, while levels of miR-224–3p have been lower in these patients compared with controls. Notably, ROC curve analyses have indicated the ability of serum levels of SNHG8 in distinguishing atherosclerotic patients. Moreover, the levels of miR-224–3p have been negatively correlated with those of SNHG8 [34].

SNHG8 has also been identified as an important participant in the pathogenesis of acute myocardial infarction through an RNA-seq analysis and subsequent construction of the lncRNA-miRNA-mRNA axes. This lncRNA has been shown to have significant diagnostic value for diagnosis of this disorder (Table 7) [43].

8. Discussion

SNHG8 has been shown to contribute to the pathogenesis of cancers via regulation of miR-634/ZBTB20, miR-335–5p/PYGO2, miR588/ATG7, miR-152/c-MET, miR-1270/BACH1, miR-491/PDGFRA, miR-512–5p/TRIM28, miR-149–5p/PPM1F, miR-542–3p/CCND1/CDK6, miR-656–3p/SERBP1, miR-656–3p/SATB1, miR-1270/S100A11 and miR-384/ axes as well as Wnt/β-catenin pathway. Moreover, it can affect pathogenesis of atherosclerosis, chronic cerebral ischemia, acute gouty arthritis, ischemic stroke and myocardial infarction through modulation of a number of molecular axes such as SNHG8/miR-384/Hoxa13/FAM3A and miR-335/RASA1 as well as NF-κB signaling pathway.

SNHG8 has been found to affect patients' prognosis in a variety of cancers, being associated with pathological characteristics that define the course of cancer progression. Therefore, this lncRNA can be used as a prognostic marker, particularly in cancers. However, the diagnostic value of SNHG8 has not been evaluated in the context of cancer. Another issues that complicate the application of SNHG8 as a diagnostic tool in cancers is the observed up-regulation of this lncRNA in non-malignant conditions such as atherosclerosis and acute myocardial infraction. This issue should also been considered when assessing the impact of SNHG8 dysregulation in the prognosis of patients with different types of cancers.

Although tens of miRNAs have been found to be sponged by SNHG8, the comprehensive network between miRNAs and SNHG8 has not been illustrated yet. Moreover, the impact of transcription factors on expression of SNHG8 has not been evaluated. Therefore, it is necessary to conduct high throughput studies to find the SNHG8-interacting non-coding RNAs and mRNAs, depict the comprehensive overview of functional interactions between these transcripts and identify the mostly enriched cellular mechanisms and signaling pathways in this regard. These types of studies would help in design of more appropriate and effective treatment strategies, particularly for malignant conditions.

Ethics approval and consent to Participant

Not applicable.

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CRediT authorship contribution statement

SGF wrote the manuscript and revised it. MT supervised and designed the study. AH, SAA and BMH collected the data and designed the figures and tables. All authors read and approved the submitted version.

Conflict of interest

The authors declare they have no conflict of interest.

Table 4
Level of SNHG8 expression in various cancers and its relation with disease prognosis using clinical samples (ANCTs: adjacent non-cancerous tissues, TCGA: the cancer genome atlas, GEPIA: gene expression profiling interactive analysis, EBVaGC: EBER positive GC, EBVnGC: EBER negative GC, OS: overall survival, PFS: progression-free survival, DFS: disease-free survival, FBG: fasting blood glucose, FIGO: international federation of gynecology and obstetrics, TNM: tumor-node-metastasis, PTA: pairs of tumor tissues and ANCTs).

Tumor type	Samples	Expression (tumor vs. normal)	Kaplan-Meier analysis (impact of SNHG8 overexpression)	Prognostic factors (univariate/multivariate cox regression analysis)	Association of SNHG8 expression with clinicopathologic characteristics	References
Breast Cancer	16 PTAs	High	_	_	_	[8]
	30 PTAs	High	_	_	_	[41]
Colorectal Cancer	286 tumor tissues and 41 normal tissues (TCGA data)	High	_	_	_	[3]
	40 PTAs + TCGA data	High	Poor prognosis	_	Metastasis	[40]
Endometrial Cancer	60 tumor tissues, 25 normal tissues	High	Shorter survival time	_	Lymph node metastasis, FIGO stage, histological grade	[35]
Esophageal Cancer	20 PTAs + TCGA data	High	_	_	_	[33]
Gastric Cancer (GC)	30 PTAs (15 males, 15 females)	High	_	_	_	[37]
	42 PTAs + TCGA data	High	_	_	cancer stage	[42]
	217 PTAs (follow up study)	High (non survivors vs. survivors)	Shorter survival time Poor prognosis (after radical gastrectomy)	The interaction of SNHG8 expression and FBG (predictive for cancer mortality)	_	[20]
Epstein-Barr Virus-Associated Gastric Cancer (EBVaGC)	61 PTAs	High	Poor OS	_	Tumor size, Vascular tumor thrombus	[44]
	61 EBVaGC tissues 20 EBVnGC tissues	High (EBVaGC vs. EBVnGC)	_	_	_	[44]
	39 pairs of EBVaGC tissues and ANCTs + 49 EBVnGC tissues	High (EBVaGC vs. ANCT and EBVnGC)	_	_	_	[17]
Hepatocellular Carcinoma	23 PTAs TCGA data: 49 PTAs and 376 unpaired tumor samples	High	Higher recurrence rates (no association with OS)	SNHG8 expression and T stage were independent predictive factors for tumor recurrence.	No relationship with assessed clinicopathological features	[6]
Diffuse Large B-Cell Lymphoma	337 tumor samples and 47 normal samples (GEPIA database)	High	_	_	_	[19]
Non-Small-Cell Lung Cancer	120 PTAs	High	Shorter OS and PFS Shorter survival time	_	Lymph node metastasis, TNM stages	[2]
Melanoma	32 PTAs	High	Shorter OS	_	_	[28]
Nasopharyngeal Carcinoma	21 tumor tissues and normal tissues	High	_	_	_	[32]
Osteosarcoma	60 PTAs (37 males, 23 females)	High	Shorter OS	_	Increased tumor size Advanced Enneking stage	[14]
Ovarian Cancer	19 PTAs	High	Shorter OS	_	No association with cancer grade	[34]
Pancreatic Adenocarcinoma	40 PTAs 40 tumor tissues and 10 normal tissues	High	Shorter OS	_	Tumor stage Differentiation level	[29]
Prostate Cancer	53 PTAs + GEPIA data	High	Shorter OS and DFS	_	Lymph node metastasis, TNM stage, Gleason score	[1]

Table 5
Cell line studies to determine the role of SNHG8 in other disease. (OGD: oxygen and glucose deprivation).

Disease	Cell line	Molecular targets/ Regulators and pathways	Function	Reference
Atherosclerosis	HA-VSMC (human aortic vascular smooth muscle cell line)	miR-224–3 P	ΔSNHG8: ↓cell growth ↓cell migration	[34]
Chronic Cerebral Ischemia (CCI)	HT22(the mouse hippocampal neuronal cell line): CCI group and control group	SNHG8/miR-384/ Hoxa13/FAM3A axis	↑SNHG8: ↓CCI-induced apoptosis	[21]
Acute Gouty Arthritis (GA)	THP-1 (the human monocytic cell line)	miR-542–3p, AP3D1	SNHG8→ Δ miR-542–3p→ ↑ AP3D1→ regulating GA progression	[9]
Ischemic Stroke	BMEC (the mouse brain microvascular endothelial cell line) OGD-treated microglia cell model	miR-425–5p, SIRT1, NF-κB signaling pathway	↑SNHG8: ↓IL-1β, IL-6, TNF-α, ↓inflammatory response ↓cell damage	[31]
	HAPI (rat microglia, highly and aggressively proliferating immortalized cell line): OGD-treated microglia cell model	miR-449c-5p, SIRT1/ FoxO1	↑SNHG8: ↓microglia activation ↓IL-1β, IL-6, TNF-α releasing ↑anti-inflammatory factors releasing (IL-4, IL-10, TGF-β)	[36]
Myocardial Infraction	H9C2 (rat cardiomyocyte cell line): Hypoxia-induced H9C2	NF-κB signaling pathway	↑SNHG8: ↑CK-MB and cTnI releasing, ↓mitochondrial viability, ↓cell viability,↑ apoptosis, ↑cleaved-caspase3 expression, ↑inflammatory factors secretion	[39]
Hypoxia-Ischemic-Reoxygenation-induced myocardial injury (HI/R-induced myocardial injury)	H9C2 (the embryonic rat cardiomyocyte-derived cell line)	miR-335/RASA1	ΔSNHG8: ↑cell viability, ↑proliferation, ↓apoptosis → ↓cell damage	[23]
Acute Myocardial Infraction	NMCM (neonatal mouse cardiomyocyte cell line): Hypoxia-treated NMCM	miR-203–3p, VEGFA, Postn	ΔSNHG8: ↑cell viability ↑angiogenesis ↓cell apoptosis	[16]

Table 6
The effect of SNHG8 in animal models of non-malignant diseases (MSU: monosodium urate, MCAO: middle cerebral artery occlusion, BBB: blood-brain barrier).

Disease	Animal model	Expression of SNHG8 (disease-induced group vs. control group)	Results	Effect of SNHG8 overexpression	Reference
Chronic Cerebral Ischemia (CCI)	Male C57BL/6 mice (CCI mice group and control group)	Down	↑SNHG8 (in combination with ΔmiR-384): ↓neuronal apoptosis	Protective effect	[21]
Acute Gouty Arthritis (GA)	C57BL/6 mice (MSU-induced GA mice group and control group)	High	ΔSNHG8: ↓paw swelling, ↓IL-6, TNF-α, IL-1β, ↓Inflammation	Progressive effect	[9]
Ischemic Stroke (IS)	C57BL/6 mice (MCAO mice)	Not reported	↑SNHG8: ↓cell apoptosis, ↓neuron damage, ↓cerebral edema, ↓endothelial cell damage, ↑vascular integrity, ↓microglia activation, ↓inflammatory factors and inflammatory response	Protective effect	[31]
	Rat (p-MCAO model and control group)	Down	↑SNHG8: ↓neurological deficit, ↓brain edema, ↓brain damage, ↓microglia activation, ↓BBB permeability, ↓BBB damage ↓inflammatory reaction(↓IL-1β,IL-6, TNF-α and ↑IL-4, IL-10, TGF-β)	Protective effect	[36]

Table 7
Human studies to determine expression and diagnostic value of SNHG8 in non-malignant diseases.

Disease	Sample size	Expression (patient group vs. control group)	Distinguish between	Area under the curve (AUC)	Sensitivity (%)	Specificity (%)	Reference
Atherosclerosis	Sera from 83 patients and 84 controls	High	AS patients vs. healthy controls	0.905	81.9	88.1	[34]
Acute Myocardial Infraction	115 patients and 115 controls	High	AMI patients vs. healthy controls	0.85	_	_	[43]

Data Availability

The analyzed data sets generated during the study are available from the corresponding author on reasonable request.

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Consent of publication

Not applicable.

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