Mohtasham *et al.*
Egyptian Journal of Medical Human Genetics (2024) 25:77
https://doi.org/10.1186/s43042-024-00531-4

Egyptian Journal of Medical Human Genetics

RESEARCH

Open Access

Serum mir-31-5p is a reliable biomarker in patients with oral squamous cell carcinoma and oral lichen planus

Nooshin Mohtasham[1,2], Zahra Ghorbani[3], Hossein Ayatollahi[4], Fatemeh Arab[5], Seyed Hamid Aghaee-Bakhtiari[6], Bashir Rasoulian[7] and Farnaz Mohajertehran[3*]

Abstract

Background MicroRNAs have been proposed as a novel regulatory biomarker for gene expression and early diagnosis of cancers. In this study, we evaluate the expression level of miR-31-5p in the serum of patients with oral squamous cell carcinoma, oral lichen planus, and a healthy control group to obtain a primary diagnostic biomarker.

Materials and methods Serum was collected from patients with oral lichen planus ($n=32$), patients with oral squamous cell carcinoma ($n=35$), and healthy subjects ($n=32$). MicroRNA was isolated from serum and cDNA was made from it. Then, the quantitative and qualitative expression of miR-31-5p levels among the samples was checked by the qRT-PCR method.

Results In this study, three groups were quantitatively and qualitatively analyzed for miR-31-5p expression in serum. The results showed that there was a statistically significant correlation between the mean quantitative and qualitative expression of miR-31-5p among the three groups ($P<0.05$).

Conclusions The expression of miR-31-5p was significantly higher in patients with oral squamous cell carcinoma and oral lichen planus compared with healthy controls. MiR-31-5p can be considered as a biomarker in serum that could be potentially reliable in the diagnosis and prognosis of oral squamous cell carcinoma and also in the transformation of lichen planus.

Keywords Serum microRNA, Oral squamous cell carcinoma, Oral lichen planus, qRT-PCR

*Correspondence:
Farnaz Mohajertehran
mohajertf@mums.ac.ir
[1] Oral and Maxillofacial Diseases Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
[2] Department of Oral and Maxillofacial Pathology, School of Dentistry, Mashhad University of Medical Sciences, Azadi Sq., Mashhad, Iran
[3] Dental Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
[4] Cancer Molecular Pathology Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[5] Department of Medical Genetics and Molecular Medicine, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[6] Department of Medical Biotechnology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[7] Sinus and Surgical Endoscopic Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Introduction

Determining serum biomarkers is considered a valuable method for diagnosis, setting treatment goals, and making prognosis assessments for various types of tumors. The concentration of serum biomarkers changes during tumor formation and development. These biomarkers can be proteins, nucleic acid, or metabolites. These markers can inform the prognosis, recurrence, or metastasis of a tumor because the growth of malignant tumors changes their concentration [1, 2]. Using a serum is easier, cheaper, and more acceptable to patients than a biopsy. However, the use of serum biomarkers for various types of cancers still requires further studies [3, 4]. One of these biomarkers is miRNA, which is a single-stranded

Springer Open

© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

non-coding RNA and plays a role in various physiological processes such as cell growth and division, differentiation, cell aging, apoptosis, stress and immune response, and carcinogenic processes [3–7]. MiRNAs are secreted in different body fluids such as saliva, serum, and urine [3]. The expression of miRNA in some tumors changes significantly compared to healthy tissue, and in addition, it has been determined that there is a specific type of miRNA for each type of cancer [5, 8]. Dysregulation of some miRNAs such as miR-138, miR-99a, miR-21, miR-375, miR-181a, miR-24, miR-222, and miR-7 has been implicated in the progression and metastasis of head and neck cancer and oral squamous cell carcinoma [3, 6, 9]. One of these miRNAs is miR-31-5p, whose gene is located in the p21.39 regions. Its function includes increasing cell migration and increasing the power of tumor invasion. New evidence has shown that miR-31-5p is upregulated in various neoplasms including OSCC and acts as an oncogenic miRNA, and high expression of miR-31-5p is associated with a poor overall survival rate [10] and that miR-31-5p can act as a useful biomarker for examining clinical prognosis [11, 12]. Regarding oral lichen planus (OLP), several miRNAs, including miR125, miR137, miR147a, miR155, miR181, and miR223, have been investigated and have been associated with the pathogenesis and malignant changes of OLP through their tissue expression and function [13]. Therefore, considering that OSCC is a malignant lesion and OLP is a premalignant lesion, a quick and timely diagnosis of OSCC and OLP is very useful for the effective treatment of this disease. In this study, we decided to evaluate the expression level of miR-31-5p in the serum of patients with OSCC, OLP, and a healthy control group to achieve a primary diagnostic biomarker.

Materials and methods

Study *subjects and serum sample collection*

The study was approved by the Department of Research Council of Mashhad University of Medical Sciences, Faculty of Dentistry, Mashhad, Iran (No. 991557), and by the Ethics Committee of Mashhad University of Medical Sciences [IR.MUMS.DENTISTRY.REC. 1399.165]. All participating subjects provided signed informed consent. The total sample size for the study was 99 participants in three groups: OLP ($n=32$), OSCC ($n=35$), and a healthy control group ($n=32$).

Inclusion and exclusion criteria

Healthy control subjects had no history of malignant, inflammatory, or systemic disease. Also, they were similar to the patient groups in age and sex. Eligible patients had not received anti-tumor therapy whose disease was confirmed by biopsy; their samples had the quality to perform real-time PCR tests; and they had no other history of malignancy. Participants with a history of other malignancies and an unwillingness to cooperate to continue the project, as well as samples that were not of the required quality, were excluded from the study.

Serum processing and RNA isolation

In this study, miRNAs were manually extracted from serum samples with high quality and purity, which was one of the most important achievements of this study. The procedure was as follows: 400–450 µl of each sample was collected in a 1.5-ml microtube and 800 µl of RNX-plus (SinaClon, Iran) was added to it, and the samples vortexed for 15 s to homogenize and then were placed at room temperature for 3–4 min. 250 µl of chloroform was added to each microtube and shaken by hand for 15 s, incubated for 3–5 min at room temperature, and then centrifuged for 20 min (12,000 RPM, 4 °C). About 500 µl of supernatant was carefully transferred to new 1.5-ml DNase and RNase-free microtubes. Then, for RNA precipitation, 500 µl of isopropanol (Merck Co.) was added to each tube. The microtubes were gently covered and incubated overnight at − 20 °C. After the incubation period, the samples were centrifuged for 45 min (12,000 RPM, 4 °C) and supernatant was removed, and the RNA pellet was washed with 1 ml of cold 80% ethanol and centrifuged for 20 s (12,000 RPM, 4 °C). This step was done twice. Then, the pellet was dissolved in 20 µl of DEPC water and incubated for 5 min at room temperature. To determine the quantity and purity of the extracted miRNAs, NanoDrop 2000c (Thermo Scientific 2000, USA) was used based on absorbance ratio of 260/280 nm. RNAs with sufficient quantity (50 mg/µl) and purity (ratio 2–1.5) were used for the synthesis of complementary DNA (cDNA).

Reverse transcription

An Adscriptc DNA synthesis kit (REF: 22,701, Bio-Tech, Addbio, Korea) was used to synthesize cDNA using an ABI thermocycler (One Step, USA) in a final volume of 20 µl containing 10 µl of 2X reaction buffer, 2 µl of 10 mM dNTP mixture, 6 µl of RNA, 1 µl of RT primer (1 pM) for U6 or miR 31 5p, and 1 µl of 20X enzyme. Reverse transcription (RT) was performed using a temperature cycle procedure that included preincubation at 25 °C for 10 min, RT at 50 °C for 60 min, RT inactivation at 80 °C for 5 min, and holding at 12 °C.

Real-time PCR (qPCR)

The qPCR was performed to examine relative expression of miR-31-5p compared with U6 as a reference gene using SYBR Green method. The following primers were used: miR-31-5p forward, 5′-GAGGCAAGATGCTGGC-3′

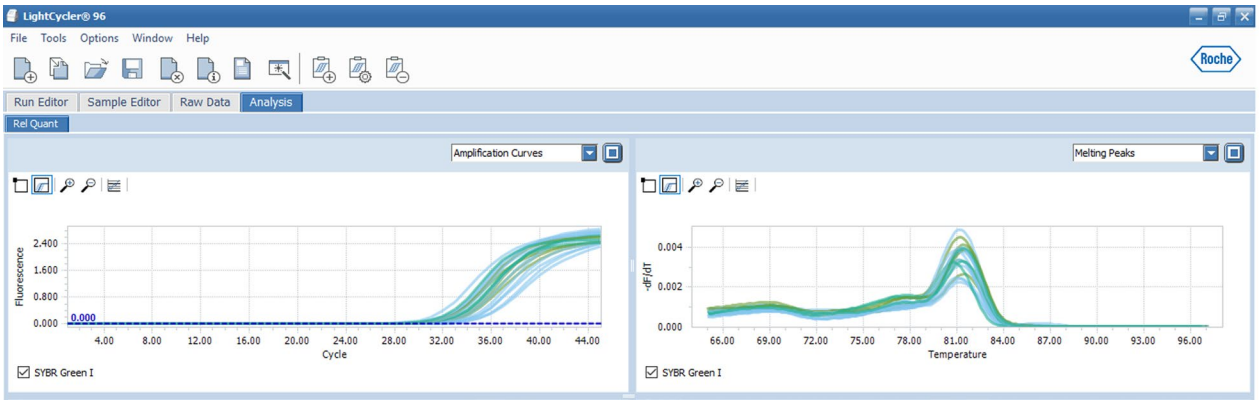

Fig. 1 The melting curve (right) and amplification plot (left) of miR-31-5p and U6 expressions in real-time PCR

and reverse, 5′-GTCGTATGCAGAGCAGGGTCCGAG GTATTCGCACTGCATACGACAAAATATGG-3′; U6 forward, 5′-AAGGATGACACGCAAATTC-3' and reverse, 5′-GTCGTATGCAGAGCAGGGTCCGAGGTA TTCGCACTGCATACGACAAAATATGG-3′. All reactions were carried out in duplicate in separate wells of 20 µl total volume. 0.5 µl of each primer (10 pM), 10 µl of SYBR Green master mix (XX) (SMOBIO, Taiwan), 7 µl of distilled sterile water, and 2 µl of cDNA were used in each reaction. Following a preincubation phase at 95 °C for 30 s, 50 cycles at 95 °C for 5 s for denaturation, and 60 °C for 30 s for annealing were performed using the Light Cycler 96 (Roche, Germany). The ΔΔCT technique was utilized to examine relative expression of qPCR data. Additionally, we examined the melting curve to verify precise target amplification (Fig. 1).

Analytical statistics

SPSS software was used for all data analysis (version 25). The relative miRNA expression level was computed as $2^{-\Delta\Delta CT}$, which is a frequently used measure of miRNA expression after the data had been normalized by the threshold cycle number ΔCt. A *P* value less than 0.05 was considered significant.

Results

Characteristics of study subjects

In this study, miR-31-5p expression was evaluated in the serum of 35 OSCC, 32 OLP patients, and 32 healthy controls. A total of 99 individuals were studied, including 51 women (51.5%) and 48 men (48.5%). Age and sex values of the study groups and the control group were compared, and differences were not statistically significant ($P > 0.05$). The results showed that the expression level of miRNA-32-5p in the study groups was higher than that in the control group, and the differences were statistically significant (Table 1 and Fig. 2). The increase in the expression of miRNA-31-5p qualitatively and quantitatively in the OSCC group was significant compared to the other two groups. However, the expression of miRNA-31-5P in OSCC and OLP groups was not significantly different from each other.

Table 1 Comparison of the expression levels of miR-31-5p between the study groups

Groups	Numbers	Mean ± SD	*P* value
miR-31-5p expression			
Control	32	0.74 ± 0.74	$P < 0.0001$
OLP	32	2.71 ± 2.15	
OSCC	35	4.40 ± 3.62	
Total	99	2.67 ± 2.91	

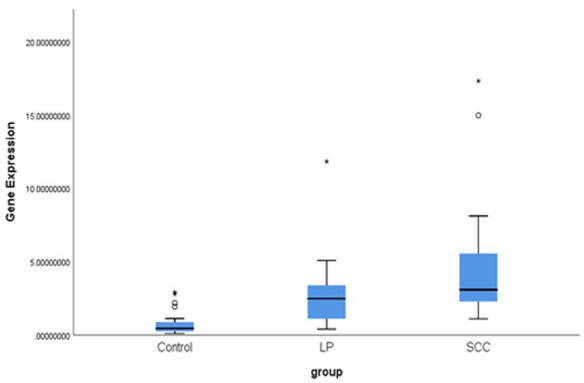

Fig. 2 Expression level of miRNA-32-5p in the study groups

Multiple comparisons of miR-31-5p expression in study groups

The Kruskal–Wallis test was performed to determine which specific group rejected the null hypothesis.

Table 2 Multiple comparisons of miR-31-5p expression in study groups

Group (I)	Group (J)	*P* value	Adj. *P* value[a]
OSCC	OLP	< 0.0001	< 0.0001
	Healthy control	< 0.0001	< 0.0001
OLP	Healthy control	0.056	0.169

Table 3 Comparison of miR-31-5p quantitative expression in OSCC group (by grades) and control

Groups	Numbers	Mean ± SD	
miR-31-5p expression			
Control	32	0.74 ± 0.74	*P* < 0.0001
I	14	3.08 ± 1.49	
II	16	5.20 ± 4.80	
III	5	5.52 ± 2.70	

According to this test, the OSCC group showed statistically significant differences from other groups ($P < 0.05$) (Table 2).

Comparison of miR-31-5p expression in the OSCC group based on grades and stages

The statistical analysis by Fisher's exact test showed differences between grades I, II, and III in OSCC patients ($P < 0.05$). The quantitative expression of miR-31-5p in grade III was higher than in grades II and I (Table 3). The average qualitative expression of miRNA-31-5P in grades I, II, and III was 3.08 ± 1.49, 5.20 ± 4.80, and 5.52 ± 2.70, respectively (Table 4). Our findings revealed a significant difference between OSCC stages ($P < 0.05$). The mean quantitative expression of miR-31-5p in the early stage was 2.49 ± 1.02, and in the advanced stage, it was 6.67 ± 4.27. The mean expression of miR-31-5p in early-stage patients was higher than in advanced-stage patients (Fig. 3).

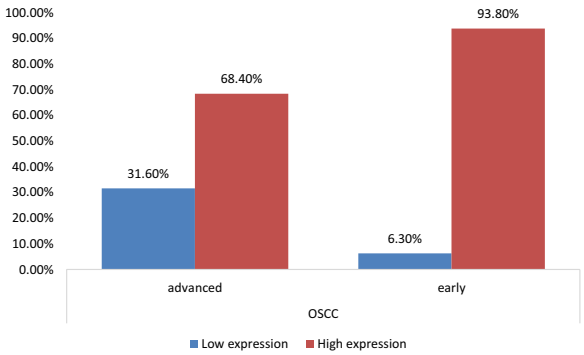

Fig. 3 Quantitative expression of miR-31-5p in OSCC patients based on stages

Comparison of miRNA-31-5P quantitative expression in the OSCC group (by tumor size)

In Table 5, it can be seen that the average quantitative expression of miRNA-31-5P in CM2 tumor size was 3.11 ± 1.7, and in CM2 tumor size it was 5.01 ± 7.23. The average expression of miRNA-31-5P in patients with tumor sizes greater than 2 cm was significantly higher than the average expression of the gene in patients with tumor sizes less than 2 cm (*P* 0.05).

Comparison of miRNA-31-5P quantitative expression in the OSCC group at the levels of lymph node involvement

In Table 5, it can be seen that the quantitative expression ranges of the miRNA-31-5P gene related to level two are greater than level one and zero and this difference was significant ($P < 0.05$).

Discussion

Human body tissues and fluids are a rich source of biomarkers that are used in clinical diagnosis. Many researchers have shown that microRNAs can be used as non-invasive markers for diagnosis and prognosis. Studies conducted on cancer cells and laboratory animals show that the dysregulation of miRNAs in their primary form or by suppressing a miRNA can effectively play a role in tumorigenesis or tumor progression [14,

Table 4 Qualitative expression of miR-31-5p in OSCC group (by grades)

Group		Qualitative expression of miR-31-5p		Total	Fisher's Exact test
		high expression	Low expression		*P* value
I	Frequency (%)	10 (71.4)	4 (28.6)	14	< 0.0001
II	Frequency (%)	13 (81.3)	3 (18.8)	16	
III	Frequency (%)	5 (100.0)	0 (0.0)	5	
Control	Frequency (%)	3 (9.4)	29 (90.6)	32	
Total	Frequency (%)	31 (3.46)	36 (7.53)	67	

Table 5 Comparison of miRNA-31-5p quantitative expression in OSCC group at the levels of lymph node involvement and tumor size

	Numbers	Mean ± SD	*P* value	Mann–Whitney test
miR-31-5p expression				
Lymph node involvement				
0	23	3.08 ± 1.70	< 0.0001	–
1	8	4.59 ± 2.54		
2	4	11.64 ± 5.35		
Total	35	4.40 ± 3.62		
Tumor size				
< 2 cm	24	3.11 ± 1.70	0.007	Z = – 2.684
> 2 cm	11	7.23 ± 5.01		

15]. Therefore, today, early diagnosis based on serum biomarker analysis, such as miRNAs, is one of the most important perspectives of modern medicine, which will be effective for screening, early diagnosis, treatment, and prognosis of these patients with oral malignancies. Oral cancer is one of the most common cancers in the world [16, 17]. Epidemiological studies show that the prevalence of oral cancer is different in different parts of the world, and its frequency varies from below 0.1% to above 40%. OSCC is the most common head and neck malignancy and has a poor survival rate. Its 5-year survival rate is 80% when it is detected in the early stages (T1), and it is remarkably low and reaches 20–40% if it is detected in the late stages (T3–T4) [18]. Therefore, the use of miRNA as a biomarker in serum is a fast, non-invasive, and accessible method for the early identification and diagnosis of patients [19]. We investigated the expression of miR-31-5p in three groups: OSCC and OLP patients, as well as healthy individuals. For the first time, we compared serum miR-31-5p expression in patients with pre-malignant and malignant lesions with healthy controls. This is also the first study of miR-31-5p expression in OLP patients. We report significant up-regulation of miR-31-5p in the serum samples of OSCC and OLP patients. The results of our study showed that 80% of OSCC patients and 62.5% of OLP patients demonstrated high expression of miR-31-5p, while the control group exhibited 90.6% lower expressions. So, the levels of miR-31-5p expression in serum revealed significant sensitivity and specificity to differentiate between OSCC, OLP patients, and healthy controls. It was so significant in OSCC patients compared to the OLP and health control groups. The average quantitative expression of miRNA-31-5P in the early stage was significantly higher than in the advanced stage in OSCC patients ($P < 0.05$). The average expression of miRNA-31-5P in tumor size, lymph node involvement, and TNM levels in OSCC patients had a significant difference ($P < 0.05$). Scholtz et al. [20] showed that the expression of miR-31-5p can be a suitable biomarker for the prognosis and diagnosis of OSCC. Lu et al. [3] evaluated the expression of miR-31-5p in serum, in healthy individuals and patients with oral cancer. Their results also showed that miR-31-5p expression is a biomarker and therapeutic target for the development of diagnosis in patients with OSCC. Lai et al. [21] demonstrated that increasing miR-31-5p levels was effective in the treatment and migration of cancer cells in OSCC patients. Previous studies suggested that miR-31-5p can be used as a novel biomarker for predicting the development and prognosis of colorectal cancer [22–24] and that high miR-31-5p expression promotes colon adenocarcinoma progression [25]. Furthermore, our experiment was consistent with previous findings. In this study, we also examined the expression of miR-31-5p in OLP patients, which was higher than in healthy controls. Based on our searches in different databases, there are no studies for the evaluation of miR-let-7a-5p as a biomarker during precancerous changes of OLP. Therefore, we are reporting novel biomarkers (miR-31-5p) in serum that we have identified to find lesions with malignant transformation potential.

Conclusion

Due to the novelty of the subject and the technical problems and difficulties regarding the study of microRNAs in patients' serum, very few studies have been conducted in this field. According to the searches conducted in reliable databases, the present study is the first study that investigated the expression of miRNA-31-5p in three groups: OSCC, OLP, and a healthy control group. According to the results of the present study, it is recommended that this microRNA be considered a target for future therapeutic strategies and an effective biomarker.

Acknowledgements

All authors thank the Department of the Research Council of Mashhad University of Medical Sciences, Faculty of Dentistry.

Author contributions

FM and NM made the design of the work, supervised and supported this study, and quality control of data and algorithms. FM made substantial contributions to the conception. NM and ZG and HA carried out the research, collected the data for this study and performed the data extraction, management, and interpretation of the results and draft of this paper, and contributed to writing the manuscript. FA and SHAB and BR helped in the interpretation and article editing. All the authors have read and approved the final manuscript.

Funding

The Department of the Research Council of Mashhad University of Medical Sciences, Faculty of Dentistry, supported the project financially (Grant number: 4001578). The data that support the findings of this study are available from [Dr. Farnaz Mohajertehran] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not

publicly available. Data are, however, available from the authors upon reasonable request and with permission of [Dr. Farnaz Mohajertehran].

Availability of data and material
The data supporting this study's findings are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Department of Research Council of Mashhad University of Medical Sciences, Faculty of Dentistry, Mashhad, Iran (No. 991557), and by the Ethics Committee of Mashhad University of Medical Sciences [IR.MUMS.DENTISTRY.REC. 1399.165]. All participating subjects provided signed informed consent. This article does not contain any studies with animals performed by any of the authors.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 10 April 2023 Accepted: 6 May 2024
Published online: 05 July 2024

References

1. Voiculescu V, Calenic B, Ghita M, Lupu M, Caruntu A, Moraru L, et al. (2016) From normal skin to squamous cell carcinoma: a quest for novel biomarkers. Dis Markers
2. Fernández-Olavarría A, Mosquera-Pérez R, Díaz-Sánchez R-M, Serrera-Figallo M-A, Gutiérrez-Pérez J-L, Torres-Lagares D (2016) The role of serum biomarkers in the diagnosis and prognosis of oral cancer: a systematic review. J Clin Exp Dent 8(2):e184
3. Lu Z, He Q, Liang J, Li W, Su Q, Chen Z et al (2019) miR-31-5p is a potential circulating biomarker and therapeutic target for oral cancer. Mol Ther Nucl Acids 16:471–480
4. Al Rawi N, Elmabrouk N, Kou RA, Mkadmi S, Rizvi Z, Hamdoon Z (2021) The role of differentially expressed salivary microRNA in oral squamous cell carcinoma. A systematic review. Arch Oral Biol 125:105108
5. Piotrowski I, Zhu X, Saccon TD, Ashiqueali S, Schneider A, de Carvalho-Nunes AD et al (2021) miRNAs as biomarkers for diagnosing and predicting survival of head and neck squamous cell carcinoma patients. Cancers 13(16):3980
6. Cristaldi M, Mauceri R, Di Fede O, Giuliana G, Campisi G, Panzarella V (2019) Salivary biomarkers for oral squamous cell carcinoma diagnosis and follow-up: current status and perspectives. Front Physiol 10:1476
7. Troiano G, Mastrangelo F, Caponio V, Laino L, Cirillo N, Lo ML (2018) Predictive prognostic value of tissue-based microRNA expression in oral squamous cell carcinoma: a systematic review and meta-analysis. J Dent Res 97(7):759–766
8. Fadhil RS, Wei MQ, Nikolarakos D, Good D, Nair RG (2020) Salivary microRNA miR-let-7a-5p and miR-3928 could be used as potential diagnostic bio-markers for head and neck squamous cell carcinoma. PLoS ONE 15(3):e0221779
9. Libório-Kimura TN, Jung HM, Chan EK (2015) miR-494 represses HOXA10 expression and inhibits cell proliferation in oral cancer. Oral Oncol 51(2):151–157
10. Liu C-J, Tsai M-M, Hung P-S, Kao S-Y, Liu T-Y, Wu K-J et al (2010) miR-31 ablates expression of the HIF regulatory factor FIH to activate the HIF pathway in head and neck carcinoma. Can Res 70(4):1635–1644
11. Wang S, Hu J, Zhang D, Li J, Fei Q, Sun Y (2014) Prognostic role of microRNA-31 in various cancers: a meta-analysis. Tumor Biol 35(11):11639–11645
12. Ma Y, Chen Y, Lin J, Liu Y, Luo K, Cao Y et al (2017) Circulating miR-31 as an effective biomarker for detection and prognosis of human cancer: a meta-analysis. Oncotarget 8(17):28660
13. Aghbari SM, Zayed SO, Shaker OG, Abushouk AI (2019) Evaluating the role of tissue micro RNA-27b as a diagnostic marker for oral lichen planus and possible correlation with CD 8. J Oral Pathol Med 48(1):68–73
14. Alles J, Fehlmann T, Fischer U, Backes C, Galata V, Minet M et al (2019) An estimate of the total number of true human miRNAs. Nucl Acids Res 47(7):3353–3364
15. Ma Y, Shen N, Wicha MS, Luo M (2021) The roles of the Let-7 family of microRNAs in the regulation of cancer stemness. Cells 10(9):2415
16. Roush S, Slack FJ (2008) The let-7 family of microRNAs. Trends Cell Biol 18(10):505–516
17. Balzeau J, Menezes MR, Cao S, Hagan JP (2017) The LIN28/let-7 pathway in cancer. Front Genet 8:31
18. Liu C, Chen Z, Fang M, Qiao Y (2019) MicroRNA let-7a inhibits proliferation of breast cancer cell by downregulating USP32 expression. Transl Cancer Res 8(5):1763
19. Luo M, Clouthier SG, Deol Y, Liu S, Nagrath S, Azizi E, et al. (2015) Breast cancer stem cells: current advances and clinical implications. Mammary Stem Cells. 1–49
20. Scholtz B, Horváth J, Tar I, Kiss C, Márton IJ (2022) Salivary miR-31-5p, miR-345-3p, and miR-424-3p are reliable biomarkers in patients with oral squamous cell carcinoma. Pathogens 11(2):229
21. Lai Y-H, Liu H, Chiang W-F, Chen T-W, Chu LJ, Yu J-S et al (2018) MiR-31-5p-ACOX1 axis enhances tumorigenic fitness in oral squamous cell carcinoma via the promigratory prostaglandin E2. Theranostics 8(2):486
22. Liu C, Wu W, Chang W, Wu R, Sun X, Wu H et al (2022) miR-31-5p-DMD axis as a novel biomarker for predicting the development and prognosis of sporadic early-onset colorectal cancer. Oncol Lett 23(5):1–13
23. Peng H, Wang L, Su Q, Yi K, Du J, Wang Z (2019) MiR-31-5p promotes the cell growth, migration and invasion of colorectal cancer cells by targeting NUMB. Biomed Pharmacother 109:208–216
24. Kim SB, Zhang L, Barron S, Shay JW (2014) Inhibition of microRNA-31-5p protects human colonic epithelial cells against ionizing radiation. Life Sci Space Res 1:67–73
25. Mi B, Li Q, Li T, Liu G, Sai J (2020) High miR-31-5p expression promotes colon adenocarcinoma progression by targeting TNS1. Aging (Albany NY) 12(8):7480

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.