Int J Clin Exp Pathol 2016;9(11):11639-11645
www.ijcep.com /ISSN:1936-2625/IJCEP0034082

Original Article

Up-regulation of long non-coding RNA SUMO1P3 is associated with poor prognosis in NSCLC patients

Xiao Liu[1], Bo Liu[1], Wei Chen[1], Gang Hu[1], Yun Zhao[2], Jun Wang[1]

Departments of [1]Respiratory Diseases, [2]Thoracic Surgery, The Fifth People's Hospital of Chengdu, Chengdu, Sichuan, China

Received June 20, 2016; Accepted September 12, 2016; Epub November 1, 2016; Published November 15, 2016

Abstract: Recently, long noncoding RNAs (lncRNAs) have been shown to have crucial regulatory roles in human cancer biology and may be used for cancer diagnosis, prognosis, and potential therapeutic targets. LncRNA SUMO1P3 (Small ubiquitin-like modifier 1 pseudogene 3) is a newly identified lncRNA that was previously reported to be up-regulated in gastric cancer and bladder cancer, however, its role in non-small cell lung cancer (NSCLC) remains unclear. The aim of this study was to investigate the expression and clinical significance of lncRNA SUMO1P3 in NSCLC. Our results showed that SUMO1P3 was significantly up-regulated in NSCLC tissues compared with paired-adjacent nontumorous tissues ($P<0.01$) and healthy tissues ($P<0.01$). Its expression level was significantly correlated with TNM stage ($\chi^2=12.49$, $P=0.0019<0.001$) and tumor size ($\chi^2=10.20$, $P=0.0014<0.001$). Receiver operating characteristics (ROC) curve indicated that SUMO1P3 could be a potential tumor marker of NSCLC (AUC=0.7284; 95% CI: 0.664-0.761; $P=0.0012$). Kaplan-Meier survival analysis revealed that patients with high SUMO1P3 expression level had poorer overall survival (OS; $P=0.0001$) and progression free survival (PFS; $P=0.0031$) than those with low SUMO1P3 expression. Further multivariable Cox regression analysis suggested that increased SUMO1P3 was an independent prognostic indicator for this disease. In conclusion, SUMO1P3 is involved in the development and progression of NSCLC and may be a potential diagnostic and target for new therapies in patients with NSCLC.

Keywords: Long non-coding RNA, SUMO1P3, NSCLC, prognosis

Introduction

Non-small cell lung cancer (NSCLC) accounts for about 80-85% of all lung cancer, which is the most frequently diagnosed cancer as well as the leading cause of cancer death worldwide [1]. Although in recent years there are mounting advances in clinical treatment and experimental oncology, the prognosis of NSCLC remains dismal, with the 5-year overall survival time of only about 11%-15% [2]. For that is closely correlated with high potential for invasion and metastasis, as well as the lack of molecular biomarkers [3]. To diagnose and develop novel therapies for NSCLC, it is required to identify more precise prognostic markers of underlying development and progression of the disease.

Long non-coding RNAs (lncRNAs), a recently discovered subclass of non-coding RNA (ncRNA) by high throughput trancriptome analysis, are over 200 nucleotides (nt) in length with no or limited coding protein capacity [4]. LncRNAs are predicted to modulate chromatin or to function as genetic regulators, which depend on their location to the nucleus. To date, over 3000 lncRNAs have been identified; however, functions for only 1% of them have been well characterized [5]. Recently, a number of cancer-related has suggested lncRNAs are involved in multiple biological processes, including tumorigenesis and tumor progression. Among the lncRNA family, the pseudogene-expressed lncRNAs are one of the major types. Recently, Zhan et al. showed that small ubiquitin-like modifier (SUMO) 1 pseudogene 3, SUMO1P3, one of the pseudogene-expressed lncRNAs, was significantly up-regulated in bladder cancer [6]. Furthermore, they also found it was closely associated with the poor prognosis and tumor growth, as well as metastasis in bladder cancer. Previously, Mei et al. found that SUMO1P3

Table 1. The relationship between SUMO1P3 expression and clinicopathological factors of 126 NSCLC patients

Characteristics	Number	Expression of SUMO1P3		χ^2	*P* value
		Low (n=63)	High (n=63)		
Sex					
Male	80	38	42	0.5478	0.4592
Female	46	25	21		
Age (years)					
≤60	51	28	23	0.8235	0.3642
>60	75	35	40		
Histological grade					
Low or undiffer	16	8	8	0.2559	0.8799
Middle	47	22	25		
High	63	23	30		
Histological classification					
Squamous cell carcinoma	79	40	39	0.3746	0.8292
Adenocarcinoma	35	18	17		
Other	12	5	7		
TNM stage					
I and II	43	13	30	10.20	0.0014**
III and IV	83	50	33		
Lymph node metastasis					
Negative	48	28	20	2.154	0.1422
Positive	78	35	43		
Tumor size					
≤3 cm	41	29	11	12.49	0.0019**
3-7 cm	65	26	39		
>7 cm	20	7	13		
History of smoking					
Ever	96	46	50	0.7000	0.4028
Never	30	17	13		

**$P<0.01$.

was overexpressed in gastric cancer and identified as a potential prognostic and therapeutic target for gastric cancer [7]. However, the relationship between the lncRNA SUMO1P3 and NSCLC is entirely unknown.

In this study, we investigated the relationship between SUMO1P3 expression and clinicopathological parameters, as well as prognosis in NSCLC. We found that SUMO1P3 is significantly up-regulated in NSCLC cancer tissues juxtaposed with adjacent normal tissues, and may be used as a novel marker of poor prognosis and potential therapeutic target.

Materials and methods

Patients and sample collection

Fresh cancer tissues and pair-matched adjacent normal tissues were obtained from 126 patients with NSCLC between July 2010 and May 2012 at the Fifth People's Hospital of Chengdu, Sichuan, China. All specimens from transbronchial lung biopsy (TBLB), percutancous lung biopsy, bronchial mucosal biopsy and resection surgery were frozen and stored in liquid nitrogen until needed. All patients did not receive preoperative treatment such as radiation or chemotherapy before collecting specimens. This study was performed with the approval of the Research Ethics Committee of the Fifth People's Hospital of Chengdu, Sichuan, China. Written informed consents were taken from all subjects. **Table 1** summarizes the clinical characteristics of all the patients. In addition, 57 people without NSCLC or other malignancies were recruited to act as healthy controls. All patients were under a close follow-up observation for disease recurrence at no less than 3-month intervals during the first postoperative years and no less than every 6 months thereafter. Overall survival (OS) time was calculated from the date of the initial surgery to death. Progression-free survival (PFS) time was calculated from the date of the initial surgery until the first evidence of local regional, or distant tumor progression of disease.

RNA extraction and quantitative real-time polymerase chain reaction (qRT-PCR)

The total RNA of the tissue samples were extracted using the Trizol reagent (Invitrogen, Shanghai, China) according to the manufactur-

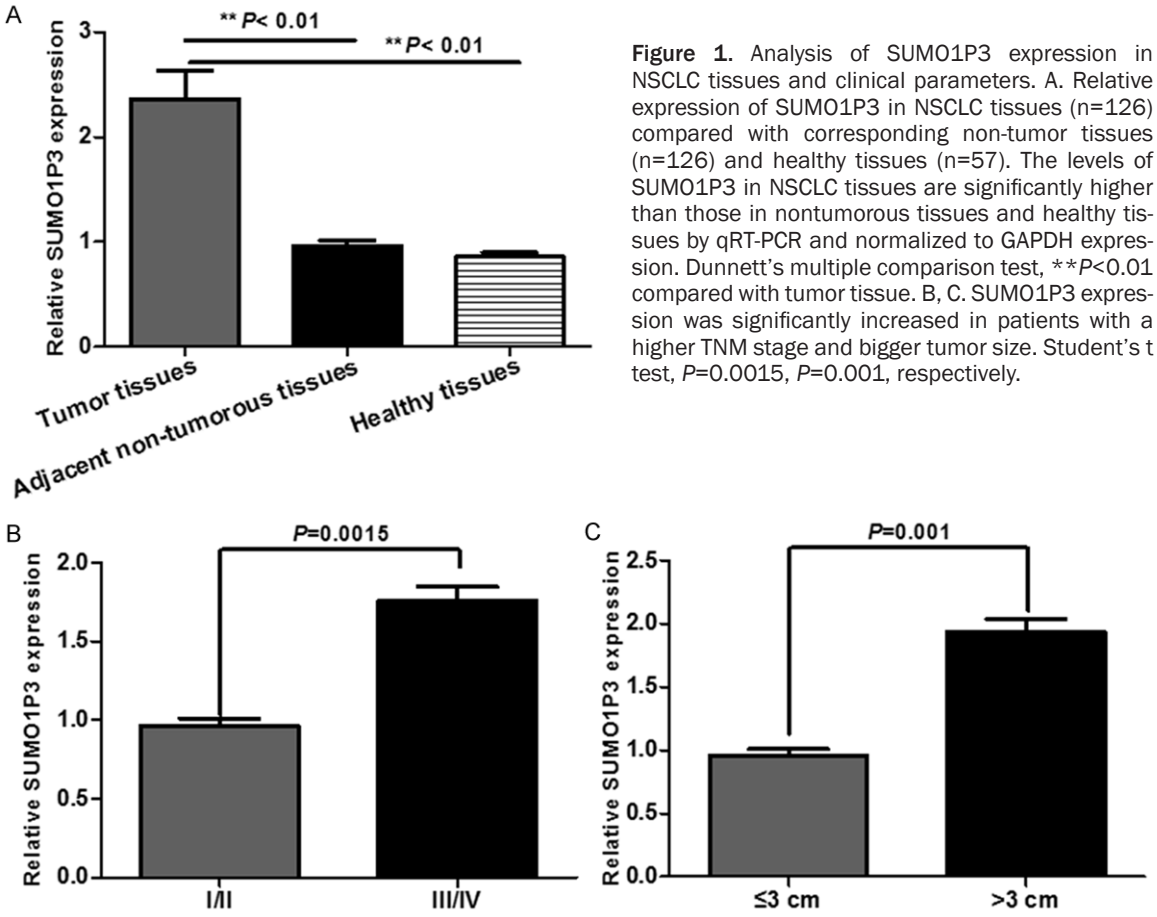

Figure 1. Analysis of SUMO1P3 expression in NSCLC tissues and clinical parameters. A. Relative expression of SUMO1P3 in NSCLC tissues (n=126) compared with corresponding non-tumor tissues (n=126) and healthy tissues (n=57). The levels of SUMO1P3 in NSCLC tissues are significantly higher than those in nontumorous tissues and healthy tissues by qRT-PCR and normalized to GAPDH expression. Dunnett's multiple comparison test, $**P<0.01$ compared with tumor tissue. B, C. SUMO1P3 expression was significantly increased in patients with a higher TNM stage and bigger tumor size. Student's t test, $P=0.0015$, $P=0.001$, respectively.

er's instructions. The concentration and purity of the total RNA were detected with NanoDrop ND-2000 Spectrophotometer (Thermo Scientific) at 260 nm and the electrophoresis detection showed good quality of purified RNA. By using a Reverse Transcription Kit (Takara, Dalian, China) according to the instructions, cDNA was converted from total RNA. Quantitative real-time PCR was performed with SYBR Green (Takara) and the data collection was carried out on the M×3000P StrataGene QPCR (Agilent Technologies) according to the manufacturer's instructions. The primers were synthesized by Biosune (Shanghai, China). Their sequences were as follows: SUMO1P3 primers, forward: 5'-ACTGGGAATGGAGGAAGA-3', reverse: 5'-TGAGAAAGGATTGAGGGAAAAG-3'; GAPDH primers, forward: 5'-CGCTCTCTGCTCCTCCTGTTC-3', reverse: 5'-ATCCGTTGACTCCGACCTTCAC-3'. The average value in each triplicate was used to calculate the relative amount of SUMO1P3 using $2^{-\Delta\Delta Ct}$ methods. Experiments were repeated no less than three times.

Statistical analysis

All experimental data from three independent experiments were analyzed by SPSS software 19.0 and results were expressed as mean ± SD. Using one-way analysis of variance (ANOVA), differences of SUMO1P3 levels between NSCLC cancer tissues and adjacent nontumor tissues were analyzed. The chi-square and t tests were performed to explore the associations between SUMO1P3 level and clinicopathological factors. Survival analysis was performed using the Kaplan-Meier method, and the log-rank test was used to compare the differences between patient groups. Survival data were evaluated using univariate and multivariate Coxproportional hazards model. Variables with a value of $P<0.05$ in the univariate analysis were used in the subsequent multivariate analysis on the basis of Cox regression analyses. To discriminate the studied groups, receiver operating characteristic (ROC) curve was established to evaluate the diagnostic value for the perfor-

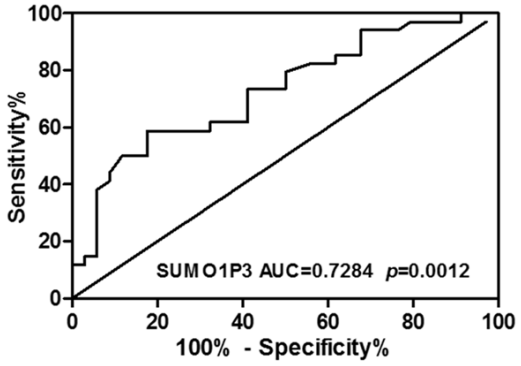

Figure 2. The ROC curve of SUMO1P3 expression for distinguishes NSCLC. The area under the ROC curve (AUC) was calculated for the diagnosis of tumor tissues vs. nontumourous control.

mance of SUMO1P3. *P*-values of less than 0.05 were considered to be statistically significant. GraphPad Prism 5.0 plotted all graphs.

Results

Expression of SUMO1P3 was up-regulated in NSCLC tissues

We first examined the relative expression level of SUMO1P3 in NSCLC tissues (n=126) contrasted with corresponding non-tumor tissues (n=126) and healthy tissues (n=57) by qRT-PCR, and normalized to GAPDH. As shown in **Figure 1A** and Supplemental Data, the SUMO1P3 level was significantly up-regulated in NSCLC tissues compared with corresponding adjacent non-tumorous tissues ($P<0.01$) and healthy tissues ($P<0.01$). These data suggested that abnormal SUMO1P3 expression may be associated with NSCLC pathogenesis.

Relationship of SUMO1P3 expression level with the clinicopathological factors in patients with NSCLC

We used *t* test to examine the correlation of SUMO1P3 expression level with the clinicopathological factors in NSCLC. As shown in **Figure 1B** and **1C**, there was an obvious positive correlation between increased SUMO1P3 levels and advanced TNM stage (0.9603 ± 0.1533 versus 1.7570 ± 0.2705, $P=0.0015$) and larger tumor size (0.9712 ± 0.1433 versus 1.9371 ± 0.3021, $P=0.0010$). Tumor size less than 3 cm or stages in I/II were associated with lower SUMO1P3 level, whereas tumor size greater than 3 cm or stages in III/IV were associated with higher SUMO1P3 expression. Moreover, according to the median value of SUMO1P3 levels in cancer tissues, we divided the samples into high SUMO1P3 expression groups (above the mean, n=63) and low SUMO1P3 expression groups (below the mean, n=63). Chi-square test was then performed to evaluate clinicopathological factors between the two groups. As shown in **Table 1**, SUMO1P3 level was also correlated to tumor size ($\chi^2=10.20$, $P=0.0014<0.001$) and TNM stage ($\chi^2=12.49$, $P=0.0019<0.001$). No relationship between SUMO1P3 expression and other factors, e.g., sex (male, female), age (≤60, >60), histological grade (low or undiffer, middle or high), histological classification (SCC, AD, or other), lymph node metastasis (negative, positive), or history of smoking (ever, never) were found within our study.

Diagnostic value of SUMO1P3

To investigate the characteristics of SUMO1P3 as potential tumor markers of NSCLC, ROC curve and the area under the ROC curves (AUC) were performed on NSCLC tissues and corresponding adjacent nontumorous tissues control. The ROC curves illustrated strong separation between the tumor tissues and the control group,with an AUC of 0.7284 (95% CI: 0.664-0.761; $P=0.0012$) for SUMO1P3 (**Figure 2** and Supplemental Data).

High expression of SUMO1P3 predicts poor prognosis in patients with NSCLC

Firstly, to determine the relationship between SUMO1P3 expression and NSCLC patients' prognosis, we used Kaplan-Meier analysis and log-rank test to evaluate the correlation between SUMO1P3 expression and the clinicopathological characteristics on overall survival (OS) and progression-free survival (PFS). As shown in **Figure 3A**, **3B** and Supplemental Data, 5 years of OS for low SUMO1P3 expression was 20.6%, whereas high SUMO1P3 expression was only 11.5%. The median survival time for low SUMO1P3 expression was 48 months, where as high SUMO1P3 expression was 23 months. Moreover, the median PFS for low SUMO1P3 was 36 months, while high SUMO1P3 expression was 19 months. Remarkably, patients with high SUMO1P3 expression level had poorer overall survival ($P=0.0001$) and progression-free survival

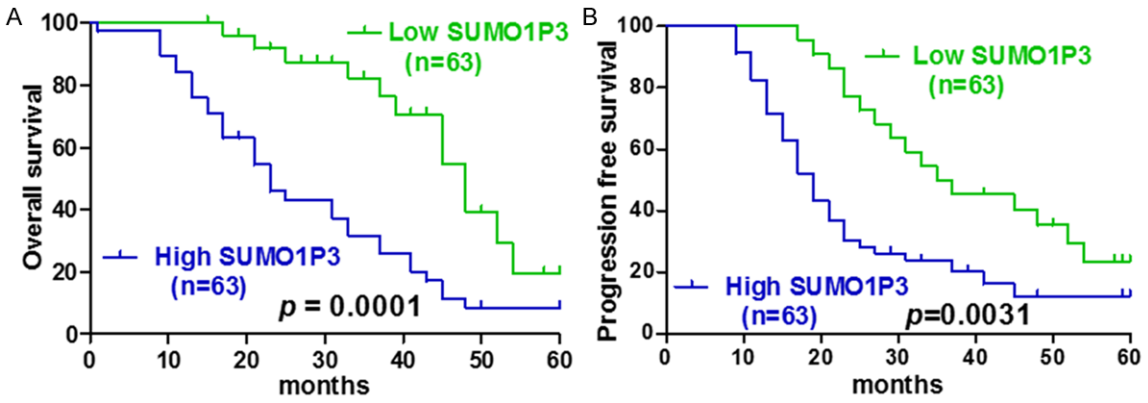

Figure 3. Kaplan-Meier curves of the overall survival and progression-free survival of 126 patients with NSCLC. A, B. Overall survival rate and progression-free survival rate in patients with high SUMO1P3 expression was significantly lower than that in patients with low SUMO1P3 expression (Log-Rank test, *P*=0.0181, *P*<0.001).

Table 2. Univariate and multivariate analysis of clinic-pathologic factors for PFS or OS in 126 patients with NSCLC

Variables	PFS			OS		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Univariate analysis						
Age (≤60 vs. >60)	1.164	0.825~1.317	0.653	1.267	0.784~1.732	0.765
Gender (male vs. female)	1.214	0.891~1.846	0.317	1.527	0.872~2.145	0.261
Tumor size (≤3 cm vs. >3 cm)	1.347	0.984~1.526	0.456	1.260	0.938~1.692	0.316
History of smoking (never vs. ever)	1.136	0.755~1.319	0.576	1.317	1.103~1.851	0.571
Histologic classification (SCC, AD, or other)	1.572	1.136~1.771	0.371	1.104	0.774~1.632	0.183
Lymph node metastasis (N vs. P)	1.319	1.124~1.983	0.561	1.739	0.933~3.240	0.082
TNM stage (I+II vs. III+IV)	0.459	0.347~0.617	<0.001**	0.638	0.437~1.132	0.007**
Histologic grade (low, middle, high)	2.599	1.987~2.871	0.018*	2.143	1.681~2.756	0.014**
Expression of SUMO1P3 (high vs. low)	0.189	0.071~0.535	0.001**	0.325	0.141~0.764	0.008**
Multivariate analysis						
TNM stage (I+II vs. III+IV)	0.416	0.344~0.671	0.015*	0.421	0.257~0.962	0.018*
Histologic grade (low, middle, high)	2.431	1.793~2.795	0.001**	2.148	1.651~2.368	0.016*
Expression of SUMO1P3 (high vs. low)	0.276	0.099~0.768	0.014*	0.192	0.070~0.528	0.001**

PFS, progression-free survival; OS, overall survival; HR, hazard ratio; N, negative; P, positive; SSC, Squamous cell carcinoma; AD, Adenocarcinoma; *P<0.05, **P<0.01.

(*P*=0.0031). These results together suggested up-regulated expression of SUMO1P3 in NSCLC significantly decreased the survival time of patients.

Up-regulated expression of SUMO1P3 is an independent prognostic predictor for patient with NSCLC

To further confirm the prognostic role of SUMO1P3 in NSCLC patients, the univariate and multivariate survival analyses (Cox proportional hazards regression model) were performed for PFS or OS in 126 patients with NSCLC, respectively. Univariate analysis identified three prognosis factors (histological grade (low, middle, or high), TNM stage (I/II, III/IV) and SUMO1P3 expression) that were statistically significant risk factors affecting PFS or OS of patients. The other clinicopathological characteristics, such as sex, tumor size, histological classification, history of smoking, and lymph node metastasis were found to be statistically insignificant prognosis factors (*P*>0.05). Multivariate analysis further revealed that SUMO1P3 expression, histological classification, and TNM stage could

be regarded as significant independent predictors of poor survival and progression-free survival in NSCLC patients (P<0.05) (**Table 2**). Taken together, these results indicated that up-regulated expression of SUMO1P3 might play an important role in the development of NSCLC.

Discussion

Recently, many lncRNAs have been identified, and the participation of lncRNAs in a wide repertoire of biological processes has been a topic of intense contemporary research, as virtually every step in the life cycle of genes from transcription to mRNA splicing, RNA decay, and translation can be influenced by these molecules [8, 9]. Furthermore, the identification of cancer-associated lncRNAs and investigation of their clinical significance and biological functions in cancers have begun in recent studies. For instance, HOTAIR is an lncRNA that is overexpressed in various tumors and significantly associated with cancer metastasis [10-12]. Overexpression of lncRNA CCAT2 is linked with poor prognosis in patients with colorectal cancer (CRC) [13, 14]. LncRNA MALAT1 (metastasis-associated lung adenocarcinoma transcript 1) is up-regulated in NSCLC and can be used as an independent prognostic marker of patient survival [15]. Other well-studied lncRNAs, such as MEG3, GAS5, and lncRNA H19, have instead demonstrated tumor suppressive roles indiverse human cancers [16-18]. These findings indicate that, similar to protein-coding genes and miRNAs, lncRNAs could serve as diagnostic and prognostic biomarkers. However, the overall pathophysiological roles of lncRNAs to NSCLC cancer remain largely unknown.

Small ubiquitin-like modifier 1 pseudogene 3 (SUMO1P3) is one member of the SUMO pseudogene family, which is a newly indentified long non-coding RNA [19]. SUMO1P3 has been shown to be up-regulated and identified as a potential prognostic and therapeutic target for gastric cancer and bladder cancer [6, 7]. For gastric cancer, the expression of SUMO1P3 is connected with tumor size, differentiation, lymph node metastasis, and invasion of patients with gastric cancer [7]. Additionally, inhibited proliferation, increased apoptosis, and suppressed migration were observed in SUMO1P3 siRNA-transfected bladder cells [6].

However, the expression and clinical significance of SUMO1P3 in NSCLC remains largely unknown. Our results found that the expression of SUMO1P3, one of the transcripts of pseudogenes, is un-regulated in NSCLC (**Figure 1A**). This is the first report about SUMO1P3 expression in NSCLC to our knowledge.

Furthermore, we also evaluated the prognostic value of SUMO1P3 by Kaplan-Meier and Cox regression analysis. Our findings suggest lncRNA SUMO1P3 may represent a novel indicator of poor prognosis in NSCLC cancer, and may be a potential therapeutic target for diagnosis and gene therapy.

In further studies, we will expand the samples for additional investigation and try to identify the biological functions of lncRNA SUMO1P3, along with elucidating the concise molecular mechanisms underlying the altered expression of SUMO1P3 in NSCLC.

In summary, we demonstrate that the increased SUMO1P3 expression is a common event underlying NSCLC juxtaposed with paired-adjacent nontumorous tissues and healthy tissues. This indicates that SUMO1P3 may play a key oncogenic role as an indicator of poor survival rate and a negative prognostic factor for patients with NSCLC. These new findings suggest that SUMO1P3 may be used as a potential prognostic and therapeutic target of NSCLC.

Acknowledgements

This work was funded by the National Science Foundation Projects of Sichuan Province (100044).

Disclosure of conflict of interest

None.

Address correspondence to: Jun Wang, Department of Respiratory Diseases, The Fifth People's Hospital of Chengdu, Chengdu 611130, Sichuan, China. Tel: +86 13568926135; +86 28-82724558; E-mail: wangjun201605@yahoo.com

References

[1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016; 66: 7-30.

[2] Chen Z, Fillmore CM, Hammerman PS, Kim CF, Wong KK. Non-small-cell lung cancers: a heterogeneous set of diseases. Nat Rev Cancer 2014; 14: 535-546.

[3] Rosell R, Bivona TG, Karachaliou N. Genetics and biomarkers in personalisation of lung cancer treatment. Lancet 2013; 382: 720-731.

[4] Huarte M. The emerging role of lncRNAs in cancer. Nat Med 2015; 211: 1253-1261.
[5] Rinn JL, Chang HY. Genome regulation by long noncoding RNAs. Annu Rev Biochem 2012; 81: 145-166.
[6] Zhan Y, Liu Y, Wang C, Lin J, Chen M, Chen X, Zhuang C, Liu L, Xu W, Zhou Q, Sun X, Zhang Q, Zhao G, Huang W. Increased expression of SUMO1P3 predicts poor prognosis and promotes tumor growth and metastasis in bladder cancer. Oncotarget 2016; 7: 16038-48.
[7] Mei D, Song H, Wang K, Lou Y, Sun W, Liu Z, Ding X, Guo J. Up-regulation of SUMO1 pseudogene 3 (SUMO1P3) in gastric cancer and its clinical association. Med Oncol 2013; 30: 709.
[8] Flynn RA, Chang HY. Long noncoding RNAs in cell-fate programming and reprogramming. Cell Stem Cell 2014; 14: 752-761.
[9] Turner M, Galloway A, Vigorito E. Noncoding RNA and its associated proteins as regulatory elements of the immune system. Nat Immunol 2014; 15: 484-491.
[10] Gupta RA, Shah N, Wang KC, Kim J, Horlings HM, Wong DJ, Tsai MC, Hung T, Argani P, Rinn JL, Wang Y, Brzoska P, Kong B, Li R, West RB, van de Vijver MJ, Sukumar S, Chang HY. Long non-coding RNA HOTAIR reprograms chromatin state to promote cancer metastasis. Nature 2010; 464: 1071-1076.
[11] Hajjari M, Salavaty A. HOTAIR: an oncogenic long non-coding RNA in different cancers. Cancer Biol Med 2015; 12: 1-9.
[12] Du M, Wang W, Jin H, Wang Q, Ge Y, Lu J, Ma G, Chu H, Tong N, Zhu H, Wang M, Qiang F, Zhang Z. The association analysis of lncRNA HOTAIR genetic variants and gastric cancer risk in a Chinese population. Oncotarget 2015; 6: 31255-31262.
[13] Ling H, Spizzo R, Atlasi Y, Nicoloso M, Shimizu M, Redis RS, Nishida N, Gafà R, Song J, Guo Z, Ivan C, Barbarotto E, De Vries I, Zhang X, Ferracin M, Churchman M, van Galen JF, Beverloo BH, Shariati M, Haderk F, Estecio MR, Garcia-Manero G, Patijn GA, Gotley DC, Bhardwaj V, Shureiqi I, Sen S, Multani AS, Welsh J, Yamamoto K, Taniguchi I, Song MA, Gallinger S, Casey G, Thibodeau SN, Le Marchand L, Tiirikainen M, Mani SA, Zhang W, Davuluri RV, Mimori K, Mori M, Sieuwerts AM, Martens JW, Tomlinson I, Negrini M, Berindan-Neagoe I, Foekens JA, Hamilton SR, Lanza G, Kopetz S, Fodde R, Calin GA. CCAT2, a novel noncoding RNA mapping to 8q24, underlies metastatic progression and chromosomal instability in colon cancer. Genome Res 2013; 23: 1446-1461.
[14] He X, Tan X, Wang X, Jin H, Liu L, Ma L, Yu H, Fan Z. C-Myc-activated long noncoding RNA CCAT1 promotes colon cancer cell proliferation and invasion. Tumour Biol 2014; 35: 12181-12188.
[15] Gutschner T, Hammerle M, Eissmann M, Hsu J, Kim Y, Hung G, Revenko A, Arun G, Stentrup M, Gross M, Zörnig M, MacLeod AR, Spector DL, Diederichs S. The noncoding RNA MALAT1 is a critical regulator of the metastasis phenotype of lung cancer cells. Cancer Res 2013; 73: 1180-1189.
[16] Sun M, Jin FY, Xia R, Kong R, Li JH, Xu TP, Liu YW, Zhang EB, Liu XH, De W. Decreased expression of long noncoding RNA GAS5 indicates a poor prognosis and promotes cell proliferation in gastric cancer. BMC Cancer 2014; 14: 319.
[17] Liang WC, Fu WM, Wong CW, Wang Y, Wang WM, Hu GX, Zhang L, Xiao LJ, Wan DC, Zhang JF, Waye MM. The lncRNA H19 promotes epithelial to mesenchymal transition by functioning as miRNA sponges in colorectal cancer. Oncotarget 2015; 6: 22513-22525.
[18] Yin DD, Liu ZJ, Zhang E, Kong R, Zhang ZH, Guo RH. Decreased expression of long noncoding RNA MEG3 affects cell proliferation and predicts a poor prognosis in patients with colorectal cancer. Tumour Biol 2015; 36: 4851-4859.
[19] Wright MW, Bruford EA. Naming 'junk': human non-protein coding RNA (ncRNA) gene nomenclature. Hum Genomics 2011; 5: 90-98.