Вестник РУДН. Серия: МЕДИЦИНА
RUDN Journal of MEDICINE. ISSN 2313-0245 (Print). ISSN 2313-0261 (Online)
2026;30(3)
http://journals.rudn.ru/medicine

DOI 10.22363/2313-0245-2025-30-3-314–327
EDN KBUNAB

ОРИГИНАЛЬНОЕ ИССЛЕДОВАНИЕ
ORIGINAL RESEARCH

Comparative characteristics of the molecular biological portrait of the head and neck squamous cell carcinoma tumor and peritumoral tissue

Enar D. Jumaniyazova[1] ✉, Irina V. Arutyunyan[1, 2], Anna G. Soboleva[1, 2], Polina A. Vishnyakova[1, 3], Marina A. Gulieva[1], Anastasia V. Lokhonina[1], Andrey V. Makarov[1, 4], Konstantin B. Gordon[1, 5]

[1] RUDN University, *Moscow, Russian Federation*
[2] Avtsyn Research Institute of Human Morphology, Petrovsky National Research Centre of Surgery, *Moscow, Russian Federation*
[3] V.I. Kulakov National Medical Research Center of Obstetrics, Gynecology and Perinatology, *Moscow, Russian Federation*
[4]Pirogov Russian National Research Medical University, *Moscow, Russian Federation*
[5]A. Tsyb Medical Radiological Research Center, National Medical Research Center of Radiology, *Obninsk, Russian Federation*
✉ enar2017@yandex.ru

Abstract: *Relevance*. Head and neck squamous cell cancer (HNSCC) accounts for about 890,000 new cases of malignant neoplasms (approximately 4.5% of all diagnosed cancer cases worldwide) and 450,000 deaths per year. Even with radical antitumor treatment, more than 40–50% of patients develop relapse, 20–30% of them develop distant metastases, and the five-year survival rate in advanced cases is 25%. Patients with recurrent HNSCC have an unfavorable clinical prognosis with a median overall survival of about 12 months. A high recurrence rate indicates the possible existence of a “source” of tumor cells, which may be located near the primary tumor, namely in the peritumoral tissue, which necessitates its study. The aim of the study was to compare the structure and expression of genes in the tumor and peritumoral tissues of HNSCC. *Materials and methods*. Biopsy material of tumor and peritumoral (located at a distance of 2 cm from the tumor border) tissues was obtained from 35 patients with HNSCC. Biopsies were examined by histological method, then the levels of mRNA expression of *EGFR, PIK3CA, PTEN, YAP, SLC26A6, ARIH2, UBE2Z, PITX1* genes were determined by real-time polymerase chain reaction in samples of tumor tissue and peritumoral region. The RNA Solo kit was used for RNA isolation, and the MMLV RT Kit (Evrogen, Russia) was used for reverse transcription. The amplification reaction with real-time detection was performed on a Real-Time DTprime amplifier (DNA Technology, Russia). *Results and discussion*. All tumor samples, regardless of anatomical localization, exhibited characteristic morphological features of squamous cell carcinoma. The peritumoral specimens represented visually unchanged tissue with

preserved epithelial architecture. The expression of *EGFR* and *PIK3CA* genes was higher in tumor tissue samples, while *PITX1* expression was higher in peritumoral tissue samples. *Conclusion*. Increased expression of *EGFR* and *PIK3CA* genes in tumor tissue confirms the activation of signaling pathways associated with tumor cell proliferation, survival, and disease progression. In contrast, the higher expression of the putative tumor suppressor gene *PITX1* in peritumoral tissue suggests the preservation of regulatory mechanisms limiting malignant transformation outside the tumor focus.

Keywords: squamous cell carcinoma of the head and neck, peritumoral tissue, tumor tissue, gene expression

Funding. This work was supported by the tripartite agreement of the Russian Science Foundation № 24-24-00296 dated 29.12.2023 on the project "The effect of proton therapy on the molecular portrait of the microenvironment of head and neck tumors" of the competition 2023 "Conducting basic scientific research and search scientific research by small individual scientific groups" between RSCF, Lokhonina A.V. and RUDN.

Author contributions. Jumaniyazova E.D. — the concept and design of the study, analysis of the data obtained, writing the text; Arutyunyan I.V. — the concept and design of the study, processing of the material and conducting the experiment; Soboleva A.G. — processing of the material and conducting the experiment, analysis of the data obtained; Gulieva M.A. — writing the text; Vishnyakova P.A. — text editing, analysis of the data obtained; Lokhonina A.V. — responsible for document management; Makarov A.V. — text editing; Gordon K.B. — collection of clinical material. All authors made a substantial contribution to the study and writing the manuscript, read and approved the final version before publication.

Conflicts of interest statement. The authors declare that there are no obvious or potential conflicts of interest related to the publication of this article.

Ethics approval. The study was approved by the Independent Ethics Committee (Protocol No. 634 dated 11/17/2021, Protocol No. 684 dated 03/02/2022).

Acknowledgements — not applicable.

Consent for publication. All patients signed an informed consent to participate in the study.

Received 10.06.2025. Accepted 01.07.2025.

For citation: *Jumaniyazova ED, Arutyunyan IV, Soboleva AG, Gulieva MA, Vishnyakova PA, Lokhonina AV, Makarov AV, Gordon KB.* Comparative characteristics of the molecular biological portrait of the head and neck squamous cell carcinoma tumor and peritumoral tissue. *RUDN Journal of Medicine.* 2026;30(3):314–327. doi: 10.22363/2313-0245-2026-30-3-314-327 EDN: KBUNAB

Introduction

The most common morphological form of tumors of the head and neck is squamous cell carcinoma. According to data published by GLOBOCAN (2020), head and neck squamous cell carcinoma (HNSCC) ranks sixth in prevalence among other types of malignant neoplasms in the world. According to current data, HNSCC accounts for an estimated 890 000 incident cases of malignant neoplasms per annum, corresponding to approximately 4.5% of the global incidence of diagnosed cancers, and approximately 450 000 cancer-related deaths annually [1]. This type of cancer is more common in adults over 50 years of age, with a male-dominated gender ratio (the ratio of men to women is approximately 2:1) [2]. To date, the increase in the incidence of acute respiratory viral infections among young able-bodied people has become socially significant. The main generally recognized etiological factors are tobacco smoking, alcohol consumption, infection with human papillomavirus (HPV) or Epstein-Barr virus (EBV), as well as betel chewing, common among the peoples of Southeast Asia. Clinically, HNSCC is characterized by late diagnosis, aggressive course, locally widespread

growth pattern, and frequent relapses [3]. The lack of screening leads to late diagnosis, complex anatomical localization complicates the radical surgical stage of treatment, and the proximity of critical structures leads to complications during RT. In the early stages of HNSCC (stages I and II), surgical treatment and RT are highly effective, with one- and two-year survival rates of 88.7 and 79.8%, respectively [4]. However, more than half of the patients (approximately 2/3 of the patients) already have a locally advanced form of the disease (stages III and IV) at the time of diagnosis, which is a prognostically unfavorable factor. Even with radical antitumor treatment, more than 40–50% of patients develop relapse, 20–30% of them develop distant metastases [5, 6], and the overall five-year survival rate is 25%. Patients with recurrent HNSCC have an unfavorable clinical prognosis with a median overall survival of about 12 months [7]. It was shown that in the most unfavorable cohort of patients (with a low–grade tumor negative for HPV type 16), the recurrence rate in the first six months after treatment is 50.6%, within 1 year — 72.5%, within 2 years — 88.6%. Such statistical data indicate the possible existence of a source of preserved or, conversely, induced by the therapeutic effect of tumor cells, which may be located near the localization of the primary tumor, namely, in the peritumoral tissue, which necessitates its study.

The aim of our study was to compare the structure and expression of genes in the tumor and peritumoral tissues of squamous cell carcinoma of the head and neck.

Based on a literature review, genes were selected that play a key role in tumor progression, including long-known regulators of tumor progression, as well as genes whose role in tumor growth has become known relatively recently.

Materials and methods

Characteristics of the biomaterial

The biopsy material of the tumor and peritumoral tissue (located at a distance of 2 cm from the tumor border) of the patients was obtained from the A. Tsyb Medical Radiological Research Center (MRSC). During the study, biomaterials from 35 patients obtained during the surgical stage of treatment were analyzed, information about patients is presented in the Table 1.

Biomaterial was obtained from patients meeting the following criteria:

1. Men and women over the age of 18.

2. Morphologically or radiologically verified diagnosis of squamous cell carcinoma in the head and neck (C00-C14, C30-C33).

3. General condition on the Karnovsky scale of at least 70 points.

4. Informed consent to participate in the study.

Table 1

General characteristics of patients

Parameters	Patients n, %
Total quantity	35 (100%)
Gender	
Men Women	22 (62.8%) 13 (37.1%)
Age (years)	
Median Range	57.3 19—83
Grade of malignancy	
G1 *G2* *G3*	25 (71.4.4%) 8 (22.8.8%) 2 (5.7.7%)

Ending tabl. 1

Parameters	Patients n, %
Keratinization	
Keratinizing	17 (48.57%)
Non-keratinizing	18 (51.4%)
T stage	
1	3 (8.57%)
2	15 (42.8%)
3	10 (28.5%)
4	7 (20%)
N stage	
0	9 (25.7%)
1	18 (51.4%)
2	8 (22.8%)
M stage	
0	22 (62.8%)
1	13 (37.2%)
Localization	
Oral cavity	15 (42.8%)
Tongue	8 (22.8%)
Larynx	10 (28.5%)
Maxillary sinus	2 (5.7%)

Primary processing of the received material

The material was thoroughly washed from possible contaminating agents in a phosphate-salt buffer containing 0.02% EDTA (Versin solution), then in a phosphate-salt buffer containing 1× antibiotic-antimycotic, then in a phosphate-salt buffer or Hanks solution without additives. In each solution, the tissue was washed 3 times. Then the material was divided into 2 unequal parts: the fragment was preserved in RNAlater solution for subsequent PCR-RT and stored at –80˚C until the study, the rest of the tissue was used for morphological examination.

Morphological examination

To verify the diagnosis of squamous cell carcinoma, a histological examination of the obtained tissue samples (tumor and peritumoral) was performed. Unfixed tissue samples were transferred to a foil mold filled with Tissue-Tek O.C.T. Compound (Sakura Finetek), frozen at –80 °C until the mounting medium completely solidified, then stored at –20 °C until use. Cryosections with a thickness of 5 microns were made using a Leica CM1200 cryotome using Super Frost Gold (Menzel) glasses and dried at room temperature for 1 hour. For routine histological examination, cryosections were stained with hematoxylin and eosin, dehydrated in standard wiring, and enclosed in a mounting medium (Biovitrum). The survey was carried out using a Leica DM 4000 B direct microscope.

PCR-RT

The levels of mRNA expression of *EGFR, PIK3CA, PTEN, YAP, SLC26A6, ARIH2, UBE2Z,* and *PITX1* genes were determined using real-time polymerase chain reaction in samples of tumor tissue and the peritumoral region (Table 2). The RNA Solo kit was used for RNA isolation, and the MMLV RT Kit (Evrogen, Russia) was used for reverse transcription. The amplification reaction with real-time detection was performed on a Real-Time DTprime amplifier (DNA Technology, Russia). The relative mRNA concentration of these genes was calculated by direct data comparison using

the formula: [A]0/[B]0 = E DC(T), where [A]0 is the initial concentration of the gene's mRNA in the PCR mixture, [B]0 is the initial concentration of *GAPDH* mRNA in the PCR mixture, E is the reaction efficiency (assumed to be 1.98), DC(T) is the difference between the threshold cycles of *GAPDH* and the desired gene.

Table 2

Sequences of used primers

Gene	Sequence	
GAPDH	Forward	GCACCGTCAAGGCTGAGAAC
	Reverse	TGGTGAAGACGCCAGTGGA
EGFR	Forward	CCCCCTGACTCCGTCCAGTA
	Reverse	CCCAACTGCGTGAGCTTGTT
PIK3CA	Forward	TTCCGGGGGATTGTAGGCTC
	Reverse	TTCCGGGGGATTGTAGGCTC
YAP	Forward	CAGCAACTCCAACCAGCAGC
	Reverse	CAGCAACTCCAACCAGCAGC
SLC26A6	Forward	AGACAGCCAGAGATGCTGCC
	Reverse	GTAGGTGACCACGAAGCCGA
UBE2Z	Forward	CGGCACGAGACCATCAGAGT
	Reverse	TGGTAGTCAAAGTGGCCCCG
PTEN	Forward	CCCAGTCAGAGGCGCTATGT
	Reverse	CCCAGTCAGAGGCGCTATGT
TIMP1	Forward	CCTTCCAGGTGTTTCCCTGTT
	Reverse	CCTTCCAGGTGTTTCCCTGTT
TIMP2	Forward	GACCCACAAGGAGATTGGGG
	Reverse	GACCCACAAGGAGATTGGGG
PITX1	Forward	AACCGCTACCCCGACATGAG
	Reverse	CTGCACTAGGCCGCTGAACT

Statistical methods

The statistical analysis of the obtained data was carried out in the Statistica 8.0 program, using the Shapiro – Wilk test to assess the normality of the distribution, the Mann – Whitney criteria and the t-test for pairwise comparison. The differences were considered statistically significant at a significance level of $p<0.05$.

Results and discussion

In all the presented samples of tumor tissue, extensive invasion of tumor cells into their own plate of the mucous membrane was noted, and the integrity of the basement membrane was disrupted (Figure 1, 2). Histological preparations stained with hematoxylin and eosin revealed a pattern characteristic of squamous cell carcinoma: abundant invasive growth of tumor cells into the underlying tissues in the form of rounded clusters, strands or individual cells. Normal architectonics were preserved in the peritumoral tissue samples: the multilayer epithelium is separated from its own plate of the mucous membrane by a preserved basement membrane (Figure 1, 2).

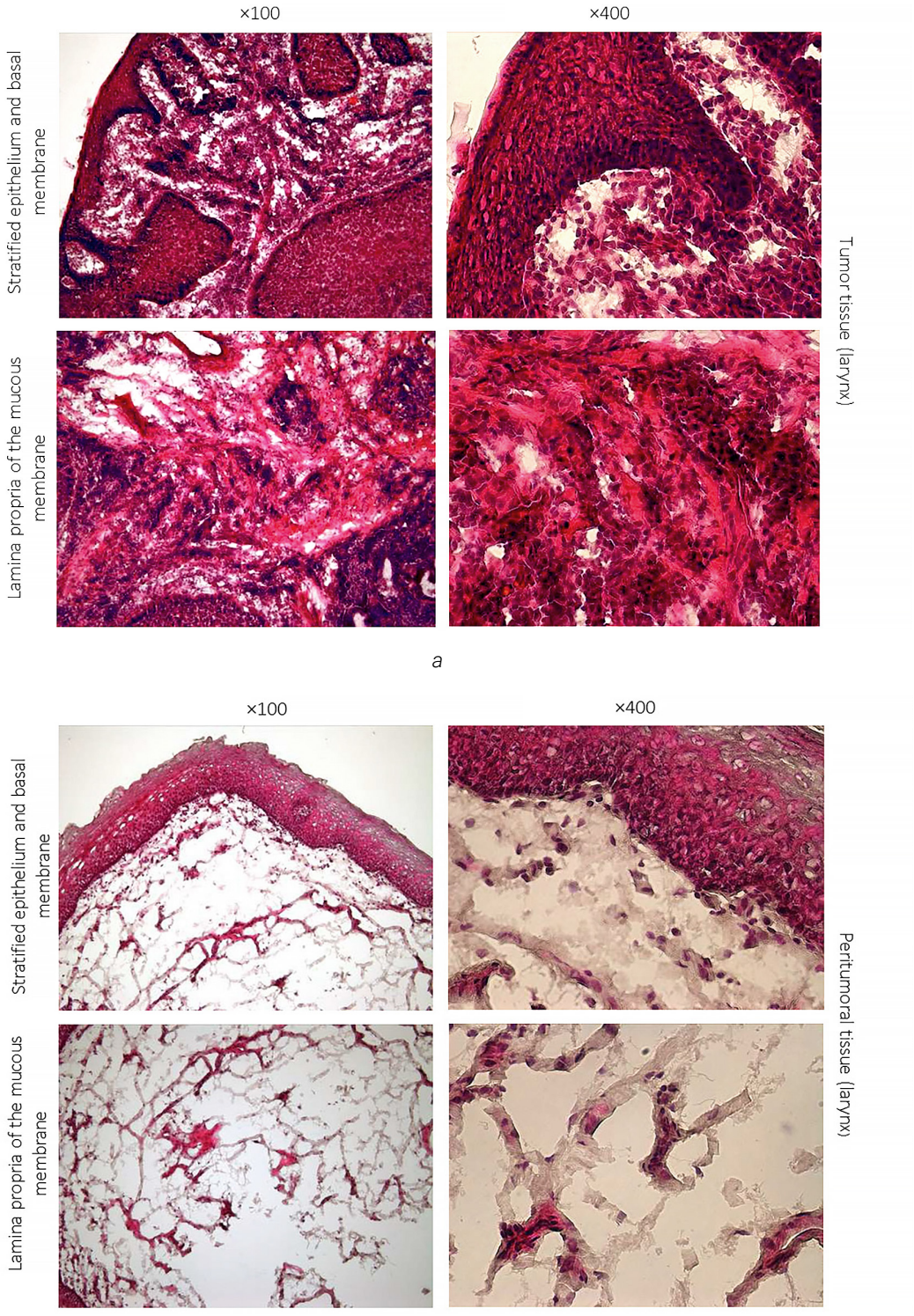
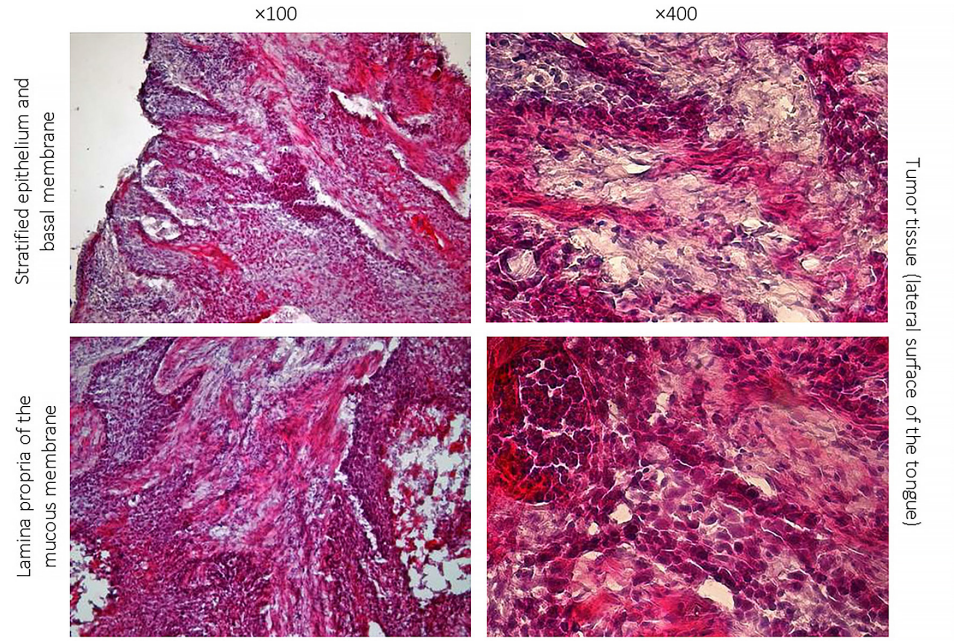
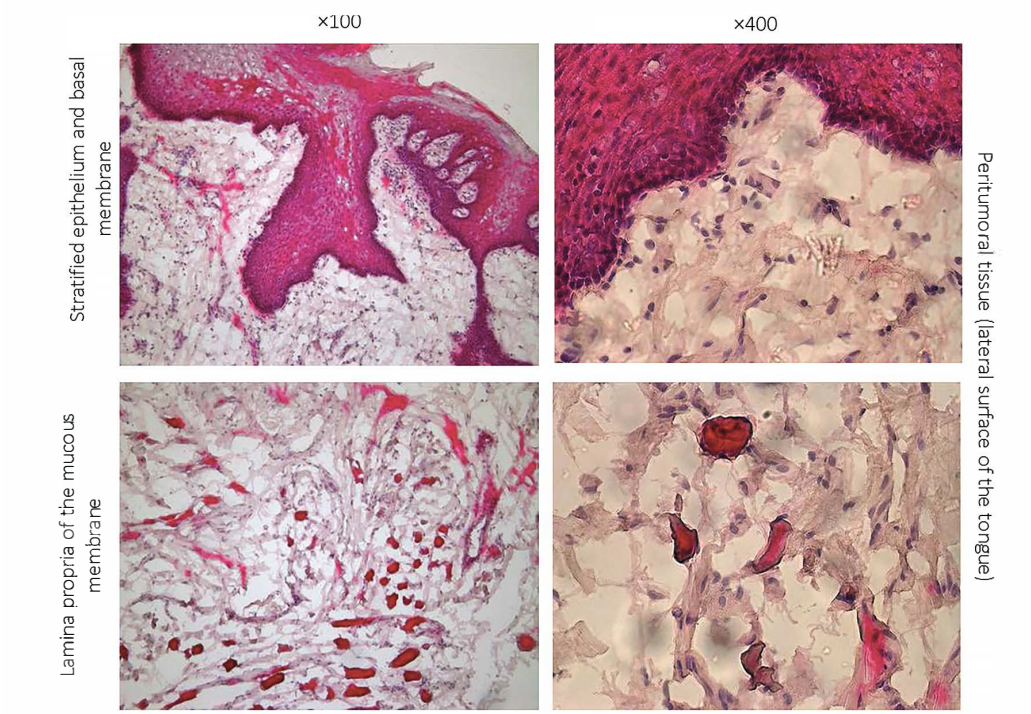


Figure 1. Squamous cell carcinoma of the larynx: tumor (*a*) and peritumoral (*b*) tissues. Hematoxylin and eosin staining. Light-field microscopy. The length of the scale segment is 100 microns and 50 microns



a



b

Figure 2. Squamous cell carcinoma of the tongue: tumor (*a*) and peritumoral (*b*) tissues. Hematoxylin and eosin staining. Light-field microscopy. The length of the scale segment is 100 microns and 50 microns

The levels of mRNA expression of the *PTEN*, *TIMP1*, *TIMP2*, *YAP*, *PIK3CA*, *EGFR*, *ARIH2*, *SLC26A6*, *UBE2Z*, and *PITX1* genes were evaluated using real-time polymerase chain reaction in tumor tissue and peritumoral tissue samples.

PTEN is a tumor suppressor gene that regulates the cell cycle and apoptosis by modulating the PI3K-PKB/Akt signaling pathway. Approximately 30% of cases of HNSCC have decreased *PTEN* expression. Moreover, the lack of *PTEN* expression often leads to the development of aggressive tumors and is associated with low disease-free and overall survival of patients [8, 9].

YAP is a transcriptional coactivator of genes involved in growth and tumor formation. Increased *YAP* expression is associated with an unfavorable prognosis of HNSCC and resistance to chemo and radiotherapy [10] (Figure 3).

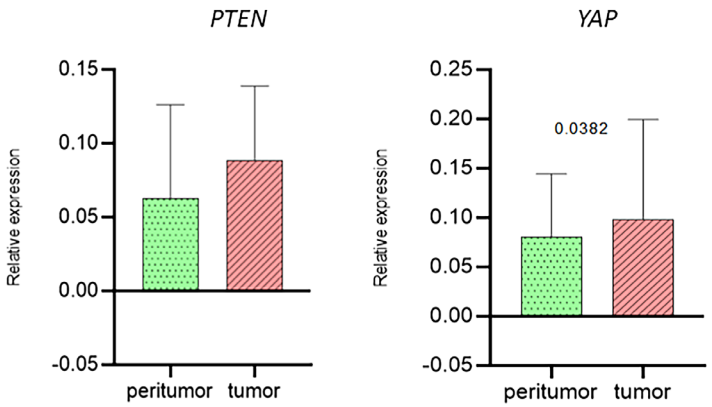


Figure 3. The level of relative expression of the *PTEN, YAP* genes in tumor and peritumoral tissues

Tissue metalloproteinase inhibitors (TIMPs) block the activity of matrix metalloproteinases, which leads to suppression of tumor progression [11], but their role in HNSCC is controversial. There was no significant difference in the expression of these genes in the samples of tumor and peritumoral tissues studied by us (Figure 4).

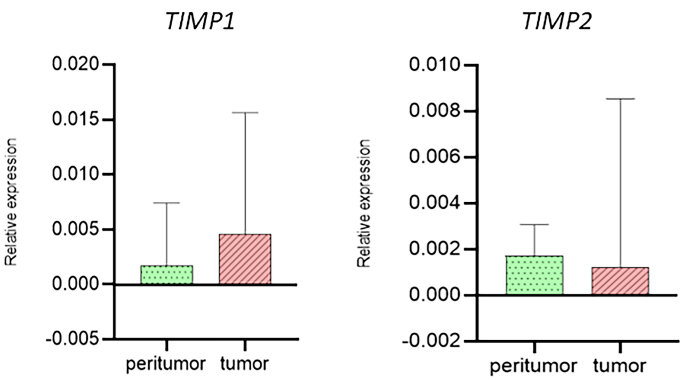


Figure 4. The level of relative expression of the *TIMP1* and *TIMP2* genes in tumor and peritumoral tissues

PIK3CA is one of the most frequently mutating oncogenes in PRGS: mutations were detected in 13.7% of cases (TCGA, Firehose Legacy). *PIK3CA* encodes p110a, a Class 1A PI3K catalytic subunit. With abnormal activation, PI3K stimulates several downstream signaling cascades, which leads to uncontrolled proliferation, survival, and migration of tumor cells [12].

We found that the expression level of the epidermal growth factor receptor (EGFR) is significantly higher in tumor tissue than in peritumoral tissue (Figure 5). *EGFR* is overexpressed in more than 90% of cases of HNSCC, and its increased expression correlates with an unfavorable outcome in patients [13]. Binding of ligands to EGFR leads to a conformational change in the receptor, followed by autoactivation of tyrosine kinase from the intracellular domain of the receptor. This process activates the intracellular signaling pathway, which leads to inhibition of apoptosis, activation of cell proliferation and angiogenesis, as well as to an increase in the potential for metastatic spread [14].

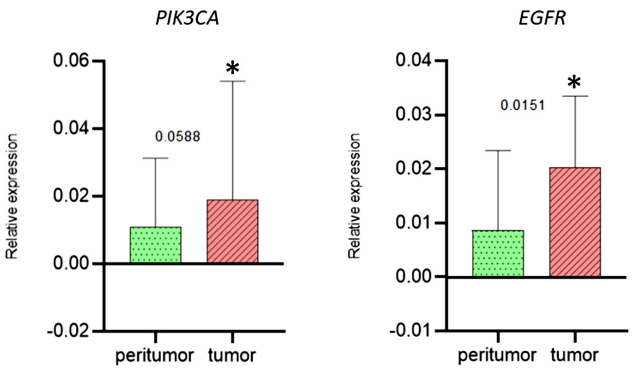


Figure 5. The level of relative expression of *PIK3CA* and *EGFR* genes in tumor and peritumoral tissues

Note: * — $p < 0.05$

The *ARIH2* gene is expressed everywhere, demonstrating the highest levels of expression in granulocytes [15]. Ubiquitin-protein ligase E3, encoded by the *ARIH2* gene, catalyzes the ubiquitination of target proteins and plays a key role in posttranslational modifications in various cellular processes. *ARIH2* is involved in DNA repair under genotoxic stress [16].

The family of solute carrier proteins 26 (SLC26) includes multifunctional transporters of substrates, including oxalate, sulfate, and chloride, and plays an important role in the physiology and pathophysiology of the kidneys [17]. One of the members of this family, SLC26A6, is of particular interest because it has some non-canonical properties. For example, it has recently been demonstrated that *SLC26A6* acts as an oncogene in hepatocellular carcinoma [18] and lung cancer [19]. In the studied samples, the expression levels of the *ARIH2* and *SLC26A6* genes were approximately the same in the tumor and peritumoral tissues (Figure 6).

Ubiquitination is one of the types of protein modification that modulates many cellular signaling processes, including DNA repair, transcription, cell membrane receptor recycling, intracellular transport, endocytosis, angiogenesis, and inflammatory signaling [20]. Ubiquitination occurs as a result of the joint work of three types of enzymes: ubiquitin-activating enzymes (E1), ubiquitin-conjugating enzymes (E2) and ubiquitin ligases (E3), respectively (Upregulation of ubiquitin-conjugating enzyme E2Z is associated with human hepatocellular carcinoma). More and more studies show that most of the enzymes involved in ubiquitination play a significant role in the development of tumors [21]. Paired homeodomain transcription factor 1 (PITX1), also known as pituitary homeobox 1 (Ptx1), refers to highly conserved homeobox genes that encode sequence-specific transcription factors (SSTFS) that are involved in osteogenesis [22]. It is assumed that *PITX1* can act as a tumor suppressor gene and a potential biomarker for predicting the chemoresistance of tumor stem cells of HNSCC [23]. In our study, a decrease in the expression of this gene was noted in the samples of the tumor tissue of the HNSCC, compared with the tissue of the peritumoral region (Figure 7).

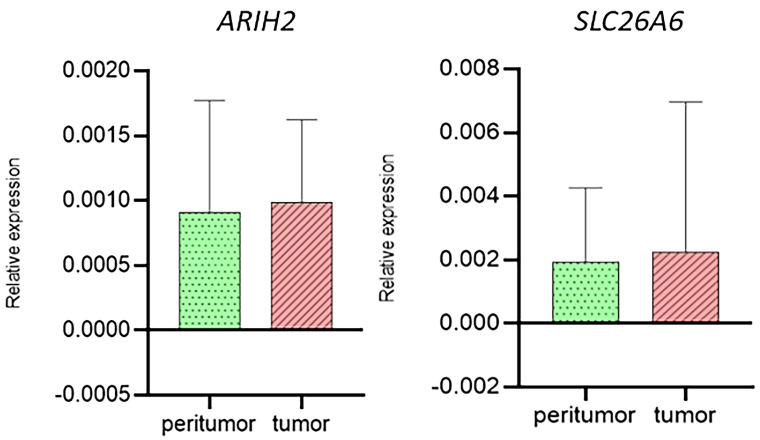


Figure 6. The level of relative expression of the *ARIH2, SLC26A6* genes in tumor and peritumoral tissues

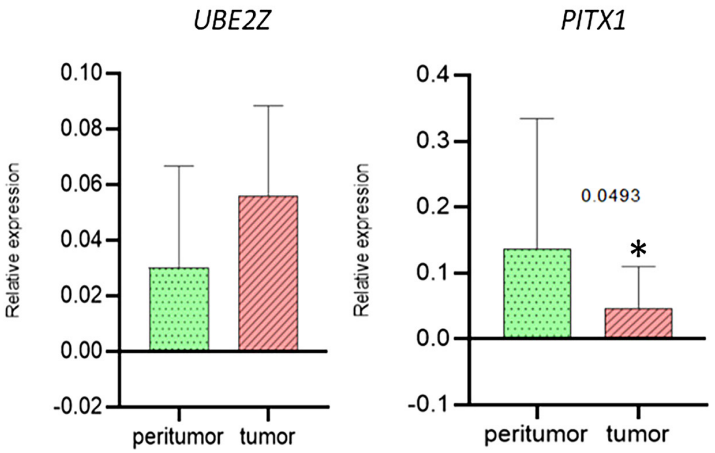


Figure 7. The level of relative expression of the *UBE2Z and PITX1* genes in tumor and peritumoral tissues

Note: * — $p < 0.05$

Conclusion

Increased expression of *EGFR* and *PIK3CA* genes in tumor tissue confirms the activation of signaling pathways associated with tumor cell proliferation, survival, and progression. In contrast, the higher expression of the putative tumor suppressor gene *PITX1* in peritumoral tissue suggests the preservation of regulatory mechanisms limiting malignant transformation outside the tumor focus.

The obtained results emphasize the importance of studying not only the tumor itself but also its surrounding peritumoral microenvironment, which may contribute to disease progression and recurrence. The identified molecular markers can be considered promising candidates for further studies aimed at improving prognostic assessment, identifying patients at high risk of relapse, and developing personalized therapeutic strategies for *HNSCC*.

Reference/Список литературы

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*. 2021;71(3):209–249. doi: 10.3322/caac.21660

2. Barsouk A, Aluru J S, Rawla P, Saginala K, Barsouk A. Epidemiology, risk factors, and prevention of head and neck squamous cell carcinoma. *Medical Sciences*. 2023;11(2):42. doi: 10.3390/medsci11020042

3. Jumaniyazova ED, Sentyabreva AV, Kosyreva AM, Lokhonina AV. Molecular genetic signatures of head and neck squamous cell carcinoma and their changes induced by proton irradiation. *RUDN Journal of Medicine*. 2024;28(4):413–426. doi: 10.22363/2313–0245–2024–28–4–413–426

4. Eden D, Ghose A, Moschetta M, Perez-Fidalgo J A, Rassy E, Boussios S. Immunotherapy combined with standard therapies in head and neck squamous cell carcinoma–a meta-analysis. *Anticancer Research*. 2024;44(3):861–878. doi: 10.21873/anticanres.16880

5. Machiels J P, Leemans C R, Golusinski W, Grau C, Licitra L, Gregoire V. Squamous cell carcinoma of the oral cavity, larynx, oropharynx and hypopharynx: EHNS–ESMO–ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2020;31(11):1462–1475. doi: 10.1016/j.annonc.2020.07.011

6. Ionna F, Bossi P, Guida A, Alberti A, Muto P, Salzano G, Perri F. Recurrent/metastatic squamous cell carcinoma of the head and neck: a big and intriguing challenge which may be resolved by integrated treatments combining locoregional and systemic therapies. *Cancers*. 2021;13(10):2371. doi: 10.3390/cancers13102371

7. Samra B, Tam E, Baseri B, Shapira I. Checkpoint inhibitors in head and neck cancer: current knowledge and perspectives. *Journal of Investigative Medicine*. 2018;66(7):1023–1030. doi: 10.1136/jim-2018–000743

8. Squarize CH, Castilho RM, Abrahao A C, Molinolo A, Lingen MW, Gutkind JSL. PTEN deficiency contributes to the development and progression of head and neck cancer. *Neoplasia*. 2013;15(5):461–471. doi: 10.1593/neo.121024

9. Vidotto T, Melo CM, Castelli E, Koti M, Dos Reis RB, Squire JA. Emerging role of PTEN loss in evasion of the immune response to tumours. *British journal of cancer*. 2020;122(12):1732–1743. doi: 10.1038/s41416–020–0834–6

10. Segrelles C, Paramio JM, Lorz C. The transcriptional co-activator YAP: A new player in head and neck cancer. *Oral Oncology*. 2018;86:25–32. doi: 10.1016/j.oraloncology.2018.08.020

11. Abdel-Hamid N M, Abass S A. Matrix metalloproteinase contribution in management of cancer proliferation, metastasis and drug targeting. *Molecular biology reports*. 2021;48(9):6525–6538. doi: 10.1007/s11033–021–06635-z

12. Vanhaesebroeck B, Stephens L, Hawkins P. PI3K signalling: the path to discovery and understanding. *Nature reviews Molecular cell biology*. 2012;13(3):195–203. doi: 10.1038/nrm3290

13. Rothenberg SM, Ellisen LW. The molecular pathogenesis of head and neck squamous cell carcinoma. *The Journal of clinical investigation*. 2012;122(6):1951–1957. doi: 10.1172/JCI59889

14. Hong Y, He J, Deng D, Liu Q, Zu X, Shen Y. Targeting kinases that regulate programmed cell death: a new therapeutic strategy for breast cancer. *Journal of Translational Medicine*. 2025;23(1):439. doi: 10.1186/s12967–025–06367–9.

15. Vinci M, Treccarichi S, Galati Rando R, Musumeci A, Todaro V, Federico Calì F. A de novo ARIH2 gene mutation was detected in a patient with autism spectrum disorders and intellectual disability. *Scientific Reports*. 2024;14(1):15848. doi: 10.1038/s41598–024–66475–2

16. Von Stechow L, Typas D, Carreras Puigvert J, Oort L, Siddappa R, Pines A Danen EH. The E3 ubiquitin ligase ARIH1 protects against genotoxic stress by initiating a 4EHP-mediated mRNA translation arrest. *Molecular and cellular biology*. 2015; *35*(7): 1254–1268. doi: 10.1128/mcb.01152–14

17. Li J, Huang S, Liu S, Liao X, Yan S, Liu Q. SLC26 family: a new insight for kidney stone disease. *Frontiers in Physiology*. 2023;14:1118342. doi: 10.3389/fphys.2023.1118342

18. Cao J, Wang P, Chen J, He X. Systemic characterization of the SLC family genes reveals SLC26A6 as a novel oncogene in hepatocellular carcinoma. *Translational Cancer Research*. 2021;10(6):2882. doi: 10.21037/tcr-20–1751

19. Lee D, Lee P C, Hong JH, Shin DM. Estrogen treatment reduced oxalate transporting activity and enhanced migration through the involvement of SLC26A6 in lung cancer cells. *Toxicology in Vitro*. 2023;82*:105373*. doi: 10.1016/j.tiv.2022.105373

20. Bui QT, Hong JH, Kwak M, Lee JY, Lee PCW. Ubiquitin-conjugating enzymes in cancer. *Cells*. 2021;10(6): 1383. doi: 10.3390/cells10061383.

21. Shi X, Wang B, Chen X, Zheng Y, Ding Y, Wang C. Upregulation of ubiquitin-conjugating enzyme E2Z is associated with human hepatocellular carcinoma. *Biochemical and Biophysical Research Communications*. 2020;523(1):25–32. doi: 10.1016/j.bbrc.2019.11.170

22. Kioussi C, Shih H P, Loflin J, Gross MK. Prediction of active nodes in the transcriptional network of neural tube patterning. *Proceedings of the National Academy of Sciences*. 2006;103(49):18621–18626. doi: 10.1073/pnas.0609055103

23. Takenobu M, Osaki M, Fujiwara K, Fukuhara T, Kitano H, Kugoh H, Okada F. PITX1 is a novel predictor of the response to chemotherapy in head and neck squamous cell carcinoma. *Molecular and Clinical Oncology*. 2016;5(1):89–94. doi: 10.3892/mco.2016.880

Сравнительная характеристика молекулярно-биологического портрета опухолевой и перитуморальной тканей плоскоклеточного рака головы и шеи

Э.Д. Джуманиязова[1] ✉, И.В. Арутюнян[1, 2], А.Г. Соболева[1, 2], П.А. Вишнякова[1, 3], М.А. Гулиева[1], Лохонина А.В.[1], А.В. Макаров[1, 4], К.Б. Гордон[1, 5]

[1] Российский университет дружбы народов, *г. Москва, Российская Федерация*
[2] Научно-исследовательский институт морфологии человека имени академика А.П. Авцына ФГБНУ «Российский научный центр хирургии имени академика Б.В. Петровского», *г. Москва, Российская Федерация*
[3]Национальный медицинский исследовательский центр акушерства, гинекологии и перинатологии имени академика В.И. Кулакова, *г. Москва, Российская Федерация*
[4]Российский национальный исследовательский медицинский университет имени Н.И. Пирогова, *г. Москва, Российская Федерация*
[5]Медицинский радиологический научный центр им. А. Цыба — филиал Национального медицинского исследовательского центра радиологии *г. Обнинск, Российская Федерация*
✉ enar2017@yandex.ru

Аннотация: *Актуальность*. На долю плоскоклеточного рака головы и шеи (ПРГШ) приходится около 890 000 новых случаев злокачественных новообразований (примерно 4,5 % всех диагностированных случаев в мире) и 450 000 смертей в год. Даже при проведении радикального противоопухолевого лечения у более чем 40–50 % пациентов развивается рецидив, у 20–30 % из них появляются отдаленные метастазы, а общая пятилетняя выживаемость составляет примерно 25%. Пациенты с рецидивами ПРГШ имеют неблагоприятный клинический прогноз с медианой общей выживаемости около 12 месяцев. Высокая частота местных рецидивов свидетельствует о возможном существовании «источника» опухолевых клеток, который может быть локализован недалеко от первичной опухоли, а именно — в перитуморальной ткани, что обуславливает актуальность ее изучения. *Цель исследования* — сравнительная оценка строения и экспрессии генов в опухолевой и перитуморальной тканях ПРГШ. *Материалы и методы*. Биопсийный материал опухолевой и перитуморальной (расположенной на расстоянии 2 см от границы опухоли) тканей получен от 35 пациентов с ПРГШ. Образцы биоптатов последовательно исследовали: на первом этапе — гистологическим методом, на втором — методом полимеразной цепной реакции; в образцах опухолевой ткани и перитуморальной области определяли уровни экспрессии мРНК генов *EGFR, PIK3CA, PTEN, YAP, SLC26A6, ARIH2, UBE2Z, PITX1*. Для выделения РНК использовали набор RNA Solo, а для обратной транскрипции — MMLV RT Kit (все — «Евроген», Россия). Реакцию амплификации с детектированием в режиме реального времени проводили на Real-Time амплификаторе DTprime («ДНК-Технология», Россия). *Результаты и обсуждение*. Все образцы опухоли, вне зависимости от анатомической локализации, имели характерную для плоскоклеточного рака картину. Образцы перитуморальной зоны представляли собой визуально неизмененную ткань с сохранной архитектоникой эпителия. Экспрессия генов *EGFR, PIK3CA* была выше в образцах опухолевой ткани, в то время как экспрессия *PITX1* была выше в образцах перитуморальной ткани. *Выводы*. Повышенная экспрессия генов *EGFR* и *PIK3CA* в опухолевой ткани указывает на активацию сигнальных путей, связанных с пролиферацией, выживанием клеток и опухолевой прогрессией. Напротив, более высокая экспрессия предполагаемого гена-супрессора опухолей *PITX1* в перитуморальной ткани указывает на сохранение регуляторных механизмов, ограничивающих злокачественную трансформацию за пределами опухолевого очага.

Ключевые слова: плоскоклеточный рак головы и шеи, перитуморальная ткань, опухолевая ткань, экспрессия генов.

Информация о финансировании. Работа выполнена при поддержке трёхстороннего соглашения Российского научного фонда № 24-24-00296 от 29.12.2023 по проекту «Влияние протонной терапии на молекулярный портрет микроокружения опухолей головы и шеи» конкурса 2023 года «Проведение фундаментальных научных исследований и поисковых научных исследований малыми индивидуальными научными коллективами» между РНФ, Лохониной А.В. и РУДН.

Вклад авторов. Джуманиязова Э.Д. — концепция и дизайн исследования, анализ полученных данных, написание текста; Арутюнян И.В. — концепция и дизайн исследования, обработка материала и проведение эксперимента; Соболева А.Г. — обработка материала и проведение эксперимента, анализ полученных данных; Гулиева М.А. — написание текста; Вишнякова П.А. — редактирование текста, анализ полученных данных; Лохонина А.В. — ответственная за документооборот; Макаров А.В. — редактирование текста; Гордон К.Б. — сбор клинического материала. Все авторы внесли существенный вклад в проведение исследования и подготовку рукописи, прочитали и одобрили окончательную версию перед публикацией.

Информация о конфликте интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией данной статьи.

Этическое утверждение. Исследование одобрено независимым комитетом по этике (протокол № 634 от 17.11.2021, протокол № 684 от 02.03.2022).

Благодарности — неприменимо.

Информированное согласие на публикацию. Все пациенты подписали информированное согласие на участие в исследовании.

Поступила 10.06.2025. Принята 01.07.2025.

Для цитирования: *Jumaniyazova E.D., Arutyunyan I.V., Soboleva A.G., Gulieva M.A., Vishnyakova P.A., Lokhonina A.V., Makarov A.V., Gordon K.B.* Comparative characteristics of the molecular biological portrait of tumor and peritumoral tissue of the head and neck squamous cell carcinoma // Вестник Российского университета дружбы народов. Серия: Медицина. 2026. Т. 30. № 3. С. 314–327. doi: 10.22363/2313-0245-2026-30-3-314-327 EDN: KBUNAB

Corresponding author: Jumaniyazova E.D. — Assistant of the Department of Histology, Cytology and Embryology, RUDN University, 6 Miklukho-Maklaya st, 117198, Moscow, Russian Federation. E-mail: enar2017@yandex.ru
Jumaniyazova E.D. SPIN 1780-5326, ORCID 0000-0002-8226-0433
Arutyunyan I.V. SPIN 5220-1893, ORCID 0000-0002-4344-8943
Soboleva A.G. SPIN 2582-5511, ORCID 0000-0002-9158-1933
Vishnyakova P.A. SPIN 3406-3866, ORCID 0000-0001-8650-8240
Gulieva M.A. SPIN 3536-3784, ORCID-0000-0002-8226-0433
Lokhonina A.V. SPIN 4521-2250, ORCID 0000-0001-8077-2307
Makarov A.V. SPIN 3534-3764, ORCID 0000-0003-2133-2293
Gordon K.B. SPIN 2045-4565, ORCID 0000-0002-3146-5615

Ответственный за переписку: Джуманиязова Энар Денисовна — ассистент кафедры гистологии, цитологии и эмбриологии Медицинского института, научный сотрудник лаборатории молекулярной патофизиологии клетки Научно-исследовательского института молекулярной и клеточной медицины Российского университета дружбы народов, Российская Федерация, 117198, г. Москва, ул. Миклухо-Маклая, д. 6. E-mail: enar2017@yandex.ru
Джуманиязова Э.Д. SPIN 1780-5326, ORCID 0000-0002-8226-0433
Арутюнян И.В. SPIN 5220-1893, ORCID 0000-0002-4344-8943
Соболева А.Г. SPIN 2582-5511, ORCID 0000-0002-9158-1933
Вишнякова П.А. SPIN 3406-3866, ORCID 0000-0001-8650-8240
Гулиева М.А. SPIN 3536-3784, ORCID 0000-0002-8226-0433
Лохонина А.В. SPIN 4521-2250, ORCID 0000-0001-8077-2307
Макаров А.В. SPIN 3534-3764, ORCID 0000-0003-2133-2293
Гордон К.Б. SPIN 2045-4565, ORCID 0000-0002-3146-5615