

## PERSPECTIVE

# Unveiling roles of non-coding RNAs in cancer through advanced technologies

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National Institutes of Health, Grant/Award Numbers: R01HG011633, R01CA262623

**Abstract**

Non-coding RNAs (ncRNAs) have emerged as key regulators in tumorigenesis. In this perspective, we briefly review the significance of ncRNA in cancer biology and highlight recent technological advancements in characterization of ncRNA in cancer research. Specifically, we discuss how these advanced approaches, such as Patho-DBiT, CRISPR screens, and snoKARR-seq, hold the potential to revolutionize ncRNA research by offering comprehensive insights into their spatial expression patterns and functional roles.

**KEYWORDS**

cancer, CRISPR screens, ncRNAs, patho-DBiT, snoKARR-seq, spatial transcriptomics

## 1 | INTRODUCTION

Non-coding RNAs (ncRNAs) are RNA transcripts that do not encode for a protein. Extensive research has explored the functional roles of various ncRNAs, such as long non-coding RNAs (lncRNAs), microRNAs (miRNAs), transfer RNAs (tRNAs), small nucleolar RNAs (snoRNAs), and small nuclear RNAs (snRNAs), in human cancers [1–3]. These ncRNAs play pivotal roles in regulating gene expression, modulating cellular signalling pathways, and influencing critical processes such as proliferation, apoptosis, metastasis, and immune evasion [1, 4]. Their profound impact in cancer biology underscores their potential as diagnostic biomarkers and therapeutic targets. However, the complex mechanisms and spatial dynamics of ncRNAs remain challenging to dissect, necessitating innovative technologies. This perspective briefly reviews the roles of ncRNAs in cancer and highlights technological advancements that enable their functional characterization.

## 2 | FUNCTIONAL SIGNIFICANCE OF ncRNAs IN CANCER

ncRNAs are emerging as pivotal regulators in the intricate landscape of gene expression, playing essential roles in cancer research. These ncRNAs influence key cellular processes through diverse regulatory mechanisms, which are briefly summarized in this section with a focus in cancer research. With their functional versatility and broad impact on gene regulation, ncRNAs hold significant promise as biomarkers and/or therapeutic targets in oncology.

### 2.1 | lncRNA

lncRNAs (>200 nucleotides) are critical regulators of various biological processes, including tumorigenesis, proliferation, metabolism, and immune responses. In tumorigenesis, lncRNAs modulate oncogenic and

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tumour suppressor pathways, influencing key processes such as invasion, metastasis and angiogenesis [5]. They also play a central role in metabolic reprogramming by regulating genes involved in glycolysis, lipid metabolism, and mitochondrial function, thereby supporting the metabolic demands of cancer cells [6]. Additionally, lncRNAs control cell cycle progression and apoptosis, acting as either promoters or inhibitors of cell growth, depending on the cellular context [7]. In immune responses, lncRNAs regulate immune cell differentiation, cytokine production, and interactions within the tumour microenvironment (TME), shaping the immune landscape of tumours [8]. lncRNAs often exhibit tissue- and cell-specific expression, and their dysregulation, arising from mutations, deletions, or altered biogenesis, is closely related to cancer progression [9]. For example, lncRNA LINK-A promotes immune evasion and metastasis in triple-negative breast cancer by disrupting antigen presentation and tumour suppressor pathways through G-protein-coupled receptor signalling, leading to peptide-loading complex, Rb and p53 degradation, while its inhibition sensitizes tumours to immune checkpoint blockade therapy [10].

## 2.2 | miRNA

MicroRNAs (miRNAs) are small ncRNAs (18–25 nucleotides) that post-transcriptionally regulate gene expression by targeting messenger RNAs (mRNAs) for degradation or translational repression [11]. As oncogenes, miRNAs drive cancer progression by promoting cell proliferation, survival and metastasis through the suppression of tumour suppressor genes [12]. Conversely, they can also act as tumour suppressors by inhibiting oncogenic pathways, thereby reducing tumour growth, and preventing metastatic spread [12]. Dysregulation of miRNAs, whether through mutations, deletions, amplifications or defective biogenesis, significantly contributes to tumour initiation and advancement [13–16]. Furthermore, transcriptional regulation by oncogenic or tumour-suppressive factors, such as c-Myc or p53, integrates miRNAs into the intricate network of cancer biology [17].

## 2.3 | tRNA

tRNAs (70–87 nucleotides) not only support protein translation but also contribute to cancer by overcoming translational bottlenecks and promoting oncogenic protein synthesis [18–20]. Upregulation of tRNAs in cancer cells enhance the synthesis of oncogenic proteins by resolving translational bottlenecks, facilitating rapid tumour growth and proliferation [21]. Alterations in tRNA expression are further coupled with dysregulation of translational enzymes, such as tRNA modification

enzymes and aminoacyl-tRNA synthetases, which amplify translational efficiency and tumour growth [21, 22]. In addition to their functional roles, tRNAs exhibit tissue-specific expression patterns and have strong associations with clinical outcomes, making them promising biomarkers for cancer diagnosis, prognosis and monitoring disease progression [23]. Dysregulated tRNAs also offer therapeutic potential that targeting abnormal tRNA expression or translational processes may reduce oncogene abundance [24], improve drug sensitivity [25] and even generate neoantigens for immunotherapy [26].

## 2.4 | snoRNA

snoRNAs (60–300 nucleotides) are traditionally known for guiding post-transcriptional RNA modifications, such as 2'-O-methylation and pseudouridylation, essential for ribosomal RNA and snRNA stability and function [27]. Beyond these canonical functions, snoRNAs actively contribute to cancer by modulating oncogenic signalling pathways, thereby promoting tumour proliferation, survival, and metastasis through interactions with key molecular players [28]. They also influence gene translation by modifying rRNAs and interacting with mRNAs, enhancing the production of proteins critical for tumour growth and progression [28]. Additionally, certain snoRNAs regulate alternative splicing, affecting the production of oncogenic or tumour-suppressive isoforms and adding complexity to cancer transcriptomes [28]. The dysregulation of snoRNAs has been associated with clinical outcomes [29–34], positioning them as promising biomarkers for cancer diagnosis, prognosis and therapeutic targets.

## 2.5 | snRNA

snRNAs, approximately 150 nucleotides in length, are essential components of spliceosomes and play a critical role in RNA splicing [35]. Emerging evidence highlights that dysregulation of snRNAs in cancer leads to altered splicing patterns, resulting in the production of oncogenic transcripts while reducing the expression of tumour suppressors, thereby driving tumorigenesis [36]. Mutations or aberrant expression of snRNAs can disrupt normal alternative splicing, affecting key cancer signalling pathways such as cell cycle regulation, apoptosis, DNA repair, PI3K/AKT and mitogen-activated protein kinase, promoting tumour growth and metastasis [37–39]. Additionally, snRNAs have been associated with clinical outcomes, including cancer prognosis and therapeutic response, making them valuable biomarkers for cancer diagnosis and treatment monitoring [40, 41]. Targeting dysregulated snRNAs or correcting their associated splicing errors offers a

promising avenue for anti-cancer strategies, potentially restoring normal splicing and inhibiting oncogenic pathways [42].

### 3 | TECHNOLOGICAL ADVANCEMENTS FOR CHARACTERIZATION OF ncRNAs

The functional analysis of ncRNAs has been constrained by technical limitations, particularly in degraded formalin-fixed paraffin-embedded (FFPE) tissues, which are essential for clinical diagnostics [43]. Recent innovations are transforming ncRNA research and enabling unprecedented insights into their roles in cancer (Figure 1).

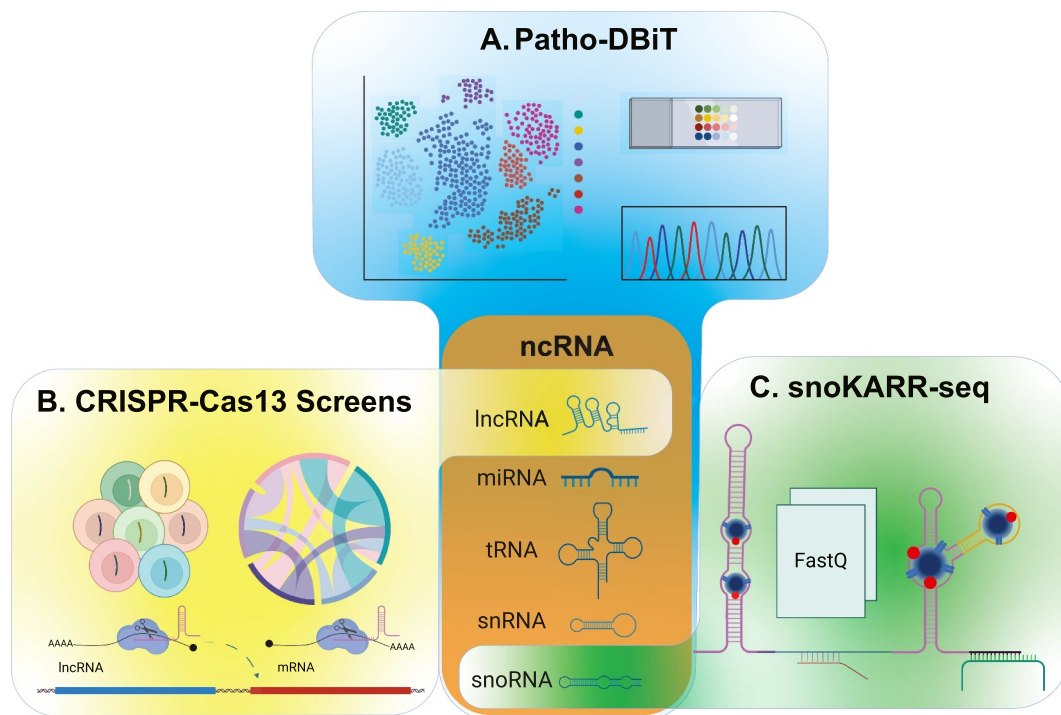
#### 3.1 | ncRNA-spatial transcriptomics (ST)

ST combines spatially resolved molecular profiling with transcriptome-wide analysis, enabling the precise mapping of RNA expression within intact tissue environments [44–47]. This approach enhances our understanding of tumour heterogeneity, therapeutic resistance and the role of the TME in disease progression [48–50]. Recent advancement Patho-DBiT

extends the power of ST by enabling high-sensitivity profiling of diverse RNA species in FFPE tissues [51]. By combining polyadenylation with spatial barcoding, Patho-DBiT accurately maps a broad range of ncRNAs. For example, Patho-DBiT enhances gene body coverage and significantly increases 5' untranslated region read mapping, enabling the detection of a diverse range of ncRNAs [51], including lncRNAs, miRNAs, tRNAs, snRNAs, and snoRNAs (Figure 1A). This technology has been instrumental in reconstructing spatial cellular compositions and uncovering molecular pathways in archival cancer tissues, bridging histopathology and genomics. Patho-DBiT's ability to reveal region-specific ncRNA activities, tumour vulnerabilities, drug-resistant clones and patient-specific targets positions it as a transformative tool in precision oncology. By overcoming technical barriers associated with FFPE tissues, it enables high-resolution exploration of ncRNA biology, providing unprecedented insights into ncRNA-mediated mechanisms and tumour heterogeneity.

#### 3.2 | RNA-targeting CRISPR screens

CRISPR interference (CRISPRi) and CRISPR activation (CRISPRa) are CRISPR-Cas9-based technologies



**FIGURE 1** Overview of advanced technologies for ncRNA research in cancer biology. (A) Patho-DBiT enables high-sensitivity profiling of diverse RNA species, uncovering patient-specific vulnerabilities. (B) RNA-targeting CRISPR-Cas13 screens systematically perturb lncRNAs with strand and transcript specificity, identifying and comparing essential lncRNAs involved in different human cell lines. (C) snoKARR-seq employs chemical crosslinking to identify transcriptome-wide snoRNA-mRNA interactions, revealing noncanonical functions of snoRNAs in mRNA dynamics relevant to cancer progression. KARR-seq, kethoxal assisted RNA-RNA interaction sequencing; lncRNAs, long non-coding RNAs; mRNA, messenger RNA; ncRNA, noncoding RNA; snoRNAs, small nucleolar RNAs.

designed for gene regulation [52, 53]. CRISPRi employs a catalytically inactive Cas9 (dCas9) fused with a transcriptional repressor to silence gene expression at specific genomic loci [52], while CRISPRa uses dCas9 fused to transcriptional activators to enhance gene expression [53]. These approaches have proven invaluable for identifying functional lncRNAs by modulating their expression levels. Recently, the development of CRISPR-Cas13, an RNA-targeting system, has revolutionized lncRNA screening [54] (Figure 1B). Unlike DNA-based perturbation, CRISPR-Cas13 directly targets lncRNA transcripts with strand- and transcript-specific precision, minimizing unintended effects on neighbouring genes or genomic elements. By perturbing about 6200 lncRNAs across multiple human cell lines, these screens have identified hundreds of lncRNAs with context-specific or broad essentiality. For example, they identified cell-type-specific essential lncRNAs, *XLOC\_013548* (essential in HAP1) and *XLOC\_044949* (essential in THP1), which showed variable expression across cell lines [54]. In contrast, broadly essential lncRNAs exhibited more consistent expression and depletion patterns [54]. Importantly, many essential lncRNAs operate independently of nearby protein-coding genes, emphasizing their unique functional roles.

### 3.3 | snoKARR-seq

Kethoxal assisted RNA–RNA interaction sequencing (Figure 1C) is a cutting-edge technique that uses N<sub>3</sub>-kethoxal labelling and multifunctional chemical cross-linkers to covalently capture RNA–RNA interactions and higher-order RNA structures directly within cells, independent of local protein binding [55]. This method provides highly sensitive and accurate detection of widespread intermolecular RNA–RNA interactions and RNA folding dynamics. Building upon this foundation, snoKARR-seq, a recent breakthrough, extends these capabilities to systematically identify RNA targets of snoRNAs across the transcriptome [56]. This chemical crosslinking-based approach has uncovered thousands of previously unrecognized snoRNA–mRNA interactions, revealing non-canonical snoRNA functions beyond their traditional roles in RNA modifications. Notably, snoKARR-seq has demonstrated that snoRNAs can regulate mRNA dynamics and enhance the secretion of secretory and membrane proteins, processes highly relevant to cancer progression and the TME. For example, *SNORA73*, one of these snoRNAs, targets mRNAs encoding secretory and membrane proteins and interacts with 7SL RNA, a component of the signal recognition particle (SRP) essential for protein secretion. The mRNA–*SNORA73*–7SL RNA interactions strengthen the association between *SNORA73*-targeted

mRNAs and SRP, thereby enhancing the secretion of the encoded proteins [56].

## 4 | DISCUSSION AND PERSPECTIVE

Recent advancements in ST, RNA-targeting CRISPR screens and snoRNA-target profiling have revolutionized ncRNA research in cancer (Figure 1), providing unparalleled insights into their roles in tumour heterogeneity, progression and therapy resistance. Integrating these technologies with multi-omics approaches and advanced computational tools promises to enhance the understanding of ncRNA-mediated mechanisms and facilitate the identification of clinically actionable targets.

### AUTHOR CONTRIBUTIONS

**Runhao Wang:** Investigation; visualization; writing—original draft. **Leng Han:** Writing—review and editing; project administration; supervision.

### ACKNOWLEDGMENTS

This work was supported by the National Institutes of Health (NIH) (R01HG011633 and R01CA262623) to Leng Han.

### CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

### ETHICS STATEMENT

This article is a perspective article and does not contain any studies with human or animal subjects performed by any of the authors.

### DATA AVAILABILITY STATEMENT

The authors have nothing to report.

### REFERENCES

- [1] Nemeth K, Bayraktar R, Ferracin M, Calin GA. Non-coding RNAs in disease: from mechanisms to therapeutics. *Nat Rev Genet.* 2024;25(3):211–32.
- [2] Zhang Z, Zhang J, Diao L, Han L. Small non-coding RNAs in human cancer: function, clinical utility, and characterization. *Oncogene.* 2021;40(9):1570–7.
- [3] Xiang Y, Ye Y, Zhang Z, Han L. Maximizing the utility of cancer transcriptomic data. *Trends Cancer.* 2018;4(12):823–37.
- [4] Winkle M, El-Daly SM, Fabbri M, Calin GA. Noncoding RNA therapeutics — challenges and potential solutions. *Nat Rev Drug Discov.* 2021;20(8):629–51.
- [5] Liu CG, Li J, Xu Y, Li W, Fang SX, Zhang Q, et al. Long non-coding RNAs and circular RNAs in tumor angiogenesis: from mechanisms to clinical significance. *Mol Ther Oncolytics.* 2021;22:336–54.
- [6] Lin W, Zhou Q, Wang CQ, Zhu L, Bi C, Zhang S, et al. LncRNAs regulate metabolism in cancer. *Int J Biol Sci.* 2020; 16(7):1194–206.
- [7] Peng WX, Koirala P, Mo YY. LncRNA-mediated regulation of cell signaling in cancer. *Oncogene.* 2017;36(41):5661–7.

- [8] Guo Y, Xie Y, Luo Y. The role of long non-coding RNAs in the tumor immune microenvironment. *Front Immunol.* 2022; 13:851004.
- [9] Kornienko AE, Guenzl PM, Barlow DP, Pauler FM. Gene regulation by the act of long non-coding RNA transcription. *BMC Biol.* 2013;11(1):59.
- [10] Hu Q, Ye Y, Chan LC, Li Y, Liang K, Lin A, et al. Oncogenic lncRNA downregulates cancer cell antigen presentation and intrinsic tumor suppression. *Nat Immunol.* 2019;20(7):835–51.
- [11] Ratti M, Lampis A, Ghidini M, Salati M, Mirchev MB, Valeri N, et al. MicroRNAs (miRNAs) and long non-coding RNAs (lncRNAs) as new tools for cancer therapy: first steps from bench to bedside. *Target Oncol.* 2020;15(3):261–78.
- [12] Chen LL, Kim VN. Small and long non-coding RNAs: past, present, and future. *Cell.* 2024;187(23):6451–85.
- [13] Fernandez N, Cordiner RA, Young RS, Hug N, Macias S, Cáceres JF. Genetic variation and RNA structure regulate microRNA biogenesis. *Nat Commun.* 2017;8(1):15114.
- [14] Pekarsky Y, Balatti V, Croce CM. BCL2 and miR-15/16: from gene discovery to treatment. *Cell Death Differ.* 2018;25(1):21–6.
- [15] He L, Thomson JM, Hemann MT, Hernando-Monge E, Mu D, Goodson S, et al. A microRNA polycistron as a potential human oncogene. *Nature.* 2005;435(7043):828–33.
- [16] Annese T, Tamma R, De Giorgis M, Ribatti D. microRNAs biogenesis, functions and role in tumor angiogenesis. *Front Oncol.* 2020;10:581007.
- [17] Marson A, Levine SS, Cole MF, Frampton GM, Brambrink T, Johnstone S, et al. Connecting microRNA genes to the core transcriptional regulatory circuitry of embryonic stem cells. *Cell.* 2008;134(3):521–33.
- [18] Grewal SS. Why should cancer biologists care about tRNAs? tRNA synthesis, mRNA translation and the control of growth. *Biochim Biophys Acta.* 2015;1849(7):898–907.
- [19] Gomez-Roman N, Grandori C, Eisenman RN, White RJ. Direct activation of RNA polymerase III transcription by c-Myc. *Nature.* 2003;421(6920):290–4.
- [20] Dever TE, Green R. The elongation, termination, and recycling phases of translation in eukaryotes. *Cold Spring Harbor Perspect Biol.* 2012;4(7):a013706.
- [21] Zhang Z, Ye Y, Gong J, Ruan H, Liu CJ, Xiang Y, et al. Global analysis of tRNA and translation factor expression reveals a dynamic landscape of translational regulation in human cancers. *Commun Biol.* 2018;1:234.
- [22] Hernandez-Alias X, Benisty H, Schaefer MH, Serrano L. Translational efficiency across healthy and tumor tissues is proliferation-related. *Mol Syst Biol.* 2020;16(3):e9275.
- [23] Zhang Z, Ruan H, Liu CJ, Ye Y, Gong J, Diao L, et al. tRic: a user-friendly data portal to explore the expression landscape of tRNAs in human cancers. *RNA Biol.* 2020;17(11):1674–9.
- [24] Goodarzi H, Nguyen HCB, Zhang S, Dill BD, Molina H, Tavazoie SF. Modulated expression of specific tRNAs drives gene expression and cancer progression. *Cell.* 2016;165(6):1416–27.
- [25] Wang X, Chow CR, Ebine K, Lee J, Rosner MR, Pan T, et al. Interaction of tRNA with MEK2 in pancreatic cancer cells. *Sci Rep.* 2016;6(1):28260.
- [26] Santos M, Fidalgo A, Varanda AS, Oliveira C, Santos MAS. tRNA deregulation and its consequences in cancer. *Trends Mol Med.* 2019;25(10):853–65.
- [27] Dupuis-Sandoval F, Poirier M, Scott MS. The emerging landscape of small nucleolar RNAs in cell biology. *Wiley Interdiscip Rev RNA.* 2015;6(4):381–97.
- [28] Liang J, Wen J, Huang Z, Chen X, Zhang B, Chu L. Small nucleolar RNAs: insight into their function in cancer. *Front Oncol.* 2019;9:587.
- [29] Mannoor K, Shen J, Liao J, Liu Z, Jiang F. Small nucleolar RNA signatures of lung tumor-initiating cells. *Mol Cancer.* 2014; 13(1):104.
- [30] Yang Y, Zhang H, Xie Y, Zhang S, Zhu J, Yin G, et al. Preliminary screening and identification of differentially expressed metastasis-related ncRNAs in ovarian cancer. *Oncol Lett.* 2018;15:368–74.
- [31] Cui L, Nakano K, Obchoei S, Setoguchi K, Matsumoto M, Yamamoto T, et al. Small nucleolar noncoding RNA SNORA23, up-regulated in human pancreatic ductal adenocarcinoma, regulates expression of spectrin repeat-containing nuclear envelope 2 to promote growth and metastasis of xenograft tumors in mice. *Gastroenterology.* 2017;153(1):292–306.e2.
- [32] Gong J, Li Y, Liu C, Xiang Y, Li C, Ye Y, et al. A pan-cancer analysis of the expression and clinical relevance of small nucleolar RNAs in human cancer. *Cell Rep.* 2017;21(7):1968–81.
- [33] Liu Y, Ruan H, Li S, Ye Y, Hong W, Gong J, et al. The genetic and pharmacogenomic landscape of snoRNAs in human cancer. *Mol Cancer.* 2020;19(1):108.
- [34] Wang R, Chen C, Liu Y, Luo M, Yang J, Chen Y, et al. The pharmacogenomic and immune landscape of snoRNAs in human cancers. *Cancer Lett.* 2024;605:217304.
- [35] Chen W, Moore MJ. Spliceosomes. *Curr Biol CB.* 2015;25(5):R181–3.
- [36] Dvinge H, Guenthoer J, Porter PL, Bradley RK. RNA components of the spliceosome regulate tissue- and cancer-specific alternative splicing. *Genome Res.* 2019;29(10):1591–604.
- [37] Inoue D, Guo-Liang C, Liu B, Lee SC, Michel BC, Pangallo J, et al. Spliceosomal disruption of the non-canonical SWI/SNF chromatin remodeling complex in SF3B1 mutant leukemias. *Blood.* 2019;134(Suppl 1):637.
- [38] Shuai S, Suzuki H, Diaz-Navarro A, Nadeu F, Kumar SA, Gutierrez-Fernandez A, et al. The U1 spliceosomal RNA is recurrently mutated in multiple cancers. *Nature.* 2019; 574(7780):712–6.
- [39] Suzuki H, Kumar SA, Shuai S, Diaz-Navarro A, Gutierrez-Fernandez A, De Antonellis P, et al. Recurrent noncoding U1 snRNA mutations drive cryptic splicing in SHH medulloblastoma. *Nature.* 2019;574(7780):707–11.
- [40] Oh JM, Venters CC, Di C, Pinto AM, Wan L, Younis I, et al. U1 snRNP regulates cancer cell migration and invasion in vitro. *Nat Commun.* 2020;11:1.
- [41] Dong X, Ding S, Yu M, Niu L, Xue L, Zhao Y, et al. Small nuclear RNAs (U1, U2, U5) in tumor-educated platelets are downregulated and act as promising biomarkers in lung cancer. *Front Oncol.* 2020;10:1627.
- [42] Bradley RK, Anczuków O. RNA splicing dysregulation and the hallmarks of cancer. *Nat Rev Cancer.* 2023;23(3):135–55.
- [43] Mathieson W, Thomas GA. Why formalin-fixed, paraffin-embedded biospecimens must be used in genomic medicine: an evidence-based review and conclusion. *J Histochem Cytochem.* 2020;68(8):543–52.
- [44] Baysoy A, Bai Z, Satija R, Fan R. The technological landscape and applications of single-cell multi-omics. *Nat Rev Mol Cell Biol.* 2023;24(10):695–713.
- [45] Bressan D, Battistoni G, Hannon GJ. The dawn of spatial omics. *Science.* 2023;381(6657):eabq4964.
- [46] Deng Y, Bai Z, Fan R. Microtechnologies for single-cell and spatial multi-omics. *Nat Rev Bioeng.* 2023;1(10):769–84.
- [47] Chen J, Larsson L, Swarbrick A, Lundberg J. Spatial landscapes of cancers: insights and opportunities. *Nat Rev Clin Oncol.* 2024;21(9):660–74.

- [48] Rao A, Barkley D, França GS, Yanai I. Exploring tissue architecture using spatial transcriptomics. *Nature*. 2021;596(7871):211–20.
- [49] Jin Y, Zuo Y, Li G, Liu W, Pan Y, Fan T, et al. Advances in spatial transcriptomics and its applications in cancer research. *Mol Cancer*. 2024;23(1):129.
- [50] Zhang L, Chen D, Song D, Liu X, Zhang Y, Xu X, et al. Clinical and translational values of spatial transcriptomics. *Signal Transduct Targeted Ther*. 2022;7(1):111.
- [51] Bai Z, Zhang D, Gao Y, Tao B, Zhang D, Bao S, et al. Spatially exploring RNA biology in archival formalin-fixed paraffin-embedded tissues. *Cell*. 2024;187(23):6760–79.e24.
- [52] Liu SJ, Malatesta M, Lien BV, Saha P, Thombare SS, Hong SJ, et al. CRISPRi-based radiation modifier screen identifies long non-coding RNA therapeutic targets in glioma. *Genome Biol*. 2020;21(1):83.
- [53] Joung J, Engreitz JM, Konermann S, Abudayyeh OO, Verdine VK, Aguet F, et al. Genome-scale activation screen identifies a lncRNA locus regulating a gene neighbourhood. *Nature*. 2017;548(7667):343–6.
- [54] Liang WW, Müller S, Hart SK, Wessels HH, Méndez-Mancilla A, Sookdeo A, et al. Transcriptome-scale RNA-targeting CRISPR screens reveal essential lncRNAs in human cells. *Cell*. 2024:S0092867424012030.
- [55] Wu T, Cheng AY, Zhang Y, Xu J, Wu J, Wen L, et al. KARR-seq reveals cellular higher-order RNA structures and RNA–RNA interactions. *Nat Biotechnol*. 2024;42(12):1909–20.
- [56] Liu B, Wu T, Miao BA, Ji F, Liu S, Wang P, et al. snoRNA-facilitated protein secretion revealed by transcriptome-wide snoRNA target identification. *Cell*. 2024:S0092867424012698.

**How to cite this article:** Wang R, Han L. Unveiling roles of non-coding RNAs in cancer through advanced technologies. *Quantitative Biology*. 2025;e70005. <https://doi.org/10.1002/qub2.70005>