International Journal of Research in Environmental Science
Volume 4, Issue 1, 2018, PP 1-8
ISSN No. (Online) 2454-9444
DOI: http://dx.doi.org/10.20431/2454-9444.0401001
www.arcjournals.org

A Case-Control Study of the Relationship between LINC01495, TRAPPC9 Polymorphisms and Lung Cancer Susceptibility in Northeast Chinese Population

Qianru Yang[1,2], Yangwu Ren[1,2], Ruoyi Qu[1,2], Hang Li[1,2], Chang Zheng[1,2], Zhihua Yin[1,2], Yuxia Zhao[3], Baosen Zhou[2,4*]

[1.] *Department of Epidemiology, School of Public Health, China Medical University, Shenyang, 110122, China.*

[2.] *Key Laboratory of Cancer Etiology and Prevention (China Medical University), Liaoning Provincial Department of Education, Liaoning, China.*

[3.] *Department of Cancer Radiotherapy, Fourth Affiliated Hospital, China Medical University, Shenyang 110001, China.*

[4.] *Department of Clinical Epidemiology, First Affiliated Hospital, China Medical University, Shenyang 110001, China.*

***Corresponding Author:** *Baosen Zhou, Department of Clinical Epidemiology, First Affiliated Hospital, China Medical University, Shenyang 110001, China.*

Abstract: ***Background****: Long non-coding RNAs (LncRNAs) have been shown playing important roles in the pathogenesis and progression of multiple tumors. Meanwhile, we also identified some loci associated with emphysema distribution at genome-wide significance. It included a new association near TRAPPC9. So far, the effect of LINC01495 and TRAPPC9 polymorphisms on lung cancer risk were unclear. Rs2665675 and rs2665936 are single nucleotide polymorphisms located in LINC01495 and TRAPPC9, respectively. This study aimed to investigate the association between rs2665675 of LINC01495 and rs2665936 of TRAPPC9 polymorphisms and the risk of lung cancer in Northeast Chinese population.*

Methods*: A hospital-based case-control study of 640 patients and 699 matched controls was conducted. Then 10 ml venous blood was donated for genotype test by Taqman allelic discrimination method. And statistical analyses were performed using SPSS software.*

Result*: We found that TT genotype in rs2665675 (OR = 1.518, 95%CI = 1.099-2.097, P = 0.011) compared with CC genotype and GG genotype in rs2665936 (OR = 1.943, 95%CI = 1.361-2.774, P < 0.001) compared with AA genotype demonstrated that significantly increased the risk of lung cancer.*

Conclusion*: LINC01495 rs2665675 and TRAPPC9 rs2665936 polymorphisms might be associated with lung cancer risk in northeastern Chinese population.*

Keywords: *LINC01495; TRAPPC9; polymorphism; susceptibility; lung cancer*

1. INTRODUCTION

Lung cancer is the most common cancer worldwide[1]. It causes more deaths per year than other cancers and the mortality has been high for recent decades among both men and women[2]. Non-small cell lung cancer (NSCLC) epitomizes the most frequently diagnosed subtype of this fatal malignancy[3]. Over the past 50 years, NSCLC accounts for 85% to 90% of lung cancer, especially squamous cell carcinoma (SCC) and adenocarcinoma (ADC)[4]. There are many causes for lung cancer. Smoking, including passive exposure to tobacco, is the principal cause of lung cancer. However, many lung cancer patients did not have the history of smoking and a lot of smokers didn't

develop lung cancer. So, genetic susceptibility and other environmental factors also affect lung cancer development[5].

LncRNAs play important roles in tumor initiation, progression and metastasis through modulating oncogene and suppressing tumor pathways which are longer than 200 bases and are lack of protein coding capability[6, 7]. For example, metastasis-associated lung adenocarcinoma transcript 1 (MALAT-1) of the lncRNA has been reported to be increased in lung cancer and to be associated with metastasis[8]. And long stress-induced noncoding transcripts (LSINCTs) that are over-expressed in 4-(methylnitrosamino)-1-(3-pyridy1)-1-butanone (NNK)-treated bronchial epithelial cells in normal people[9]. LncRNA enhance proliferation of the cell and play critical roles in tumor progression in breast and ovarian cancers[10]. Because of their important regulatory effects of cancer progression, it is reasonable to infer that there is an association between lncRNAs and lung cancer[11].

Trafficking Protein Particle Complex 9 (TRAPPC9) was named NIBP, for it is consistent to yeast Trs120 protein and it is a necessary and sole subunit for the complex of TRAPP II which regulating exit process of the *trans*-Golgi [12-15]. For cancer development, it is necessary to the trans-Golgi network and possible represent a new target for anti-cancer therapy[16]. TRAPPC9 and specific subunits of other TRAPP II are required for autophagy proteins' transport from the trans-Golgi to assembly of a phagophore [17]. Autophagy is known to be a pivotal mediator for tumorigenesis as well[18, 19]. Thence, TRAPPC9 may adjust the function of trans-Golgi and the formation of autophagosome during cancer development. Studies have confirmed that transcription of TRAPPC9 exists in various cell lines and tumor tissues, and clinical studies have also reported TRAPPC9 transcripts with human breast[20], colon cancer[21], osteosarcoma[22], and lymphoma[23, 24].

Recent some genetic susceptibility studies of lung cancer have focus on single nucleotide polymorphisms (SNPs) in lncRNAs. But to our knowledge, no study has reported the association between polymorphisms in LINC01495 nor TRAPPC9 and NSCLC. So we conducted this case-control study in order to identify the relationship of LINC01495-rs2665675 and TRAPPC9-rs2665936 polymorphisms and NSCLC risk in northeastern Chinese population.

2. MATERIALS AND METHODS

In this hospital-based case-control study, the case group consisted of 640 diagnosed histologically lung cancer patients from The Fourth Affiliated Hospital of China Medical University in Shenyang, located in northeast China. At the same time, 699 controls were selected from medical examination centers of the hospital mentioned above in the same period. All subjects were unrelated ethnic Han Chinese. Each subject was interviewed to collect the demographic characteristics date by questionnaire when they were admitted to the hospital and donated 10ml of venous blood for detection. Individual with a total of 100 cigarettes in his lifetime was defined as a smoker, otherwise he was considered as a non-smoker.

SNP isolation and genotyping

We isolated genomic DNA samples from the venous blood of all participants by Phenol-chlo-roform method. SNP genotyping was performed on an Applied Biosystems 7500 FAST Real-Time PCR System(Foster City, CA, USA) using Taqman® allelic discrimination(Applied Biosystem, Foster City, CA) with primer probe set. When genotyping was performed, appropriate negative controls were included in each run, two investigators randomly selected 10% of samples and performed twice the genotyping of these samples. For quality control, the results were examined to be concordant by different investigators.

Statistical analysis

T test and χ^2 test were used to examine differences in the distributions of demographic characteristics,

selected variables and genotypes among cases and controls. The associations of genotypes of LINC01495 and TRAPPC9 with risk of lung cancer were assessed by the odds ratios (OR) and their 95% confidence intervals (CI) from logistic regression models with both univariate and multivariate in case-control analysis. All the analyses were adjusted by age and gender. All above analyses were two-sided, and performed using the Statistical Product and Service Solutions software (v.21.0, SPSS Institute Cary, Chicago, IL, USA). A value of $P < 0.05$ was considered statistical significantly.

3. RESULTS

The demographic characteristics of the studying subjects are shown in Table 1.There were 640 lung cancer patients and 699 controls in this study. Among the lung cancer patients, there were 457 adenocarcinomas and 183 squamous cell carcinomas. There was no significant difference in the distributions of age ($P = 0.095$) between the cases(58.80 ± 10.59 years) and controls (59.15 ± 11.43 years). Meanwhile, the distribution of gender was no significant differences($P = 0.994$). While, the distribution of smoking status was of significant differences($P < 0.001$), so the next study was adjusted by smoking statues, age and gender.

Table 1. *Characteristics of lung cancer cancers and controls*

Variables		**Cases (%)**	**Controls (%)**	***P* value**
Gender	Male	164(25.6)	179(25.6)	
	Female	476(74.4)	520(74.4)	0.994[b]
Age	mean±SD	58.80±10.59	59.15±11.43	0.095[a]
Smoking	Never	499(78.0)	612(87.6)	
	Yes	141(22.0)	87(12.4)	**<0.001**[b]
Histology	Adencarcinoma	457(71.4)		
	Squamous cell carcinoma	183(25.6)		

[a] *p* value was calculated by the t-test; [b] *p* value was calculated by the chi-square test; Abbreviations: SD, standard deviation

Results of genotype distributions in case and control group and the relationship of genotypes of rs2665675 and rs2665936 with lung cancer risk are showed in Table 2. With the CC genotype of rs2665675 as reference group in LINC01495, after adjusted by age, gender and smoking, analyses showed that individuals carrying heterozygous CT (adjust OR = 1.187, 95%CI = 0.901-1.563, $P = 0.222$) was no statistically significant association. Conversely, homozygous TT genotypes (adjust OR = 1.518, 95%CI = 1.099-2.097, $P = 0.011$) was of statistically significant association that had increased risk of lung cancer comparing to the homozygous wild CC genotype. Increased risk also found in recessive model (adjust OR = 1.346, 95%CI = 1.040-1.741, $P = 0.024$) which was taken wild CC genotype and heterozygous CT as reference. No significant difference was observed in dominant model (adjusted OR = 1.280, 95%CI = 0.984-1.664, $P = 0.066$) which was taken wild CC as reference. Further analyses were carried out by allele comparison and the T allele of rs2665675 was found to be associated with an increased risk of lung cancer with marginally significant OR of 1.227 (95%CI = 1.054-1.552, $P = 0.008$). Similarly, no statistically significant association for rs2665936 was found when heterozygous AG (adjusted OR = 1.258, 95%CI = 0.989-1.599, $P = 0.061$) compared with wild AA genotype as reference. Meanwhile, there were statistically significant association that GG genotype carriers (adjusted OR = 1.943, 95%CI = 1.361-2.774, $P < 0.001$) compared with AA genotype carriers which increased the risk of lung cancer. Increased risk also found in dominant model (adjusted OR = 1.375, 95%CI = 1.093-1.730, $P = 0.007$) which was taken wild AA genotype as reference and recessive model (adjusted OR = 1.696, 95%CI = 1.224-2.350, $P < 0.001$) which was taken wild AA genotype and heterozygous AG as reference. Likewise, the G allele of rs2665936 was found to be associated with an increased risk of lung cancer (adjusted OR = 1.324, 95%CI = 1.130-1.552, $P < 0.001$).

Table 2. *Genotype frequencies of the LINC01495 and TRAPPC9 polymorphisms among lung cancer cases and controls and their associations with risk of lung cancer.*

SNP		Cases(%)		Controls(%)		Adj.OR(95%CI)	*P* value
rs2665675							
CC		131(20.5)		177(25.3)		1.00	
CT		341(53.3)		376(53.8)		1.187 (0.901-1.563)	0.222
TT		168(26.2)		146(20.9)		**1.518(1.099-2.097)**	**0.011**
CC		131(20.5)		177(25.3)		1	
CT/TT		509(79.5)		522(74.7)		1.280(0.984-1.664)	0.066
CC/CT		472(73.8)		553(79.1)		1.00	
TT		168(26.2)		146(20.9)		**1.346(1.040-1.741)**	**0.024**
C allele		603(47.1)		730(52.2)		1.00	
T allele		677(52.9)		668(47.8)		**1.227(1.054-1.428)**	**0.008**
rs2665936							
AA		206(32.2)		271(38.8)		1.00	
AG		327(51.1)		356(50.9)		1.258(0.989-1.599)	0.061
GG		107(16.7)		72(10.3)		**1.943(1.361-2.774)**	**<0.001**
AA		206(32.2)		271(38.8)		1.00	
AG/GG		434(67.8)		428(61.2)		**1.375(1.093-1.730)**	**0.007**
AA/AG		533(83.3)		627(89.7)		1.00	
GG		107(16.7)		72(10.3)		**1.696(1.224-2.350)**	**0.001**
A allele		739(57.7)		898(64.2)		1.00	
G allele		541(42.3)		500(35.8)		**1.324(1.130-1.552)**	**0.001**

OR, odds ratio; CI, confidence interval; ORs and 95%CIs were calculated by logistic regression adjusted by age, gender and smoking.

This study investigated the interaction of tobacco exposure and SNPs by cross-over analysis showed in Table 3. Relative to rs2665675 non-smoking and CC genotype, the OR (6.943) for TT genotype with tobacco exposure was lower than the OR (7.592) for CC genotype with tobacco exposure. Analogous results were acquired when rs2665936 tobacco exposure were investigated. Above cross-over results showed that SNPs-tobacco exposure interaction may not exist.

Meanwhile, the relationship between the tobacco exposure and gender in lung cancer cases and controls were showed in Table 4. There was no significant difference in smoking population (adjusted OR = 6.011, 95%CI = 0.744-48.589, P = 0.093), conversely in non-smoking population, the result was a significant difference (adjusted OR = 2.519, 95%CI = 1.660-3.812, $P < 0.001$). Therefore, there was no evident difference between the tobacco exposure and gender.

Table 5 summarized the relationships of LINC01495-rs2665675 and TRAPPC9-rs2665936 genotypes in lung cancer cases and controls, stratified by histology type. We obtained a statistically significant difference increased association between the rs2665675 polymorphism and adencarcinoma risk in two genetic models (TT vs CC: adjusted OR = 1.701, 95%CI = 1.190-2.431, P = 0.004 for heterogeneity; CT+TT vs CC: adjusted OR = 1.414, 95%CI = 1.053-1.899, P = 0.021 for heterogeneity). Also as described in Table 5, two genetic models (GG vs AA: adjusted OR = 2.174, 95%CI = 1.485-3.183, $P < 0.001$ for heterogeneity; AG+GG vs AA: adjusted OR = 1.444, 95%CI = 1.121-1.861, P = 0.005 for heterogeneity) increased the risk between the rs2665936 polymorphism and adencarcinoma were statistically significant association. For squamous cell carcinoma, there were no statistically significant association between squamous cell carcinoma risk and the rs2665675 polymorphism (CT vs CC: adjusted OR = 0.888, 95%CI = 0.579-1.362, P = 0.587 for heterogeneity; TT vs CC: adjusted

OR = 1.063, 95%CI = 0.641-1.764, *P* = 0.813 for heterogeneity; CT+TT vs CC: adjusted OR = 0.938, 95%CI = 0.625-1.406, *P* = 0.755 for heterogeneity) and the rs2665936 polymorphism (AG vs AA: adjusted OR = 1.250, 95%CI = 0.853-1.831, *P* = 0.253 for heterogeneity; GG vs AA: adjusted OR = 1.467, 95%CI = 0.820-2.626, *P* = 0.196 for heterogeneity; AG+GG vs AA: adjusted OR = 1.288, 95%CI = 0.892-1.858, *P* = 0.177 for heterogeneity).

Table 3. *Interaction of LINC01495 and TRAPPC9 variants and tobacco exposure on lung cancer*

SNP	Smoking	Cases	Controls	Adj.OR(95%CI)	*P* value
rs2665675					
CC	-	98	161	1.00	
CT	-	267	324	1.321(0.976-1.789)	0.072
TT	-	134	127	**1.672(1.173-2.383**	**0.004**
CC	+	33	16	**7.592(3.622-15.913)**	**<0.001**
CT	+	74	52	**5.199(2.970-9.101)**	**<0.001**
TT	+	34	19	**6.943(3.388-14.232)**	**<0.001**
rs2665936					
AA	-	150	240	1.00	
AG	-	261	313	**1.375(1.055-1.792)**	**0.018**
GG	-	88	59	**2.361(1.595-3.495)**	**<0.001**
AA	+	56	31	**6.992(3.792-12.893)**	**<0.001**
AG	+	66	43	**5.832(3.295-10.322)**	**<0.001**
GG	+	19	13	**5.432(2.354-12.124)**	**<0.001**

ORs were adjusted by age and gender

Table 4. *Distribution of smoking and gender in LINC01495 and TRAPPC9*

	Gender	Cases(%)	Controls(%)	Adj.OR(95%CI)	*P* value
Smoking	male	131(92.9)	86(98.9)	1.00	
	female	10(7.1)	1(1.1)	6.011(0.744-48.589)	0.093
Non-smoking	male	33(6.6)	93(15.2)	1.00	
	female	466(93.4)	519(84.8)	**2.519(1.660-3.821)**	**<0.001**

ORs were adjusted by age.

Table 5. *The effect of the SNPs rs2665675 and rs2665936 in the region on lung cancer risk in pathological subgroup.*

SNP		Cases(%)	Controls(%)	Adj.OR(95%CI)	*P* value
rs2665675					
Adenocarcinoma	CC	86(18.8)	177(25.3)	1.00	
	CT	246(53.8)	376(53.8)	1.303(0.957-1.774)	0.093
	TT	125(27.4)	146(20.9)	**1.701(1.190-2.431)**	**0.004**
	CT/TT	371(81.2)	522(74.7)	**1.414 (1.053-1.899)**	**0.021**
Squamous cell carcinoma	CC	45(24.6)	177(25.3)	1.00	
	CT	95(51.9)	376(53.8)	0.888 (0.579-1.362)	0.587
	TT	43(23.5)	146(20.9)	1.063(0.641-1.764)	0.813
	CT/TT	138(75.4)	522(74.7)	0.938 (0.625-1.406)	0.755
rs2665936					
Adenocarcinoma	AA	141(30.8)	271(38.8)	1.00	
	AG	233(51.0)	356(50.9)	1.293 (0.991-1.686)	0.058
	GG	83(18.2)	72(10.3)	**2.174 (1.485-3.183)**	**<0.001**
	AG/GG	316(69.1)	428(61.2)	**1.444 (1.121-1.861)**	**0.005**
Squamous cell carcinoma	AA	65(35.5)	271(38.8)	1.00	
	AG	94(51.4)	356(50.9)	1.250(0.853-1.831)	0.253
	GG	24(13.1)	72(10.3)	1.467(0.820-2.626)	0.196
	AG/GG	118(64.5)	428(61.2)	1.288(0.892-1.858)	0.177

ORs were adjusted by age, gender and smoking.

4. DISCUSSION

In recent years, the study of lung cancer is still popular all over the world with multiple etiological, which the results are inconsistent. This is the first study of investigating whether the two genetic variants (LINC01495-rs2665675 and TRAPPC9-rs2665936) are associated with lung cancer risk in

northeast Chinese population. To our knowledge, smoking cannot fully explain the etiology of lung cancer. Chinese women who smoke rarely developed lung cancer more often. Besides tobaccos smoking, environmental factors, gene-environment interaction and passive smoking and so on are likely to impact the risk of lung cancer. However, cigarette smoking also can't be ignored. So we chose both male and female in northeast Chinese population as study subjects to analyze the association of lung cancer risk with genetic polymorphisms in LINC01495 and TRAPPC9.

Few studies have investigated the interaction between polymorphisms in LINC01495 and TRAPPC9 and tobacco exposure on lung cancer. Because smoking is major environmentanl risk for the develoment of lung cancer which has been established, gene-environment interactions may have potential effect. Then, we studied the interaction between smoking and two SNPs. We found that tobacco exposure and SNPs interaction may exist. Another result suggest that the difference of gender in smoking population was no statistically significant association, it turned out just the opposite in non-smoking population. So it proved that other environment exposures could affect the risk of lung cancer like oil fume exposure exclude tobacco exposure.

Previous studies have proved that lncRNAs play critical roles in tumor initiation, progression and metastasis by modulating oncogenic and tumor-suppressing pathways. Studies proved that upregulated lncRNAs ANRIL[25], AK001796[8], BCYRN1[26] and HNF1A-AS1[27] induced cell migration and tumor metastasis of NSCLC[6]. Although the function of most lncRNAs are still unknown, the numbers and accumulating evidence involved in cancers are increasing. As for long intergenic non-protein coding RNA, only several studies has reported in NSCLC[28, 29], let alone the rs2665675 of LINC01495. Meanwhile, TRAPPC9 impact the development of cancer because it regulates the trans-Golgi exit process which is essential for cancer development. In the previous study, TRAPPC9 is highly expressed in many cancer lines and tumor tissues, and the evidence that TRAPPC9 plays a critical role in regulating viability, proliferation, migration and tumorigenesis has been provided[17]. The current studies of TRAPPC9 have reported as a novel biomarker in breast cancer and colon cancer. But Boueiz A[30] found five loci associated with emphysema distribution at genome-wide significance including TRAPPC9. For TRAPPC9, the polymorphism of rs2665936 was still an innovative study.

Throughout the entire study, the results of this study suggest the T allele of rs2665675 and G allele of rs2665936 were risk factors that increasing the possible of lung cancer occurrence. Meanwhile, TT genotype carriers of rs2665675, as well as GG genotypes of rs2665936 were still significantly dangerous for risk of lung cancer, compared with wild genotypes. Based on our results, homozygous TT genotype and homozygous TT genotype with heterozygous CT genotype of LINC01495, as well as homozygous GG genotype and homozygous GG genotype with heterozygous AG genotype of TRAPPC9 contributed to risk of lung adenocarcinoma, but for squamous cell carcinoma, there are no significant associations with LINC01495 and TRAPPC9. It confirmed our conclusion that the polymorphisms of the rs2665675-LINC01495 and rs2665936-TRAPPC9 and the susceptibility of lung cancer have association was established. The cause of lung cancer should be combination of genetic factors and environmental risk factors. But in this study, we can't obtain the data of other environment exposure, so we can't assess other effect for lung cancer risk.

In summary, our study brought to light the relationship between polymorphisms in LINC01495 and TRAPPC9 and susceptibility of lung cancer in northeast Chinese population. While, there are still some limitations which should be considered in this study. Firstly, this is a hospital-based study, controls' selection may be not approximate representative. Secondly, the sample size may be not large enough to get statistical power. Thirdly, the information of environment exposure was not comprehensive that may cause some bias. More noteworthy is that our study was a explorative subject, additional larger studies are needed to validate the association between rs2665675 of LINC01495 and rs2665936 of TRAPPC9 polymorphisms and the risk of lung cancer in northeast Chinese population.

5. Conclusion

In conclusion, the present study provides that polymorphisms rs2665675 in LINC01495 and rs2665936 in TRAPPC9 are associated with non-small cell lung cancer risk. T allele and G allele are risk factors, especially in lung adenocarcinoma.

Acknowledgments

This study is support bygrant no.81602923 from National Nature Science Foundation of China.

References

[1] Theodoratou E, Timofeeva M, Li X et al. Nature, Nurture, and Cancer Risks: Genetic and Nutritional Contributions to Cancer. Annu Rev Nutr 2017; 37: 293-320.

[2] Lemjabbar-Alaoui H, Hassan OU, Yang YW, Buchanan P. Lung cancer: Biology and treatment options. Biochim Biophys Acta 2015; 1856: 189-210.

[3] Rahal Z, El Nemr S, Sinjab A et al. Smoking and Lung Cancer: A Geo-Regional Perspective. Front Oncol 2017; 7: 194.

[4] Wakelee H, Kelly K, Edelman MJ. 50 Years of progress in the systemic therapy of non-small cell lung cancer. Am Soc Clin Oncol Educ Book 2014; 177-189.

[5] Couraud S, Zalcman G, Milleron B et al. Lung cancer in never smokers--a review. Eur J Cancer 2012; 48: 1299-1311.

[6] Tantai J, Hu D, Yang Y, Geng J. Combined identification of long non-coding RNA XIST and HIF1A-AS1 in serum as an effective screening for non-small cell lung cancer. Int J Clin Exp Pathol 2015; 8: 7887-7895.

[7] Zhou B, Yuan W, Li X. Long Intergenic Noncoding RNA 319 (linc00319) Promotes Cell Proliferation and Invasion in Lung Cancer Cells by Directly Downregulating the Tumor Suppressor MiR-32. Oncol Res 2017.

[8] Yang Q, Xu E, Dai J et al. A novel long noncoding RNA AK001796 acts as an oncogene and is involved in cell growth inhibition by resveratrol in lung cancer. Toxicol Appl Pharmacol 2015; 285: 79-88.

[9] Mercer TR, Dinger ME, Mattick JS. Long non-coding RNAs: insights into functions. Nat Rev Genet 2009; 10: 155-159.

[10] Muller-Tidow C, Diederichs S, Thomas M, Serve H. Genome-wide screening for prognosis-predicting genes in early-stage non-small-cell lung cancer. Lung Cancer 2004; 45 Suppl 2: S145-150.

[11] Li N, Wang Y, Liu X et al. Identification of Circulating Long Noncoding RNA HOTAIR as a Novel Biomarker for Diagnosis and Monitoring of Non-Small Cell Lung Cancer. Technol Cancer Res Treat 2017; 1533034617723754.

[12] Cox R, Chen SH, Yoo E, Segev N. Conservation of the TRAPPII-specific subunits of a Ypt/Rab exchanger complex. BMC Evol Biol 2007; 7: 12.

[13] Kummel D, Oeckinghaus A, Wang C et al. Distinct isocomplexes of the TRAPP trafficking factor coexist inside human cells. FEBS Lett 2008; 582: 3729-3733.

[14] Westlake CJ, Baye LM, Nachury MV et al. Primary cilia membrane assembly is initiated by Rab11 and transport protein particle II (TRAPPII) complex-dependent trafficking of Rabin8 to the centrosome. Proc Natl Acad Sci U S A 2011; 108: 2759-2764.

[15] Zong M, Satoh A, Yu MK et al. TRAPPC9 mediates the interaction between p150 and COPII vesicles at the target membrane. PLoS One 2012; 7: e29995.

[16] Wlodkowic D, Skommer J, McGuinness D et al. ER-Golgi network--a future target for anti-cancer therapy. Leuk Res 2009; 33: 1440-1447.

[17] Zhang Y, Liu S, Wang H et al. Elevated NIBP/TRAPPC9 mediates tumorigenesis of cancer cells through NFkappaB signaling. Oncotarget 2015; 6: 6160-6178.

[18] Di X, Zhang G, Zhang Y et al. Accumulation of autophagosomes in breast cancer cells induces TRAIL

resistance through downregulation of surface expression of death receptors 4 and 5. Oncotarget 2013; 4: 1349-1364.

[19] Vazquez-Martin A, Oliveras-Ferraros C, Menendez JA. Autophagy facilitates the development of breast cancer resistance to the anti-HER2 monoclonal antibody trastuzumab. PLoS One 2009; 4: e6251.

[20] Wetterskog D, Shiu KK, Chong I et al. Identification of novel determinants of resistance to lapatinib in ERBB2-amplified cancers. Oncogene 2014; 33: 966-976.

[21] Kim JC, Kim SY, Roh SA et al. Gene expression profiling: canonical molecular changes and clinicopathological features in sporadic colorectal cancers. World J Gastroenterol 2008; 14: 6662-6672.

[22] Cain JE, McCaw A, Jayasekara WS et al. Sustained Low-Dose Treatment with the Histone Deacetylase Inhibitor LBH589 Induces Terminal Differentiation of Osteosarcoma Cells. Sarcoma 2013; 2013: 608964.

[23] Ghobrial IM, Roccaro A, Hong F et al. Clinical and translational studies of a phase II trial of the novel oral Akt inhibitor perifosine in relapsed or relapsed/refractory Waldenstrom's macroglobulinemia. Clin Cancer Res 2010; 16: 1033-1041.

[24] Ross CW, Ouillette PD, Saddler CM et al. Comprehensive analysis of copy number and allele status identifies multiple chromosome defects underlying follicular lymphoma pathogenesis. Clin Cancer Res 2007; 13: 4777-4785.

[25] Lin L, Gu ZT, Chen WH, Cao KJ. Increased expression of the long non-coding RNA ANRIL promotes lung cancer cell metastasis and correlates with poor prognosis. Diagn Pathol 2015; 10: 14.

[26] Hu T, Lu YR. BCYRN1, a c-MYC-activated long non-coding RNA, regulates cell metastasis of non-small-cell lung cancer. Cancer Cell Int 2015; 15: 36.

[27] Wu Y, Liu H, Shi X et al. The long non-coding RNA HNF1A-AS1 regulates proliferation and metastasis in lung adenocarcinoma. Oncotarget 2015; 6: 9160-9172.

[28] Li W, Zheng J, Deng J et al. Increased levels of the long intergenic non-protein coding RNA POU3F3 promote DNA methylation in esophageal squamous cell carcinoma cells. Gastroenterology 2014; 146: 1714-1726.e1715.

[29] Zhu SP, Wang JY, Wang XG, Zhao JP. Long intergenic non-protein coding RNA 00858 functions as a competing endogenous RNA for miR-422a to facilitate the cell growth in non-small cell lung cancer. Aging (Albany NY) 2017; 9: 475-486.

[30] Boueiz A, Lutz SM, Cho MH et al. Genome-Wide Association Study of the Genetic Determinants of Emphysema Distribution. Am J Respir Crit Care Med 2017; 195: 757-771.

Citation: *Q. Yang et al., " A Case-Control Study of the Relationship between LINC01495, TRAPPC9 Polymorphisms and Lung Cancer Susceptibility in Northeast Chinese Population ", International Journal of Research in Environmental Science, vol. 4, no. 1, p. 1-8, 2018. http://dx.doi.org/10.20431/2454-9444.0401001*