MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE
SUMY STATE UNIVERSITY
ACADEMIC AND RESEARCH MEDICAL INSTITUTE

Eastern Ukrainian Medical Journal

116, Kharkivska st., Sumy 40007, Ukraine eumj.med.sumdu.edu.ua
e-mail: eumj@med.sumdu.edu.ua ISSN: 2663-5909 (print)/2664-4231 (online)

How to cite: Stroi Ye, Volkohon A, Moskalenko Yu. Association analysis between MALAT1 rs619581-polymorphism and urinary tract cancer development in Ukrainian population. *East Ukr Med J*. 2025;13(3):748-756

DOI: https://doi.org/10.21272/eumj.2025;13(3):748-756

ABSTRACT

Yelizaveta Stroi
https://orcid.org/0000-0003-3366-8800
Department of Physiology and Pathophysiology with a Course in Medical Biology, Sumy State University, Sumy, Ukraine

Andriy Volkohon
https://orcid.org/0000-0003-0835-0657
Sumy Regional Clinical Oncology Center, Sumy, Ukraine

Yuliia Moskalenko
https://orcid.org/0000-0002-5398-0298
Department of Oncology and Radiology of Sumy State University, Sumy, Ukraine

ASSOCIATION ANALYSIS BETWEEN MALAT1 RS619581-POLYMORPHISM AND URINARY TRACT CANCER DEVELOPMENT IN UKRAINIAN POPULATION

Introduction. A key component in the pathogenesis of oncological diseases is the disruption of genetic and epigenetic regulation of cellular processes, in which long non-coding RNAs play an important role. Of particular significance in the context of cancer development at various sites and its metastasis is the long non-coding RNA MALAT1, which influences tumorigenesis, chemoresistance, and immunotherapy. Therefore, the aim of our study was to investigate the possible association between the genetic marker rs619581 of *MALAT1* and the development of urinary tract malignancies.

Materials and Methods. The study involved 242 patients with urinary tract cancer (UTC) (101 with clear cell renal cell carcinoma (CCRCC) and 141 with transitional cell carcinoma of urinary bladder (TCCUB)) and 100 individuals without UTC (control group). Among patients with UTC, 97 had metastases, while 145 individuals had no metastases. Genotyping of patients for the rs619581 polymorphism of the *MALAT1* gene was performed by real-time polymerase chain reaction using TaqMan assays (TaqMan®SNP Assay C_1060479_10). Statistical analysis of the obtained results was carried out using Prism (version 10.4.1) and R (version 4.4.2) software.

Results. The distribution of genotypes for the rs619581 polymorphism in the group of patients with UTC was AA – 216 (89.3%), AG + GG – 26 (10.7%); in the control group, respectively – 96 (96%), 4 (4%) (P = 0.045). The results of the regression analysis of the association of rs619581 genotypes with the development of RCC were close to the level of statistical significance (P = 0.054). And after adjusting for age, sex, smoking habits and BMI, the association became statistically significant: carriers of the minor allele (AG + GG) have a 3.43-fold higher risk of developing RCC than homozygotes for the major allele (AA) (P = 0.037). Among patients with metastases, the

distribution of genotypes was as follows: AA – 81 (83.5%), AG + GG – 16 (16.5%), while in individuals without metastases, respectively, AA – 135 (93.1%), AG + GG – 10 (6.9%) (P = 0.02). In patients who are carriers of the minor allele (AG + GG), the risk of developing metastases is 2.67-fold higher than in homozygotes for the major allele (AA) (P = 0.02).

Conclusions. In patients with urinary tract cancer, the minor G-allele of the rs619581 polymorphism of the *MALAT1* gene is more frequent than in the control group (P=0.039; χ^2=4.264). There is an association between rs619581 polymorphism and the development of urinary tract malignancies: carriers of the minor allele (AG + GG) have a higher risk than homozygotes for the major allele (AA) according to multivariable logistic regression, 3.43-fold higher (P = 0.037)). In patients with AG and GG genotypes, the risk of developing metastases is 2.67-fold higher than in homozygotes for the major allele AA (P = 0.02).

Keywords: gene polymorphism, long non-coding RNA, MALAT1, urinary tract cancer.

Corresponding author: *Yelizaveta Stroi, PhD student of the Department of Physiology and Pathophysiology with a Course in Medical Biology of Sumy State University, Sumy, Ukraine*
e-mail: yelizavetastroi@gmail.com

РЕЗЮМЕ

Єлізавета Строй
https://orcid.org/0000-0003-3366-8800
Кафедра фізіології і патофізіології з курсом медичної біології, Сумський державний університет, Суми, Україна

Андрій Волкогон
https://orcid.org/0000-0003-0835-0657
Сумський обласний клінічний онкологічний центр, Суми, Україна

Юлія Москаленко
https://orcid.org/0000-0002-5398-0298
Кафедра онкології і радіології, Сумський державний університет, Суми, Україна

АСОЦІАЦІЯ МІЖ RS619581-ПОЛІМОРФІЗМОМ ГЕНА MALAT1 І РОЗВИТКОМ ОНКОЛОГІЧНИХ ЗАХВОРЮВАНЬ СЕЧОВИДІЛЬНОЇ СИСТЕМИ В УКРАЇНСЬКІЙ ПОПУЛЯЦІЇ

Вступ. Основною ланкою патогенезу онкологічних захворювань є порушення генетичної та епігенетичної регуляції клітинних процесів, важливе місце в якому посідають довгі некодуючі РНК. Особлива значення у контексті розвитку раку різної локалізації і його метастазування належить довгій некодуючій РНК MALAT1, яка впливає на пухлиногенез, хіміорезистентність та імунотерапію. Тому метою нашого дослідження стало вивчення можливого зв'язку генетичного маркеру rs619581 *MALAT1* з розвитком онкологічних захворювань сечовидільної системи.

Матеріали і методи дослідження. У дослідженні взяли участь 242 пацієнти з раком сечовидільної системи (РСС) (101 з світлоклітинним раком нирки (СКРН) і 141 з перехідноклітинним раком сечового міхура (ПКРСМ)) і 100 осіб без РСС (група контролю). Серед пацієнтів з РСС 97 мали метастази, у 145 осіб метастазів не було. Генотипування пацієнтів за rs619581 поліморфізмом гена *MALAT1* проводили методом полімеразної ланцюгової реакції у реальному часі з використанням TaqMan assays (TaqMan®SNP Assay C_1060479_10). Статистичну обробку отриманих результатів проводили за допомогою програм Prism (версія 10.4.1) та R (версія 4.4.2).

Результати. Розподіл генотипів за rs619581 поліморфізмом у групі пацієнтів із РСС становив: AA – 216 (89,3 %), AG + GG – 26 (10,7 %); у групі контролю відповідно – 96 (96 %), 4 (4 %) (P = 0,067). Результати регресивного аналізу зв'язку rs619581-генотипів з розвитком РСС були близькі до рівня статистичної достовірності (P = 0,054). А після введення поправок на на вік, стать, звичку палити та ІМТ зв'язок став статистично значущим: у носіїв

мінорного алеля (AG + GG) ризик розвитку РСС у 3,43 рази більший, ніж у гомозигот за основним алелем (AA) (P = 0,037). Серед пацієнтів з метастазами розподіл генотипів був наступним: AA – 81 (83,5 %), AG + GG – 16 (16,5 %), тоді як осіб без метастазів відповідно: AA – 135 (93,1 %), AG + GG – 10 (6,9 %) (P = 0.02). У пацієнтів, що є носіями мінорного алеля (AG + GG) ризик розвитку метастазів у 2,67 рази більший, ніж у гомозигот за основним алелем (AA) (P = 0,02).

Висновки. У пацієнтів з раком сечовидільної системи мінорний G-алель за rs619581 поліморфізмом гена *MALAT1* зустрічається частіше, ніж у осіб контрольної групи (P=0,039; χ^2=4,264). Існує зв'язок rs619581-поліморфізму з розвитком онкологічних захворювань сечовидільної системи: у носіїв мінорного алеля (AG + GG) ризик більший, ніж у гомозигот за основним алелем (AA) (згідно мільтиваріабельної логістичної регресії у 3,43 рази (P = 0,037). У пацієнтів з генотипами AG і GG ризик розвитку метастазів у 2,67 рази більший, ніж у гомозигот за основним алелем AA (P = 0,02).

Ключові слова: поліморфізм генів, довга некодуюча РНК MALAT1, рак сечовидільної системи.

***Автор, відповідальний за листування**: Єлізавета Строй, кафедра фізіології і патофізіології з курсом медичної біології, Сумський державний університет, м. Суми, Україна*
e-mail: yelizavetastroi@gmail.com

INTRODUCTION

The main link in the pathogenesis of oncological diseases is the disruption of genetic and epigenetic regulation of cellular processes. Today, it is established that 90% of the human genome is actively transcribed, while only 2% of these are protein-coding genes. Therefore, the majority of transcripts are non-coding RNAs, which regulate the expression of more than 75% of human genes.

Considerable data has been published regarding the influence of short non-coding RNAs on the development of oncological diseases, which is implemented mainly through the suppression of mRNA expression. The significance of long non-coding RNAs in this process remains less studied. [1].

Scientists are paying special attention to the long non-coding RNA MALAT1 (Metastasis Associated Lung Adenocarcinoma Transcript 1), also known as NEAT2 (Nuclear Enriched Abundant Transcript 2) [2; 3]. Its role has been proven in the processes of alternative splicing and epigenetic modulation of gene expression [4; 5], especially genes whose products are involved in metastasis formation [3].

Scientific research on the role of the long non-coding RNA MALAT1 in oncogenesis is being conducted in several directions. The first research direction aims to study the role of MALAT1 expression in the pathogenesis of oncological diseases. It should be noted that MALAT1 was first identified as a transcript with increased expression in primary non-small cell lung cancer tumors that had a high propensity for metastasis [6]. Later, MALAT1 overexpression was registered in various types of cancer [7], with the expression level of this lncRNA correlating with tumor progression and metastasis. In experimental models, particularly in a murine metastatic cancer model, it has been shown that genetic knockdown leads to differentiation of the primary tumor and significant reduction in metastasis. [8]. In the lung cancer homing model, MALAT1 knockdown and its knockout caused a reduction in the homing of cancer cells to lung tissue [9].

The second research direction is related to studying the connection between single nucleotide polymorphism of the *MALAT1* gene with the development of oncological diseases of various locations, their association with different cancer characteristics and stages, including metastasis. In particular, it has been shown that lung cancer patients who carry the T-allele at the rs3200401 polymorphic locus of the *MALAT1* gene have a greater average life expectancy than dominant CC homozygotes [10]. Women with the CT genotype for the rs3200401 polymorphism have a lower risk of developing breast cancer compared to CC homozygotes. [11]. The protective significance of the minor T-allele for the rs3200401 polymorphism of the *MALAT1* gene has been demonstrated: carriers of the minor allele (T/T and C/T genotypes) have a lower risk

of developing clear cell renal carcinoma compared to dominant homozygotes (C/C) [12]. It was discovered that the rs3200401 polymorphism is significantly associated with transitional cell carcinoma of the urinary bladder (TCCUB) progression. Specifically, individuals with the TT genotype demonstrate a later onset of TCCUB compared to those with CC and CT genotypes, suggesting a potential genetic marker for predicting disease trajectory [13]. It should be emphasized that data regarding the connection between polymorphic loci of the *MALAT1* gene and urinary tract cancer development are scarce. Regarding the rs619581 polymorphism, such studies have only just begun. In particular, it is known that there is no difference in the distribution of rs619581 *MALAT1* genotypes in patients with transitional cell carcinoma of the urinary bladder and individuals without TCCUB [14]. Therefore, our scientific efforts were directed towards studying the possible connection between the genetic marker rs619581 *MALAT1* and urinary tract cancer development in the Ukrainian population.

MATERIALS AND METHODS

STUDY POPULATION

The study involved 242 patients with urinary tract cancer (UTC) (101 with clear cell renal cell carcinoma (CCRCC) and 141 with transitional cell carcinoma of urinary bladder (TCCUB)) and 100 individuals without oncological diseases of the urinary system (control group). The clinical characteristics of the patients are presented in Table 1. Among patients with UTC, 97 had metastases and 145 individuals did not have metastases (Table 2).

Table 1 – Clinical characteristics of the patients with urinary tract cancer and control

Parameter	Main group (n=242)	Control (n=100)	P
Age, years ± SD	65.1±11.8	77.38±8.499	<0.0001
Sex, female/male	69/173	34/66	0.3143
Smokers, n (%)	119 (49.2)	27 (27.0)	0.0002
Obesity (%)	61 (25.2)	18 (18.0)	0.15
Body weight, kg	78.8±11.9	74.31±11.38	0.0015
Height, cm	171±7.6	165.8±10.26	<0.0001
BMI	26.97±4.31	27.13±4.3	0.766
Blood glucose, mmol/l	55.1±15.8	52.68±7.905	0.14

Note: n – number of cases; P – indicator of statistical significance. Categorical variables were compared by χ^2-test, quantitative variables – by t-test

Table 2 – Clinical characteristics of the patients with and without metastasis

Parameter	With metastasis (n = 97)	Without metastasis (n = 145)	P
Age, years ± SD	68±11.2	63.2±11.8	0.0017
Sex, female/male	25/72	44/101	0.44
Smokers, n (%)	48 (49.5)	71 (49)	0.94
Drinkers, n (%)	60 (61.8)	104 (71.7)	0.107
Obesity (%)	26 (26.8)	35 (24.1)	0.64
Body weight, kg	79.2±10.6	78.5±12.8	0.65
Height, cm	172±7.78	171±7.5	0.47
BMI	27.01±4.03	26.95±4.5	0.9
Blood glucose, mmol/l	58.2±17.7	53.1±14.1	0.014
Diabetes (%)	28 (28.9)	25 (17.2)	0.03
Arterial hypertension (%)	58 (59.8)	83 (57.2)	0.69

Note: n – number of cases; P – indicator of statistical significance. Categorical variables were compared by χ^2-test, quantitative variables – by t-test

Between March 2001 and May 2020, patients with cancer were monitored and received diagnoses at the Sumy Regional Clinical Oncology Center. All oncological patients received radical tumor excision followed by histological analysis. The cancer patients were all classified as clinical stage II according to the TNM Classification of Malignant Tumors. The final morphological diagnosis was determined in accordance with the European Association of Urology Guidelines [15]. The research protocol adhered to the Declaration of Helsinki's principles and received approval from the Ethics Committee of the Educational and Scientific Medical Institute at Sumy State University (№5/07.2022). All study participants provided their voluntary written informed consent.

GENOTYPING

For the study of *MALAT1* gene rs619581 polymorphism, venous blood was collected under sterile conditions in 2.7 ml monovettes containing potassium ethylenediaminetetraacetic acid (11.7 mM) as an anticoagulant (Sarstedt, Germany). Blood samples were frozen and stored at -20°C. DNA was extracted from whole blood leukocytes using GeneJET Whole Blood Genomic DNA Purification Mini Kit (Thermo Fisher Scientific, USA). Genotyping of the rs619581 polymorphic locus was performed at the Scientific Laboratory of Molecular Genetic Research at Sumy State University using real-time polymerase chain reaction (Real-time PCR) on a Quant Studio 5 DX Real-Time instrument (Applied Biosystems, USA). The study employed TaqMan assays (TaqMan®SNP Assay C___1060479_10) and PCR Real-Time reagent kit (Thermo Fisher Scientific, USA). Amplification consisted of initial denaturation at 95ºC for 10 minutes followed by 45 cycles of 15 seconds at 95ºC and 30 seconds at 60°C. The resulting curves were analyzed using software supplied with the Quant Studio 5 DX Real-Time system.

STATISTICAL ANALYSIS

Statistical processing of the obtained results was conducted using Prism software (version 10.4.1) and R (version 4.4.2). The conformity of genotype distribution to Hardy-Weinberg equilibrium was verified using the online resource Equilibrium WpCalc (https://wpcalc.com/en/equilibrium-hardy-weinberg/). The analysis of rs619581-genotype distribution between groups was performed using Pearson's χ^2 test, the comparison of means between groups was conducted using two-tailed Student's t-test. The risk of developing urinary tract cancer depending on the genotype for the rs619581 polymorphism of the MALAT gene was calculated using logistic regression in the dominant inheritance model (AA versus AG+GG). To identify the association of rs619581 polymorphic variants with the risk of urinary tract cancer after adjusting for sex, age, body mass index (BMI) of patients and their smoking habits, multivariable logistic regression was applied. Statistical significance was set at $P < 0.05$, with all tests being two-tailed.

RESULTS

The distribution of genotypes in the comparison groups corresponded to Hardy-Weinberg equilibrium (χ^2=0.648, P>0,05 – for patients with UTC and χ^2=0.042, P>0,05 – for the control group). As a result of the conducted research, the distribution of genotypes and alleles for the rs619581 polymorphism of the MALAT gene was studied in patients with urinary tract cancer (UTC) and individuals in the control 0group (Table 3). It was shown that in patients with UTC, the minor G-allele occurs more frequently than in the control (P=0.039; χ^2=4.264). The distribution of genotypes for the studied polymorphism in the group of patients with UTC was as follows: AA – 216 (89.3%), AG + GG – 26 (10.7%); in the control group, respectively – 96 (96%), 4 (4%). The P-value, calculated using Pearson's χ^2-test, was 0.067, which indicates the existence of differences in the distribution of genotypes for the rs619581 polymorphism of the *MALAT1* gene between patients with UTC and individuals in the control group.

The analysis of the association between the rs619581 polymorphism of the *MALAT1* gene and urinary tract cancer was conducted using binary and multivariable logistic regression within the framework of the dominant inheritance model (Table 4). The results of the regression analysis of the association of rs619581 genotypes with the development of RCC were close to the level of statistical significance (P = 0.054). And after adjusting for age, sex, smoking habits and BMI, the association became statistically significant: carriers of the minor allele (AG + GG) have a 3.43-fold higher risk of developing RCC than homozygotes for the major allele (AA) (P = 0.037).

The next step of the analysis was to study the characteristics of the association between the rs619581 polymorphism of the *MALAT1* gene and the development of UTC in patients with and without metastases. Table 5 presents data on the frequency of genotypes for the rs619581 locus of the *MALAT1* gene in patients with UTC who have metastases and in individuals without metastases. Thus, among patients with metastases, the distribution of genotypes was as follows: AA – 81 (83.5%), AG + GG – 16 (16.5%), while for individuals without metastases, respectively, AA – 135 (93.1%), AG + GG – 10 (6.9%) (P = 0.02).

Table 3 – Distribution of alleles and genotypes for the MALAT1 rs619581-polymorphism among patients main group and control

	Main group (n=242)		Control (n=100)		P (χ^2)
	n	%	n	%	
Genotypes					
AA	216	89,3	96	96	0.067 (3.363)
AG + GG	26	10,7	4	4	
Alleles					
A	453	94.4	196	98	0.039 (4.264)
G	27	5.6	4	2	

Note: n – number of cases; P – indicator of statistical significance

Table 4 – Analysis of the association between the MALAT1 rs619581-polymorphism and the development of urinary tract cancer

Model	P_c	OR_c (95.7 % CI)	P_a	OR_a (95.7 % CI)
Dominant	0.054	2.89 (0.98 – 8.5)	0.037	3.43 (1.07 – 10.97)

Note. Pc: crude P value; ORc: crude odds ratio; CI: confidence interval; Pa: P value adjusted for age, sex, BMS and smoking; ORa: adjusted odds ratio

Table 5 – Distribution of alleles and genotypes for the MALAT1 rs619581-polymorphism among patients with and without metastasis

	With metastasis (n = 97)		Without metastasis (n = 145)		P (χ^2)
	n	%	N	%	
Genotypes					
AA	81	83.5	135	93.1	0.02 (5.58)
AG + GG	16	16.5	10	6.9	
Alleles					
A	176	90.7	280	96.5	0.62 (0.249)
G	18	9.3	10	3.5	

Note: n – number of cases; P – indicator of statistical significance

Table 6 presents the results of regression analysis of the association between the rs619581 polymorphism of the *MALAT1* gene and the development of urinary tract cancer in patients with metastases within the framework of the dominant inheritance model. It was found that in patients who are carriers of the minor allele (AG + GG), the risk of developing metastases is 2.67 times higher than in homozygotes for the main allele (AA) (P = 0.02). After adjusting for age, sex, smoking habits, and BMI, the association maintained statistical significance: the risk increased to 2.74 times (P = 0.02).

DISCUSSION

MALAT1 is a long non-coding RNA that is highly conserved in mammals and actively expressed in many cells and tissues of the body, such as kidneys, adrenal glands, prostate, lungs, heart, liver, brain, ovaries, thyroid gland, intestines, and skeletal muscles [16]. The transcript of the *MALAT1* gene was first described in the study of multiple endocrine neoplasia type 1 [17]. In 2003, MALAT1 was identified as a transcript associated with metastasis in patients with early-stage non-small cell lung cancer [6]. Today, it is believed that the main function of MALAT1 is the regulation of gene expression related to metastases [3]. Additionally, it is known that the long non-coding RNA MALAT1 is located in nuclear paraspeckles, indicating its involvement in processing [18] and maturation of mRNA [19]. In experiments using genetic knockout, the important role of MALAT1 in the activation of certain transcription factors, particularly SRF1 (Strubbelig-

receptor family 1 protein) and SC35 (Serine/arginine-rich splicing factor SC35), has been elucidated [20].

The *MALAT1* gene is located on the long arm of chromosome 11, contains 8708 base pairs, and has 2 exons [21]. According to NCBI (National Center for Biotechnology Information) data, as of February 2025, 7517 single nucleotide polymorphisms are known in the human *MALAT1* gene [22]. The rs619581 polymorphism is located in the non-coding region of the gene and manifests as a substitution of adenine for guanine at position 46598443.

Table 6 – Analysis of the association between the MALAT1 rs619581-polymorphism and the development of metastasis of urinary tract cancer

Model	P_c	OR_c (95.7 % CI)	P_a	OR_a (95.7 % CI)
Dominant	0.02	2.67 (1.15 – 6.15)	0.02	2.74 (1.16 – 6.48)

Note. Pc: crude P value; ORc: crude odds ratio; CI: confidence interval; Pa: P value adjusted for age, sex, BMS and smoking; ORa: adjusted odds ratio

As already indicated, there is currently no data regarding the genotyping of individuals with UTC for the rs619581 polymorphic locus, and our presented study is the first in this direction. We studied the distribution of alleles and genotypes for this genetic marker in patients with urinary tract cancer and found that the minor G-allele occurs more frequently in them than in individuals without this pathology. In addition, we demonstrated an association of the rs619581 polymorphism with the risk of developing UTC in patients with AG and GG genotypes, as well as demonstrated a greater risk of developing metastases in them.

Regarding the role of other polymorphic loci of *MALAT1* in the development of urinary tract cancer in patients of the Ukrainian population, it is known about the connection of the rs3200401 polymorphism with the development of clear cell renal cell carcinoma [12] and transitional cell carcinoma of urinary bladder [23], as well as the association of this polymorphism with metastasis [24] and survival of patients with bladder cancer [13].

Thus, the active search for genetic markers of urinary tract cancer, which is taking place today in oncourology, is important in addressing the issue of early diagnosis of these diseases, personalized treatment, and prognosis.

CONCLUSIONS

The conducted research is the first to search for an association between the rs619581 site of the *MALAT1* gene and the occurrence of urinary tract cancer both in the Ukrainian population and worldwide. It was shown that in patients with UTC, the minor G-allele occurs more frequently than in individuals of the control group (P=0.039).

An association of the rs619581 polymorphism of the MALAT1 gene with the development of urinary tract cancer was identified: carriers of the minor allele (AG + GG) have a higher risk of developing UTC than homozygotes for the main allele (AA) (according to multivariable logistic regression by 3.43 times (P = 0.037)).

It was proven that in patients with AG and GG genotypes, the risk of developing metastases is 2.67 times higher than in homozygotes for the main allele AA (P = 0.02).

STUDY LIMITATIONS

Increasing the size of the control group would have increased the representativeness of the study.

PROSPECTS FOR FUTURE RESEARCH

Prospects for future research: to investigate the association of polymorphisms of other long non-coding RNAs in the development of UTC in order to predict the risk of disease occurrence.

AUTHOR CONTRIBUTIONS

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

FUNDING

This research has been performed with the financial support provided by the Ministry of Education and Science of Ukraine: Grant №0123U101850.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Chi Y, Wang D, Wang J, Yu W, Yang J. Long Non-Coding RNA in the Pathogenesis of Cancers. Cells. 2019 Sep 1;8(9):1015. https://doi.org/10.3390/cells8091015
2. Liu J, Peng WX, Mo YY, Luo D. MALAT1-mediated tumorigenesis. Front Biosci (Landmark Ed). 2017 Jan 1;22(1):66-80. https://doi.org/10.2741/4472.
3. Sun Y, Ma L. New Insights into Long Non-Coding RNA MALAT1 in Cancer and Metastasis. Cancers (Basel). 2019 Feb 13;11(2):216. https://doi.org/10.3390/cancers11020216
4. Xu D, Wang W, Wang D, Ding J, Zhou Y, Zhang W. Long noncoding RNA MALAT-1: A versatile regulator in cancer progression, metastasis, immunity, and therapeutic resistance. Noncoding RNA Res. 2024 Feb 1;9(2):388-406. https://doi.org/10.1016/j.ncrna.2024.01.015
5. Zhang X, Hamblin MH, Yin KJ. The long noncoding RNA Malat1: Its physiological and pathophysiological functions. RNA Biol. 2017 Oct 6;14(12):1705-14. https://doi.org/10.1080/15476286.2017.1358347.
6. Ji P, Diederichs S, Wang W, Böing S, Metzger R, Schneider PM, et al. MALAT-1, a novel noncoding RNA, and thymosin beta4 predict metastasis and survival in early-stage non-small cell lung cancer. Oncogene. 2003 Sep 11;22(39):8031-41. https://doi.org/10.1038/sj.onc.1206928
7. Wei Y, Niu B. Role of MALAT1 as a Prognostic Factor for Survival in Various Cancers: A Systematic Review of the Literature with Meta-Analysis. Dis Markers. 2015;2015:164635. https://doi.org/10.1155/2015/164635
8. Arun G, Diermeier S, Akerman M, Chang KC, Wilkinson JE, Hearn S, et al. Differentiation of mammary tumors and reduction in metastasis upon Malat1 lncRNA loss. Genes Dev. 2016 Jan 1;30(1):34-51. https://doi.org/10.1101/gad.270959.115
9. Gutschner T, Hämmerle M, Eissmann M, Hsu J, Kim Y, Hung G, et al. The noncoding RNA MALAT1 is a critical regulator of the metastasis phenotype of lung cancer cells. Cancer Res. 2013 Feb 1;73(3):1180-9. https://doi.org/10.1158/0008-5472.CAN-12-2850
10. Wang JZ, Xiang JJ, Wu LG, Bai YS, Chen ZW, Yin XQ, et al. A genetic variant in long non-coding RNA MALAT1 associated with survival outcome among patients with advanced lung adenocarcinoma: a survival cohort analysis. BMC Cancer. 2017 Mar 3;17:167. https://doi.org/10.1186/s12885-017-3151-6
11. Peng R, Luo C, Guo Q, Cao J, Yang Q, Dong K, et al. Association analyses of genetic variants in long non-coding RNA MALAT1 with breast cancer susceptibility and mRNA expression of MALAT1 in Chinese Han population. Gene. 2018 Feb 5;642:241-8. https://doi.org/10.1016/j.gene.2017.11.013
12. Volkogon AD, Roshchupkin AA, Chumachenko YD, Harbuzova VY, Ataman AV. Assotiation of MALAT1 rs3200401 gene polymorphism with kidney cancer in Ukrainian population. East. Ukr. Med. J. 2019 Jun 208;7(2):121-5. Retrieved from: https://eumj.med.sumdu.edu.ua/index.php/journal/article/view/18
13. Volkogon A, Kolnoguz O, Harbuzova V, Ataman A. Long Non-Coding RNA MALAT1 Gene Polymorphism is Associated with Disease-Free Survival in Bladder Cancer Patients. Galician Med J. 2020 Jun 30;27(2):E202025. https://doi.org/10.21802/gmj.2020.2.5
14. Stroy YA, Moskalenko YV, Obukhova OA. Allelic variant frequency of the MALAT1 gene by rs619581 polymorphism in patients with transitional cell carcinoma of the bladder. Biopolym Cell. 2024 Sept 10;40(3):200. https://doi.org/10.7124/bc.000AE6
15. Powles T, Albiges L, Staehler M, Bensalah K, Dabestani S, Giles RH, et al. Updated European Association of Urology Guidelines: Recommendations for the Treatment of First-line Metastatic Clear Cell Renal Cancer. Eur Urol. 2018 Mar;73(3):311-15. https://doi.org/10.1016/j.eururo.2017.11.016
16. Arun G, Aggarwal D, Spector DL. MALAT1 Long Non-Coding RNA: Functional Implications. Non Coding RNA. 2020 Jun;6(2):22. https://doi.org/10.3390/ncrna6020022
17. Marx SJ. Molecular genetics of multiple endocrine neoplasia types 1 and 2. Nat Rev Cancer. 2005 May;5(5):367-75. https://doi.org/10.1038/nrc1610
18. Lin Y, Schmidt BF, Bruchez MP, McManus CJ. Structural analyses of NEAT1 lncRNAs suggest long-range RNA interactions that may contribute to paraspeckle architecture. Nucleic Acids Res. 2018 Apr 20;46(7):3742-52. https://doi.org/10.1093/nar/gky046
19. Skeparnias I, Bou-Nader C, Anastasakis DG, Fan L, Wang YX, Hafner M, et al. Structural basis of MALAT1 RNA maturation and mascRNA biogenesis. Nat Struct Mol Biol. 2024 Jul 2;31:1655-68. https://doi.org/10.1038/s41594-024-01340-4
20. Tripathi V, Ellis JD, Shen Z, Song DY, Pan Q, Watt AT, et al. The nuclear-retained noncoding RNA MALAT1 regulates alternative splicing by modulating SR splicing factor phosphorylation. Mol Cell. 2010 Sep 24;39(6):925-38. https://doi.org/10.1016/j.molcel.2010.08.011

21. Goyal B, Yadav SRM, Awasthee N, Gupta S, Kunnumakkara AB, Gupta SC. Diagnostic, prognostic, and therapeutic significance of long non-coding RNA MALAT1 in cancer. Biochim Biophys Acta Rev Cancer. 2021 Apr;1875(2):188502. https://doi.org/10.1016/j.bbcan.2021.188502
22. National Library of Medicine. MALAT1 homo sapiens – SNP. Retrieved from: https://www.ncbi.nlm.nih.gov/snp/?term=MALAT1+homo+sapiens
23. Volkohon AD, Chumachenko YD, Roshchupkin AA, Harbuzova VYu, Ataman AV. [Association between rs3200401 long non-coding RNA MALAT1 gene polymorphism and bladder cancer development]. Bukovinian Med Her. 2019 Aug 29;23(3(91)):23-7. https://doi.org/10.24061/2413-0737.xxiii.3.91.2019.57
24. Volkogon AD, Harbuzova VYu, Ataman AV. [The Relation between Genetic Polymorphism of Long Non-Coding RNA Malat1 and Bladder Cancer Metastasis]. Ukrainian Journal of Medicine, Biology and Sports. 2020;5(1(23)):308-12. https://doi.org/10.26693/jmbs05.01.308

Received 22.03.2025 ***Accepted 11.06.2025***

INFORMATION ABOUT THE AUTHORS

Строй Єлізавета Антонівна, аспірант кафедри фізіології і патофізіології з курсом медичної біології Сумського державного університету, м. Суми, Україна
yelizavetastroi@gmail.com
https://orcid.org/0000-0003-3366-8800

Волкогон Андрій Дмитрович, лікар-уролог Сумського обласного клінічного онкологічного центру, м. Суми, Україна
volkohon@ukr.net
https://orcid.org/0000-0003-0835-0657

Москаленко Юлія Василівна, доцент кафедри онкології та радіології Сумського державного університету, м. Суми, Україна
yl.moskalenko@med.sumdu.edu.ua
https://orcid.org/0000-0002-5398-0298