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Oncogenic Long Non-Coding RNAs in Cancer: Comparative Analysis of HOTAIR and MINCR in Modulating Transcriptional and Post Transcriptional Pathways

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ABSTRACT

***Background**: Long non-coding RNAs (lncRNAs) have emerged as key regulators of gene expression in cancer, modulating chromatin architecture, transcriptional programs, and post-transcriptional processes. HOTAIR and MINCR are two prototypical oncogenic lncRNAs that have been independently linked to tumour progression, metastasis, and therapy resistance, but their comparative roles in shaping transcriptional and post-transcriptional oncogenic pathways remain incompletely synthesised. **Objective**: To compare the molecular functions of HOTAIR and MINCR in human malignancies, focusing on their roles in transcriptional and post-transcriptional regulation, oncogenic signalling, and clinically relevant outcomes, and to evaluate their potential as prognostic biomarkers and therapeutic targets. **Methods**: A narrative comparative review was conducted using PubMed, Embase, Web of Science, and Google Scholar up to December 2024 to identify mechanistic, translational, and clinical studies of HOTAIR and MINCR in cancer. Eligible studies included experimental models, clinical cohorts, and meta-analyses reporting molecular mechanisms, cellular phenotypes, or associations with stage, treatment response, or survival. Data on chromatin remodelling, MYC signalling, microRNA interactions, and clinical endpoints were extracted and summarised in comparative tables. **Results**: HOTAIR predominantly functions as an epigenetic scaffold that recruits PRC2 and LSD1/CoREST complexes to enforce transcriptional silencing of tumour suppressor genes, promoting EMT, metastasis, and chemoresistance. Meta-analytic data show that high HOTAIR expression approximately doubles the hazard of death across multiple cancers. MINCR is a MYC-induced lncRNA that amplifies MYC transcriptional programs, enhances expression of cell-cycle regulators, and promotes proliferation and survival, particularly in MYC-positive lymphomas and NSCLC. MINCR is consistently upregulated in tumour tissues, and its silencing reduces proliferation and induces apoptosis, although large pooled survival analyses remain limited. **Conclusion**: HOTAIR and MINCR exemplify distinct yet convergent oncogenic lncRNA mechanisms—epigenetic suppression and transcriptional amplification—that cooperatively drive malignant progression and therapy resistance. HOTAIR currently has stronger prognostic validation, whereas MINCR represents a promising biomarker and target in MYC-driven cancers. Integrating both lncRNAs into biomarker panels and therapeutic strategies may enhance precision in cancer diagnosis, risk stratification, and targeted treatment.*

Keywords
long non-coding RNA; HOTAIR; MINCR; MYC; chromatin remodelling; epigenetics; transcriptional regulation; cancer prognosis; chemoresistance.

INTRODUCTION

Cancer remains a leading cause of morbidity and mortality worldwide, driven by uncontrolled cellular proliferation, evasion of apoptosis, invasion, and metastatic spread across diverse tissue types (1). Despite major advances in molecular oncology, targeted therapy, and immuno-oncology, tumour evolution and therapy resistance continue to undermine durable responses, reflecting the profound biological complexity and adaptability of malignant cells and their microenvironment (2). Within this landscape, non-coding elements of the genome—once dismissed as "junk" DNA and RNA—are now recognised as central regulators of oncogenic signalling, immune evasion, and treatment failure.

Among non-coding RNAs, long non-coding RNAs (lncRNAs), defined as transcripts longer than 200 nucleotides without protein-coding potential, have emerged as key regulators of genome architecture and gene expression at transcriptional and post-transcriptional levels (3). LncRNAs interact with chromatin-modifying complexes, transcription factors, RNA-binding proteins, and microRNAs to regulate chromatin state, transcription initiation and elongation, RNA splicing, stability, and translation. Through these mechanisms, they influence developmental processes, cellular differentiation, stress responses, and multiple hallmarks of cancer, including sustained proliferative signalling, resistance to cell death, invasion, metastasis, and therapy resistance (3).

LncRNAs can act as oncogenes or tumour suppressors depending on cellular context. Oncogenic lncRNAs are typically overexpressed in malignant tissues, promote cell-cycle progression, inhibit apoptosis, enable epithelial–mesenchymal transition (EMT), and foster metastatic dissemination. Conversely, tumour-suppressive lncRNAs restrain proliferation or promote apoptosis and are often silenced in advanced tumours. HOTAIR (HOX

transcript antisense intergenic RNA) is one of the most extensively studied oncogenic lncRNAs. It is transcribed from the HOXC locus and functions as a modular scaffold that recruits chromatin-modifying complexes, particularly Polycomb Repressive Complex 2 (PRC2) and the LSD1/CoREST complex, to specific genomic regions, inducing H3K27 trimethylation and H3K4 demethylation, thereby enforcing transcriptional silencing of tumour suppressor genes (4,10). HOTAIR is frequently overexpressed in breast, liver, lung, gastrointestinal, and urogenital cancers, where its upregulation correlates with higher tumour stage, lymph node involvement, distant metastasis, and poor survival (5–7,9,10). It has also been implicated in endocrine crosstalk and is transcriptionally induced by estradiol in hormone-responsive tumours, further integrating tumour biology with systemic signalling (4).

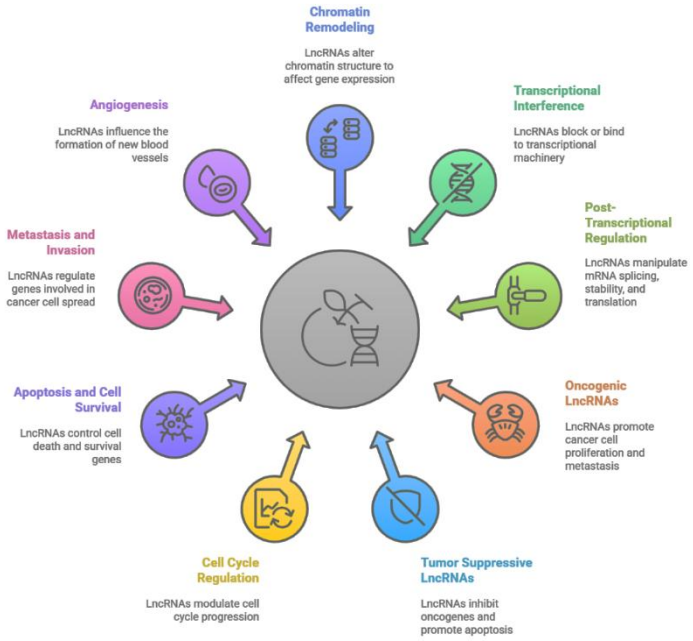

Figure 1 LncRNA-Mediated Gene Regulation in Cancer

MINCR (MYC-induced long non-coding RNA) represents a more recently characterised oncogenic lncRNA that is tightly linked to MYC-driven transcriptional programs. Initially identified in MYC-positive B-cell lymphomas, MINCR shows strong positive correlation with MYC expression and modulates expression of MYC target genes that control cell cycle progression and DNA replication (12). In experimental models, MINCR knockdown leads to impaired cell-cycle progression and decreased expression of MYC-regulated cell-cycle genes, whereas its overexpression reinforces MYC-driven proliferation (12). Subsequent work in non-small cell lung cancer (NSCLC) has shown that MINCR is upregulated in tumour tissue and NSCLC cell lines, where it promotes proliferation, cell-cycle progression, and resistance to apoptosis by enhancing c-Myc levels and downstream effectors such as cyclin A, cyclin D, CDK2, and CDK4 (13). Beyond lymphoma and NSCLC, MINCR dysregulation has been reported in hepatocellular carcinoma, gallbladder cancer, colorectal cancer, nasopharyngeal carcinoma, and glioma, where it frequently acts as an oncogenic driver and prognostic biomarker (14).

A growing body of evidence highlights that HOTAIR and MINCR converge on critical oncogenic pathways yet differ strikingly in their primary modes of action. HOTAIR predominantly reprograms the epigenetic landscape by recruiting chromatin-remodelling complexes to silence tumour suppressor loci and rewire transcriptional networks (4,5,8,10,11). MINCR, in contrast, functions mainly as a transcriptional amplifier within the MYC axis, reinforcing MYC-driven gene expression programs and affecting cell-cycle regulators and apoptosis pathways (12–14). Both lncRNAs have been individually linked to chemoresistance, EMT, and metastatic behaviour, and both show promise as biomarkers and potential therapeutic targets (5–9,13,14). However, existing literature is fragmented: reviews typically focus either on HOTAIR or on MINCR, or they address lncRNAs in aggregate without directly comparing these two archetypal oncogenic lncRNAs in terms of their molecular architecture, pathway crosstalk, and clinical translation (5,8,9,14).

Accordingly, the present narrative review addresses a focused PICO-style question: in patients with solid and haematological malignancies (Population), how does dysregulated expression of HOTAIR and MINCR (Intervention/exposure) compared with lower expression or absence of these lncRNAs (Comparator) influence transcriptional and post-transcriptional regulation, oncogenic phenotypes, and clinically relevant outcomes such as survival, metastasis, and therapy resistance (Outcomes)? The objective of this study is to synthesise and compare the molecular mechanisms by which HOTAIR and MINCR modulate chromatin, transcriptional networks, and post-transcriptional processes across cancer types, and to critically appraise the evidence supporting their roles as prognostic biomarkers and therapeutic targets. This review specifically seeks to clarify how their distinct mechanistic profiles translate into overlapping yet non-identical oncogenic signatures, thereby informing rational strategies for biomarker development and lncRNA-targeted interventions.

MATERIALS AND METHODS

This work was conceived as a focused narrative, comparative review of the roles of HOTAIR and MINCR in human malignancies. The study design was chosen to integrate mechanistic, translational, and clinical evidence, allowing detailed pathway-level comparison while maintaining enough flexibility to incorporate diverse study types, including in vitro and in vivo functional studies, clinical cohorts, and meta-analyses. The primary analytic perspective was mechanistic and translational rather than epidemiological, with the goal of mapping how these lncRNAs shape transcriptional and post-transcriptional landscapes and how those molecular effects relate to tumour phenotype and clinical outcomes.

The literature search was conducted in PubMed, Embase, Web of Science, and Google Scholar for articles published up to December 2024. The search strategy combined controlled vocabulary and free-text terms related to lncRNAs, HOTAIR, MINCR, and cancer. Representative search strings were: ("HOTAIR" OR "HOX transcript antisense RNA") AND (cancer OR carcinoma OR neoplasm); ("MINCR" OR "MYC-induced long non-coding RNA") AND (cancer OR lymphoma OR "non-small cell lung cancer"); and "long noncoding RNA" AND (transcriptional regulation OR epigenetic OR chemoresistance) (3–5,8,9,12–14). Reference lists from relevant primary studies, reviews, and meta-analyses were manually screened to identify additional eligible publications. No language restrictions were applied at the search stage; however, only full-text articles in English were finally included to ensure consistent detailed data extraction.

Eligible studies were required to meet at least one of the following criteria: (i) experimental studies (cell lines, organoids, or animal models) interrogating HOTAIR or MINCR function in oncogenic processes such as proliferation, apoptosis, EMT, invasion, metastasis, angiogenesis, or drug resistance; (ii) clinical observational studies correlating HOTAIR or MINCR expression with tumour stage, histopathological features, treatment response, or patient outcomes (e.g., overall survival, disease-free survival, progression-free survival); or (iii) systematic reviews or meta-analyses focused on HOTAIR or MINCR in cancer. Studies were excluded if they lacked primary mechanistic or clinical data (e.g., commentaries, editorials), focused on non-malignant conditions only, did not clearly specify the lncRNA under investigation, or provided insufficient detail for extracting molecular mechanisms or outcome associations (5–9,12–14).

Two reviewers independently screened titles and abstracts for relevance, followed by full-text assessment of potentially eligible records. Disagreements were resolved by discussion, with emphasis on conservative inclusion when studies provided novel mechanistic insights or clinically relevant associations. Although this review did not adhere to a formal PRISMA protocol, the selection process aimed to reduce selection bias by prespecifying inclusion criteria, systematically screening multiple databases, and cross-checking reference lists for saturation of major mechanistic and clinical themes (5,8,9,12–14).

For each included study, data were extracted into structured templates capturing: cancer type and model system; sample size and key clinical or experimental characteristics; method of lncRNA quantification; primary and secondary outcomes; effect estimates (hazard ratios, odds ratios, relative expression changes, or mean differences) with corresponding 95% confidence intervals and p-values when available; and mechanistic details, including interacting proteins, chromatin modifiers, transcription factors, microRNAs, signalling pathways, and downstream gene sets (4–14). Where possible, we extracted summary statistics directly from tables or text; when only graphical data were provided, direction and significance of associations were recorded qualitatively. No novel pooling of effect sizes was undertaken; instead, we relied on reported summary estimates from published meta-analyses or individual studies.

Variables of interest were operationally defined as follows. Molecular endpoints included changes in chromatin marks (e.g., H3K27 trimethylation), recruitment of PRC2 or LSD1, modulation of MYC and its downstream targets, alterations in EMT markers (E-cadherin, N-cadherin, vimentin), and changes in expression of apoptotic regulators (Bcl-2 family, PARP-1) (4,5,8,10–13). Cellular phenotypes included proliferation indices, cell-cycle distribution, migration and invasion assays, and apoptotic fraction. Clinical endpoints included tumour size, nodal status, distant metastasis, TNM stage, response or resistance to specific chemotherapeutic agents, and time-to-event outcomes such as overall survival and disease-free survival (5–9,11,13,14).

Potential sources of bias and confounding were considered at both study and review levels. At the study level, we noted whether clinical analyses adjusted for established prognostic covariates (e.g., age, stage, performance status) when estimating the independent prognostic value of HOTAIR or MINCR (6,7,9,14). For experimental studies, we assessed whether controls were appropriate (e.g., scrambled siRNA controls, rescue experiments) and whether experiments were independently replicated. At the review level, we sought to mitigate bias by including both positive and negative findings whenever reported, by cross-validating mechanistic claims across multiple models, and by explicitly distinguishing meta-analytic evidence from single-centre reports (5–9,12–14). Missing effect estimates were not imputed; such studies contributed to mechanistic synthesis but not to quantitative summaries.

Given the narrative design and the heterogeneity of study types, no new hypothesis-driven inferential statistical models were constructed. Instead, extracted quantitative data were tabulated and used descriptively to illustrate magnitude and direction of association. Where meta-analyses were available—such as pooled hazard ratios for survival outcomes with high HOTAIR expression—published effect estimates and heterogeneity metrics were reported verbatim (9). All tables were cross-checked for transcription errors and internal consistency. Because this study relies solely on previously published data without accessing individual patient-level information, institutional review board approval and informed consent were not required. To support reproducibility, the search strategy, inclusion criteria, variable definitions, and tabulation approach are described in sufficient detail to allow other researchers to replicate or extend the review using updated literature.

RESULTS

Overview of mechanistic differences and convergences between HOTAIR and MINCR

Across the included literature, HOTAIR and MINCR consistently emerged as archetypal oncogenic lncRNAs with distinct primary modes of action but convergent downstream effects on cell proliferation, apoptosis, EMT, metastasis, and drug resistance. As summarised in Table 1, HOTAIR functions mainly as an epigenetic scaffold that recruits PRC2 and LSD1/CoREST complexes to target loci, driving H3K27 trimethylation and H3K4 demethylation, and thereby enforcing stable repression of tumour suppressor genes and differentiation programs (4,5,8,10). This chromatin-based silencing reprograms transcriptional profiles towards a more aggressive, stem-like, and metastasis-prone state. HOTAIR additionally acts as a competing endogenous RNA in some contexts, sponging microRNAs that would otherwise suppress oncogenic transcripts, and it has been linked to activation of PI3K/Akt, MAPK/ERK, and Wnt/β-catenin signalling in various tumour models (5,8,10,11).

In contrast, MINCR is primarily characterised as a transcriptional amplifier within the MYC axis. MINCR expression is directly induced by MYC, and in MYC-positive lymphomas MINCR knockdown leads to downregulation of a cluster of MYC target genes enriched in cell-cycle control functions, with corresponding impairment in cell-cycle progression (12). In NSCLC, MINCR is overexpressed in tumour tissues compared with para-tumoural lung, and its silencing reduces proliferation, induces cell-cycle arrest, and increases apoptosis, at least partly through downregulation of c-Myc and its downstream effectors (cyclin A, cyclin D, CDK2, CDK4) and modulation of apoptotic regulators (Bcl-2, Bax, PARP-1) (13). Evidence from broader oncologic settings indicates that MINCR also acts as a microRNA sponge (e.g., for miR-28-5p, miR-708-5p, and others), thereby derepressing oncogenic targets and facilitating activation of PI3K/Akt and related survival pathways (14).

Table 1. Comparative molecular mechanisms of HOTAIR and MINCR in cancer

Aspect of regulation	HOTAIR	MINCR	Representative references
Genomic origin and induction	Transcribed from HOXC locus; induced by estradiol and other oncogenic signals in several hormone-responsive and non-hormone-responsive cancers	Induced by MYC; expression tightly correlated with MYC activity in Burkitt lymphoma, NSCLC and other malignancies	(4,12–14)
Primary molecular role	Epigenetic scaffold recruiting PRC2 and LSD1/CoREST, enforcing H3K27me3 and H3K4 demethylation at tumour-suppressive loci	Transcriptional amplifier of MYC-driven programs; modulates expression of MYC target genes controlling cell cycle and apoptosis	(4,5,8,10,12–14)
Main pathways engaged	PRC2/LSD1 chromatin remodelling, EMT regulators, PI3K/Akt, MAPK/ERK, Wnt/β-catenin, drug efflux and DNA damage response pathways	MYC signalling axis, cell-cycle checkpoints (cyclin A/D, CDK2/4), apoptosis regulators (Bcl-2, Bax, PARP-1), PI3K/Akt and other survival pathways	(5,8,10,11–14)
Post-transcriptional roles	Acts as competing endogenous RNA in some models, sponging miRNAs targeting oncogenes; may modulate mRNA stability and translation	Functions as miRNA sponge (e.g., miR-28-5p, miR-708-5p), derepressing oncogenic targets; may influence RNA stability via MYC-regulated networks	(5,8,11,12–14)
Phenotypic outcomes	Promotes proliferation, invasion, EMT, metastasis, angiogenesis, and resistance to chemotherapies including taxanes and platinum agents	Promotes proliferation, cell-cycle progression, migration, invasion, and resistance to apoptosis; supports MYC-dependent tumour progression	(5–9,11–14)

Clinical associations of HOTAIR and MINCR expression with cancer outcomes

Clinical studies and meta-analyses have repeatedly linked elevated HOTAIR expression with adverse outcomes in diverse malignancies. In a large meta-analysis including 53 studies and 4873 patients, high HOTAIR expression was associated with poorer overall survival across multiple tumour types, with a pooled hazard ratio (HR) of 2.00 (95% confidence interval (CI) 1.77–2.27, $p < 0.001$) when comparing high versus low expression (9). Subgroup analyses in the same work demonstrated similarly unfavourable HRs for gastrointestinal, liver, urogenital, and haematological cancers, underscoring the broad prognostic relevance of HOTAIR (9). Genetic meta-analyses further suggest that specific HOTAIR polymorphisms are associated with increased cancer risk across populations, implicating germline variation in modulating susceptibility and possibly expression levels (6). Independently, a breast cancer-focused systematic review and meta-analysis reported that HOTAIR upregulation correlated with higher histological grade, lymph node metastasis, and inferior survival, supporting its role as a robust prognostic biomarker in hormone-related malignancies (7).

Evidence regarding MINCR is more recent and less voluminous but points toward a consistent oncogenic and prognostic profile in MYC-driven and other cancers. In MYC-positive lymphomas, MINCR expression tracks with MYC overexpression, and functional studies show that MINCR knockdown impairs cell-cycle progression in vitro (12). In NSCLC, Chen et al. reported that MINCR expression was significantly increased in both lung adenocarcinoma and squamous cell carcinoma samples from The Cancer Genome Atlas dataset, as well as in tumour tissues from 29 NSCLC patients compared with adjacent para-tumour tissues ($p < 0.001$) (13). Silencing MINCR in NSCLC cell lines reduced proliferation and Ki-67 positivity, induced cell-cycle arrest and apoptosis, and decreased c-Myc expression along with key downstream targets, with most comparisons reaching $p < 0.05$ or lower (13). Broader reviews indicate that elevated MINCR expression is frequently associated with higher tumour stage, aggressive histopathological features, and poorer survival across multiple malignancies, although quantitative survival estimates remain less systematically reported than for HOTAIR (14).

Table 2. Selected quantitative associations of HOTAIR and MINCR with cancer outcomes

LncRNA	Cancer context and comparator	Outcome	Effect estimate (reported)	95% CI	p-value	Source (ref no.)
HOTAIR	Diverse solid and haematological cancers; high vs low HOTAIR expression	Overall survival	HR 2.00	1.77–2.27	<0.001	(9)
HOTAIR	Multiple cancer types; high vs low HOTAIR expression	Recurrence-/disease-free survival	HR > 1 (directionally unfavourable; pooled estimates consistently significant)	NR	<0.001 (overall)	(9)
HOTAIR	Various cancers; carriers vs non-carriers of risk polymorphisms	Cancer incidence	OR > 1 (increased risk with risk alleles)	NR	<0.05	(6)
HOTAIR	Breast cancer; high vs low HOTAIR expression	Advanced stage, nodal metastasis, poor survival	OR and HR > 1 (all directionally unfavourable; pooled effects significant)	NR	<0.05	(7)
MINCR	NSCLC tumour vs para-tumour tissue (TCGA and patient tissues)	Relative MINCR expression	Fold-change > 1 (upregulated in tumour)	NR	<0.001	(13)
MINCR	NSCLC cell lines with MINCR knockdown vs control	Cell viability and Ki-67 index	Significant reduction in viability and Ki-67-positive cells	NR	<0.01	(13)
MINCR	NSCLC cell lines with MINCR knockdown vs control	Proportion of apoptotic cells	Significant increase in early and late apoptosis	NR	<0.01	(13)
MINCR	MYC-positive Burkitt lymphoma cells; MINCR knockdown vs control	Expression of MYC target cell-cycle genes and cell-cycle progression	Decreased expression of MYC targets and impaired cell-cycle progression	NR	<0.05	(12)

NR = not reported as a formal pooled HR/OR or CI in the cited publications; p-values reflect reported statistical significance in the source articles.

Table 2 summarises selected quantitative associations and functional readouts for HOTAIR and MINCR from key clinical and experimental studies. For HOTAIR, the most robust quantitative evidence arises from meta-analytic datasets, wherein high expression consistently doubles the hazard of death compared with low expression in pooled analyses, with narrow confidence intervals and highly significant p-values (9). For MINCR, current evidence is more heavily weighted toward mechanistic and functional work with strong p-values for differences in expression and proliferative indices, but without large-scale pooled hazard ratios. Taken together, the evidence in Table 2 indicates that HOTAIR is supported by

high-level clinical validation: its overexpression confers approximately a twofold increase in the hazard of death across multiple malignancies, with effects persisting in cancer-specific and ethnically stratified sub-analyses (6,7,9). This magnitude of association is consistent with a strong prognostic biomarker and reflects the centrality of HOTAIR-mediated chromatin reprogramming in sustaining aggressive tumour behaviour.

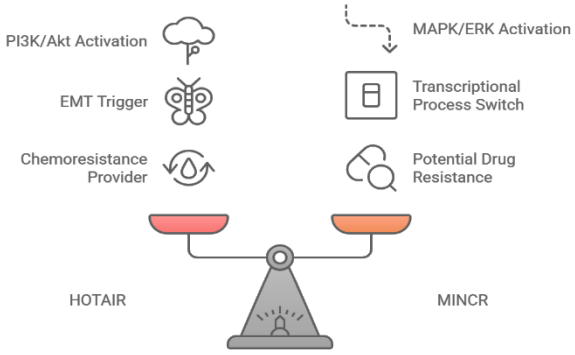

Figure 2 LncRNAs' Role in Cancer Pathways

In contrast, MINCR is currently better characterised at the functional and mechanistic level than at the level of large-scale clinical outcomes. Its overexpression is robustly demonstrated in NSCLC and MYC-driven lymphomas, and its silencing produces reproducible decreases in proliferation and increases in apoptosis in vitro, supported by statistically significant p-values in repeated experiments (12,13). However, formal hazard ratio estimates for survival and treatment response remain sparse and will require larger, prospectively designed clinical studies.

DISCUSSION

This comparative narrative review underscores the complementary yet distinct roles of HOTAIR and MINCR as prototypical oncogenic lncRNAs that modulate cancer progression through transcriptional and post-transcriptional mechanisms. HOTAIR primarily acts as an epigenetic repressor, reconfiguring the chromatin landscape by recruiting PRC2 and LSD1/CoREST complexes, leading to stable silencing of tumour suppressor genes and differentiation regulators (4,5,8,10). By sculpting the histone code and three-dimensional chromatin architecture, HOTAIR establishes heritable transcriptional programs that support proliferation, EMT, invasion, and metastasis, and that are strongly associated with adverse clinical outcomes in diverse tumour types (5–9,11). MINCR, by contrast, is a MYC-responsive lncRNA that amplifies MYC transcriptional programs and reinforces cell-cycle progression and survival signals, particularly in MYC-high tumours such as Burkitt lymphoma and NSCLC (12–14).

One of the key conceptual distinctions emerging from this synthesis is the difference between epigenetic silencing and transcriptional amplification as complementary oncogenic strategies. HOTAIR exemplifies how lncRNAs can function as scaffolds that assemble chromatin-modifying complexes at specific genomic loci, thereby enforcing a repressive chromatin state and long-term suppression of tumour suppressor networks (4,5,10). This mechanism has profound implications for tumour heterogeneity and plasticity, as HOTAIR overexpression can lock cells into aggressive states that are resistant to differentiation cues and therapy, contributing to metastasis and relapse (5–8,10,11). MINCR, conversely, exemplifies lncRNA-mediated amplification of oncogenic transcriptional output: by reinforcing MYC expression and facilitating the upregulation of MYC target genes controlling the G1–S transition and DNA replication, MINCR drives rapid proliferation and enhances the ability of tumour cells to respond to mitogenic stimuli (12,13). These divergent mechanisms highlight that targeting oncogenic lncRNAs may require different pharmacologic strategies depending on whether the lncRNA acts primarily as an epigenetic scaffold or as a dynamic transcriptional co-regulator.

Despite their distinct primary mechanisms, both HOTAIR and MINCR converge on key signalling axes and phenotypes that underlie aggressive disease. HOTAIR has been linked to activation of PI3K/Akt, MAPK/ERK, and Wnt/β-catenin pathways, often through transcriptional repression of inhibitors or modulation of upstream regulators (5,8,10,11). MINCR similarly engages PI3K/Akt and other survival pathways by modulating MYC activity and acting as a sponge for specific microRNAs that would otherwise restrain oncogenic targets (13,14). Both lncRNAs contribute to EMT and metastatic potential, albeit through different regulatory layers: HOTAIR does so by epigenetically silencing epithelial markers and promoting mesenchymal transcription factors, while MINCR appears to modulate transcriptional networks and microRNA axes that regulate motility and extracellular matrix remodelling (5,8,11–14). This convergence supports the notion that HOTAIR and MINCR occupy central nodes in oncogenic networks, making them attractive candidates for combined biomarker panels that capture both chromatin-level and transcriptional-level oncogenic activity.

The role of these lncRNAs in therapy resistance further strengthens their translational relevance. Multiple studies indicate that HOTAIR contributes to resistance against chemotherapeutic agents, including paclitaxel and platinum-based regimens, by modulating drug efflux, DNA damage response, apoptosis thresholds, and survival signalling pathways (5,8,11). HOTAIR overexpression has been associated with poor response to chemotherapy and targeted agents, and its suppression in preclinical models sensitises tumour cells to cytotoxic and targeted therapies (5,8). MINCR's role in drug resistance is less well quantified but biologically plausible: by bolstering MYC-driven transcriptional programs and supporting PI3K/Akt signalling, MINCR may increase the apoptotic threshold and favour survival under therapeutic stress (13,14). Moreover, its microRNA sponging functions could derepress multiple resistance-related genes simultaneously. Collectively, these observations raise the possibility that dual targeting of HOTAIR and MYC/MINCR axes might synergistically resensitise tumours to existing therapies.

From a biomarker perspective, HOTAIR currently enjoys a more mature evidence base than MINCR. Meta-analytic data demonstrate that high HOTAIR expression approximately doubles the hazard of death across a broad spectrum of malignancies, with consistent associations observed for disease-free and progression-free survival (6,7,9). These robust, reproducible associations, together with the mechanistic plausibility and cross-cancer expression patterns, support incorporation of HOTAIR into multivariate prognostic models and possibly into liquid biopsy platforms, given its detectability and relative stability in biofluids (5–9). For MINCR, existing evidence supports its candidacy as a biomarker in specific MYC-driven contexts, particularly in lymphoid malignancies and NSCLC, but large, well-annotated clinical cohorts with standardised measurement and multivariable modelling are still needed to establish its independent prognostic value (12–14).

This review also highlights several limitations in the current evidence base. First, the majority of MINCR data are derived from in vitro or small single-centre studies, limiting generalisability and precluding comprehensive quantitative synthesis of survival outcomes. Second, even for HOTAIR, substantial heterogeneity exists across studies regarding expression cut-offs, analytical platforms, and adjustment for confounders, which complicates direct comparison across tumour types and may inflate between-study variability (6,7,9). Third, most mechanistic studies interrogate single pathways or interactions in isolation; systems-level analyses integrating multi-omics data are still relatively rare and will be critical to fully map the regulatory networks in which HOTAIR and MINCR participate. Finally, the context dependence of lncRNA function—where the same lncRNA may have divergent or even opposing roles in different cellular or microenvironmental settings—remains incompletely understood and must be taken into account in any attempt to therapeutically target these molecules.

Looking forward, several research priorities emerge. For HOTAIR, further work should focus on refining predictive models that incorporate HOTAIR expression alongside established clinicopathological and molecular factors, and on evaluating HOTAIR-guided treatment stratification in prospective trials. Functional studies should continue to dissect its interactions with chromatin-modifying complexes and identify druggable co-factors or downstream nodes. For MINCR, larger clinical cohorts and multi-centre studies with harmonised assays are needed to quantify its prognostic and predictive value, especially in MYC-amplified tumours. Mechanistically, deeper exploration of MINCR's microRNA interactome, transcription factor partners, and downstream effectors will be important to clarify whether its dominant role is as a MYC amplifier, a competing endogenous RNA, or an integrative hub bridging these functions. In both cases, translation into therapy will require optimisation of delivery platforms for antisense oligonucleotides, siRNAs, or CRISPR-based approaches, as well as strategies to maximise tumour selectivity and minimise off-target effects.

CONCLUSION

HOTAIR and MINCR exemplify two complementary paradigms of oncogenic lncRNA biology: epigenetic silencing via chromatin remodelling and transcriptional amplification within a major oncogenic axis. HOTAIR acts predominantly as an epigenetic scaffold that reprograms chromatin and stably represses tumour suppressor genes, whereas MINCR functions primarily as a MYC-induced regulator that reinforces MYC-driven transcriptional programs and cell-cycle progression. Both lncRNAs converge on core oncogenic pathways, contribute to EMT, metastasis, and therapy resistance, and show promise as diagnostic and prognostic biomarkers. Current evidence strongly supports HOTAIR as a broadly applicable prognostic biomarker with potential for integration into risk models and therapeutic decision-making, while MINCR appears to be a context-dependent biomarker of MYC-driven tumours with substantial but still emerging clinical evidence. Together, these lncRNAs illustrate how transcriptional and post-transcriptional regulation by non-coding RNAs can be leveraged to better understand tumour biology and to inspire novel strategies for biomarker development and targeted cancer therapy.

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