in vivo *38*: 1448-1450 (2024)
doi:10.21873/invivo.13588

Letter to the Editor

Elevating Precision Oncology: Unraveling the Role of microRNA Analysis in the Comprehensive Staging of Oral Cavity Carcinoma

MARCEL EBELING[1,2*], MARIO SCHEURER[1*], SEBASTIAN PIETZKA[1,2], SPYRIDOULA DERKA[3], GEORGIA VAIRAKTARI[3], ALEXANDER SCHRAMM[1,2], FRANK WILDE[1,2] and ANDREAS SAKKAS[1,2]

[1]*Department of Oral and Plastic Maxillofacial Surgery, Military Hospital Ulm, Academic Hospital of the University of Ulm, Ulm, Germany;*
[2]*Department of Oral and Plastic Maxillofacial Surgery, University of Ulm, Ulm, Germany;*
[3]*Department of Oral and Maxillofacial Surgery, Attikon General University Hospital of Athens, Chaidari, Greece*

This letter emphasizes the potential of microRNA (miRNA) analysis in the staging of oral cavity carcinoma. It highlights the role of miRNA analysis in predicting critical aspects, such as lymphonodular recurrence, preoperative tumor grading, perineural invasion, angiolymphatic invasion, and extracapsular nodal spread of metastasis. The intricate landscape of miRNAs and their significance in refining our understanding of cancer is discussed, and examples of specific miRNAs implicated in each dimension are provided. The convenience and less invasive nature of miRNA profiling through saliva samples will also be highlighted. This could pave the way for a paradigm shift in staging procedures and personalized cancer care.

Oral cavity carcinoma, which includes various subtypes and significantly impacts patients' quality of life, requires a precise staging approach for optimal therapeutic decision-making. Traditional staging methods, based on clinical and histopathological parameters, provide a fundamental understanding. However, miRNA analysis is emerging as a powerful tool that can enhance our understanding of the disease's complexities and contribute to precision oncology.

Predicting Lymphonodular Recurrence: miRNA as a Prognostic Indicator

miRNA analysis can provide valuable prognostic insights for predicting lymphonodular recurrence. Specific miRNA signatures have demonstrated correlations with the likelihood of nodal involvement, offering a predictive tool for assessing the risk of recurrence.

For instance, miR-155 and miR-99a-5p have been identified as a significant factor in lymph node metastasis and recurrence in oral cavity carcinoma (1, 2). High levels of miR-155 and miR-99a-5p have been associated with an increased risk of nodal metastasis, indicating its potential as a biomarker for identifying patients at higher risk. By including miR-155 and miR-99a-5p analysis in the staging process, clinicians can obtain valuable information to customize surveillance strategies and implement targeted interventions for patients with a higher probability of recurrence.

Preoperative Tumor Grading: miRNA as a Molecular Stratifier

Preoperative tumor grading is a crucial aspect of staging precision, and miRNA analysis can contribute to this. Certain miRNAs have shown associations with the aggressiveness and differentiation of oral cavity carcinoma tumours.

For example, miR-26b (3), miR-137 (4) and miR-195-5p (5), all well-studied miRNA in cancer research, have been correlated with advanced tumor stages and poorer differentiation in oral cavity carcinoma when its levels are elevated. Integrating miR-26b, miR-137 and miR-195-5p (5) profiling into preoperative assessments allows clinicians to comprehensively understand the biological behavior of the

*These Authors contributed equally to this study.

Correspondence to: Dr. Marcel Ebeling, University Hospital Ulm, Albert-Einstein-Allee 11, 89081 Ulm, Germany. Tel: +49 0731 1710 35806, e-mail: mrclebeling@gmail.com

Key Words: miRNA, staging, oral cavity carcinoma.

tumor. This molecular insight helps in surgical planning and may influence the extent of resection required, contributing to a more tailored and effective therapeutic approach.

Perineural Invasion and Angiolymphatic Invasion: Implications for Survival and Therapeutic Strategies

Assessing perineural invasion and angiolymphatic invasion is crucial in determining the aggressiveness of oral cavity carcinoma. Certain miRNAs regulate genes involved in these invasion processes, affecting both survival prognosis and treatment strategies.

For instance, reduced expression of miR-205 has been linked to increased perineural invasion and angiolymphatic invasion, which may result in the spread of cancer cells through blood vessels. Profiling miR-205 levels can provide insights into the tumor's potential to invade blood vessels, which can affect both prognosis and therapeutic planning. Integrating miR-205 analysis into the staging process provides a more comprehensive understanding of the tumor microenvironment, which can impact therapeutic decisions aimed at reducing nerve infiltration (6).

Extracapsular Nodal Spread of Metastasis: miRNA as a Prognostic Indicator

Extracapsular nodal spread of metastasis is a crucial factor in determining the prognosis of oral cavity carcinoma. Certain miRNAs have been linked to the probability of extracapsular spread, which could serve as a biomarker for predicting nodal involvement beyond the primary tumor capsule.

For instance, miR-375, a miRNA with tumor-suppressive properties, has shown promise in this regard. Reduced expression of miR-375 has been associated with an increased risk of extracapsular spread and poorer prognosis in patients with oral cavity carcinoma. Profiling miR-375 levels helps to refine nodal staging, providing valuable prognostic information and informing decisions regarding the intensity of adjuvant therapies (7).

Convenience and Less Invasiveness of Saliva-based miRNA Profiling

miRNA analysis is essential for refining staging procedures. A significant breakthrough in this analysis is the mode of sample collection. Saliva samples can be used for miRNA profiling, providing a less invasive and more patient-friendly alternative to traditional biopsy methods.

Saliva-based miRNA analysis is a convenient and fast alternative that aligns with patient-centric care principles. This approach not only reduces discomfort for patients but also expedites the diagnostic process. Saliva samples are increasingly used for miRNA profiling as a reliable and minimally invasive method for molecular characterization of oral cavity carcinoma (8, 9).

Conclusion: Toward a Future of Precision Oncology

In conclusion, miRNA analysis is a crucial aspect of comprehensive oral cavity carcinoma staging. It influences predictions of lymphonodular recurrence, preoperative tumor grading, nerve and vascular invasion, and extracapsular nodal spread of metastasis. The examples highlighted underscore the transformative potential of miRNA analysis, offering a multidimensional view of the disease and paving the way for more personalized and effective cancer care.

As we progress towards a future of precision oncology, the integration of miRNA profiling through saliva samples represents a significant change in staging procedures. This alternative is less invasive and patient-friendly, aligning with the principles of patient-centric care. It provides a comprehensive molecular snapshot of the tumor's characteristics. The potential impact of miRNA analysis is significant, as it offers new opportunities for personalized cancer care and optimized therapeutic strategies.

Conflicts of Interest

The Authors declare that no funds, grants, or other support were received during the preparation of this manuscript. The Authors have no relevant financial or non-financial interests to disclose.

Authors' Contributions

All Authors contributed to the manuscript conception and design. Material preparation, data collection and analysis were performed by Marcel Ebeling, Mario Scheurer and Andreas Sakkas. The first draft of the manuscript was written by Marcel Ebeling and Mario Scheurer, and all Authors commented on previous versions of the manuscript. All Authors read and approved the final manuscript. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1 Baba O, Hasegawa S, Nagai H, Uchida F, Yamatoji M, Kanno NI, Yamagata K, Sakai S, Yanagawa T, Bukawa H: MicroRNA-155-5p is associated with oral squamous cell carcinoma metastasis and poor prognosis. J Oral Pathol Med 45(4): 248-255, 2016. DOI: 10.1111/jop.12351

2 Cousseau CPV, Sorroche BP, De Jesus Teixeira R, De Carvalho AC, Melendez ME, De Castro Capuzzo R, Laus AC, Da Silva LS, De Menezes NS, Carvalho AL, Arantes LMRB: miR-99a-5p as a biomarker for lymph node metastasis prediction in oral squamous cell carcinoma patients. Head Neck 45(10): 2489-2497, 2023. DOI: 10.1002/hed.27459

3 Cao J, Guo T, Dong Q, Zhang J, Li Y: miR-26b is downregulated in human tongue squamous cell carcinoma and

regulates cell proliferation and metastasis through a COX-2-dependent mechanism. Oncol Rep 33(2): 974-980, 2015. DOI: 10.3892/or.2014.3648

4 Sun C, Li J: Expression of MiRNA-137 in oral squamous cell carcinoma and its clinical significance. J BUON 23: 167-172, 2018.

5 Wang T, Ren Y, Liu R, Ma J, Shi Y, Zhang L, Bu R: miR-195-5p suppresses the proliferation, migration, and invasion of oral squamous cell carcinoma by targeting TRIM14. Biomed Res Int 2017: 7378148, 2017. DOI: 10.1155/2017/7378148

6 Kolenda T, Guglas K, Teresiak A, Bliźniak R, Lamperska K: Low let-7d and high miR-205 expression levels positively influence HNSCC patient outcome. J Biomed Sci 26(1): 17, 2019. DOI: 10.1186/s12929-019-0511-3

7 Wang P, Xu L, Li L, Ren S, Tang J, Zhang M, Xu M: The microRNA-375 as a potentially promising biomarker to predict the prognosis of patients with head and neck or esophageal squamous cell carcinoma: a meta-analysis. Eur Arch Otorhinolaryngol 276(4): 957-968, 2019. DOI: 10.1007/s00405-019-05325-8

8 Liu C, Lin S, Yang C, Cheng H, Chang K: Exploiting salivary miR-31 as a clinical biomarker of oral squamous cell carcinoma. Head Neck 34(2): 219-224, 2012. DOI: 10.1002/hed.21713

9 Zahran F, Ghalwash D, Shaker O, Al-Johani K, Scully C: Salivary microRNAs in oral cancer. Oral Dis 21(6): 739-747, 2015. DOI: 10.1111/odi.12340

Received January 17, 2024
Revised February 8, 2024
Accepted February 9, 2024