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Original Article

LncRNA GAS5 expression in non-small cell lung cancer tissues and its correlation with Ki67 and EGFR

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Abstract: Objective: This research explored and analyzed LncRNA GAS5 expression in non-small cell lung cancer (NSCLC) tissues and its correlation with Ki67 and EGFR. Methods: A total of 130 samples of paraffin-embedded NSCLC tissues and para-cancerous normal tissues that were collected in the Department of Pathology from January 2014 to April 2016 were selected. The relative expression of LncRNA GAS5 and Ki67/EGFR in both NSCLC tissues and para-cancerous normal tissues were detected via RT-PCR and immunohistochemistry respectively. Subsequently, we analyzed the relative expression of LncRNA GAS5, the expression of Ki67/EGFR and its correlation with clinicopathological features and prognosis of patients, and studied the correlation between LncRNA GAS5 and Ki67/EGFR. Results: The relative expression of LncRNA GAS5 in NSCLC tissues was substantially less than that of the para-cancerous normal tissues (*P<0.05*). The positive expression rate of Ki67/EGFR in NSCLC tissues remarkably exceeded that in para-cancerous normal tissues (*P<0.05*). The relative expression of LncRNA GAS5 was correlated with the degree of tumor differentiation, TNM staging and lymph node metastasis *(P<0.05*). The positive expression rate of Ki67 and EGFR in NSCLC tissues was related to TNM stage and metastasis of lymph node (*P<0.05*). In addition, the survival of patients with high LncRNA GAS5 expression was obviously superior to those with low LncRNA GAS5 expression (*P<0.05*), patients with negative Ki67 had superior survival than those with positive Ki67 (*P<0.05*), and patients with negative EGFR had increased survival over those with positive EGFR (*P<0.05*). Moreover, the positive rates of Ki67 and EGFR in patients with low LncRNA GAS5 expressions were obviously higher than those with high LncRNA GAS5 expressions (*P<0.05*). The relative expression level of LncRNA GAS5 in NSCLC patients had a remarkably negative correlation with Ki67 and EGFR (*P<0.05*). Conclusion: The decrease in LncRNA GAS5 expression and the over-express of Ki67/EGFR occur in NSCLC tissues, the expressions of LncRNA GAS5, Ki67 and EGFR are connected with the progression, metastasis and prognosis of tumor; and LncRNA GAS5 is related to the expression of Ki67 and EGFR. These three factors are involved in the tumorigenesis and growth of the NSCLC process.

Keywords: Non-small cell lung cancer, LncRNA GAS5, Ki67, EGFR

Introduction

Malignant tumor poses a threat to human health and life in modern society. Among the different types, non-small cell lung cancer (NSCLC) occurs mostly in clinical, and is the key factor leading to the death of patients [1]. As the aging process of population continues to intensify, the incidence of NSCLC has been increasing year by year. At the same time, as the disease is insidious in the early stages, and most patients are clinically diagnosed in middle-late stages with poor prognosis [2, 3]. Current studies suggest that the tumorigenesis and growth of NSCLC are related to factors of genes, environmental degradation, and infection, etc. While the exact molecular mechanism of the disease remains unclear [4, 5]. In recent years, it has been found that long non-coding RNA (LncRNA) plays a crucial role in tumorigen-

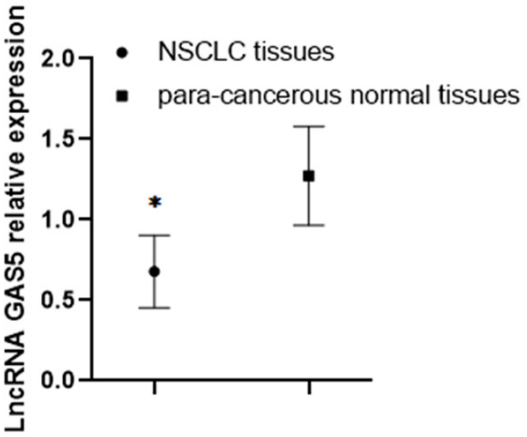

Figure 1. Comparison of LncRNA GAS5 relative expression in NSCLC tissues and para-cancerous normal tissues. Note: compare with para-cancerous normal tissues.

esis and growth, and has been widely involved in gene expression and regulation in term of epigenetic, genetic transcription and post-transcriptional levels. Maternally expressed gene 3 (MEG3) is the first LncRNA found to have a tumor suppressor function [6]. Epidermal growth factor receptor (EGFR) and proliferated cell nuclear protein Ki67 are two tumor markers that are usually used and have a crucial function in the tumorigenesis and growth of NSCLC diseases [7, 8]. This research explored and analyzed the LncRNA MEG3 expression in NSCLC and its correlation with EGFR and Ki67, and provided potential biological indicators for elaborating the molecular mechanism and early diagnosis of NSCLC. The research details are stated as follows:

Material and methods

Research subjects

A total of 130 specimines of paraffin-embedded NSCLC tissues and para-cancerous normal tissues that collected in the Department of Pathology from January 2014 to April 2016 were selected. The para-cancerous tissues, the lung tissues at least 2 cm over the tumor, were confirmed with H&E stains as normal controls. The research was authorized by the hospital ethics committee.

Inclusive and exclusive criteria

Inclusive criteria: (1) Patient that was diagnosed with NSCLC by postoperative pathological examination; (2) No radiotherapy or chemotherapy treated before surgery; (3) The Karnofsky percentage system (KPS) score of patient ≥70; (4) The estimated survival length >3 months; (5) Full sets of clinical, pathological and follow-up data were available; (6) No deterioration or damage with tissue samples; (7) Patients or family members voluntarily signed the informed consent.

Exclusive criteria: (1) Patients with additional primary malignant tumors; (2) Patients with severe body dysfunctions such as in the heart, liver or kidney. (3) Patients with severe metabolic dysfunction, neurological abnormalities or cognitive dysfunction; (4) Patients with acute or chronic infectious diseases.

Detection of LncRNA GAS5 expression by RT-PCR

We extracted the total RNA in cancer tissues as well as para-cancerous ones by TRIzol, and measured the purity and concentration of total RNA by a trace ultraviolet spectrophotometer. The total RNA was made into cDNA by TaqMan miRNA reverse transcription reagent, and PCR amplification was done by taking cDNA as the template. The kit used was SYBR Green fluorescence quantitative PCR kit, and the primer sequences of lncRNA GAS5 were designed and synthesized by Sangong Biotech (Shanghai) Co., Ltd. The forward and reverse primers of LncRNA GAS5 were 5'-CTTGCCTGGACCAGCTTAAT-3' and 5'-CAAGCCGACTCTCCATACCT-3'; The forward and reverse primers of the internal reference U6 were 5'-CTCGGTTCGGCAGCACA-3' and 5'-AACGCTTCACGAATTTG CGT-5'. The total reaction system of PCR was 20 μL, including 1 μL template cDNA, 0.5 μL forward and reverse primers respectively, 8 μL SYBR Green Premix, and 10 μL RNase-free deionized water. The reaction was carried out under 95°C (3 min), 95°C (30 s), and 60°C (30 s), with a total of 40 cycles. All reactions were performed on ABI 7500 real-time fluorescent quantitative PCR. Using U6 as the internal reference, the relative expression of the targeted genes were calculated by $2^{-\Delta\Delta Ct}$. Repeated the detection was performed three times and we adopted the average value for reference.

Expression of Ki67 and EGFR detected by IHC

All specimens were fixed in 10% formaldehyde solution, embedded in paraffin, and sliced continuously at 4 μm and dried. Using the SP method to measure the expression of EGFR and

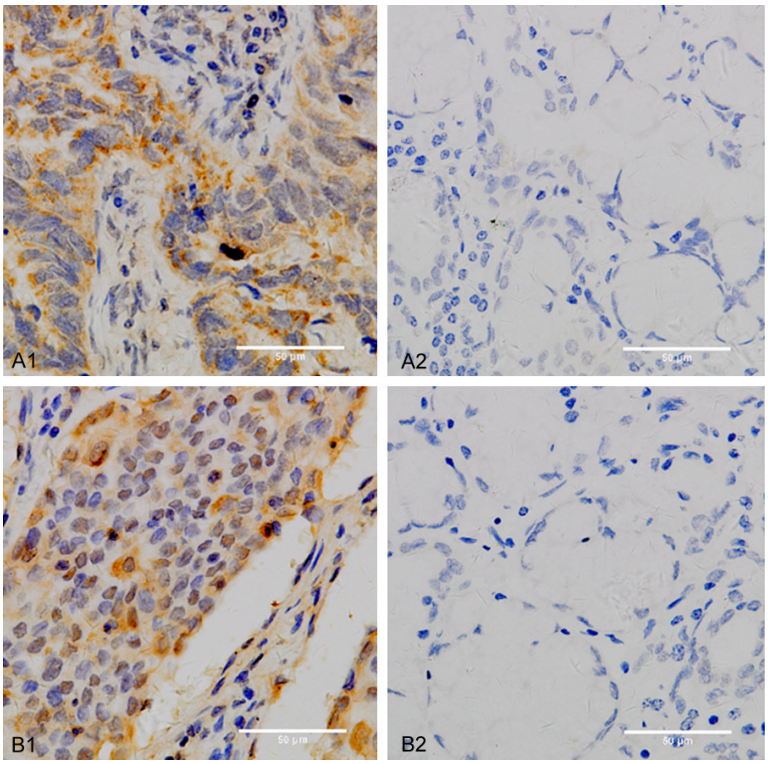

Figure 2. The expression of Ki67 and EGFR detected by immunohistochemistry. A1: Expression of EFGR in NSCLC; A2: Expression of EFGR in paracancerous tissues; B1: Expression of Ki67 in NSCLC; B2: Expression of Ki67 in paracancerous tissues.

Ki67, and set the negative control. The humanised anti-epidermal growth factor receptor (EGFR) monoclonal antibody and the humanised monoclonal antibody Ki67 were purchased from Beijing Zhongshan Biotechnology Co., Ltd.

The EGFR was localized to cytoplasm and Ki67 to the nucleus. Positive staining referred to that when viewing under the microscope, the accurately positioned brown-yellow particles in cells are clearly observed and, and the background is clear. The staining of the cells was divided into 4 grades according to the proportion of positive cells in total number of cancer cells: Negative (-) means that there is no brown yellow staining or the quantity of stained positive cells is less than 10%; Weakly positive (+) means that the proportion of positive cells is 10%-25%; Moderately positive (++) means that the amount of positive cells accounts for 25%-50%; and strong positive (+++) indicates that the positive cells quantity is ≥50%. Results were evaluated according to the above criteria: 0 points: negative; 1 point: weakly positive; 2 points: moderately positive and 3 points: strong positive.

Follow-up of patients

The patients were followed up postoperatively, and the overall survival time (OS) was recorded with the deadline of June 1, 2020. OS refers to the time from the day after surgery to death caused by any reason.

Statistical analysis

Statistical software SPSS 25.0 was applied for data processing and analysis. The measurement data were compared by *t*-test, and the enumeration data was compared by χ^2 test. We adopted the Kaplan Meier curve to obtain the survival situation, Log-rank to compare the survival curve, and Pearson correlation analysis for correlation analysis. The difference was statistically accepted with significance by $P<0.05$.

Results

Clinical data

There was total of 130 NSCLC patients, including 83 males and 47 females who ranged from 39 to 72 years old. The average age was 58.94±12.84 years. According to histology types, 88 cases were adenocarcinoma and 42 were non adenocarcinoma; and according to WHO classification, 34 cases were in stage I, 47 cases in stage II, 39 in stage III, and 10 in stage IV.

LncRNA GAS5 expression

LncRNA GAS5 relative expression in NSCLC tissues was critically inferior to that of the paracancerous normal ones ($P<0.05$), see **Figure 1**.

Expression of Ki67/EGFR

The positive rate of Ki67 expression was 80.77% (105/130) in NSCLC tissues and 10.77% (14/130) in para-cancerous normal tissues; The positive rate of EGFR expression was 66.92% (87/130) in NSCLC tissues and 16.92% (22/130) in para-cancerous normal tissues.

Table 1. The relationship between LncRNA GAS5 and the clinicopathological characteristics

Clinicopathological characteristics	Number of cases	Relative expression of LncRNA GAS5	t	P
Gender				
Male	83	0.637±0.125	1.364	0.175
Female	47	0.601±0.174		
Age (years old)				
>60	61	0.598±0.227	1.080	0.282
≤60	69	0.639±0.206		
Type of histology				
Adenocarcinoma	88	0.628±0.264	0.347	0.729
Non-adenocarcinoma	42	0.612±0.203		
Smoking history				
YES	46	0.602±0.178	0.910	0.365
NO	84	0.637±0.225		
Differentiation degree of tumor				
Well-differentiated	67	0.674±0.204	3.769	0.000
Moderately and poorly differentiated	63	0.548±0.175		
Tumor size (CM)				
≥3	58	0.583±0.264	1.213	0.228
<3	72	0.644±0.301		
TNM Stage				
Stage I~II	81	0.652±0.229	3.425	0.001
Stage III~IV	49	0.521±0.178		
Lymph node metastasis				
YES	45	0.519±0.227	2.335	0.021
NO	85	0.664±0.382		

That of Ki67/EGFR positive expressions in NSCLC tissues remarkably exceeded than that in para-cancerous normal tissues (*P<0.05*), as illustrated in **Figure 2**.

Correlation between LncRNA GAS5 and the clinicopathological characteristics of patients

The relative expression of LncRNA GAS5 was connected with the degree of tumor differentiation, TNM stage and metastasis of lymph nodes *(P<0.05*), as shown in **Table 1**.

Correlation between Ki67/EGFR and the clinicopathological features of patients

The positive expression rate of Ki67 and EGFR in NSCLC was related to the TNM staging and metastasis of lymph node (*P<0.05*), as shown in **Table 2**.

Relationship between LncRNA GAS5, Ki67, EGFR and the prognosis of patients

Taking the median value as the boundary, we divided the relative expression of LncRNA GAS5 in NSCLC into high-expression and low-expression. The survival of patients with high LncRNA GAS5 expression was obviously superior to whom with low LncRNA GAS5 expression (*P<0.05*), patients with negative Ki67 had greater survival than those with positive Ki67 (*P<0.05*), and patients with negative EGFR had increased survival to those with positive EGFR (*P<0.05*), as illustrated in **Figure 3**.

Correlation between LncRNA GAS5 and Ki67/EGFR

The positive rates of Ki67 and EGFR in patients with low LncRNA GAS5 expressions were obviously higher than those with high LncRNA GAS5 expressions (*P<0.05*) (**Table 3**).

Correlation analysis

The results of correlation analysis are consistent, that the relative expression level of LncRNA GAS5 in NSCLC patients had a remarkably negative correlation with Ki67 and EGFR (P<0.05), as shown in **Figure 4**.

Table 2. Relationship between Ki67/EGFR expressions and clinicopathological features of patients

Clinicopathological characteristics	Number of cases	Positive rate of Ki67 (n, %)	X^2	P	Positive rate of EGFR (n, %)	X^2	P
Gender							
Male	83	69 (83.13)	0.826	0.364	53 (63.86)	0.976	0.323
Female	47	36 (76.60)			34 (72.34)		
Age (years old)							
>60	61	50 (81.97)	0.106	0.745	38 (62.30)	1.112	0.292
≤60	69	55 (79.71)			49 (71.10)		
Type of histology							
Adenocarcinoma	88	67 (76.14)	3.764	0.052	60 (68.18)	0.195	0.659
Non-adenocarcinoma	42	38 (90.48)			27 (64.29)		
Smoking history							
YES	46	35 (76.09)	1.005	0.316	33 (71.74)	0.746	0.388
NO	84	70 (83.33)			54 (64.29)		
Differentiation degree of tumor							
Well-differentiated	67	50 (74.63)	3.358	0.067	40 (59.70)	3.257	0.071
Moderately and poorly differentiated	63	55 (87.30)			47 (74.60)		
Tumor size (CM)							
≥3	58	48 (82.76)	0.227	0.606	41 (70.69)	0.671	0.413
<3	72	57 (79.17)			46 (63.89)		
TNM Stage							
Stage I~II	81	60 (74.07)	6.202	0.013	49 (60.49)	4.013	0.045
Stage III~IV	49	45 (91.84)			38 (77.55)		
Lymph node metastasis							
YES	45	41 (91.11)	4.739	0.030	36 (80.00)	5.317	0.021
NO	85	64 (75.29)			51 (60.00)		

Discussion

Non-coding gene sequences account for about 97% of the human genome. The genome expresses a large number of non-coding RNAs, and they impose a significant regulatory functions in cellular life activities and development [9]. In recent years, studies have shown that abnormal expression of non-coding RNA exists in tissues of non-small cell lung tumor, colorectal tumor, etc. and they affect the tumorigenesis and progression of tumors by regulating or inhibiting the oncogene expression. Therefore, non-coding RNA may be treated as a biological marker for diagnosis of certain tumors and a potential therapeutic target [10, 11]. LncRNA is a class of RNA molecules with over 200 nucleotides and a variety of regulatory functions. LncRNA can participate in the tumorigenesis and progression of chronic inflammation, autoimmune diseases and malignant tumors by regulating the biological processes such as chromatin remodeling, transcription and post-transcriptional modification [12, 13]. Studies by scholars have shown that LncRNA can regulate gene expression through transcription and post-transcriptional levels, and at the same time exert or inhibit the oncogenes by regulating a variety of target genes, thus affecting the tumorigenesis and development of tumors [14, 15]. GAS5, a member of the LncRNA family, is located on chromosome 1q25.1. In recent years, it has been discovered that LncRNA GAS5 can affect the expression of target genes by directly acting or interacting with miRNA, and exerting an anti-cancer role in a variety of malignant tumors [16, 17]. This study analyzed LncRNA GAS5 expression in NSCLC tissues. The research shows that the relative expression of LncRNA GAS5 in NSCLC tissues was inferior to that of the para-cancerous normal tissues; LncRNA GAS5 was related to tumor differentiation, TNM stage and metastasis of lymph node; and the survival of subjects with high LncRNA GAS5 expression was superior to those whom with low LncRNA GAS5 expression. The results, which are consistent with the related research conclusions by other scholars

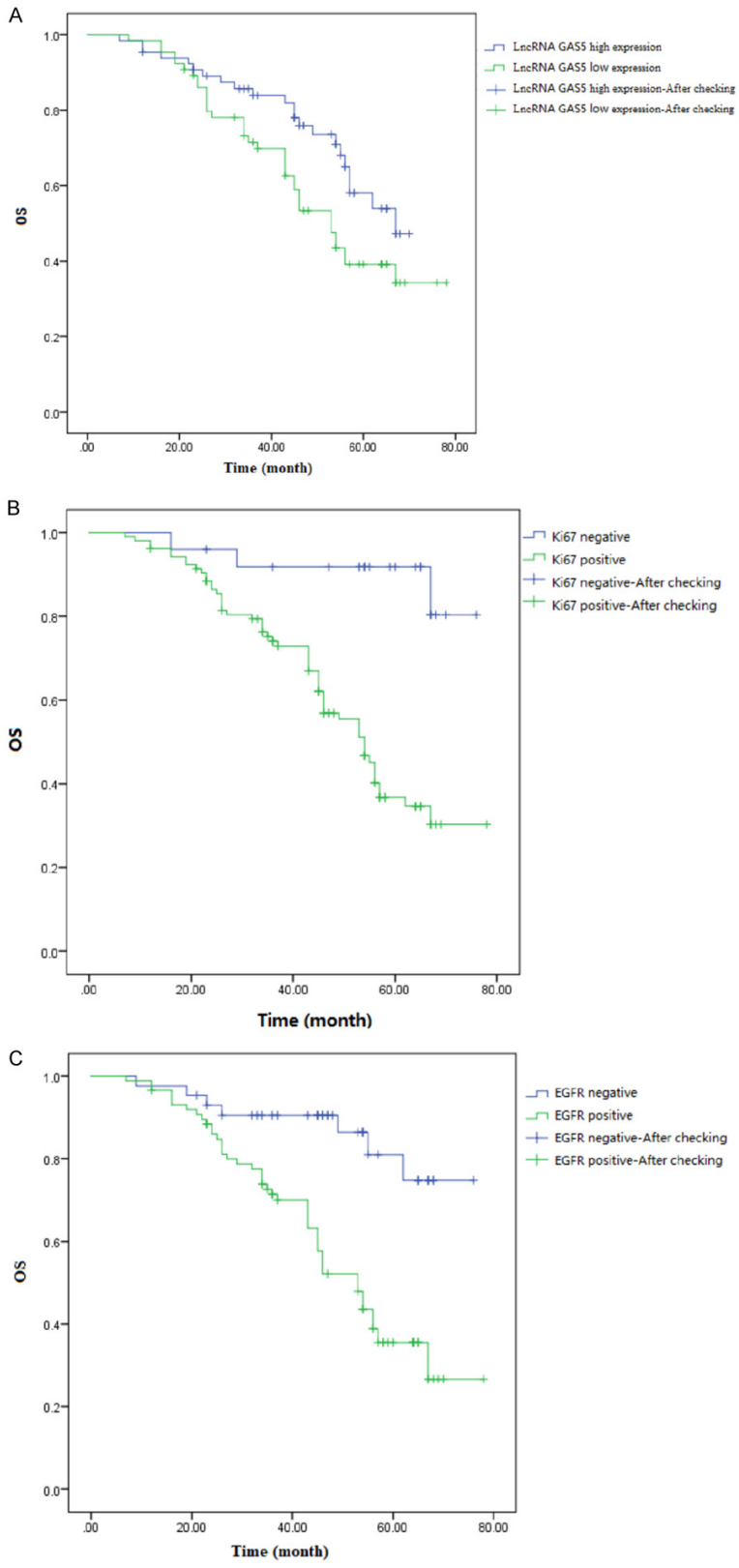

Figure 3. LncRNA GAS5, Ki67, EGFR and overall survival. A: LncRNA GAS5; B: Ki67; C: EGFR.

[18], indicate that LncRNA GAS5 may act with tumor suppressor effects in NSCLC, and impose crucial functions in the tumorigenesis and growth of NSCLC. LncRNA GAS5 is associated with the proliferation, invasion and metastasis of tumors, and has an important impact on clinical prognosis of patients.

Ki67, which is located on chromosome 10 and distributed only in the nucleus, is a nuclear antigen related to cell proliferation. The expression of Ki67 appears in the middle to late G1 period, gradually increases in S and G2 phases, reaches the peak during the mitosis period, and then rapidly decreases after mitosis [19]. The expression degree of Ki67 can reflect the multiplication of tumor cells, which is only expressed in proliferating cells. EGFR is the expression product of the proto-oncogene C-erbB-1. It is a cell membrane receptor with a relative molecular mass of 170×103. EGFR can activate the receptor's tyrosine kinase through the combination of epidermal growth factor (EGF) and transforming growth factor (TGF-α), resulting in phosphorylation of tyrosine residues in the receptor itself and cells, thus leading to cell division and proliferation [20, 21]. Studies have shown that EGFR is overexpressed in a variety of malignant tumors, suggesting that tumor cells are poorly differentiated and have strong invasion and metastasis ability [22, 23]. In this study, we adopted immunohistochemistry to detect Ki67 and EGFR expression in NSCLC and para-cancerous normal tis-

Table 3. The relationship between LncRNA GAS5 and Ki67/EGFR

LncRNA GAS5 Expression	Number of cases	Positive rate of Ki67 (n, %)	Positive rate of EGFR (n, %)
Low-expression	66	61 (92.42)	54 (81.82)
High-expression	64	44 (68.75)	33 (51.56)
X^2	-	11.724	13.437
P	-	0.000	0.000

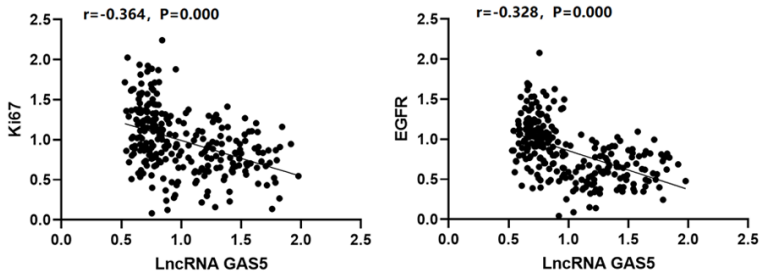

Figure 4. Correlation analysis.

sues. The positive expression rate of Ki67 and EGFR in NSCLC tissues remarkably exceeded than that in para-cancerous normal tissues. The positive expression rate of Ki67 and EGFR in NSCLC tissues was related to the TNM staging and metastasis of lymph node; sufferers with negative Ki67 had improved survival than those with positive Ki67, and patients with negative EGFR had better survival than those with positive EGFR. The empirical conclusions are in line with those conclusions by scholars [24, 25], that Ki67 and EGFR are overexpressed in NSCLC and it has a connection with the malignant proliferation, invasion and disease growth of lung cancer cells. Tumors positive for Ki67 and EGFR have stronger mitotic proliferation and infiltration, and are also important indicators that affect the prognosis of patients.

At present, the effect mechanism of LncRNA GAS5 on NSCLC remains uncovered. This research made further comparisons between LncRNA GAS5 and the traditional tumor markers Ki67 and EGFR. The results displayed that the positive rates of Ki67 and EGFR in patients with low LncRNA GAS5 expressions and were obviously higher than whom with high LncRNA GAS5 expressions, indicating that the inhibiting function of LncRNA GAS5 on tumors may be related to the regulation of Ki67 and EGFR expression. However, further fundamental experiments are needed to verify its specific action pathway.

To conclude, the decrease in LncRNA GAS5 expression and the over-expression of Ki67 and EGFR occur in NSCLC, expression of LncRNA GAS5, Ki67 and EGFR are correlated with the progression, metastasis and prognosis of tumors, and LncRNA GAS5 is related to the expression of Ki67 and EGFR. These three factors are jointly involved in tumorigenesis and growth of NSCLC disease process.

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Disclosure of conflict of interest

None.

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References

[1] Su WZ and Yuan X. LncRNA GASL1 inhibits tumor growth of non-small cell lung cancer by inactivating TGF-beta pathway. Eur Rev Med Pharmacol Sci 2018; 22: 7282-7288.

[2] Lei Y, Guo W, Chen B, Chen L, Gong J and Li W. Tumor-released lncRNA H19 promotes gefitinib resistance via packaging into exosomes in non-small cell lung cancer. Oncol Rep 2018; 40: 3438-3446.

[3] Lu W, Zhang H, Niu Y, Wu Y, Sun W, Li H, Kong J, Ding K, Shen HM, Wu H, Xia D and Wu Y. Long non-coding RNA linc00673 regulated non-small cell lung cancer proliferation, migration, invasion and epithelial mesenchymal transition by sponging miR-150-5p. Mol Cancer 2017; 16: 118.

[4] Zhang W, Cai X, Yu J, Lu X, Qian Q and Qian W. Exosome-mediated transfer of lncRNA RP11-838N2.4 promotes erlotinib resistance in non-

small cell lung cancer. Int J Oncol 2018; 53: 527-538.
[5] Ao X, Jiang M, Zhou J, Liang H, Xia H and Chen G. lincRNA-p21 inhibits the progression of non-small cell lung cancer via targeting miR-17-5p. Oncol Rep 2019; 41: 789-800.
[6] Lin T, Fu Y, Zhang X, Gu J, Ma X, Miao R, Xiang X, Niu W, Qu K, Liu C and Wu Q. A seven-long noncoding RNA signature predicts overall survival for patients with early stage non-small cell lung cancer. Aging (Albany NY) 2018; 10: 2356-2366.
[7] Zhang YX, Yuan J, Gao ZM and Zhang ZG. LncRNA TUC338 promotes invasion of lung cancer by activating MAPK pathway. Eur Rev Med Pharmacol Sci 2018; 22: 443-449.
[8] Liu J, Yao L, Zhang M, Jiang J, Yang M and Wang Y. Downregulation of LncRNA-XIST inhibited development of non-small cell lung cancer by activating miR-335/SOD2/ROS signal pathway mediated pyroptotic cell death. Aging (Albany NY) 2019; 11: 7830-7846.
[9] Chen ZY, Liu HY, Jiang N and Yuan JM. LncRNA HOST2 enhances gefitinib-resistance in non-small cell lung cancer by down-regulating miRNA-621. Eur Rev Med Pharmacol Sci 2019; 23: 9939-9946.
[10] Liu L, Chen Y, Li Q and Duan P. lncRNA HNF1A-AS1 modulates non-small cell lung cancer progression by targeting miR-149-5p/Cdk6. J Cell Biochem 2019; 120: 18736-18750.
[11] Yu L, Fang F, Lu S, Li X, Yang Y and Wang Z. lncRNA-HIT promotes cell proliferation of non-small cell lung cancer by association with E2F1. Cancer Gene Ther 2017; 24: 221-226.
[12] Wang L, Ma L, Xu F, Zhai W, Dong S, Yin L, Liu J and Yu Z. Role of long non-coding RNA in drug resistance in non-small cell lung cancer. Thorac Cancer 2018; 9: 761-768.
[13] Xu W, Xu Q, Kuang D, Wang Z, Lu Q, Lin Q, Wu H and Chen L. Long non-coding RNA SLNCR1 regulates non-small cell lung cancer migration, invasion and stemness through interactions with secretory phospholipase A2. Mol Med Rep 2019; 20: 2591-2596.
[14] Miao F, Chen J, Shi M, Song Y, Chen Z and Pang L. LncRNA HAND2-AS1 inhibits non-small cell lung cancer migration, invasion and maintains cell stemness through the interactions with TGF-beta1. Biosci Rep 2019; 39: BSR20181525.
[15] Zhu ZJ and He JK. TINCR facilitates non-small cell lung cancer progression through BRAF-activated MAPK pathway. Biochem Biophys Res Commun 2018; 497: 971-977.
[16] Niu Y, Ma F, Huang W, Fang S, Li M, Wei T and Guo L. Long non-coding RNA TUG1 is involved in cell growth and chemoresistance of small cell lung cancer by regulating LIMK2b via EZH2. Mol Cancer 2017; 16: 5.
[17] Zhou Y, Shi H, Du Y, Zhao G, Wang X, Li Q, Liu J, Ye L, Shen Z, Guo Y and Huang Y. lncRNA DLEU2 modulates cell proliferation and invasion of non-small cell lung cancer by regulating miR-30c-5p/SOX9 axis. Aging (Albany NY) 2019; 11: 7386-7401.
[18] Wang R, Feng N, Wang Y, Gao S, Zhang F, Qian Y, Gao M, Yu H, Zhou B and Qian B. SNPs in LncRNA genes are associated with non-small cell lung cancer in a Chinese population. J Clin Lab Anal 2019; 33: e22858.
[19] Esfandi F, Kholghi Oskooei V, Taheri F, Kiani A, Taheri M and Ghafouri-Fard S. Expression analysis of OIP5-AS1 in non-small cell lung cancer. Klin Onkol 2018; 31: 260-263.
[20] Cai Y, Dong ZY and Wang JY. LncRNA NNT-AS1 is a major mediator of cisplatin chemoresistance in non-small cell lung cancer through MAPK/Slug pathway. Eur Rev Med Pharmacol Sci 2018; 22: 4879-4887.
[21] Wang S, Lan F and Xia Y. lncRA ANCR inhibits non-small cell lung cancer cell migration and invasion by inactivating TGF-beta pathway. Med Sci Monit 2018; 24: 6002-6009.
[22] Qian B, Wang X, Mao C, Jiang Y, Shi Y, Chen L, Liu S, Wang B, Pan S, Tao Y and Shi H. Long non-coding RNA linc01433 promotes migration and invasion in non-small cell lung cancer. Thorac Cancer 2018; 9: 589-597.
[23] Tian LJ, Wu YP, Wang D, Zhou ZH, Xue SB, Zhang DY, Wei YG and Liu W. Upregulation of long noncoding RNA (lncRNA) X-inactive specific transcript (XIST) is associated with cisplatin resistance in non-small cell lung cancer (NSCLC) by downregulating microRNA-144-3p. Med Sci Monit 2019; 25: 8095-8104.
[24] Yu DJ, Li YH and Zhong M. LncRNA FBXL19-AS1 promotes proliferation and metastasis via regulating epithelial-mesenchymal transition in non-small cell lung cancer. Eur Rev Med Pharmacol Sci 2019; 23: 4800-4806.
[25] Han B. LncRNA LINC02418 regulates proliferation and apoptosis of non-small cell lung cancer cells by regulating miR-4677-3p/SEC61G. Eur Rev Med Pharmacol Sci 2019; 23: 10354-10362.