JCMS
OPEN ACCESS

www.jclinmedsurgery.com

Journal of
Clinical & Medical Surgery

Short Commentary

SNHG8/mir-335-5p/PYGO2 Axis: A New Targets of Triple Negative Breast Cancer

Xiao Chen[1]; Tong Tang[2]*; WenJun Jia[3]

[1]Institute of AnHui Medical University, Hefei, China.

[2]Institute of the second hospital of Anhui medical university, Hefei, China.

***Corresponding Author: Tong Tang**
Institute of the second hospital of Anhui medical university, Hefei, China.
Tel: +86-15298388310; Email: tt20164@126.com

Article Info

Received: May 05, 2022

Accepted: Jun 08, 2022

Published: Jun 15, 2022

Archived: www.jclinmedsurgery.com

Abstract...

The relationship between long non-coding RNAs (lncRNAs) and human diseases has been widely studied. lncRNAs are considered to be an important participant in cancer. Small Nucleolar RNA Host Gene 8 (SNHG8) is a newly discovered lncRNA belonging to the Small Nucleolar RNA Host Gene (SNHG) family. Firstly, this study introduces the carcinogenicity of SNHG8 and discusses its mechanism in many types of cancer. Previous studies have shown that SNHG8 promotes cancer through mir-335-5p/PYGO2 axis in triple negative breast cancer (TNBC). Therefore, we further analyzed the role of PYGO2 protein in tumor progression in various cancers. SNHG8,mir-335-5p and PYGO2 can be used as biomarkers for TNBC evaluation and potential targets for treatment. We hoped to provide new insights for cancer diagnosis, prognosis and treatment.

Key words: SNHG8; PYGO2; Triple negative breast cancer.

Introduction

In the worldwide, breast cancer is the most common malignancy in women. According to GLOBOCAN data in 2020, there were 230 new cases of breast cancer, accounting for 11.7% of all new cancer cases. Breast cancer is the fifth leading cause of cancer death worldwide [1]. Among them, TNBC accounts for 15-20% in invasive breast cancer, and is significantly different from Estrogen Receptor (ER), Progesterone Receptor (PR) and human epidermal growth factor receptor 2 (HER-2) in molecular genetics, histopathology and clinical features. Compared with other molecular typing of breast cancer, TNBC has a higher malignancy and worse prognosis. Although there are many ways to treat TNBC, such as surgery, chemotherapy and radiotherapy, TNBC still has a high risk of death and recurrence. Therefore, it is urgent to explore new therapeutic targets for TNBC.

Citation: Chen X, Tang T, Jia WJ. SNHG8/mir-335-5p/PYGO2 Axis: A New Targets of Triple Negative Breast Cancer. J Clin Med Surgery. 2022; 2(1): 1016.

With the development of high-throughput RNA sequencing technology, only 1.2-2% of the human genome have protein-coding function. Most of the rest have been transcribed into non-coding RNA. LncRNA is a long chain non-coding RNA with a length of 200 nt-100 KB [2]. LncRNA does not translate proteins, but can be used as a molecular sponge of miRNA to regulate the stability, translation and post transcriptional modification of mRNA. So that LncRNA participate in many processes such as embryonic development, cell proliferation, cell differentiation and tumor progression [2]. Many studies have revealed the key role of lncRNA in tumor progression. LncRNA can pass through many signaling pathways, such as p53,NF-κB and PI3K / Akt. LncRNA can affect the expression of tumor genes and have great potential as tumor biomarkers or therapeutic targets [3].

SNHGs are a group of small nucleolar host lncRNAs, which are located in the cytoplasm and nucleus. Small nucleolar RNA is produced by selective splicing [4]. LncRNA SNHG8 belongs to SNHG family, with a total length of 1062nt and located on chromosome 4q26 [5]. SNHG8 is a research hotspot of SNHG family, which was found to be related to the malignant proliferation and differentiation of many tumors. However, few studies have further explored the expression and regulation mechanism of SNHG8 in breast cancer. High expression was detected in tissues and cells of a variety of malignant tumors, including breast cancer [6], gastric cancer [7], osteosarcoma [8], hepatocellular carcinoma [9] and non-small cell lung cancer (NSCLC) [10]. In addition, SNHG8 has been shown to be carcinogenic by targeting MicroRNAs (miRNAs) in a variety of cancers (Table 1). For example, in colorectal cancer, SNHG8 can promote the proliferation and invasion of tumor cells by sponging mir-663 and mir-588 [11,12]. SNHG8 negatively regulates mir-542-3p in the progression of NSCLC by regulating downstream effectors such as CCND1 and CDK6, which has shown great potential in the treatment of NSCLC [10]. SNHG8 can also regulate different miRNAs and affect the expression of downstream factors, so as to promote the occurrence and development of tumors.In addition, recent studies have found that SNHG8 passes Wnt/β-Catenin pathway to promote the proliferation, migration and epithelial mesenchymal transformation (EMT) of tumor cells in ovarian cancer [13].

Table 1: The relationship between SNHG8 and target genes and downstream effectors.

Cancer type	Target gene	Downstream effect factor	Reference
Non-small-cell Lung Cancer	miR-542-3p	CCND1/CDK6	[1]
Hepatocellular Carcinoma	miR-149-5p		[2]
Breast Cancer	miR-634/	ZBTB20	[3]
Triple-negative Breast Cancer	miR-335-5p	PYGO2	[4]
Osteosarcoma	miR-876-5p		[5]
Osteosarcoma	miR-542-3p		[6]
Colorectal Cancer	miR-588	ATG7	[7]
Prostate Cancer	miR-384	HOXB7	[8]
Esophageal Squamous Cell Carcinoma	miR-411	KPNA2	[9]
Nasopharyngeal Carcinoma	miR-656-3p	SATB1	[10]
Ovarian Cancer	miR-1270	S100A11	[11]
Endometrial Carcinoma	miR-152	c-MET	[12]
Diffuse Large B-Cell Lymphoma	miR-335-5p		[13]
Gastric Cancer	miR-491	PDGFRA	[14]
Epstein-Barr Virus-Associated Gastric Cancer	miR-512-5p	TRIM28	[15]
Colorectal Cancer	miR-663		[16]

The above results reveal the important role of SNHG8 in the development of malignant tumors. Our previous studies have shown that SNHG8 is highly expressed in TNBC cells and promotes the growth, proliferation, migration and EMT progress of tumor cells. In depth studies on the downstream pathway of SNHG8 show that SNHG8 regulates TNBC cells through mir-335-5p/ PYGO2 axis [14-24] .

PYGO2 protein is located on chromosome 1q213 position, with a total length of 233 amino acids, which include two important structures: N-terminal NHD domain and C-terminal PhD domain [25]. PYGO2 is involved in the morphogenesis and development of many tissues, including the brain, eyes, hair follicles, lungs, kidneys and pancreas [26]. PYGO2 is an important functional protein of Wnt/ β- Catenin signaling pathway. Wnt/β-Catenin signal transduction pathway is involved in embryonic development, cell growth, stem cell proliferation and tumorigenesis,and is related to a variety of female reproductive system diseases and plays an important role in the occurrence and development of tumors [27]. PYGO2 is highly expressed in human glioma. Inhibiting PYGO2 expression can inhibit the growth and proliferation of human glioma cells [28]. PYGO2 has tumor promoting function. The number and size of chemically induced tumors were significantly reduced in PYGO2 deficient internal tumor mice [29]. Studies have shown that pygopus 2 promotes the proliferation and invasion of renal cell carcinoma cells both in vivo and in vitro [30]. PYGO2 was up-regulated by, which promoted the resistance of pancreatic cancer to gemcitabine [31].

It is worth noting that PYGO2 has been proved to be up-regulated in breast cancer. PYGO2 via Wnt/β-Catenin pathway activates MDR1 expression and mediates chemo resistance in breast cancer. Its high expression inhibits the sensitivity of breast cancer cells to chemotherapeutic agents [32]. Mir-516a-3p blocks the Wnt/β-Catenin pathway by inhibiting PYGO2,and further inhibits the growth, metastasis and EMT of tumor cells in breast cancer [33].

Knockdown of PYGO2 in glioma U251 Cell line can inhibit the growth of tumor cells [28]. PYGO2 plays a role as a driving oncogene in metastatic prostate cancer and may become a potential prognostic biomarker and therapeutic target [34].

Signal transduction plays an important role in the development of tumor. SNHG8 affects the level of PYGO2 downstream by regulating mir-335-5p, and plays an important role in tumor cell proliferation, invasion and migration. Although there are many kinds of research on SNHG8 and cancer, it is mainly in the basic research stage. More clinical application researchs are needed in the future.

Conclusion

In conclusion, SNHG8 is a new target for disease diagnosis, treatment and prognosis evaluation in TNBC. In the future, the specific pathways and signaling molecules of lncRNAs including SNHG8 in cancer will be further explored and applied to cancer prevention, diagnosis and treatment.

Declarations

Author disclosure statement: The author declares that there is no conflict of interest related to the content of this article. Abide by the code of ethics. This paper is based on previous research. The authors did not involve any new studies (on human or animal subjects).

Funding sources: This research is supported by Natural Science Foundation of Anhui Province of China (Grant no.2008085QC112) and Humanities and Social Sciences Key Project of Higher Education in Anhui Province (Grant no.SK2021A0167).

Patient consent for publication: Not applicable.

References

1. Ferlay, J., et al., Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer, 2010; 127: p. 2893-917.
2. Ali, T. and P. Grote, Beyond the RNA-dependent function of LncRNA genes. Elife, 2020: 9.
3. Peng, W.X., P. Koirala, and Y.Y. Mo, LncRNA-mediated regulation of cell signaling in cancer. Oncogene, 2017; 36(41): p. 5661-5667.
4. Qin, Y., et al., Long Non-Coding Small Nucleolar RNA Host Genes (SNHGs) in Endocrine-Related Cancers. Onco Targets Ther. 2020: 13: 7699-7717.
5. Yuan, X., Y. Yan, and M. Xue, Small nucleolar RNA host gene 8: A rising star in the targets for cancer therapy. Biomed Pharmacother, 2021; 139: 111622.
6. Fan, D., et al., LncRNA SNHG8 promotes cell migration and invasion in breast cancer cell through miR-634/ZBTB20 axis. Eur Rev Med Pharmacol Sci, 2020; 24: p. 11639-11649.
7. Zhang, P., et al., LncRNA SNHG8 promotes proliferation and invasion of gastric cancer cells by targeting the miR-491/PDGFRA axis. Hum Cell. 2020; 33: 123-130.
8. Song, Y., et al., LncRNA SNHG8 promotes the development and chemo-resistance of pancreatic adenocarcinoma. Eur Rev Med Pharmacol Sci, 2018; 22: 8161-8168.
9. Dong, J., et al., lncRNA SNHG8 Promotes the Tumorigenesis and Metastasis by Sponging miR-149-5p and Predicts Tumor Recurrence in Hepatocellular Carcinoma. Cell Physiol Biochem, 2018; 51: 2262-2274.
10. Chen, C., et al., SNHG8 is identified as a key regulator in non-small-cell lung cancer progression sponging to miR-542-3p by targeting CCND1/CDK6. Onco Targets Ther. 2018; 11: 6081-6090.
11. Zhen, Y., et al., Knockdown of SNHG8 repressed the growth, migration, and invasion of colorectal cancer cells by directly sponging with miR-663. Biomed Pharmacother. 2019; 116: p. 109000.
12. He, C., et al., Long non-coding RNA SNHG8 promotes autophagy as a ceRNA to upregulate ATG7 by sponging microRNA-588 in colorectal cancer. Oncol Lett. 2021; 22: p. 577.
13. Miao, W., et al., LncRNA SNHG8 induces ovarian carcinoma cells cellular process and stemness through Wnt/β-catenin pathway. Cancer Biomark. 2020; 28: 459-471.
14. Zou, C., et al., SNHG8 Promotes the Progression of Epstein-Barr Virus-Associated Gastric Cancer via Sponging miR-512-5p and Targeting TRIM28. Front Oncol. 2021; 11: 734694.
15. Hao, H., et al., LncRNA small nucleolar RNA host gene 8 promotes cell growth and migration of osteosarcoma in vitro and in vivo by functioning as a ceRNA of microRNA-876-5p. Am J Transl Res. 2020; 12(7): p. 3476-3488.
16. Zhong, G.B., et al., Long noncoding RNA SNHG8 promotes the proliferation of osteosarcoma cells by downregulating miR-542-3p. J Biol Regul Homeost Agents, 2020; 34(2): p. 517-524.
17. Yang, C.H., et al., LncRNA SNHG8 participates in the development of endometrial carcinoma through regulating c-MET expression by miR-152. Eur Rev Med Pharmacol Sci, 2018; 22(6): p. 1629-1637.
18. Xu, X., et al., LncRNA SNHG8 Serves as an Oncogene in Breast Cancer Through miR-634/ZBTB20 Axis. Cancer Manag Res, 2021; 13: p. 3017-3028.
19. Qian, J., et al., Long non-coding RNA SNHG8 enhances triple-negative breast cancer cell proliferation and migration by regulating the miR-335-5p/PYGO2 axis. Biol Direct, 2021; 16(1): p. 13.
20. Song, H., et al., SNHG8 is upregulated in esophageal squamous cell carcinoma and directly sponges microRNA-411 to increase oncogenicity by upregulating KPNA2. Onco Targets Ther, 2019; 12: p. 6991-7004.
21. Yu, B., et al., LncRNA SNHG8 Promotes Proliferation and Inhibits Apoptosis of Diffuse Large B-Cell Lymphoma via Sponging miR-335-5p. Front Oncol, 2021; 11: p. 650287.
22. Shi, Z., et al., Long non-coding RNA SNHG8 promotes prostate cancer progression through repressing miR-384 and up-regulating HOXB7. J Gene Med, 2021; 23(3): p. e3309.
23. Xuan, L., et al., lncRNA SNHG8 promotes ovarian cancer progression through serving as sponge for miR-1270 to regulate S100A11 expression. J Gene Med, 2021: p. e3315.
24. Tian, X., et al., lncRNA SNHG8 promotes aggressive behaviors of nasopharyngeal carcinoma via regulating miR-656-3p/SATB1 axis. Biomed Pharmacother, 2020; 131: p. 110564.

25. Cantù, C., et al., A cytoplasmic role of Wnt/β-catenin transcriptional cofactors Bcl9, Bcl9l, and Pygopus in tooth enamel formation. Sci Signal, 2017; 10(465).

26. Liang, Y., et al., Immunohistochemistry analysis of Pygo2 expression in central nervous system tumors. J Cell Commun Signal, 2019; 13(1): p. 75-84.

27. Zhan, T., N. Rindtorff, and M. Boutros, Wnt signaling in cancer. Oncogene, 2017; 36(11): p. 1461-1473.

28. Li, M., et al., Pygo2 siRNA Inhibit the Growth and Increase Apoptosis of U251 Cell by Suppressing Histone H3K4 Trimethylation. J Mol Neurosci, 2015; 56(4): p. 949-955.

29. Talla, S.B. and F.H. Brembeck, The role of Pygo2 for Wnt/ß-catenin signaling activity during intestinal tumor initiation and progression. Oncotarget, 2016; 7(49): p. 80612-80632.

30. Liu, R., et al., Pygopus 2 promotes kidney cancer OS-RC-2 cells proliferation and invasion in vitro and in vivo. Asian J Urol, 2015; 2(3): p. 151-157.

31. Zhou, C., et al., LncRNA PVT1 promotes gemcitabine resistance of pancreatic cancer via activating Wnt/β-catenin and autophagy pathway through modulating the miR-619-5p/Pygo2 and miR-619-5p/ATG14 axes. Mol Cancer, 2020; 19(1): p. 118.

32. Zhang, D., et al., Pygo2 as a novel biomarker in gastric cancer for monitoring drug resistance by upregulating MDR1. J Cancer, 2021; 12(10): p. 2952-2959.

33. Chi, Y., et al., miR-516a-3p inhibits breast cancer cell growth and EMT by blocking the Pygo2/Wnt signalling pathway. J Cell Mol Med, 2019; 23(9): p. 6295-6307.

34. Lu, X., et al., An In Vivo Screen Identifies PYGO2 as a Driver for Metastatic Prostate Cancer. Cancer Res, 2018; 78(14): p. 3823-3833.