Advances in Clinical Medicine 临床医学进展, 2026, 16(1), 876-884
Published Online January 2026 in Hans. https://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2026.161116

Hans汉斯

miRNA调控靶基因影响癌症的机制与研究进展

李文飞，万智恒*

内蒙古科技大学包头医学院第一附属医院日间腹部微创疝手术中心，内蒙古 包头

收稿日期：2025年12月7日；录用日期：2026年1月1日；发布日期：2026年1月12日

摘　要

微小RNA (miRNA)作为一类重要的非编码小分子RNA，通过特异性调控靶基因的表达，在癌症的发生、发展及转移过程中发挥着关键调节作用。近年来，随着分子生物学技术的进步，miRNA在肿瘤细胞增殖、凋亡、侵袭及化疗耐药等多方面的调控功能逐渐被揭示。然而，miRNA调控网络的复杂性和靶基因多样性使得其机制尚未完全明确，制约了其临床应用的深入发展。本文通过对促癌基因的致癌机制以及miRNA在不同癌种中的双重作用的讨论，并重点分析抑癌性miRNA调控靶基因的研究现状，旨在为癌症预防和治疗提供新的生物标志物，并基于临床实践提供新思路和新方向。

关键词

miRNA，靶基因，调控机制，癌症，疾病治疗

Mechanism and Research Progress of Cancer Influenced by miRNA Target Gene Regulation

Wenfei Li, Zhiheng Wan*

Daytime Minimally Invasive Abdominal Hernia Surgery Center, First Affiliated Hospital of Baotou Medical College, Inner Mongolia University of Science and Technology, Baotou Inner Mongolia

Received: December 7, 2025; accepted: January 1, 2026; published: January 12, 2026

Abstract

MicroRNAs (miRNAs), as a class of crucial non-coding small RNAs, play pivotal regulatory roles in cancer development, progression, and metastasis by specifically modulating target gene expression. Recent advances in molecular biology have progressively uncovered miRNA's multifaceted regulatory

*通讯作者。

文章引用: 李文飞, 万智恒. miRNA 调控靶基因影响癌症的机制与研究进展[J]. 临床医学进展, 2026, 16(1): 876-884. DOI: 10.12677/acm.2026.161116

functions in tumor cell proliferation, apoptosis, invasion, and chemotherapy resistance. However, the complexity of miRNA regulatory networks and the diversity of their target genes have hindered a comprehensive understanding of their mechanisms, limiting their clinical application potential. This study examines the carcinogenic mechanisms of oncogenes and the dual roles of miRNAs across different cancer types, with a focus on the current research status of tumor-suppressing miRNAs and their target genes. The findings aim to identify novel biomarkers for cancer prevention and treatment while providing innovative insights and directions for clinical practice.

Keywords

miRNA, Target Gene, Regulatory Mechanism, Cancer, Disease Treatment

1. 前言

微小 RNA (miRNA)是一类非编码 RNA，常与靶基因的 3’非翻译区(3’-UTR)结合，实现对靶基因的转录后调控，进而影响细胞增殖、凋亡、分化和迁移等基本生命过程。研究证实 miRNA 的异常表达可以通过多种机制影响疾病，包括基因水平异常、信号通路失衡及表观遗传调控等[1]，特别是在肿瘤的发生、发展、转移及耐药性等方面。因此，探索癌基因的致癌机制和 miRNA 与其靶基因的调控机制，对辅助早期诊断、判断预后及精准治疗等方面具有积极作用。

近年来，随着高通量测序技术和生物信息学的创新，miRNA 及其靶基因的研究取得了显著进展[2]。如胃癌(GC)细胞分泌的外泌体 miR-128-3p 可通过靶向 SASH1 促进血管内皮细胞的增殖和迁移，促进肿瘤血管生成，揭示了 miRNA 介导的肿瘤进展新机制[3]。此外，miRNA 与长链非编码 RNA (lncRNA)及环状 RNA (circRNA)构建复杂的竞争性内源 RNA (ceRNA)调控网络，通过相互“海绵”作用，调节靶基因表达，参与肿瘤细胞的增殖、侵袭和耐药等过程[4]。

miRNA 在肿瘤诊断和治疗中的潜力日益受到重视。由于 miRNA 在血液等体液中具有高稳定性且表达呈肿瘤特异性，其作为非侵入性生物标志物用于早期诊断和预后评估显示出广阔前景。例如，肺癌早期患者的 miRNA 表达谱与肿瘤微环境免疫细胞状态密切相关，部分 miRNA 可作为早期肺癌诊断的候选标志物[5]。

目前，miRNA 模拟物或抑制剂、miRNA 替代疗法和载体系统等已进入临床试验阶段，但是，miRNA 的研究应用仍面临诸多挑战，包括靶基因识别的准确性和异质性、递送效率、脱靶效应等等[6]-[8]。系统解析 miRNA 及其靶基因的分子机制，为癌症的早期诊断和靶向治疗提供了新思路和新手段。未来，结合高通量组学技术和精准医学理念，推动 miRNA 相关研究向临床应用转化，将极大促进肿瘤防治水平的提升。

2. 靶基因

人体细胞在分裂过程中，DNA 可能因自然复制错误或外界因素干扰而突变，若突变积累到一定程度，导致细胞生长失控，这些过程包括原癌基因的激活、抑癌基因的失活、细胞信号传导通路的改变，以及细胞表面至核的信号传导级联等。癌症相关基因通常根据其是否促进或抑制肿瘤发生被分类为癌基因(Oncogenes, OCG)或抑癌基因(Tumor Suppressor Genes, TSG) [9]，促癌基因主要通过表 1 所示途径驱动疾病恶性转化：

Table 1. Typical oncogenes and their mechanisms of promoting cancer
表 1. 典型的促癌基因及其促癌机制

促癌机制	关键靶基因案例	调控通路	致癌效应
持续增殖信号	MYC [10], KRAS [11] EGFR [12], Ras-GTP	MAPK/PI3K，JAK/STAT 通路激活	细胞无限增殖
凋亡抑制	BCL-2, MCL-1	抑制 BAX/BAK[13]活化	抵抗程序性死亡
侵袭转移	ZEB1, SNAI1	EMT 通路激活[14]	增强迁移与侵袭能力
血管生成	VEGF-A, HIF-1α	VEGF/VEGFR 信号放大[15]	促肿瘤新生血管形成
基因组不稳定	TP53 突变体	BRCA1 CTDNA 修复缺陷[16]	加速突变积累
融合基因产生致癌蛋白	BCR-ABL 融合基因	酪氨酸激酶活性[17]	持续激活增殖信号

临床上，靶向癌基因抑制癌症的药物研究已广泛应用，例如：第三代表皮生长因子受体酪氨酸激酶抑制剂(EGFR-TKI)获批治疗 EGFR 突变 NSCLC 患者，导致后者生存率和临床结局均得到了显著改善，被推荐为 EGFR 突变 NSCLC 患者的标准一线治疗[18]。另一项研究发现 BCR-ABL 融合基因具有高度酪氨酸激酶活性，持续激活增殖信号，使得细胞过度增殖，在慢性粒细胞白血病(CML)的发生中发挥着关键作用。目前，靶向药如伊马替尼，抑制 BCR-ABL 酪氨酸激酶活性等能够诱导肿瘤细胞分化和凋亡[19]。

3. miRNA 调控靶基因的分子机制

3.1. miRNA 与靶基因结合机制

miRNA 在调控人类 1/3 的基因表达中扮演着重要角色，其核心调控机制是通过 5’末端的种子序列(第 2~8 位的碱基序列)，识别靶 mRNA 的 3’非编码区结合位点，调控下游基因的表达和调节其稳定性，通过抑制翻译或促进 mRNA 降解，从而负调控基因表达[20]。这两种调控模式可单独或协同发挥作用，以实现对靶基因的精准调节。此外，miRNA 与其靶基因的匹配程度决定了结合的特异性和稳定性[21]，miRNA 识别靶基因具有高度的特异性，例如：血管内皮生长因子(VEGF)是血管生成的重要因子，miR-126 与 VEGF 的 3’-UTR 特异性结合后影响肿瘤血管的生产[22]，也有实验证实胃癌细胞来源的外泌体 miR-128-3p 通过靶向 SASH1 促进 GC 血管生成[3]。

另外，miRNA 具有多靶点调控特性。研究表明，miR-143 不仅在非小细胞肺癌中显著下调，还通过多种信号通路靶向多个关键靶基因如 PSME3，BCL-2，Pax6，PTK2(FAK)，CCND1，发挥抑制非小细胞肺癌增殖的作用[23]。此外，miRNA 的表达受多因素影响，包括 miRNA 基因扩增(如：miR-17-92 簇扩增[24])、增强启动子活性[25]、miRNA 加工效率提高(如：miR-103/107 高表达促进乳腺癌进展[26])、以及 miRNA 稳定性提高(如：miR-155 促进结直肠癌进展[27])，通过增强这些因素能够有效提高 miRNA 的功能。

综上所述，miRNA 通过种子序列特异性结合靶基因 mRNA 的 3’-UTR，实现对靶基因表达的双重调控模式，即 mRNA 降解和翻译抑制。其调控具有高度特异性和多靶点的复杂性，构成了细胞内精细的基因调控网络[28]。

3.2. ceRNA 调控网络

ceRNA 是一种基因调控机制，涉及不同 RNA 分子通过竞争结合相同的 miRNA 来调节彼此的表达

[29]。ceRNA 通过竞争性结合常见 miRNA 来调控基因的转录后表达[30]。lncRNA 可以通过与 miRNA 结合来调节 mRNA 的稳定性和翻译，从而影响细胞的生物学行为[31]。例如：有研究证实 LncRNA RP11-805J14.5 作为 ceRNA，通过“海绵化”肺腺癌中的 miR-34b-3p 和 miR-139-5p 来调控 CCND2 [32]。此外，circRNA 作为竞争性内源 RNA，通过与 miRNA 结合，减少这些 miRNA 与其靶 mRNA 的结合能力，从而允许目标 mRNA 更高水平地表达。例如：ciRS-7 被发现会对 miR-7 产生海绵作用，从而被认为是一种致癌的肿瘤标记物[33]。

总之，ceRNA 调控网络是 miRNA 调控靶基因的重要网络机制，研究 ceRNA 调控网络有助于深入理解基因调控的多样性和复杂性，为癌症的诊断和治疗提供新的思路。

3.3. miRNA 在癌症中扮演双重角色

通常根据靶基因功能将 miRNA 分为抑癌 miRNA (ts-miRNA)和促癌 miRNA (onco-miRNA)。Ts-miRNA 通过抑制促癌基因表达而发挥抑癌作用，其表达下调时，可能会增加相关肿瘤的发生风险。例如：miR-15a 和 miR-16 在白血病中被发现具有抑制异常白细胞增殖的作用[24]。相反，onco-miRNA 则通过激活肿瘤相关通路活性或促进癌细胞生长或转移来加速癌症进展。例如，miR-21、miR-451 在多种癌症中表达上调，分别抑制 PTEN、PDCD4、TGFBR2 以及 ZEB1 等，从而促进肿瘤细胞的增殖和存活[26]。因此，miRNA 既可充当肿瘤抑制因子，也可作为致癌基因，具体作用取决于其靶向的基因及癌症类型[34]。

3.3.1. 抑癌 miRNA 调控靶基因的核心机制

在细胞核内，RNA 聚合酶 II 转录生成初级 miRNA (pri-miRNA)，再经过切割、转运和再加工形成成熟 miRNA，与靶基因互补位点结合，调控靶基因过度水平，最终维持细胞生长、增殖、分化及凋亡的正常平衡。研究表明，miRNA 在生物合成过程中关键酶出现缺陷或者功能异常导致成熟 miRNA 水平下降，靶基因过度表达，引发细胞过度增殖、凋亡减少、无法正常分化或去分化，成为癌症等疾病发生的重要分子基础[35]。以下总结了抑癌 miRNA 通过沉默致癌靶点抑制肿瘤发展的机制分类见表 2。

Table 2. Mechanism classification of anticancer miRNA in inhibiting tumor development by silencing carcinogenic targets
表 2. 抑癌 miRNA 通过沉默致癌靶点抑制肿瘤发展的机制分类

分类依据	miRNA 类型	代表分子	核心靶点	抑制作用机制
细胞周期阻滞	周期抑制剂	miR-34a, let-7	CDK4/6, RAS, CCND1	抑制细胞周期蛋白依赖性激酶[36]→阻滞增殖
促凋亡	凋亡激活剂	miR-15, miR-16-1	BCL-2, MCL-1	沉默抗凋亡蛋白 BCL-2 [37]→诱导癌细胞死亡
转移抑制	EMT 阻遏因子	miR-200 家族	ZEB1, SNAI2	阻断转录因子 ZEB→维持上皮表型[38]，抑制转移
免疫调节	免疫检查点抑制剂	miR-138, miR-424	PD-L1, CD80	下调免疫检查点 PD-L1 [39]→增强 T 细胞杀伤活性
表观遗传修复	表观修饰调控因子	miR-101, miR-29	EZH2, DNMT3A	沉默组蛋白甲基转移酶 EZH2 [40]→逆转抑癌基因沉默

抑癌 miRNA 通过多种机制调控相关靶基因，参与多种生物过程，包括细胞增殖、凋亡、迁移，代谢调节，表观遗传修复，免疫杀伤等。目前常利用生物信息学工具和实验技术(如 qPCR、Western blot、荧

光素酶报告等)识别与特定肿瘤类型相关癌基因的表达及信号通路，并验证抑癌 miRNA 是否能够直接调控这些靶点。

3.3.2. 促进肿瘤细胞增殖与抑制凋亡

miRNA 通过靶向抑癌基因，调节细胞周期及凋亡通路，从而促进肿瘤细胞增殖与抑制凋亡。miRNA 的表达异常能影响肿瘤细胞的增殖活性和存活能力。例如，miR-21 和 miR-155 作为典型的促癌 miRNA，在多种癌症中表现出促进增殖和抑制凋亡的作用。研究表明，miR-21 不仅在肝细胞癌中显著上调，还通过调控多种靶基因如抑癌基因 PTEN 和调控细胞增殖基因，促进肿瘤细胞的增殖和存活[41]。此外，miR-155 在结直肠癌中与药物耐受性密切相关，通过抑制促凋亡基因，增强肿瘤细胞的抗凋亡能力[42]。

综上所述，特定 miRNA 通过调控抑癌或促癌基因，影响细胞周期和凋亡信号通路，促进肿瘤细胞的增殖和抑制凋亡，是肿瘤发生发展的关键机制之一。

3.4. miRNA 在癌症诊断与治疗中的研究进展

3.4.1. miRNA 作为癌症生物标志物的潜力

循环 miRNA 主要存在于血液、尿液等多种体液中，具有较高的稳定性，且能抵御体液中核酸酶的降解，因此成为理想的非侵入性诊断标志物。多项研究显示，循环 miRNA 在不同癌种中的表达谱具有很强的特异性和稳定性，如乳腺癌、结直肠癌、前列腺癌、膀胱癌等，这些 miRNA 不仅有助于癌症的早期诊断，还与患者的预后密切相关[43]-[46]。例如，乳腺癌患者血浆中独特的 miRNA 组合能有效区分肿瘤患者与健康个体，且与肿瘤的淋巴结转移和总体生存率相关[47]。研究发现 miRNA-145 作为诊断标志物帮助诊断乳腺癌[48]；此外，针对非小细胞肺癌的研究发现，结合血清 miRNA 与血清外泌体 miRNA 的检测方法，能够显著提高早期诊断的准确性和敏感性[5] [49]，例如：Seyedeh Afrooz Azimi 等人研究证实 miR-155 作为非小细胞肺癌的诊断标志物[50]。近年来，基于 CRISPR-Cas 系统的 miRNA 滚环扩增检测技术，提升了 miRNA 检测的灵敏度和特异性[51]。尽管如此，临床应用仍面临方法标准化、样本处理和数据分析一致性等挑战[52] [53]。总的来看，循环 miRNA 作为癌症生物标志物具有广阔的应用前景，是实现癌症早期诊断和动态监测的有力工具。

3.4.2. miRNA 治疗策略及个性化医疗

多项研究显示，恢复或增强 miRNA 的调控功能成为抗癌治疗的重要研究方向，主要包括：miRNA 模拟物(mimics)疗法[54] (microRNA-29a 模拟物)、miRNA 替代疗法(如 MRX34 旨在递送 miR-34a [55])，miRNA 载体系统(如 AAV 载体输送 miR-26a [56])，联合治疗(如抑制 miR-21 增加结直肠癌细胞对氟尿嘧啶的敏感性[57])。目前，miRNA 治疗方法已进入临床试验阶段，部分 miRNA 药物显示出良好的安全性和初步疗效，但仍面临递送效率、组织特异性和脱靶效应等挑战[6]-[8]。未来，结合多组学数据和精准递送技术，miRNA 治疗策略有望实现更高效、安全。此外，基于 miRNA 表达谱的个体化治疗方案设计，通过高通量测序和多组学分析，结合患者具体的 miRNA 表达特征，构建个体化的治疗模型，从而优化药物选择和剂量[7] [58] [59]，有助于实现精准医疗。然而，miRNA 调控网络复杂多变，存在多个 miRNA 与多个基因相互作用的情况，增加了个体化治疗的难度。为应对这一挑战，研究者提出利用系统生物学和机器学习方法，解析 miRNA 调控网络，筛选关键 miRNA 组合，提高治疗的针对性和有效性[60]-[62]。未来，随着技术的进步和数据积累，miRNA 联合治疗将在个体化癌症治疗中发挥愈加重要的作用。

4. 结论

miRNA 作为癌症研究领域的重要分子，不仅参与了癌细胞的增殖、凋亡、迁移和侵袭等多种生物学

过程，而且其多靶点调控的复杂性赋予了癌症调控更高的灵活性和复杂度。随着研究方法的不断进步，miRNA 的调控机制研究取得了显著突破。另外，在临床研究中，miRNA 作为癌症诊断标志物和治疗靶点的潜力日益显现，不仅推动了精准医学的发展，也为个体化癌症治疗开辟了新路径。然而，当前研究中仍存在对 miRNA 功能的异质性和靶基因多样性的争议，不同肿瘤类型中 miRNA 的表达模式及其生物学作用差异较大；同时，miRNA 的临床转化方面仍面临诸多挑战。展望未来，深入系统地解析 miRNA 调控网络，结合单细胞测序、多组学整合分析和人工智能算法，有望全面揭示 miRNA 调控网络机制并推动 miRNA 相关诊断和治疗技术的规范化和标准化，最终实现精准干预。

综上所述，本文总结了促癌靶基因与肿瘤形成之间的相互关系，系统阐述了 miRNA 对靶基因的核心调控机制以及 miRNA 在生物标志物开发、癌症治疗策略等研究方向上取得的显著进展，并分析了目前面临的挑战，未来，通过系统解析和临床转化的协同发展，miRNA 有望成为癌症防治领域的重要突破口，助力实现更精准、高效的癌症诊疗。

参考文献

[1] Ali Syeda, Z., Langden, S.S.S., Munkhzul, C., Lee, M. and Song, S.J. (2020) Regulatory Mechanism of MicroRNA Expression in Cancer. *International Journal of Molecular Sciences*, **21**, Article 1723. https://doi.org/10.3390/ijms21051723

[2] Hussen, B.M., Rasul, M.F., Abdullah, S.R., Hidayat, H.J., Faraj, G.S.H., Ali, F.A., *et al.* (2023) Targeting Mirna by CRISPR/Cas in Cancer: Advantages and Challenges. *Military Medical Research*, **10**, Article No. 32. https://doi.org/10.1186/s40779-023-00468-6

[3] Yan, H., Cai, X., Zhang, J., Zhao, H., Wu, H., Zhang, J., *et al.* (2024) Gastric Cancer Cell-Derived Exosomal miRNA-128-3p Promotes Angiogenesis by Targeting SASH1. *Frontiers in Oncology*, **14**, Article 1440996. https://doi.org/10.3389/fonc.2024.1440996

[4] Tian, Y., Zhang, M., Liu, L., Wang, Z., Liu, B., Huang, Y., *et al.* (2024) Exploring Non-Coding RNA Mechanisms in Hepatocellular Carcinoma: Implications for Therapy and Prognosis. *Frontiers in Immunology*, **15**, Article 1400744. https://doi.org/10.3389/fimmu.2024.1400744

[5] Pirlog, R., Chiroi, P., Rusu, I., Jurj, A.M., Budisan, L., Pop-Bica, C., *et al.* (2022) Cellular and Molecular Profiling of Tumor Microenvironment and Early-Stage Lung Cancer. *International Journal of Molecular Sciences*, **23**, Article 5346. https://doi.org/10.3390/ijms23105346

[6] Shah, V. and Shah, J. (2020) Recent Trends in Targeting miRNAs for Cancer Therapy. *Journal of Pharmacy and Pharmacology*, **72**, 1732-1749. https://doi.org/10.1111/jphp.13351

[7] Rasulova, K., Dilek, B., Kavak, D.E., Pehlivan, M. and Kizildag, S. (2024) Mitochondrial miRNAs and Fibromyalgia: New Biomarker Candidates. *Molecular Biology Reports*, **52**, Article No. 16. https://doi.org/10.1007/s11033-024-10110-w

[8] Qian, H., Maghsoudloo, M., Kaboli, P.J., Babaeizad, A., Cui, Y., Fu, J., *et al.* (2024) Decoding the Promise and Challenges of miRNA-Based Cancer Therapies: An Essential Update on miR-21, miR-34, and miR-155. *International Journal of Medical Sciences*, **21**, 2781-2798. https://doi.org/10.7150/ijms.102123

[9] Bashyam, M.D., Animireddy, S., Bala, P., Naz, A. and George, S.A. (2019) The Yin and Yang of Cancer Genes. *Gene*, **704**, 121-133. https://doi.org/10.1016/j.gene.2019.04.025

[10] Li, X., Moreira, D.C., Bag, A.K., Qaddoumi, I., Acharya, S. and Chiang, J. (2022) The Clinical and Molecular Characteristics of Progressive Hypothalamic/Optic Pathway Pilocytic Astrocytoma. *Neuro-Oncology*, **25**, 750-760. https://doi.org/10.1093/neuonc/noac241

[11] Qin, X., Cardoso Rodriguez, F., Sufi, J., Vlckova, P., Claus, J. and Tape, C.J. (2023) An Oncogenic Phenoscape of Colonic Stem Cell Polarization. *Cell*, **186**, 5554-5568.e18. https://doi.org/10.1016/j.cell.2023.11.004

[12] Nishimura, Y. and Itoh, K. (2019) Involvement of SNX1 in Regulating EGFR Endocytosis in a Gefitinib-Resistant NSCLC Cell Lines. *Cancer Drug Resistance*, **2**, 539-549. https://doi.org/10.20517/cdr.2019.15

[13] Patel, P., Mendoza, A., Robichaux, D.J., Wang, M.C., Wehrens, X.H.T. and Karch, J. (2021) Inhibition of the Anti-Apoptotic BCL-2 Family by BH3 Mimetics Sensitize the Mitochondrial Permeability Transition Pore through Bax and Bak. *Frontiers in Cell and Developmental Biology*, **9**, Article 765973. https://doi.org/10.3389/fcell.2021.765973

[14] Yang, Y., Zhao, B., Lv, L., Yang, Y., Li, S. and Wu, H. (2021) FBXL10 Promotes EMT and Metastasis of Breast Cancer

Cells via Regulating the Acetylation and Transcriptional Activity of Snai1. *Cell Death Discovery*, **7**, Article No. 328. https://doi.org/10.1038/s41420-021-00722-7

[15] Patel, S.A., Nilsson, M.B., Le, X., Cascone, T., Jain, R.K. and Heymach, J.V. (2022) Molecular Mechanisms and Future Implications of VEGF/VEGFR in Cancer Therapy. *Clinical Cancer Research*, **29**, 30-39. https://doi.org/10.1158/1078-0432.ccr-22-1366

[16] Arimura, A., Sakai, K., Kaneshiro, K., Morisaki, T., Hayashi, S., Mizoguchi, K., *et al.* (2024) TP53 and/or BRCA1 Mutations Based on ctDNA Analysis as Prognostic Biomarkers for Primary Triple-Negative Breast Cancer. *Cancers*, **16**, Article 1184. https://doi.org/10.3390/cancers16061184

[17] Wang, Z., Wang, X., Wang, Z., Feng, Y., Jia, Y., Jiang, L., *et al.* (2021) Comparison of Hepatotoxicity Associated with New BCR-ABL Tyrosine Kinase Inhibitors vs Imatinib among Patients with Chronic Myeloid Leukemia: A Systematic Review and Meta-Analysis. *JAMA Network Open*, **4**, e2120165. https://doi.org/10.1001/jamanetworkopen.2021.20165

[18] Fu, K., Xie, F., Wang, F. and Fu, L. (2022) Therapeutic Strategies for EGFR-Mutated Non-Small Cell Lung Cancer Patients with Osimertinib Resistance. *Journal of Hematology & Oncology*, **15**, Article No. 173. https://doi.org/10.1186/s13045-022-01391-4

[19] El-Tanani, M., Nsairat, H., Matalka, I.I., Lee, Y.F., Rizzo, M., Aljabali, A.A., *et al.* (2024) The Impact of the BCR-ABL Oncogene in the Pathology and Treatment of Chronic Myeloid Leukemia. *Pathology—Research and Practice*, **254**, Article ID: 155161. https://doi.org/10.1016/j.prp.2024.155161

[20] Hill, M. and Tran, N. (2021) miRNA Interplay: Mechanisms and Consequences in Cancer. *Disease Models & Mechanisms*, **14**, dmm047662. https://doi.org/10.1242/dmm.047662

[21] Schmitz, U. (2023) Overview of Computational and Experimental Methods to Identify Tissue-Specific MicroRNA Targets. In: Dalmay, T., Ed., *MicroRNA Detection and Target Identification*, Springer, 155-177. https://doi.org/10.1007/978-1-0716-2982-6_12

[22] Liu, Z., Ke, S. and Wan, Y. (2025) miR-126: A Bridge between Cancer and Exercise. *Cancer Cell International*, **25**, Article No. 145. https://doi.org/10.1186/s12935-025-03784-0

[23] Bartoszewska, E., Misiąg, P., Czapla, M., Rakoczy, K., Tomecka, P., Filipski, M., Wawrzyniak-Dzierżek, E. and Choromańska, A. (2025) The Role of microRNAs in Lung Cancer: Mechanisms, Diagnostics and Therapeutic Potential. *International Journal of Molecular Sciences*, **26**, 3736. https://doi.org/10.3390/ijms26083736

[24] Hutter, K., Rülicke, T., Szabo, T.G., Andersen, L., Villunger, A. and Herzog, S. (2022) The miR-15a/16-1 and miR-15b/16-2 Clusters Regulate Early B Cell Development by Limiting IL-7 Receptor Expression. *Frontiers in Immunology*, **13**, Article 967914. https://doi.org/10.3389/fimmu.2022.967914

[25] Callaway, E. and Sanderson, K. (2024) Medicine Nobel Awarded for Gene-Regulating 'MicroRNAs'. *Nature*, **634**, 524-525. https://doi.org/10.1038/d41586-024-03212-9

[26] Li, B., Cao, Y., Sun, M. and Feng, H. (2021) Expression, Regulation, and Function of Exosome-Derived miRNAs in Cancer Progression and Therapy. *The FASEB Journal*, **35**, e21916. https://doi.org/10.1096/fj.202100294rr

[27] Kawaji-Kanayama, Y., Tsukamoto, T., Nakano, M., Tokuda, Y., Nagata, H., Mizuhara, K., *et al.* (2023) miR-17-92 Cluster-BTG2 Axis Regulates B-Cell Receptor Signaling in Mantle Cell Lymphoma. *Cancer Science*, **115**, 452-464. https://doi.org/10.1111/cas.16027

[28] Xu, P., Wu, Q., Yu, J., Rao, Y., Kou, Z., Fang, G., *et al.* (2020) A Systematic Way to Infer the Regulation Relations of miRNAs on Target Genes and Critical miRNAs in Cancers. *Frontiers in Genetics*, **11**, Article 278. https://doi.org/10.3389/fgene.2020.00278

[29] Mao, M., Zhang, J., Xiang, Y., Gong, M., Deng, Y. and Ye, D. (2022) Role of Exosomal Competitive Endogenous RNA (ceRNA) in Diagnosis and Treatment of Malignant Tumors. *Bioengineered*, **13**, 12156-12168. https://doi.org/10.1080/21655979.2022.2073130

[30] Pu, X., Sheng, S., Fu, Y., Yang, Y. and Xu, G. (2024) Construction of circRNA-miRNA-mRNA Cerna Regulatory Network and Screening of Diagnostic Targets for Tuberculosis. *Annals of Medicine*, **56**, Article ID: 2416604. https://doi.org/10.1080/07853890.2024.2416604

[31] Kozłowska-Masłoń, J., Guglas, K., Paszkowska, A., Kolenda, T., Podralska, M., Teresiak, A., *et al.* (2022) Radio-lncRNAs: Biological Function and Potential Use as Biomarkers for Personalized Oncology. *Journal of Personalized Medicine*, **12**, Article 1605. https://doi.org/10.3390/jpm12101605

[32] Zhu, H., Xu, X., Zheng, E., Ni, J., Jiang, X., Yang, M., *et al.* (2022) LncRNA RP11-805J14.5 Functions as a ceRNA to Regulate CCND2 by Sponging miR-34b-3p and miR-139-5p in Lung Adenocarcinoma. *Oncology Reports*, **48**, Article No. 161. https://doi.org/10.3892/or.2022.8376

[33] Rahmati, Y., Asemani, Y., Aghamiri, S., Ezzatifar, F. and Najafi, S. (2021) CiRS-7/CDR1as; An Oncogenic Circular RNA as a Potential Cancer Biomarker. *Pathology—Research and Practice*, **227**, Article ID: 153639. https://doi.org/10.1016/j.prp.2021.153639

[34] Sarkar, N. and Kumar, A. (2020) MicroRNAs: New-Age Panacea in Cancer Therapeutics. *Indian Journal of Surgical Oncology*, **12**, 52-56. https://doi.org/10.1007/s13193-020-01110-w

[35] Ho, P.T.B., Clark, I.M. and Le, L.T.T. (2022) MicroRNA-Based Diagnosis and Therapy. *International Journal of Molecular Sciences*, **23**, Article 7167. https://doi.org/10.3390/ijms23137167

[36] Kubeczko, M., Tudrej, P., Tyszkiewicz, T., Krzywon, A., Oczko-Wojciechowska, M. and Jarząb, M. (2024) Liquid Biopsy Utilizing miRNA in Patients with Advanced Breast Cancer Treated with Cyclin-Dependent Kinase 4/6 Inhibitors. *Oncology Letters*, **27**, Article No. 181. https://doi.org/10.3892/ol.2024.14314

[37] Zhu, X., Shi, C. and Hou, C. (2022) AFAP1-AS1/Hsa-miR-15a-5p/Bcl-2 Axis Is a Potential Regulator of Cancer Cell Proliferation and Apoptosis in Gallbladder Carcinoma. *Nutrition and Cancer*, **74**, 3363-3374. https://doi.org/10.1080/01635581.2022.2059090

[38] Sestito, R., Cianfrocca, R., Tocci, P., Rosanò, L., Sacconi, A., Blandino, G., *et al.* (2020) Targeting Endothelin 1 Receptor-miR-200b/c-ZEB1 Circuitry Blunts Metastatic Progression in Ovarian Cancer. *Communications Biology*, **3**, Article No. 677. https://doi.org/10.1038/s42003-020-01404-3

[39] Shadbad, M.A., Asadzadeh, Z., Derakhshani, A., Hosseinkhani, N., Mokhtarzadeh, A., Baghbanzadeh, A., *et al.* (2021) A Scoping Review on the Potentiality of Pd-L1-Inhibiting MicroRNAs in Treating Colorectal Cancer: Toward Single-Cell Sequencing-Guided Biocompatible-Based Delivery. *Biomedicine & Pharmacotherapy*, **143**, Article ID: 112213. https://doi.org/10.1016/j.biopha.2021.112213

[40] Xue, P., Huang, S., Han, X., Zhang, C., Yang, L., Xiao, W., *et al.* (2021) Exosomal miR-101-3p and miR-423-5p Inhibit Medulloblastoma Tumorigenesis through Targeting FOXP4 and EZH2. *Cell Death & Differentiation*, **29**, 82-95. https://doi.org/10.1038/s41418-021-00838-4

[41] Vairappan, B., Mukherjee, V., Subramanian, S.B., Ram, A.K. and Ravikumar, T.S. (2025) Nimbolide Attenuates Hepatocellular Carcinoma by Regulating miRNAs 21, 145 and 221 and Their Target Gene Expression. *Gene*, **937**, Article ID: 149126. https://doi.org/10.1016/j.gene.2024.149126

[42] Hussen, B.M., Sulaiman, S.H.A., Abdullah, S.R., Hidayat, H.J., Khudhur, Z.O., Eslami, S., *et al.* (2025) miRNA-155: A Double-Edged Sword in Colorectal Cancer Progression and Drug Resistance Mechanisms. *International Journal of Biological Macromolecules*, **299**, Article ID: 140134. https://doi.org/10.1016/j.ijbiomac.2025.140134

[43] Munteanu, V.C., Munteanu, R.A., Onaciu, A., Berindan-Neagoe, I., Petrut, B. and Coman, I. (2020) miRNA-Based Inspired Approach in Diagnosis of Prostate Cancer. *Medicina*, **56**, Article 94. https://doi.org/10.3390/medicina56020094

[44] Li, X., Chen, W., Li, R., Chen, X., Huang, G., Lu, C., *et al.* (2022) Bladder Cancer Diagnosis with a Four-miRNA Panel in Serum. *Future Oncology*, **18**, 3311-3322. https://doi.org/10.2217/fon-2022-0448

[45] Cardinali, B., Tasso, R., Piccioli, P., Ciferri, M.C., Quarto, R. and Del Mastro, L. (2022) Circulating miRNAs in Breast Cancer Diagnosis and Prognosis. *Cancers*, **14**, Article 2317. https://doi.org/10.3390/cancers14092317

[46] Alves dos Santos, K., Clemente dos Santos, I.C., Santos Silva, C., Gomes Ribeiro, H., de Farias Domingos, I. and Nogueira Silbiger, V. (2020) Circulating Exosomal miRNAs as Biomarkers for the Diagnosis and Prognosis of Colorectal Cancer. *International Journal of Molecular Sciences*, **22**, Article 346. https://doi.org/10.3390/ijms22010346

[47] Samara, M., Thodou, E., Patoulioti, M., Poultsidi, A., Thomopoulou, G.E. and Giakountis, A. (2024) Integrated miRNA Signatures: Advancing Breast Cancer Diagnosis and Prognosis. *Biomolecules*, **14**, Article 1352. https://doi.org/10.3390/biom14111352

[48] Yu, A., Choi, Y.H. and Tu, M. (2020) RNA Drugs and RNA Targets for Small Molecules: Principles, Progress, and Challenges. *Pharmacological Reviews*, **72**, 862-898. https://doi.org/10.1124/pr.120.019554

[49] Wu, Q., Yu, L., Lin, X., Zheng, Q., Zhang, S., Chen, D., *et al.* (2020) Combination of Serum miRNAs with Serum Exosomal miRNAs in Early Diagnosis for Non-Small-Cell Lung Cancer. *Cancer Management and Research*, **12**, 485-495. https://doi.org/10.2147/cmar.s232383

[50] Lv, P., Zhang, Z., Hou, L., Zhang, Y., Lu, L., Wang, C., *et al.* (2020) Meta-Analysis of the Clinicopathological Significance of miRNA-145 in Breast Cancer. *Bioscience Reports*, **40**, BSR20193974. https://doi.org/10.1042/bsr20193974

[51] Ma, X., Zhou, F., Yang, D., Chen, Y., Li, M. and Wang, P. (2023) Mirna Detection for Prostate Cancer Diagnosis by Miroll-Cas: miRNA Rolling Circle Transcription for CRISPR-Cas Assay. *Analytical Chemistry*, **95**, 13220-13226. https://doi.org/10.1021/acs.analchem.3c02231

[52] Valihrach, L., Androvic, P. and Kubista, M. (2020) Circulating miRNA Analysis for Cancer Diagnostics and Therapy. *Molecular Aspects of Medicine*, **72**, Article ID: 100825. https://doi.org/10.1016/j.mam.2019.10.002

[53] Andersen, G.B. and Tost, J. (2019) Circulating miRNAs as Biomarker in Cancer. In: Schaffner, F., Merlin, J.L. and von Bubnoff, N., Eds., *Tumor Liquid Biopsies*, Springer, 277-298. https://doi.org/10.1007/978-3-030-26439-0_15

[54] Shi, Y., Liu, Z., Lin, Q., Luo, Q., Cen, Y., Li, J., *et al.* (2021) miRNAs and Cancer: Key Link in Diagnosis and Therapy. *Genes*, **12**, Article 1289. https://doi.org/10.3390/genes12081289

[55] Li, W., Wang, Y., Liu, R., Kasinski, A.L., Shen, H., Slack, F.J., *et al.* (2021) MicroRNA-34a: Potent Tumor Suppressor, Cancer Stem Cell Inhibitor, and Potential Anticancer Therapeutic. *Frontiers in Cell and Developmental Biology*, **9**, Article 640587. https://doi.org/10.3389/fcell.2021.640587

[56] Wang, C., Li, Y., Yi, Y., Liu, G., Guo, R., Wang, L., *et al.* (2022) Hippocampal MicroRNA-26a-3p Deficit Contributes to Neuroinflammation and Behavioral Disorders via P38 MAPK Signaling Pathway in Rats. *Journal of Neuroinflammation*, **19**, Article No. 283. https://doi.org/10.1186/s12974-022-02645-1

[57] Bai, Y., Xiong, Y., Zhang, Y., Cheng, L., Liu, H., Xu, K., *et al.* (2022) Tangeretin Synergizes with 5-Fluorouracil to Induce Autophagy through MicroRNA-21 in Colorectal Cancer Cells. *The American Journal of Chinese Medicine*, **50**, 1681-1701. https://doi.org/10.1142/s0192415x22500719

[58] Zhang, J., Sun, X., Zhao, X., Liu, L., Cheng, X., Yang, C., *et al.* (2022) Watson-Crick Base Pairing-Inspired Laser/GSH Activatable miRNA-Coordination Polymer Nanoplexes for Combined Cancer Chemo-Immuno-Photothermal Therapy. *ACS Applied Materials & Interfaces*, **14**, 20762-20777. https://doi.org/10.1021/acsami.2c03523

[59] Song, H., Ruan, C., Xu, Y., Xu, T., Fan, R., Jiang, T., *et al.* (2021) Survival Stratification for Colorectal Cancer via Multi-Omics Integration Using an Autoencoder-Based Model. *Experimental Biology and Medicine*, **247**, 898-909. https://doi.org/10.1177/15353702211065010

[60] Zhang, B., Tian, L., Xie, J., Chen, G. and Wang, F. (2020) Targeting miRNAs by Natural Products: A New Way for Cancer Therapy. *Biomedicine & Pharmacotherapy*, **130**, Article ID: 110546. https://doi.org/10.1016/j.biopha.2020.110546

[61] Wurm, A.A., Brilloff, S., Kolovich, S., Schäfer, S., Rahimian, E., Kufrin, V., *et al.* (2023) Signaling-Induced Systematic Repression of miRNAs Uncovers Cancer Vulnerabilities and Targeted Therapy Sensitivity. *Cell Reports Medicine*, **4**, Article ID: 101200. https://doi.org/10.1016/j.xcrm.2023.101200

[62] Gaponova, S., Patutina, O., Sen'kova, A., Burakova, E., Savin, I., Markov, A., *et al.* (2022) Single Shot vs. Cocktail: A Comparison of Mono- and Combinative Application of miRNA-Targeted Mesyl Oligonucleotides for Efficient Antitumor Therapy. *Cancers*, **14**, Article 4396. https://doi.org/10.3390/cancers14184396