miRNA and Nasopharyngeal Carcinoma: Function, Regulatory Mechanism and Research Progress

Haoyang Gui
School of Life and Science, Fujian Agriculture and Forestry University, Fuzhou, Fujian, China

Keywords: miRNA, Nasopharyngeal Carcinoma, Regulatory Mechanisms.

Abstract: Nasopharyngeal carcinoma (NPC) is a common malignant tumor in East and Southeast Asia. In this review, it was discovered that miRNAs play a diverse role in the pathogenesis, biomarkers, and treatment strategies of NPC. However, the complex regulatory mechanisms of miRNAs in NPC have not been fully elucidated. This review investigates the potential use of circulating miRNAs as indicators of NPC and looks at how miRNAs affect the biological traits of NPC cells by controlling the Hippo and TGFβ/SMAD signalling pathways, which offers a fresh viewpoint for identifying and treating NPC. These results show the wide potential of miRNA therapy in conjunction with conventional therapy and serve as a guide for future studies and treatments of miRNA in NPC. However, the specific mechanism of miRNA in NPC still needs to be further explored. To support the development of precision treatment for NPC, future studies should concentrate on the relationship between miRNA and target genes as well as the impact of the tumour microenvironment.

1 INTRODUCTION

The common head and neck cancer known as nasopharyngeal carcinoma (NPC) is caused by malignant lesions of nasopharyngeal epithelial cells, mainly squamous cell carcinoma. According to the World Health Organization, around 120,000 people are diagnosed every year worldwide, with the most cases focusing on East and Southeast Asia, particularly southern China. NPC accounted for 0. 7% of all cancer cases and 80,008 related deaths in 2020, with 133,354 new cases worldwide (Sung et al,2021). Guangxi, China, has a high incidence of NPC with a rate of 10. 71/100 000 and a mortality rate of 5. 15/100 000 (Niu et al,2022). Male, middle-aged and elderly people are more likely to be affected, and the risk factors include smoking, drinking, and Epstein-Barr virus infection. Patients with metastatic NPC have a poor prognosis and a high recurrence rate (Prawira et al,2017). The main clinical strategies for the treatment of NPC are chemotherapy and radiotherapy, which lead to many adverse reactions in patients. Therefore, it is essential to explore its pathogenesis, find therapeutic targets and explore signaling pathways.

In the post-transcriptional phase, microRNAs, a class of short regulatory RNAs without coding capacity, interact with the 3'-untranslated region (3'-UTR) of specific gene targets to regulate their degradation or diminish the production of the corresponding proteins. Numerous cellular processes in cancer, such as growth, differentiation, cell cycle advancement, programmed cell death, and resistance to chemotherapeutic agents, hinge on the binding and inhibition of particular mRNA species, which subsequently modify the expression of downstream genes. These processes influence the initiation and development of tumors (Ruggieri et al,2023; Luo et al,2024). During tumorigenesis, miRNAs can function as either promoters or inhibitors of cancer, and exert a crucial influence on the control of cell growth, programmed cell death, invasion, and spread. The chemosensitivity of tumor cells is regulated by microRNAs, as confirmed by numerous studies. (Hashemi et al, 2020). Recently, a study by Luo et al. revealed that miRNA-296-5p enhances the sensitivity of NPC cells to DDP chemotherapy by modulating the STAT3/KLF4 pathway (Luo et al,2024). MiRNAs act as regulators of gene expression by binding to sequences in the coding DNA sequences (CDS) or 3' untranslated regions (3'-UTRs) of target mRNAs, ultimately leading to their degradation.

Gui, H.
miRNA and Nasopharyngeal Carcinoma: Function, Regulatory Mechanism and Research Progress.
DOI: 10.5220/0014439700004933

In *Proceedings of the 1st International Conference on Biomedical Engineering and Food Science (BEFS 2025)*, pages 155-161
ISBN: 978-989-758-789-4

Many studies have highlighted the critical role of miRNAs in regulating malignant phenotypes (Zou et al,2023; Hu et al,2023; Song et al,2023), positioning them as potential biomarkers and therapeutic targets that have the potential to be effective (Wang et al,2022). Recently, in the study of Huang et al., it was revealed that miRNA-28-3 can reduce the expression level of BIN1 protein, indicating that miRNA-28-3p has a certain targeted regulation effect on BIN1. The abnormal high expression of miRNA-28-3p may promote the occurrence and development of NPC (Huang et al,2024).

MiRNAs mainly affect gene expression by attaching themselves to particular mRNAs. Because of the way they affect gene expression, their abundant presence in bodily tissues and fluids, and their potential to be used as biomarkers for disease. In this study, miRNA was taken as the focus of the study of NPC, and the regulatory mechanism, application prospect, and feasibility analysis of miRNA on NPC were analyzed.

2 REGULATORY MECHANISMS OF MIRNAS IN NPC

2.1 miR-340-5p Regulates the Hippo Signaling Pathway to Affect the Metastasis of NPC

Metastasis of NPC is a complex process involving a delicate interplay of multiple molecules and signaling pathways. MiRNAs are essential modulators of gene expression during this process, influencing the metastasis of NPC cells by precisely altering their target genes. Over the past few years, numerous researchers have achieved notable findings regarding the regulatory role of miRNA in the metastasis of NPC. The study by Rachmadi et al. provided further insights into the regulatory mechanism of YAP1 and miR-340-5p in NPC by protein-protein interaction (PPI) and functional enrichment analysis. This study revealed YAP1 and miR-340-5p that were not expressed in metastatic cases, suggesting their potential role as tumor suppresators in NPC (Rachmadi et al., 2024). Organ size, cell proliferation, and apoptosis are controlled by the highly conserved Hippo signaling pathway. It converts extracellular signals into modulation of gene transcription in the nucleus via a cascade of kinase reactions.

In this study, miR-340-5p was predicted to directly bind to the mRNA of YAP1, thereby inhibiting YAP1 expression. This interaction phenomenon has been observed in a variety of cancers and is considered to be one of the important pathways by which miR-340-5p exerts its tumor suppressive effect. The inhibition of YAP1 expression by miR-340-5p may lead to the inhibition of cancer cells' proliferation, migration, and invasion. YAP1 (Yes-associated Protein 1) is a downstream effector of Hippo signaling pathway and acts as a transcriptional coactivator. YAP1 is phosphorylated and kept in the cytoplasm when the Hippo signalling pathway is activated, which stops it from entering the nucleus and activating the target gene's transcription. When the Hippo signaling pathway is suppressed or the expression of miR-340-5p is decreased, the activity of YAP1 can be elevated, enabling the proliferation, migration, and invasion of NPC cells. The metastasis of NPC may be a result of this regulatory imbalance. The regulation of NPC metastasis is influenced by other signaling pathways, including the Wnt/β-catenin signaling pathway and PTEN/PI3K/AKT signaling pathway. The interactions among these signaling pathways form a complex network that collectively regulates the metastasis of NPC cells. Therefore, a deep understanding of miRNA regulation of these signaling pathways is essential for the development of effective therapeutic strategies.

2.2 Mechanisms by which miRNAs Affect the Progression of NPC by Regulating the TGFβ/SMAD Pathway

During the progression of NPC, various signaling pathways precisely regulate the progression of NPC through various miRNAs. By regulating the TGFβ/SMAD signaling pathway, miRNAs play a crucial role in the onset and progression of NPC. According to relevant studies, TGFβ/SMAD pathway has a dual role in the regulation of NPC. In the early stage of NPC, TGFβ mainly acts as a tumor suppressor through the SMAD pathway, inhibiting cell proliferation and promoting apoptosis. As the disease progresses, the TGFβ signaling pathway can shift to act as a pro-cancerous signal, enhancing the invasion and metastasis of NPC by triggering the EMT (epithelial-to-mesenchymal transition) process, facilitating immune evasion, and through additional mechanisms. According to the review paper published by Mydin et al., miRNAs can act as tumor suppressor miR or onco-miR to exert profound effects on cell cycle, apoptosis, proliferation, migration and

metastasis in NPC. (Mydin et al., 2024) For example, miR-145, miR-34a, miR-296-5p, etc., inhibit TGFβ signal transduction by directly targeting key molecules in TGFβ/SMAD pathway (such as SMAD2, SMAD4, TGFβR2, etc.), so as to play a tumor suppressor role. At the same time, there are also oncogenic miRNAs, such as miR-93, miR-21, miR-106b, etc., by targeting negative regulators or antagonists of the TGFβ /SMAD pathway, NPC can be promoted through targeting negative regulators and increasing signal transduction. Besides, this review aims to provide a summary of the functions of miRNAs in various signaling pathways in NPC, such as PTEN/PI3K/AKT, TGFβ/SMAD, RAS/MAPK, Wnt/ β-catenin and PRB-E2F. Thus, exploring how miRNAs regulate signaling pathways holds immense importance for the therapy of NPC.

2.3 Tumor Microenvironment (TME) of NPC

2.3.1 Utilizing Single-Cell RNA Sequencing (scRNA-seq) to Investigate Gene Expression Profiles of Various Cell Types in the TME of NPC

The TME denotes the microenvironment immediately adjacent to tumor cells, which includes the tumor cells, as well as immune cells, fibroblasts, vascular networks, and the extracellular matrix. TME is also an important target for tumor immunotherapy. It exerts a substantial influence on the initiation, progression, and dissemination of cancer cells. The capacity to examine transcriptomes of single cells is enabled by a high-throughput sequencing technology known as scRNA-seq. Different cell types in the TME can be studied using it to examine their gene expression characteristics. Recent years have seen the rapid advancement of single-cell sequencing technology, which has allowed researchers to examine the intricate patterns of miRNA expression in NPC with previously unheard-of resolution. According to Liu et al., scRNA-seq technology was used to deeply explore the TME of NPC (Liu et al., 2024). This study revealed the changes of gene expression during the occurrence and development of NPC cells and the complex network relationship between different types of cells in the NPC TME. They obtained high-quality scRNA-seq data by high-throughput sequencing using the single-cell sequencing platform of 10x Genomics. Quality control and filtering of sequencing data were performed using tools such as Cell Ranger to remove low-quality cell data. Seurat and other R packages were used for dimensionality reduction and cluster analysis of the processed data, and the cells were divided into different populations. For instance, T cells, B cells, macrophages/monocytes, and natural killer (NK) cells. The cell types' classification was confirmed by analyzing specific marker genes for each cell population and then analyzed according to the gene expression properties of each cell population, identifying genes that show different functional potential in different NPC types. Comparison of gene expression differences between primary tumors, metastatic tumors, and PBMC revealed gene expression changes during the initiation and progression of NPC. Finally, the interaction between different cell types was analyzed using tools such as Cellphonedb and CellChat, revealing their complex network relationships in the TME. For instance, T cells exhibit considerable heterogeneity within the NPC TME, and notable disparities exist in the gene expression patterns of T cells between initial and advanced tumor stages, mirroring the distinct immune responses of T cells towards tumors at various points of progression. This comprehensive analysis details the evolutionary dynamics at single-cell resolution and the influence of the TME, greatly advancing our understanding of NPC metastasis. Hence, examining the gene expression profiles of various cell types within the NPC TME is highly important during the targeted therapy of NPC.

2.3.2 The Influence of Animal Model Construction on the Study of TME of NPC

Researchers have developed animal models that simulate the onset, progression, and interaction of NPC with adjacent tissues in humans, aiming to gain a deeper understanding of the NPC TME and ascertain the exact functions of miRNAs in NPC. The function of miRNA is strongly supported by these animal models, which also offer a fresh avenue for a thorough investigation of the molecular mechanism underlying NPC. Cai et al. used these animal models to confirm the tumor suppressor role played by miR-143 in NPC (Cai et al., 2015). We investigated the role of Epstein-Barr virus (EBV) encoded microRNA BART1 in NPC and how it regulates NPC metastasis through PTEN-dependent signaling. EBV exhibits a robust correlation with the development of NPC and is the first human virus found to encode miRNAs. . While it is recognized that proteins encoded by EBV

have significant roles in the progression and metastasis of NPC, the precise manner in which EBV-encoded miRNAs regulate the metastatic mechanism of NPC remains to be elucidated. Their research suggests that EBV-miR-BART1 is highly expressed in NPC and shows a significant association with the clinicopathological characteristics of the disease. The migratory and invasive abilities of NPC cells were assessed through the use of migration assays utilizing transwell chambers, scratch assays to measure wound closure, and the Boyden chamber invasion test. The results revealed that the elevation of EBV-miR-BART1 expression notably enhanced the migratory and invasive capacities of NPC cells, and facilitated tumor growth and metastasis in vivo. Subsequently, NPC cell lines were implanted into nude mice to establish a xenograft system, aiming to investigate how EBV-miR-BART1 influences tumor growth and metastasis. The tumour suppressor protein PTEN was directly targeted by EBV-miR-BART1, which activated PTEN-dependent signalling pathways like PI3K-Akt, FAK-p130Cas, and Shc-MAPK/ERK1/2, according to additional validation. Furthermore, it promotes epithelial-mesenchymal transition (EMT) and the migration, invasion and metastasis of NPC cells. Therefore, the establishment of animal models has a crucial impact on the study of TME and clinical intervention strategies for NPC.

2.4 Effects of Competing Endogenous RNA (ceRNA) Interaction Network Composed of lncRNA/circRNA, miRNA and mRNA on the Regulation of NPC

The mechanism of ceRNA has been a hot topic in the field of ncRNA research in recent years. This mechanism describes how different ncRNAs compete with one another to bind to shared miRNAs, which indirectly modifies target gene expression. To elucidate the crucial role of ncRNA in the onset and progression of NPC, leveraging the ceRNA mechanism, the establishment of an interaction network comprising lncRNA/circRNA, miRNA, and mRNA offers a novel approach for disease diagnosis and treatment. By identifying the ncRNA interaction networks that are closely related to diseases, ncRNA-based biomarkers can be developed for early diagnosis and prognosis evaluation of diseases. The study by Liu et al. demonstrated that the evolution of the lncRNA/CirRNA-miRNA-mRNA network in NPC could aid in gaining a comprehensive insight into the ceRNA mechanism underlying NPC and provide novel prospective biomarkers for evaluating NPC prognosis. (Liu et al., 2024). The ceRNA network realizes the fine regulation of gene expression through the interaction between various RNA molecules. In this network, lncRNAs and circRNAs competitively bind miRNAs, thereby regulating mRNA expression. This regulatory mechanism helps to maintain the balance of gene expression in the organism. The ceRNA mechanism exerts an impact on various cellular processes, including cell proliferation, differentiation, and apoptosis, among others. For example, certain miRNAs can inhibit the translation of specific mRNAs, while lncRNAs and circRNAs may relieve this repression by competitively binding miRNAs, thereby affecting cellular functions. Therefore, modulating the expression levels of particular RNA molecules within the ceRNA network could potentially serve as a therapeutic approach for treating diseases. It holds promise as a novel therapeutic target for disease treatment in the future.

3 APPLICATION

3.1 miRNA Target Prediction and Treatment Strategy of NPC

As bioinformatics technology and high-throughput sequencing continue to advance, researchers are now able to effectively predict the target genes of miRNAs and experimentally confirm the distinct roles of these target genes in NPC. Using these methods, researchers have been able to predict and validate particular miRNAs, like miR-124, as possible targets for NPC treatment. The study by Liang et al. predicted that miR-506 targeted the LHX2 gene and showed that miR-506 targeted inhibition of LHX2 provides a promising therapeutic strategy for the treatment of NPC. (Liang et al., 2019). LHX2 is a gene encoding transcription factors and belongs to the LIM homeobox gene family. The 3'utr region of LHX2 may be directly bound by miR-506, which would then suppress LHX2 expression. Wnt/β-catenin signaling pathway plays a crucial role in diverse biological processes, such as embryonic development, cell proliferation, differentiation, and migration. miR-506 inhibited the activation of Wnt/β-catenin signaling pathway by inhibiting the expression of LHX2. As an upstream regulator of this pathway, LHX2 can directly or indirectly activate β-catenin and other key molecules, thereby promoting cell proliferation and invasion. miR-506 blocked the

activation of this signaling pathway by down-regulating LHX2, thereby blocking the NPC cells' ability to proliferate and invade. One of the associated targeted therapy approaches is miRNA mimic therapy, which can be designed and synthesized to mimic the tumor suppressor miRNAs (such as miR-375, miR-506, etc.) that are down-regulated in NPC. These mimics are able to mimic the function of endogenous miRNAs, bind to the mRNA of target genes and inhibit their expression, thereby restoring or enhancing the tumor suppressive effect of miRNAs. In addition, there are therapeutic strategies such as miRNA inhibitor therapy and miRNA-based personalized medicine. More miRNA-based treatments will be used in the clinical treatment of NPC in the future as associated technologies mature.

3.2 Correlation between miRNA Expression Profile Analysis and Progression of NPC

Comprehensive miRNA expression profiling could help us to identify key miRNAs that are closely related to NPC progression. These miRNAs can be used not only as biomarkers for early diagnosis of NPC, but also as important tools for prognostic evaluation.

Chen's research revealed that numerous miRNAs exhibited differential expression patterns in NPC tissues when compared to healthy nasopharyngeal tissues. Through their regulation of target gene expression, these differentially expressed miRNAs may have an impact on NPC cell invasion, migration, apoptosis, and proliferation. (Chen, 2011). The results of unsupervised clustering analysis indicated that the differentially expressed miRNAs were capable of markedly distinguishing NPC samples from normal ones, and further classification of the samples was possible based on the clinical stage of NPC. This study also investigated the effects of differentially expressed miRNAs on signaling pathways, constructed a regulatory network of miRNAs centered on c-Myc, and revealed the complex interaction between miRNAs and c-Myc. In clinical practice, it can be combined with traditional diagnostic methods (such as pathological examination and imaging examination), and miRNA expression profile analysis can provide more comprehensive diagnostic information. During the treatment of NPC, miRNA expression profiling can also be used to monitor the therapeutic effect. As a result, miRNA expression profiling is a useful technique for observing the distinct patterns of miRNA expression in NPC and is crucial for understanding how NPC develops.

4 EVALUATION OF CLINICAL APPLICATION PROSPECTS

4.1 Biomarkers

miRNA has a lot of potential for use as biomarkers in the clinical setting of NPC, especially in early diagnosis, treatment sensitivity's prediction, prognostic evaluation and so forth. According to the review of miRNA biomarkers by Wang et al., There is discussion of the possible use of miRNAs as therapeutic targets and biomarkers for patients with NPC. It was determined that miRNAs might be promising targets for treatment in NPC. (Wang et al., 2019) It is anticipated that miRNA-based cancer therapy will increase treatment response and cure rates, either by itself or in conjunction with conventional chemotherapy and/or radiation therapy.

4.2 Reveal the Characteristics of TME

By revealing the mechanism of miRNA in TME, it can provide new ideas and methods for the diagnosis and NPC's treatment. The research conducted by Zhang et al. highlighted that circulating miRNAs are indicators of TME changes (Zhang et al., 2019). Circulating miRNAs, found in plasma or serum, serve as non-invasive indicators for alterations in the TME of NPC. Seven miRNA signatures identified in this study, including let-7b-5p and miR-140-3p, were abnormally expressed in the plasma of NPC patients. These miRNAs may be derived from tumor cells or other cells in the TME, reflecting the presence and progression of the tumor. To increase the therapeutic effect, miRNA therapy can be used in conjunction with more conventional treatments like chemotherapy and radiation. For instance, it was proposed that miR-29c might increase NPC cells' susceptibility to radiation and chemotherapy with cisplatin. This combination treatment strategy may inhibit tumor cell growth and survival through multiple pathways, thereby overcoming the limitations of monotherapy. Second, achieving clinical application of miRNA therapy will require the development of efficient delivery systems. These systems need to be able to stably deliver miRNAs to NPC target tissues and maintain their stability and activity in vivo. At present, a variety of delivery

systems (such as liposomes, viral vectors, etc.) have been used for miRNA delivery research, but the specific delivery system for NPC still needs to be further optimized and developed. Therefore, it is important to reveal the characteristics of NPC TME for the development of these therapies.

5 CONCLUSION

In this review, we systematically sorted out the research progress of miRNA in the field of NPC, focusing on the pathogenesis of NPC, the regulatory mechanism of miRNA and Hippo, TGFβ/SMAD signaling pathway on NPC, and the role of miRNA in the TME of NPC. This review summarizes the existing miRNA therapeutic strategies and the prospective use of miRNA in NPC therapy. lncRNA and circRNA compete with mRNA by absorbing miRNA to form a regulatory network, which is significant to NPC. However, there is a lack of research on the ceRNA network of NPC that includes both lncRNA and circRNA. Although circulating miRNAs have the advantage of being non-invasive as biomarkers, their sensitivity and specificity still need to be further improved to meet the needs of clinical application. Moreover, the safety and efficacy of miRNA therapy in clinical practice need to be further verified. Future research directions should continue to deeply explore the molecular mechanism of miRNA interaction with target genes to reveal the precise pathway of miRNA action in NPC. Secondly, more sensitive circulating miRNA detection methods should be developed to improve their application value in early diagnosis and prognostic evaluation of NPC. In clinical practice, efforts should be intensified to enhance miRNA-targeted therapy strategies, aiming to boost therapeutic efficacy and minimize adverse effects through the optimization of delivery systems and combination treatments. This review summarizes recent studies on the effect of miRNA on NPC and provides new strategies for future treatment.

REFERENCES

Cai, L., Ye, Y., Jiang, Q., Chen, Y., Lyu, X., Li, J., Wang, S., Liu, T., Cai, H., Yao, K., Li, J., & Li, X. 2015. Epstein–Barr virus-encoded microRNA BART1 induces tumour metastasis by regulating PTEN-dependent pathways in nasopharyngeal carcinoma. Nature Communications, 6(1).

Chen, N. 2011. microRNA expression profiling of nasopharyngeal carcinoma. Oncology Reports, 25(5).

Hashemi, A., & Gorji-Bahri, G. 2020. MicroRNA: Promising roles in cancer therapy. Current Pharmaceutical Biotechnology, 21(12), 1186–1203.

Hu, J., Liu, W., Zhang, X., Shi, G., Yang, X., Zhou, K., Hu, B., Chen, F., Zhou, C., Lau, W., Fan, J., Wang, Z., & Zhou, J. 2023. Synthetic miR-26a mimics delivered by tumor exosomes repress hepatocellular carcinoma through downregulating lymphoid enhancer factor 1. Hepatology International, 17(5), 1265–1278.

Huang, G., Zhao, N., Wu, J., Zhou, X., & Liu, W. 2024. Labeling and Diagnostic Value of miRNA-28-3p in Patients with Nasopharyngeal Carcinoma. PubMed.

Liang, T., Zheng, Y., Wang, J., Zhao, J., Yang, D., & Liu, Z. 2019. RETRACTED ARTICLE: MicroRNA-506 inhibits tumor growth and metastasis in nasopharyngeal carcinoma through the inactivation of the Wnt/β-catenin signaling pathway by down-regulating LHX2. Journal of Experimental & Clinical Cancer Research, 38(1).

Liu, Q., Xu, J., Dai, B., Guo, D., Sun, C., & Du, X. 2024. Single-cell resolution profiling of the immune microenvironment in primary and metastatic nasopharyngeal carcinoma. Journal of Cancer Research and Clinical Oncology, 150(8).

Liu, S., Li, X., Xie, Q., Zhang, S., Liang, X., Li, S., & Zhang, P. 2024. Identification of a lncRNA/circRNA-miRNA-mRNA network in Nasopharyngeal Carcinoma by deep sequencing and bioinformatics analysis. Journal of Cancer, 15(7), 1916–1928.

Luo, H., Wang, Y., Ren, J., Zhang, Q., Chen, Y., Chen, M., Huang, N., Wu, M., Tang, X., & Li, X. 2024. MiRNA-296-5p promotes the sensitivity of nasopharyngeal carcinoma cells to cisplatin via targeted inhibition of STAT3/KLF4 signaling axis. Scientific Reports, 14(1).

Mydin, R. B. S. M. N., Azlan, A., Okekpa, S. I., & Gooderham, N. J. 2024. Regulatory role of miRNAs in nasopharyngeal cancer involving PTEN/PI3K/AKT, TGFβ/SMAD, RAS/MAPK, Wnt/β-catenin and pRB-E2F signaling pathways: A review. Cell Biochemistry and Function, 42(2).

Niu, Y., Zhang, F., Chen, D., Ye, G., Li, Y., Zha, Y., Chen, W., Liu, D., Liao, X., Huang, Q., Tang, W., Cai, G., Guo, R., Li, H., & Tang, S. 2022. A comparison of Chinese multicenter breast cancer database and SEER database. Scientific Reports, 12(1).

Prawira, A., Oosting, S. F., Chen, T. W., Santos, K. A. D., Saluja, R., Wang, L., Siu, L. L., Chan, K. K. W., & Hansen, A. R. 2017. Systemic therapies for recurrent or metastatic nasopharyngeal carcinoma: a systematic review. British Journal of Cancer, 117(12), 1743–1752.

Rachmadi, L., Hasan, F., Linggodigdo, M., Dwina, Y., Cahyanur, R., & Adham, M. 2024. Unveiling the interplay of YAP1-driven pathways and miR-340-5P expression: insights into nasopharyngeal cancer metastasis. PubMed, 28(22), 4576–4590.

Ruggieri, F., Jonas, K., Ferracin, M., Dengler, M., Jäger, V., & Pichler, M. 2023. MicroRNAs as regulators of tumor metabolism. Endocrine Related Cancer, 30(8).

Song, L., Yang, J., Qin, Z., Ou, C., Luo, R., Yang, W., Wang, L., Wang, N., Ma, S., Wu, Q., & Gong, C. 2023. Multi-Targeted and On-Demand Non-Coding RNA Regulation Nanoplatform against Metastasis and Recurrence of Triple-Negative Breast Cancer. Small, 19(23).

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021b). Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA a Cancer Journal for Clinicians, 71(3), 209–249.

Wang, J., Ge, J., Wang, Y., Xiong, F., Guo, J., Jiang, X., Zhang, L., Deng, X., Gong, Z., Zhang, S., Yan, Q., He, Y., Li, X., Shi, L., Guo, C., Wang, F., Li, Z., Zhou, M., Xiang, B., & Zeng, Z. 2022. EBV miRNAs BART11 and BART17-3p promote immune escape through the enhancer-mediated transcription of PD-L1. Nature Communications, 13(1).

Wang, S., Claret, F., & Wu, W. 2019. MicroRNAs as therapeutic targets in nasopharyngeal carcinoma. Frontiers in Oncology, 9.

Zhang, H., Zou, X., Wu, L., Zhang, S., Wang, T., Liu, P., Zhu, W., & Zhu, J. 2019. Identification of a 7-microRNA signature in plasma as promising biomarker for nasopharyngeal carcinoma detection. Cancer Medicine, 9(3), 1230–1241.

Zou, S., Chen, S., Rao, G., Zhang, G., Ma, M., Peng, B., Du, X., Huang, W., Lin, W., Tian, Y., & Fu, X. 2023. Extrachromosomal circular MiR-17-92 amplicon promotes HCC. Hepatology, 79(1), 79–95.