



The Role of miRNAs and lncRNAs in Laryngeal Squamous Cell Carcinoma – a Mini-Review

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Abstract

Laryngeal squamous cell carcinoma is a common malignancy in men. Bulgaria is one of the countries in Europe with the highest incidence and mortality rates of the aggressive, severe disease of laryngeal cancer. Proven etiological factors are the abuse of tobacco and alcohol beverages. Despite the progress of technologies of multimodal medical treatment, survival rates have not reached satisfactory levels. Over the last few decades, scientific and clinical research data have led to a growing interest in exploring potential biomarkers. In the last years, non-coding RNAs have become promising biomarkers. They are important key regulators in both normal and tumour specific biological processes as well as in the response to environmental factors and treatment, including chemo- and radiotherapy. Studies have shown ectopic expression of a number of ncRNAs in laryngeal cancer. Published data provide evidence of the lncRNAs and miRNAs that could help us better understand complex carcinogenesis in laryngeal cancer and would provide reliable diagnostic, prognostic and predictive biomarkers.

Keywords

biomarkers, lncRNAs, laryngeal cancer, LSCC, miRNAs

INTRODUCTION

Epidemiology

Worldwide, laryngeal cancer is the second most common malignancy in the group of head and neck cancers. Men are more likely to be affected than women, and there is a strong association with age, with the peak of incidence in the decade between 55 and 65 years of age. According to GLOBOCAN data for 2018 (IACR), the estimated incidence rate for laryngeal cancer worldwide was 1.10% (177 422 cases) and the registered deaths were 1.07% (94 771) (data for both sexes), with Central and Eastern Europe ranking second after the Caribbean region (Fig. 1).

According to the latest data of the National Cancer Register of Bulgaria for 2015, 554 people were diagnosed with

laryngeal carcinoma and 343 deaths were registered. These results ranked laryngeal carcinoma ninth by incidence of oncological morbidity (3.1%) and tenth by death (3.3%) among males.¹ Bulgaria ranks ninth among the countries with the highest incidence of laryngeal carcinoma in Europe (GLOBOCAN 2018, IACR), a fact indicative of the social significance of this disease (Fig. 2).

The annual distribution of laryngeal cancer incidence and mortality showed significant geographical variation in the last two decades. Increase is registered in some of the Asia countries: Pakistan, Taiwan, Thailand and China, and in the Caribbean, while the incidence has been slightly decreasing in European countries with higher life standards.^{2,3} In general, the incidence of laryngeal cancer is falling in more developed countries, due to the promotion of healthy life-style and reduction of tobacco and alcohol use.

In comparison to the developed countries, in the past 18 years, there has been no improvement in the incidence of

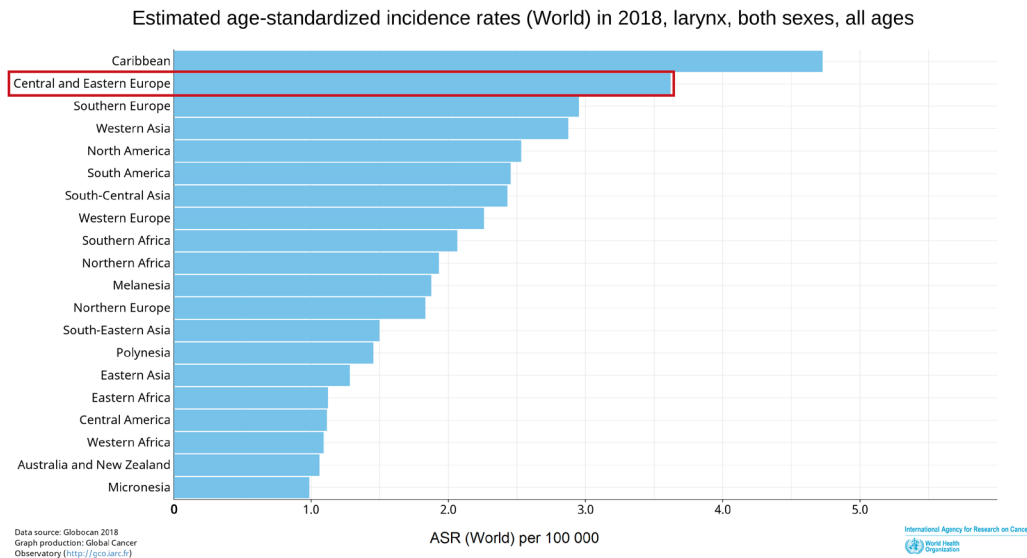


Figure 1. Description of the regions worldwide and the expected rate of incidence of laryngeal cancer in 2018. Central and Eastern Europe ranks 2nd (GLOBOCAN 2018).

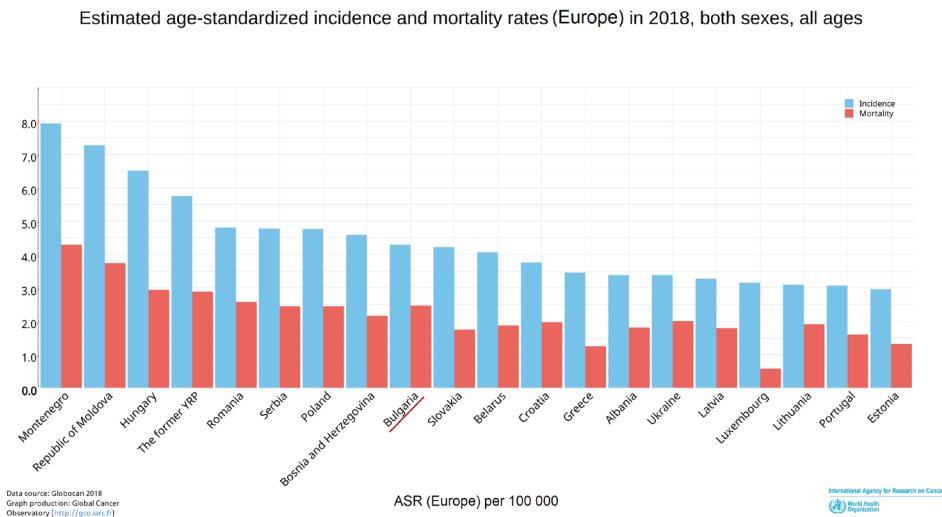


Figure 2. Description of the countries of Europe according to expected incidence rate for laryngeal cancer in 2018. Bulgaria ranks 9th (GLOBOCAN 2018).

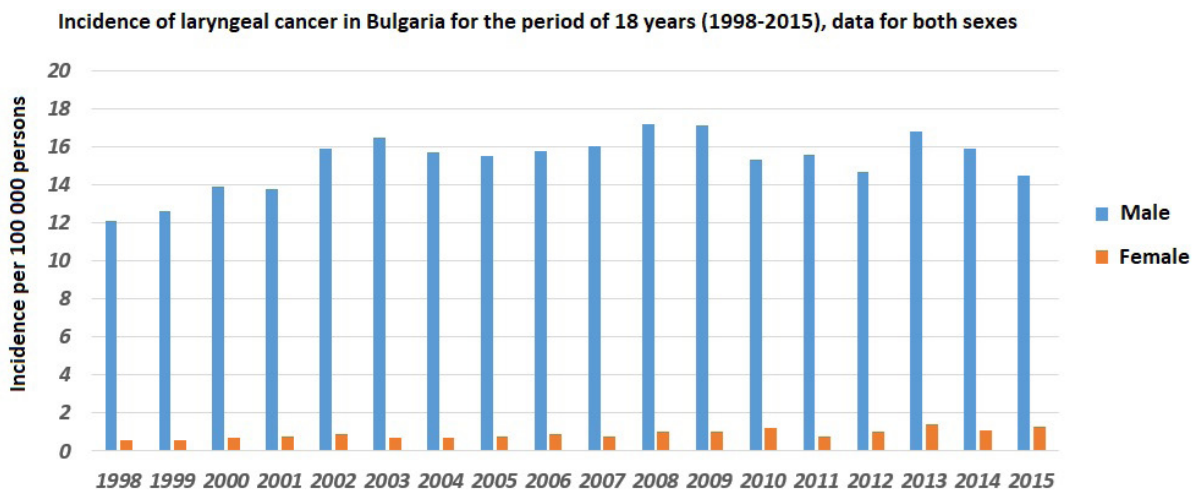


Figure 3. Laryngeal cancer incidence in men and women for a period of 18 years (1998-2015) in Bulgaria.

morbidity and mortality from laryngeal cancer in Bulgaria, which is strongly associated with an increase in the abuse of tobacco products and high consumption of alcoholic beverages, proven carcinogens for the disease⁴, and lower standard and unhealthier life style habits (Fig. 3).

Depending on the laryngeal cancer location, clinical symptoms may appear in the early stages of the disease, which is good for early diagnosis and better prognosis. However, laryngeal carcinoma remains mostly a later diagnosed disease (usually in III/IV stage),⁵ due to neglect of the symptoms by most of the patients. The long-term prognosis for advanced laryngeal carcinomas remains relatively poor, with about 30-40%⁶ of the patients surviving the late stages, recurrent carcinoma induction affecting about 60%, and metastases developing in about 15-20% of the cases⁷. According to data from the National Cancer Institute (NCI, SEER, USA), the five-year survival rate for laryngeal carcinoma of 52% for the period of 1950-1954 rose to 60.4% over the period of 2008 to 2014.⁸ This change is unsatisfactory in the light of modern advances in medicine and genetic diagnostics, and the successful treatment of laryngeal carcinoma remains challenging to medical specialists. Unlike other cancers, head and neck cancers are deficient of biomarkers and there are no other new approaches to target therapy other than cetuximab, approved by the US Food and Drug Administration (FDA) in 2006.⁹ At present, elucidation of the molecular spectrum of head and neck cancers is based on studies of primary tumors consisting only of the most common histological type,¹⁰ squamous cell carcinomas. The genetic profiles of the most difficult to treat clinically, recurrent and metastatic tumors remain unclear.

In order to improve the efficacy of laryngeal cancer treatment, it is necessary to better understand the molecular and genetic mechanisms involved in the carcinogenesis of this highly aggressive disease.

Risk factors

It is known that between 25% and 30% of all cancers in developing countries are due to tobacco abuse. The use of tobacco products is the most significant risk factor for developing of laryngeal cancer, and the risk is higher in heavy, long-time smokers or pipe users. It is considered that smoking of beedi, small cigarettes typical and often found in parts of Asia, is associated with a higher risk of developing of hypopharyngeal and laryngeal cancer, in comparison to the smoking of Western cigarettes¹¹, which is in line with increasing of laryngeal cancer incidence in Asia.

Taking large amounts of alcohol is not considered as a single risk factor for the development of laryngeal cancer but it is assumed that the cause is the prolonged impact of acetaldehyde, which is an intermediate metabolite of ethanol, and influences laryngeal cancerogenesis.¹²

Gastroesophageal reflux is considered an additional risk factor for laryngeal dysplasia and malignancy due to chronic inflammation, and tissue damage which in com-

ination with tobacco smoking represents a mutagen factor.¹³ Unlike other oncological diseases of the head and neck, the role of human papillomavirus (HPV) infection for the development of laryngeal carcinoma has not been fully established, but it is assumed that in laryngeal cancerogenesis, HPV has a weaker role than smoking and alcohol abuse. Up to 5% of the cases occur due to HPV, with prevalence serotypes HPV 16 and HPV 18.¹⁴ HPV-associated laryngeal carcinomas usually occur in younger, non-smoker and have a better overall prognosis.

Non-coding RNA

Advances in RNA Next Generation Sequencing (NGS) technologies revealed the complexity of our genome. Non-coding RNAs (ncRNAs) are the majority (98%) of the transcriptome and several different classes of regulatory RNA with important functions are detected. Understanding the importance of this RNA world is one of the most important challenges in biology, as the ncRNAs hold a great potential for new biomarkers and therapeutic targets.

Studies have found that only about 2% of the human genome encodes proteins, while the remaining 98% encodes different classes of ncRNAs¹⁵ that were considered “junk” until recently. Among these are genes that are responsible for the expression of micro RNAs (miRNAs) and long non-coding RNA (lncRNA). Many of these ncRNAs have regulatory functions at the transcriptional, post-transcriptional and epigenetic levels, and they often display changed regulation in malignant neoplasia.

Because of their proven oncogenic and tumor suppressor function in cellular processes, miRNA and lncRNA have the potential of becoming novel anticancer therapeutic molecules.^{16,17} Anti-miRNA oligonucleotides and miRNA mimics have been found to have anti-tumor properties. Both classes of ncRNAs are stable, including in body fluids,^{16,17} making them suitable for non-invasive therapies. In addition, the complete clarification of the complex regulatory chains of ncRNAs may provide additional strategies for the treatment of cancer, including laryngeal carcinoma.

Long-non coding RNA in laryngeal cancer

A number of studies discuss the involvement of lncRNAs in the regulation of gene expression through a variety of mechanisms, including interaction with polycomb repressive complex 2 (PRC2) subunits and modulation of post-transcriptional stages leading to mRNA silencing or degradation and miRNAs inhibition.¹⁸ Little is known about lncRNA profiling in head and neck cancers, especially in the cancer of the larynx. **Table 1** shows the target molecules of the most investigated lncRNAs in head and neck cancers, according to LNCREG Database (<http://bioinformatics.ustc.edu.cn/lncreg/>).

Recently, Chen J et al.¹⁹ examined the significant decrease in expression levels of lncRNA AC008440.10 in patients with advanced laryngeal cancer and the presence of

Table 1. Potential target molecules associated with lncRNA in head and neck cancers

lncRNA	Target
CDKN2B-AS1	ADIPOR1, C11ORF10, VAMP3, CARD8, Klf2, p21
FOXCUT	MMP2, MMP7, MMP9, VEGF, FoxC1
GAS5	miR-21, CDK6, C-myc, ATG7, Beclin, Cyclin D1, E2F1, LC3-II, ADAMTS4, MMP13, MMP2, MMP3, MMP9, p21, p53, PDCD4, PTEN
H19	let-7, miR-141, miR-200a, miR-200b, miR-200c, miR-429, miR-675, N-cadherin, Snail, Twist, Vimentin, Zeb1, Zeb2, Claudin1, E-cadherin, KRT19, KRT8, p53, Bax, IGF2, COL2A1, Lnsr, Lpl, Slug, CDH13, DICER, Hmga2, AKT, CDC25A, GSK3 β
HOTAIR	miR-124, miR-130a, miR-331-3p, β -catenin, Bmi1, CD11b, CD18, CD44, CD82, CD133, E-cadherin, HoxA1, HoxA4, HoxA5, HER2, KRT8, p16, p21, p53, PTEN, QKI, RBM38, SFN, WIF-1, MMP1, MMP2, MMP3, MMP9, MMP13, N-cadherin, Slug, Snail, Twist, VCAN, VEGF, Vimentin, Zeb1, Oct4
HOTTIP	HoxA7, HoxA9, HoxA10, HoxA11, HoxA13
LET	CASP3, BCL2, PCNA, Bax, p21
Linc-ROR	miR-145, miR-181, miR-205, miR-99, E-cadherin, Occludin, Fibronectin, N-cadherin, Vimentin, α -SMA, Zeb1, Zeb2, Nanog, Oct4, Sox2
MALAT1	CCT4, CTHRC1, FHL1, ROD1, SLC26a2, TMEM20, AKT, p38, PI3Kp85 α , β -catenin, CA2, E-cadherin, HNF4G, MIA2, RASSF6, ROBO1, ABCA1, ADAMTS12, AIM1, AKAP9, BMPER, CDCP1, COL6A1, CPM, CSF1, CXCL5, DRD1, GPC6, HMMR, LAYN, LPAR1, LPHN2, LY6K, MCAM, NNMT, PRKCE, Slug, Snail, STC1, Vimentin, Zeb1, Zeb2, ICAM, MMP9, PCNA, TNF- α , VEGF, Fibronectin, LTBP3, N-cadherin, p21
MEG3	CASP3, CASP9, p53, LC3-II, COL1A1, MDM2, α -SMA, CASP8, Dll4, Hes1, Iqgap1, MMP9, Timp1, Vegfa, Vegfr1, Wasl, BCL2, Bax, Cyto c, NF-kB
NEAT-1	HIV-1, ADARB2, EIF4G3, FP15737, OVC10-2, SH3PXD2A, F11R (JAM1)
UCA1	p21, CDKN2B, EP300, TGF-2, WNT6, AKT, CREB, p42, p44, ATM, Fas, PDGFB
XIST	X-chromosome, Atrx, Fgd1, Huwe1

The list of priority targets is compiled using the IncReg database at <http://bioinformatics.ustc.edu.cn/IncReg>.

lymphatic metastases compared to early-stage malignancy, finding a strong correlation between the expression of lncRNA AC008440.10 and tumor progression, the risk of developing metastases and poor prognosis. In addition, the authors disclose the potential of lncRNA AC008440.10 as a prognostic marker in combination with a CT scan of lymphatic metastases, with specificity rising to 100%.¹⁹ In head and neck malignancies, studies show a decreased expression of lncRNA MEG3²⁰, and elevated levels of lncRNA UCA1, which indicates a possible correlation with the presence of metastases in squamous cell carcinoma in tongue.²¹ Increased expression of MIR31HG correlates significantly with an advanced tumor stage and the presence of lymphatic metastases. Head and neck cancers showing lower levels of MIR31HG expression have better overall survival and lack of recurrence, facts that contribute to the proposal of MIR31HG as a potential prognostic biomarker.²² Li et al. have demonstrated that lncRNA HOTAIR (homeobox transcript antisense RNA) is significantly overexpressed in tissue samples from laryngeal cancer and participates in the methylation of the PTEN gene in a laryngeal Hep-

2 cell line.²³ In addition, they were tested in combination with miRNAs. In support of the previous study, Zhou et al. reported the involvement of HOTAIR in chemotherapeutic resistance by activating the levels of epithelium-mesenchymal transit through increasing miR-613 and decreasing levels of the SNAI2 regulatory molecule.²⁴ Wang et al. reported that the serum levels of miR-21 and HOTAIR, isolated from exosomes, were significantly higher in patients with laryngeal cancer compared to those diagnosed with a benign polyp of the voice cords. The combination of both markers successfully distinguishes the two groups of diseases with high sensitivity (94.2%) and specificity (73.5%), which could be used for the prediction of laryngeal malignancy.²⁵

Another lncRNA with elevated expression levels in squamous cell laryngeal cancer is MALAT1, which is also associated with a severe histological type or advanced clinical stage. A significant inhibition of cell proliferation and activation of apoptosis after inhibition of MALAT1 was demonstrated.²⁶ In the study of Chen et al.²⁷ modified expression levels of three highly significant lncRNAs, namely CDKN2B-AS1, HOTAIR and MALAT1 were identified and

confirmed by high-performance real-time PCR. Drastically decreased expression levels of these lncRNAs were shown following chemotherapy with cisplatin and paclitaxel.²⁷ The study suggests their use as prognostic markers.

Another lncRNA associated with the regulation of miRNAs is H19 RNA. In the study of Wu T et al., H19 was shown to be highly regulated in laryngeal cancer and negatively correlates with survival of patients with laryngeal cancer. Reduced levels of lncRNA H19 inhibit cell proliferation, migration and invasion of laryngeal cancer, with miR-148a-3p identified as an H19 target. In combination, both molecules participate in the inhibition of DNMT1 and the decrease in methylation rates in laryngeal cancer.²⁸ Recent research has established the oncogenic role of TUG1 lncRNA, which is positively associated with the tumor and clinical stages as well as the presence of lymphatic metastases. Inhibition of TUG1 levels leads to suppression of proliferation and migration of the Hep-2 cell line.²⁹ In another study, the serum levels of UCA1, a potential non-invasive marker for the diagnosis of laryngeal cancer and its high tissue levels were associated with distant metastases and low survival with poor prognosis. UCA1 promotes proliferation, migration and invasion of the AMC-HN-8 cell line by activating the Wnt/ β -catenin signalling pathway.³⁰

The list of priority targets is compiled using the lncreg database at <http://bioinformatics.ustc.edu.cn/lncreg>

MicroRNAs in laryngeal cancer

With the discovery of the functional role of miRNAs, they have become attractive markers for diagnosis, and prediction for many diseases, including laryngeal cancer.

Evaluation of miRNA expression by microarray technologies demonstrated changes in the expression profile of laryngeal cancer. This approach can be successfully used when comparing miRNAs expression profiles between normal and tumor laryngeal tissue as well as between primary laryngeal lesions and advanced laryngeal carcinoma or recurrent and metastatic tumours. RT-qPCR is often used to validate the microarray results. Recent studies have identified many miRNAs with cancer-specific promoting regulation properties (onco miRNA) or inhibiting regulation (tumor suppressive miRNA). In addition, miRNA expression profiles were analyzed in plasma from squamous cell laryngeal cancer patients and healthy individuals.³¹ **Table 2** presents miRNAs with altered regulation of laryngeal cancer as well as their validated targets and function.

A number of studies have demonstrated the potential therapeutic value of miRNAs. For example, Wang et al. show that miR-1 may affect the growth, migration and invasion by negative regulation of fibronectin 1 (FN1) in a Hep-2 cell line.³² miR-129-5p, which is decreased in primary LSCC, also has adverse effects on cell proliferation and migration and causes cell cycle arrest by targeting APC and modulating STAT3, to induce apoptosis both in vitro in Hep-2 cell lines as well as in vivo. More data

suggest that the growth of LSCC in xenograft models is significantly suppressed by miR-129-5p antisense oligonucleotides (ASO). These results effectively suggest that miR-129-5p can be considered a potential target in the treatment of LSCC.^{33,34} miR-155 has been reported to be significantly more elevated in laryngeal tumor tissues than in mucosal control tissue, its overexpression being positively associated with advanced tumor stage and activation of migration and invasion through the activation of SOCS1 and STAT3. Meanwhile, inhibition of miR-155 inhibits the growth, migration and invasion of Hep-2 cells.³⁵

Zhang et al. report that miR-206 has decreased expression in LSCC tissues and is negatively associated with the progression of T Stage, N Stage, and Clinical Stage. The authors have found that inducing elevated levels of miR-206 leads to dramatic inhibition of proliferation and invasion as apoptotic cell levels rise.³⁶ Similar to miR-206, recent studies have shown that miR-24 has decreased expression in laryngeal cancer and increased by transfection levels inhibit colony formation, increase apoptosis levels and sensitivity to radiotherapy by inhibiting X-linked inhibitor of apoptosis protein (XIAP).³⁷ Guo et al. observed similar results of ectopic miR-24 expression and inhibition of proliferation in cell line by direct targeting of S100A8.³⁸ The obtained results indicate that miR-24 can potentially have a role as a therapeutic target for laryngeal cancer.

The miRNAs that are responding to chemotherapy of laryngeal cancer are miR-31-3p, miR-210, miR-1264 and miR-3150b, which makes them a potential therapeutic target for laryngeal cancer.³⁹ In addition, the expression of miR-30b is significantly reduced in paracancerous tissues compared to malignant laryngeal forms, while overexpression of miR-30b favors p53-mediated cellular apoptosis in vivo and in vitro, thus activating the anti-tumor effect of p53 gene therapy in laryngeal cancer.⁴⁰ Xiao et al.⁴¹ found that miR-93, a clone member miR-106b-25, was significantly deregulated in LSCC. In addition, studies have shown that miR-93 overexpression enhances cell proliferation, migration and invasion, and reduces apoptosis levels, inducing cell cycle arrest by direct targeting of cyclin G2 (CCNG2), a cell cycle progression inhibitor of G1 to S-phase transition. It seems likely that the key role of miR-93 is to suppress several elements of cellular development, which may contribute to the treatment of LSCC.⁴¹

It is worth noting that the expression levels of miR-139 are significantly lower in primary laryngeal tumor formations than in metastatic laryngeal cancer and negatively correlated with the expression of chemokine receptor 4 (CXCR4). It has been concluded that miR-139 inhibits cell proliferation and metastasis of laryngeal cancer by suppressing its target molecule CXCR4.⁴² Another miRNA with tumor suppressor function in laryngeal cancer is miR-203, the expression of which is found to be back-correlated with ASAP1 expression. In addition, the miR-203 transfection results in: inhibition of cell proliferation and invasion; activation of apoptosis; G1 cell cycle arrest of Hep-2 cells in vitro by suppression of ASAP1, a well-

Table 2. Summary of potential miRNA biomarkers in cancer of the Larynx

miRNA	Target	Function	Ref.
let-7a↓	c-MYC, RAS	Affect proliferation, apoptosis and tumour differentiation	46
miR-21↑	BTG2	Inhibition of miR-21 lead to loss of G1-S phase transition and increase apoptosis	47
miR-206↓	VEGF	Inverse correlation between miR-206 expression and T grade, nodal metastasis, and clinical stage	36
miR-145↓	MYCN, FOS, YES, cyclins D2 and L1, MAP3K3 and MAPK4K4	Angiogenesis, cell cycle, proliferation	48
miR-196a↑	HOXB8, HOXC8, HOXD8 and HOXA7, annexin A1	Embryogenesis, organogenesis and oncogenesis promoted cell proliferation, anchorage-independent growth and suppressed apoptosis by targeting annexin A1	49,50
miR-1↓	FN1, ANP32B, CCND2, DDX5, E2F5, EIF4E, GAS2L, MAP4K3, MMD2 and SOX6	Suppress migration and invasion in Hep-2 cell line	32
miR-16↑	zyxin	Migration and adhesion	51
miR-19a↑	TIMP2	Proliferation and apoptosis	52
miR-27a↑	PLK2	Proliferation and inhibition of late apoptosis	53
miR-106b↑	RUNX3	Proliferation and invasion	54
miR-129-5p↑	APC, STAT3	Proliferation and migration, and cell cycle control.	33,34
miR-155↑	SOCS1, STAT3	Hep-2 cells growth, migration and invasion	35
miR-1297↑	PTEN	Proliferation and migration	55
miR-24↓	S100A8	Proliferation and invasion	38
miR-125a↓	HAX-1	Gain-of-function significantly increased the sensitivity of Hep-2 to cisplatin in vitro and in vivo	56
miR-21-5p↑, miR-34c-5p↓ and let-7a↓	Not mentioned	miR-21-5p/let-7a ratio may hold a significant clinical diagnostic potential, let-7a levels may assist in predicting lymph node metastases and miR-34c-5p could prove to be a critical biomarker for patient outcome	57
miR-34a↓	CCND1	Inversely association with advanced stage and nodal status. Overexpression of miR-34a lead to inhibition of proliferation and migration	58
miR-378↑	Not mentioned	Marker in diagnosis and postoperative curative effect of laryngeal cancer	59

Abbreviations in the table: miR: miRNA; microRNA; let-7a: lethal-7a; Ref.: Reference; ↓: underexpression; ↑: overexpression; c-MYC: c-mycproto-oncogene; RAS: retrovirus-associated DNA sequences; BTG2: B-cell translocation gene 2; VEGF: vascular endothelial growth factor; MYCN: v-Myc myelocytomatosis viral related oncogene, neuroblastoma derived (avian); FOS: FBJ murine osteosarcoma viral oncogene homolog; YES: v-yes-1 Yamaguchi sarcoma viral oncogene homolog 1; MAP3K3: mitogen-activated protein kinase kinase 3; MAPK4K4: mitogen-activated protein kinase kinase kinase 4; HOXB8: homeobox protein Hox-B8; HOXC8: homeobox protein Hox-C8; HOXA7: homeobox protein Hox-A7; FN1: fibronectin-1; ANP32B: acidic leucine-rich nuclear phosphoprotein 32 family member B; CCND2: cyclin D2; DDX5: ATP-dependent RNA helicase, DEAD-box protein 5; E2F5: E2F (Transcription Factor Activating Adenovirus E2 Gene) Transcription Factor 5; EIF4E: eukaryotic translation initiation factor 4E; GAS2L: growth arrest specific 2 like 1; SOX6: Sry-related HMG box 6; TIMP2: tissue inhibitor of metalloproteinases 2; PLK2: Polo-Like Kinase 2; RUNX3: runt related transcription factor 3; APC: adenomatous polyposis coli; STAT3: signal transducer and activator of transcription 3; PTEN: phosphatase and tensin homolog deleted on chromosome 10; S100A8: S100 calcium-binding protein A8; HAX-1: HS-1-associated protein X-1; CCND1: cyclin D1

known familial Src oncogene. Validation of cell culture results has also been achieved in animal models, suggesting that the loss of miR-203 function is key to the development of laryngeal cancer.⁴³

The current challenge is to integrate our knowledge and use combinations of miRNAs as biomarkers. A well-established marker with a diagnostic potential for squamous cell laryngeal cancer is the ratio between miR-21 and miR-375, which shows high sensitivity (94%) and specificity (94%).⁴⁴ In a study to identify potential miRNA biomarkers for early diagnosis of laryngeal carcinoma, hsa-miR-657 and hsa-miR-1287, overexpressed and decreased, respectively, show in combination high sensitivity and specificity in differentiating early laryngeal carcinoma.⁴⁵ Investigating changes in plasma miRNA levels in LSCC, Ayaz et al. (2013) found for the first time expression of miR-331-3p, 603, 1303, 660-5p and 212-3p in the plasma of LSCC patients not seen in the plasma of control individuals. They may serve as novel non-invasive biomarkers for the diagnosis of LSCC in patients.³¹

CONCLUSION

ncRNAs have a significant role in the pathological processes of laryngeal carcinogenesis. A number of studies have identified their potential oncogenic or tumour suppressor role in LSCC. The results of the studies help us better understand the pathways of carcinogenesis in LSCC and highlight the potential role of miRNA and lncRNA as biomarkers in the clinical practice. Among the miRNAs and lncRNAs with well-established ectopic ncRNA expression are miR-21, MALAT1 and HOTAIR, the oncogenic role of which has been well studied in a number of cancers, including laryngeal carcinoma. While the modified expression levels of AC008440.10, MIR31HG, MEG3, miR-205, miR-23a and miR-155 have a potential role as biomarkers for disease aggression, lncRNA CDKN2B-AS1, HOTAIR and MALAT1, miR-196a are associated with resistance to treatment. In addition to these possibilities, miR-331-3p, 603, 1303, 660-5p and 212-3p can serve as non-invasive biomarkers in the diagnosis of laryngeal cancer. Despite the expanding available research on laryngeal cancers, the precise role of ncRNAs in oncogenesis of laryngeal carcinoma has not yet been fully elucidated. More extensive research and validation studies are required to provide reliable data and to establish certain ncRNAs as diagnostic and prognostic markers in the clinical practice.

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Роль микроРНК и длинной некодирующей РНК при ларенгиальной плоскоклеточной карциноме - мини обзор

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Абстракт

Ларенгиальная плоскоклеточная карцинома (ЛПК) является распространённым злокачественным заболеванием среди мужчин. Болгария является одной из стран Европы с самой высокой заболеваемостью и смертностью от агрессивной, тяжёлой формы ларенгиального рака. Доказанными этиологическими факторами являются злоупотребление табаком и алкогольными напитками. Несмотря на достижения в области мультимодального медицинского лечения, показатели выживаемости не достигли удовлетворительного уровня. В последние десятилетия данные научных и клинических исследований привели к растущему интересу к изучению потенциальных биомаркеров. Они являются важными ключевыми регуляторами как нормальных, так и опухолевых биологических процессов, а также ответом на факторы окружающей среды и лечения, включая химиотерапию и лучевую терапию. Исследования показали эктопическую экспрессию нескольких нкРНК (ncRNA) при ларенгиальном раке. Опубликованные разработки предоставляют данные о длинных некодирующих РНК (lncRNA) и микроРНК (miRNA), которые могут помочь нам лучше понять сложный канцерогенез ларенгиального рака и обеспечат надёжные диагностические, прогностические и предиктивные биомаркеры.

Ключевые слова

биомаркеры, lncRNA, ларингеальный рак, ЛПК, miRNA
