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miR-103/107–Mediated Suppression of NKILA Enhances Oncogenic Behaviors in Human Lung Cancer Cells

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Abstract

Background: Lung cancer remains a major global health burden, and conventional therapies often fail to meet clinical needs. Although non-coding RNAs are increasingly recognized as key regulators in cancer, the role of NKILA and its modulation by the miR-103/107 cluster in lung cancer growth and metastasis is not fully characterized. This study investigates the impact of the NKILA–miR-103/107 axis on lung cancer progression and metastatic behavior.

Methods: To suppress miR-103 and miR-107 activity in the human lung cancer cell line A549, specific LNA-based inhibitors were introduced into the cells. Following *in vitro* transfection with either miR-specific LNA or a mock control, alterations in the components of the NKILA–miR-103/107 regulatory pathway were quantified using quantitative real-time PCR. The effects of miR inhibition on cellular behavior were then evaluated by measuring A549 cell growth with an MTT assay and assessing invasive capacity through a Transwell invasion test.

Results: In lung cancer A549 cells, suppression of miR-103/107 using LNA inhibitors led to a marked elevation in NKILA transcript levels. Functional assays showed that miR-103/107 inhibition was associated with a significant decrease in A549 cell viability ($p=0.0041$) and a pronounced reduction in invasive capacity ($p=0.001$).

Conclusion: In this *in vitro* study using A549 lung cancer cells, the NKILA–miR-103/107 axis was associated with lung cancer aggressiveness. miR-103/107 inhibition upregulated NKILA and was accompanied by decreased proliferation and invasion of A549 cells. These findings are preliminary and limited to a single cell line model. Further validation in additional lung cancer models and *in vivo* systems is required to determine the broader biological and therapeutic relevance of this regulatory interaction.

Keywords: Cell proliferation, Cell survival, Global health, Lung neoplasms, Lung neoplasms, MicroRNAs, Real-time polymerase chain reaction, Transfection
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Introduction

Lung cancer is one of the most frequent cancers worldwide and is responsible for a significant part of cancer-related deaths in the world. In 2025, an estimated 226,650 new cases and 124,730 deaths from lung and bronchus cancer will occur in the United States [1]. Late-stage diagnosis and subsequent ineffective treatment often contribute to the poor prognosis and increased fatality of lung cancer [2]. Although recent advancements in treatments have resulted in longer survival rates for lung cancer patients [1], the high mortality associated with the cancer places a significant burden on healthcare systems and communities [3]. Therefore,

innovative therapeutic approaches based on molecular mechanisms and tumor biology can potentially enhance lung cancer detection and treatment [4].

As one of the emerging molecular targets in cancer, Nuclear Factor-kappa B (NF-κB), a pro-inflammatory transcription factor, plays a significant role in various biological processes, including cell survival, proliferation, immune responses, inflammation, cell growth, and apoptosis [5-7]. Persistent activation of NF-κB has been observed in different types of human tumors, including lung cancer [8]. NF-κB is regarded as a key factor in lung cancer development and invasion [9]. In many solid tumors, the constant activation of NF-κB is primarily attributed to the presence of inflammatory cytokines within the tumor microenvironment [10,11].

The regulation of NF-κB signaling pathways involves proteins and non-coding RNAs, specifically long noncoding RNAs (lncRNAs) and microRNAs (miRNAs) [12,13]. lncRNAs interact with various RNAs, including miRNAs, to regulate gene expression at both transcriptional and post-transcriptional levels. Several studies have demonstrated that the interaction between miRNAs and lncRNAs plays a crucial role in the development and progression of cancer [14]. It has been reported that the NF-κB interacting lncRNA (NKILA) suppresses breast cancer progression by binding to the NF-κB inhibitor (IκB), masking the phosphorylation motifs of IκB and inhibiting IκB kinase-induced phosphorylation of IκB, which consequently prevents NF-κB activation [15]. Additionally, miR-103/107 have been found to negatively regulate NKILA and are essential for breast cancer tumorigenesis. The overexpression of miR-103/107 in cancer cells significantly decreases NKILA expression [15,16]. Further studies have shown that NKILA also inhibits the progression of malignant melanoma [17], non-small cell lung cancer [8], and esophageal squamous cell carcinoma [18]. Authors previous study suggested that NKILA may be a potential downstream target of miR-103/107 in colorectal cancer [19].

Existing literature suggests that NKILA can potentially serve as a biomarker or therapeutic target in various types of cancer [20]. Nevertheless, the contribution of the NKILA-miR103-miR107 signaling pathway to lung cancer tumorigenesis and invasion has not been investigated. Therefore, the aim of this study was to investigate the effects of miR-103/107 inhibition on NKILA expression and its impact on the proliferation and invasive behavior of A549 lung cancer cells.

Materials and Methods

Cell culture

The Pasteur Institute of Iran (Tehran, Iran) was the source of the human lung cancer cell line A549 used in the research. While STR profiling was not performed in this study, we acknowledge that the absence of formal cell line authentication is a limitation. Purchased cells were cultured in Dulbecco's Modified Eagle's medium (DMEM) (Invitrogen, London, UK). 10% Fetal Bovine Serum (FBS) (Sigma-Aldrich, London, UK) and 100 *U/ml* penicillin/streptomycin (Invitrogen, London, UK) were added to the media as supplements. Standard cell culture conditions, which consists of 5% CO_2 at 37°*C*, were provided for the cells in the medium. During incubation, the adherent cells (approximately 80% confluent) were dissociated by trypsinization using 0.25% trypsin (Sigma-Aldrich, London, UK) and then centrifuged at 400×g for 5 *min*. The cell pellets were washed with 0.1 *M* phosphate buffer at pH 7.4. The cell line was free of mycoplasma contamination.

miR-103/107 silencing by LNA-based antisense oligos

miRCURY® LNA® miRNA Power Family Inhibitor (cat no. 339160, Qiagen) was utilized simultaneously to inhibit the miR-103/107 family, as this inhibitor is designed to target conserved sequences shared by both miR-103 and miR-107 members. Approximately 24 *hr* before transfection, a six-well plate was filled with A549 cells at a density of 300,000 cells per well. Following this, serum-free DMEM was added to the medium to maximize cell culture viability. The LNA Power Inhibitor (140 *pmol*) was introduced to cells using 25 *µl* of HiPerFect Transfection Reagent (cat. no. 301704, Qiagen GmbH, Hilden, Germany), according to the manufacturer's protocol. LNA-transfected cells were extracted after 24 *hr* of incubation at 37°*C* to make a reliable assessment of the impacts of antisense oligonucleotides.

Quantitative real-time PCR assay

Total RNA was isolated from LNA-transfected and control A549 cells utilizing the RNeasy Mini spin column procedure (Qiagen, Hilden, Germany). The quality of the purified RNAs was evaluated by using a NanoDrop™ 2000 Spectrophotometer (Thermo Fisher Scientific, USA). The variation in the A260/A280 and A260/A230 ratios ranged from 1.6 to 2, representing the high standards of the extraction procedures. The miScript II Reverse Transcription Kit (Qiagen, Hilden, Germany) was utilized to produce cDNA according to the kit's instructions. miR-103 and miR-107 concentrations were detected using a StepOnePlus Real-Time PCR thermocycler with the miScript SYBR Green PCR Kit (Qiagen, Hilden, Germany, Cat. No. 218073). The PCR reaction volume was 25 *µl*, consisting of 12.5 *µl* of miScript SYBR Green Master mix, 2.5 *µl* of 10x miScript Universal primer, 2.5 *µl* of 10x miScript Primer Assay for miR103 (Qiagen, Hilden, Germany, Cat. No: MS00031241) and miR107 (Qiagen, Hilden, Germany, Cat. No: MS00003409), 6 *µl* of RNase-free water, and lastly 1.5 *µl* of template cDNA. NORD68 (Qiagen, Hilden, Germany, Cat. No: MS00033712) was selected as the reference gene for miRNA normalization based on its stable expression in A549 cells under our experimental conditions. Cycling conditions for real-time PCR were 95°*C* for 15 *min*, followed by 40 cycles of 94°*C* for 15 *s*, 55°*C* for 30 *s*, and 70°*C* for 30*s*.

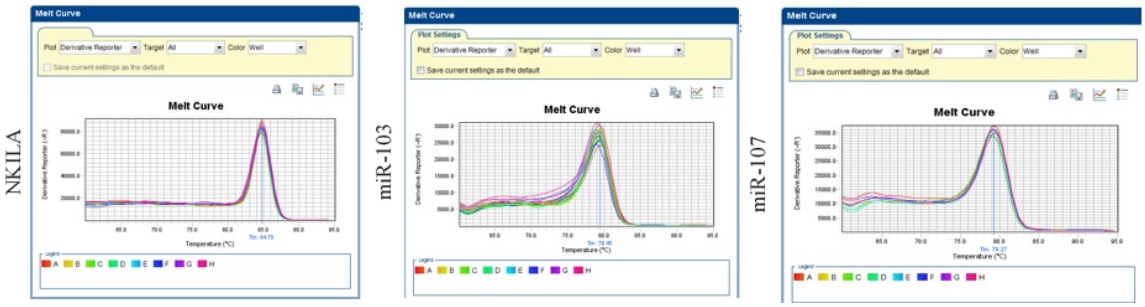

Figure 1. For qRT-PCR experiments, primer specificity was confirmed by melting curve analysis, which demonstrated single specific amplification peaks.

Extracted RNAs were used to synthesize cDNA for NKILA by the PrimeScript™ 1st strand cDNA Synthesis Kit (Takara, Dalian, China). PCR was performed in a 20 *µl* reaction volume, including 4 *µl* 5x HOT FIREPol EvaGreen qPCR Mix Plus (ROX) (Solis BioDyne, Tartu, Estonia), 1 *µl* of each primer (final concentration 10 *µM*), 12 *µl* RNase-free water, and 2 *µl* cDNA. The forward and reverse primers for NKILA were 5'-AACCAAACCTACCCACAACG-3' and 5'-ACCACT AAGTCAATCCCAGGTG-3'; and for GAPDH were 5'-ATCACCATCTTCCAGGAGCGA-3' and 5'CCTTC TCCATGGTGGTGAAGAC-3'. The PCR amplification was conducted under the following conditions: 95°*C* for 15 *min*, followed by 40 cycles at 94°*C* for 15 *s*, 59°*C* for 20 *s*, and a final extension at 72°*C* for 20 *s*. The specificity of PCR was assessed by subjecting all the PCR products to melting curve analysis (Figure 1). GAPDH gene expression was used as the normalization reference to normalize expression data. The quantity of fold changes in gene expression was measured using the 2−ΔΔCt approach.

Cell proliferation

The impact of miR-103 and miR-107 knockdown on the viability of A549 cells was evaluated using the MTT assay. Transfected and mock-transfected (vehicle-only) cells were plated in 96-well plates at a density of 1×10³ cells per well and maintained under standard culture conditions. At 24, 48, 72, and 96 *hr* post-transfection, 20 *µl* of 5 *mg/ml* MTT solution (Sigma-Aldrich, London, UK) was added to each well and incubated to allow the formation of formazan crystals. Subsequently, 100 *µl* of dimethyl sulfoxide (DMSO; Merck, Darmstadt, Germany) was added to dissolve the formazan, and absorbance was measured at 570 *nm* using a microplate spectrophotometer (Awareness Technology Inc., USA). The absorbance values served as an indicator of cell viability following miR-103/107 inhibition.

Trans well invasion assay

The invasive ability of A549 cells was assessed using 24-well Matrigel-coated invasion chambers (8 *µM* pores; Corning, NY, USA). Lower chambers were filled with DMEM containing 10% FBS as a chemoattractant, and 5×10⁴ LNA-transfected or mock-transfected (vehicle-only) cells were seeded in the upper chambers in serum-free DMEM. After 48 *hr* of incubation at 37°*C* with 5% CO_2, non-invading cells were removed from the upper surface. Invaded cells on the lower surface were fixed with 1% formaldehyde, stained with 0.2% crystal violet, and counted under an inverted microscope at 100× magnification across five random fields per well. Results were expressed as mean ± SD of three independent experiments.

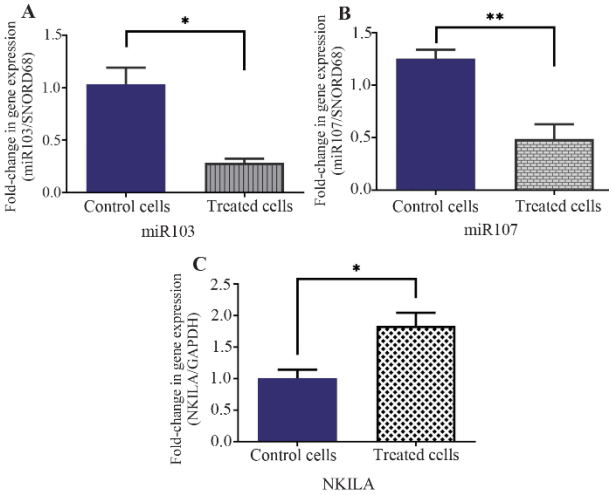

Figure 2. A and B) Quantitative RT-PCR analysis confirmed effective suppression of miR-103 and miR-107 following transfection with antisense LNA oligonucleotides. LNA treatment markedly reduced miR-103/107 levels in A549 cells compared with the negative control group (mean±SD, n=3; p=0.0147, *p=0.0026). C) Consistent with miR-103/107 inhibition, NKILA expression was significantly elevated in LNA-treated A549 cells relative to the negative control (p=0.0045).

Statistical analyses

All the data were analyzed using SPSS version 16.0 (SPSS, Chicago, IL, USA), and diagrams were created by GraphPad Prism 6.0. All cell culture experiments were conducted at least three independent times to ensure the reproducibility of the results. Differences between groups were analyzed using the Mann–Whitney U test due to the small sample size and the assumption of non-normal data distribution. Results are displayed as mean ± S.D., and $p<0.05$ was considered statistically significant.

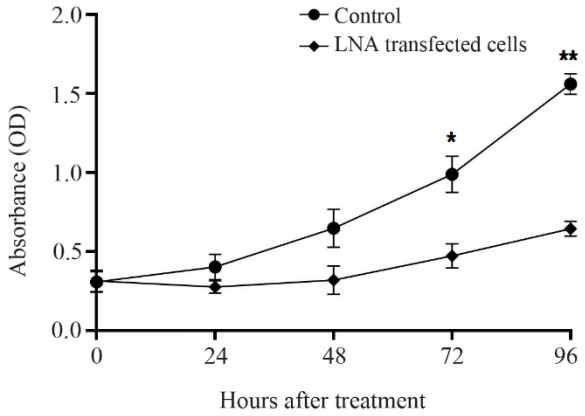

Figure 3. Downregulation of miR-103/107 substantially impaired the viability capacity of A549 cells. MTT analysis demonstrated reduced cell growth in the LNA-treated group compared with the mock-transfected (vehicle-only) cells (mean±SD, n=3; *p=0.0041).

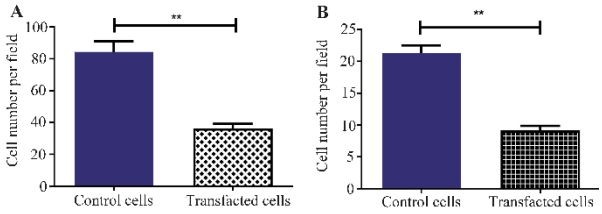

Figure 4. Silencing of miR-103/107 attenuated the invasive behavior of A549 cancer cells. Following 48 *hr* of LNA treatment, transwell assays showed a reduction in the number of invaded cells. Quantitative assessment revealed significantly lower invasion rates in the LNA group compared with the mock-transfected (vehicle-only) cells (cells on lower membrane surface: p=0.0027; cells reaching the bottom of wells: p=0.001). Data represent mean±SD from at least three independent experiments (n=3).

Results

LNA inhibition of miR-103/107 increased NKILA in A549 cells

To investigate the functional role of the NKILA regulatory axis modulated by miR-103/107, antisense LNAs were employed to specifically inhibit these microRNAs. Quantitative real-time PCR analysis revealed a significant reduction in miR-103/107 levels in LNA-transfected A549 cells compared to controls ($p<0.05$) (Figures 2A and 2B). Subsequent evaluation of NKILA expression showed a pronounced upregulation in LNA-treated cells relative to control cells, confirming that suppression of miR-103/107 enhances NKILA levels (p=0.0045) (Figure 2C).

miR-103/107 silencing reduces lung cancer cell viability

Cell viability of A549 cells was assessed at 24, 48, 72, and 96 *hr* post-transfection using the MTT assay. Compared to the negative control group, inhibition of miR-103/107 by LNA transfection led to a significant reduction in cell proliferation at all time points (Figure 3) (p=0.0041). These results suggest that silencing miR-103/107 impairs the growth capacity of lung cancer cells over time.

miR-103/107 inhibition limits A549 cell invasion

The impact of miR-103/107 suppression on the invasive and metastatic behavior of A549 cells was explored. Results from Trans well assays demonstrated that inhibition of miR-103/107 significantly reduced the cells' invasive capacity compared to control cells ($p<0.05$) (Figures 4A and 4B).

Discussion

About 57% of lung cancer patients are diagnosed with metastasis, and their survival rate is as low as 5% [21]. This staggering data implies the invasive identity of most lung cancer types. Furthermore, conventional therapies, including chemotherapy, radiation, and surgery, have proven limited abilities to address challenges such as the emerging chemoresistance of metastatic lung cancers [22] and come with considerable side effects [23]. Newer approaches, including immune checkpoint inhibitors [24], Anaplastic Lymphoma Kinase (ALK) inhibitors [25], Epidermal Growth Factor Receptor (EGFR) inhibitors [26], and Chimeric Antigen Receptor T Cell (CAR-T) therapy [27], have opened new windows into lung cancer treatment, but are not flawless and often come with limitations and side effects. The absence of a flawless and straightforward therapeutic protocol for lung cancer treatment, in particular, and for cancer in general, has led researchers to explore and consider novel and innovative approaches.

Efforts to develop innovative strategies include novel therapeutics like mRNA [28], miRNA [29], lncRNA [30] modulators and novel targets, such as factors involved in cancer-related inflammation [31,32]. The role of inflammation is firmly established in cancer invasion, metastasis, and overall pathogenesis [33-35]. Tumor-associated inflammation contributes to cancer pathogenesis by promoting immune escape, epithelial-mesenchymal transition, tumor angiogenesis, and apoptosis, among other reasons [36]. Tumors utilize various inflammatory signaling pathways, including NF-κB, to impair cytokine balance, and ultimately shift tissue dynamics to their advantage [37,38]. The role of NF-κB signaling pathway has been proven to be necessary for lung cancer development and pathology [39]. NF-κB can promote tumor resistance to anti-cancer drugs such as EGFR inhibitors [40], promote cell cycle dysregulation and apoptosis suppression in lung cancer cells [41]. Inhibition of NF-κB has proven to be effective in promoting tumor cell apoptosis [42], drug sensitivity [43] and inhibiting metastasis and angiogenesis [44]. NF-κB suppression has been achieved through different mechanisms, such as IκBα suppression, downregulation of TNFR1 protein expression, and inhibition of NF-κB by aptamers [43], among others 44.

The role of NKILA and its inhibitory effect on NF-κB and lung cancer pathogenesis has also been elucidated. NKILA can inhibit invasion [45] and proliferation [46] of lung cancer cells and generally promote the im-

mune evasion of tumors [47]. The pro-oncogenic functions of miR-103/107 have become increasingly evident in recent years. These miRNAs enhance tumor invasiveness in part by suppressing multiple tumor-modulating pathways, including DAPK [48], KLF4 [48,49], NF1 [50], Wnt/β-catenin/Axin2 [51], and OLFM4 [52], among other targets.

Our previous study demonstrated an inverse expression pattern between miR-103/107 and NKILA in colorectal cancer, suggesting that miR-103/107 may negatively regulate NKILA expression [19]. The findings of the present study in A549 lung cancer cells are consistent with this inverse association. Although NKILA is known to modulate NF-κB signaling in other cancer models, NF-κB activity was not directly measured in the current study (*e.g.*, p65 nuclear translocation or IκB phosphorylation assays were not performed). Therefore, any link between miR-103/107 suppression, NKILA upregulation, and NF-κB modulation in this model should be interpreted as hypothetical and based on prior literature rather than direct experimental evidence. Our data demonstrate that inhibition of miR-103/107 increases NKILA expression and is associated with reduced proliferation and invasion in A549 cells. However, we cannot conclusively establish a causal NKILA–NF-κB mechanistic pathway within this study. Future investigations using NF-κB reporter assays, Western blot analysis of NF-κB components, or rescue experiments are required to validate this proposed signaling interaction.

Conclusion

In conclusion, authors findings show that modulation of miR-103/107 levels significantly effects NKILA expression and is associated with changes in proliferation and invasion in A549 lung cancer cells. While these observations are consistent with a potential involvement of NF-κB signaling suggested by previous studies, the present work does not directly demonstrate NF-κB pathway inhibition. This relationship may contribute to lung cancer progression and highlights a possible regulatory interaction between miR-103/107 and NKILA. The use of a single lung cancer cell line and the absence of direct NF-κB activity assays limit mechanistic interpretation. Moreover, the findings—derived from *in vitro* assays—require validation in additional lung cancer models and *in vivo* systems. Further studies are needed to determine whether the miR-103/107–NKILA axis functionally modulates NF-κB signaling and whether it may represent a viable therapeutic target in lung cancer.

Ethics approval

This study was approved by the ethics committee of the Tehran University of Medical Sciences (IR.TUMS.CHMC.REC.1398.072).

Conflict of Interest

None to declare.

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References

1. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. CA Cancer J Clin 2025;75(1):10-45.
2. Valerio TS, Emmerick ICM, Sobreira-da-Silva MJ. Factors associated with late-stage diagnosis and overall survival for lung cancer: An analysis of patients treated in a Brazilian hospital and a US-hospital from 2009 to 2019. Cancer Epidemiol 2023;86:102443.
3. Lippiett KA, Richardson A, Myall M, Cummings A, May CR. Patients and informal caregivers' experiences of burden of treatment in lung cancer and chronic obstructive pulmonary disease (COPD): a systematic review and synthesis of qualitative research. BMJ Open 2019;9(2):e020515.
4. Li Y, Yan B, He S. Advances and challenges in the treatment of lung cancer. Biomed Pharmacother 2023;169: 115891.
5. Zhang Q, Lenardo MJ, Baltimore D. 30 Years of NF-kappaB: A Blossoming of Relevance to Human Pathobiology. Cell 2017;168(1-2):37-57.
6. Chen W, Li Z, Bai L, Lin Y. NF-kappaB in lung cancer, a carcinogenesis mediator and a prevention and therapy target. Front Biosci (Landmark Ed) 2011;16(3):1172-85.
7. Hayden MS, Ghosh S. Signaling to NF-kappaB. Genes Dev 2004;18(18):2195-224.
8. Lu Z, Li Y, Wang J, Che Y, Sun S, Huang J, et al. Long non-coding RNA NKILA inhibits migration and invasion of non-small cell lung cancer via NF-kappaB/Snail pathway. J Exp Clin Cancer Res 2017;36(1):54.
9. Batra S, Balamayooran G, Sahoo MK. Nuclear factor-κB: a key regulator in health and disease of lungs. Arch Immunol Ther Exp (Warsz) 2011;59(5):335-51.
10. DiDonato JA, Mercurio F, Karin M. NF-kappaB and the link between inflammation and cancer. Immunol Rev 2012;246(1):379-400.
11. Gupta SC, Kim JH, Prasad S, Aggarwal BB. Regulation of survival, proliferation, invasion, angiogenesis, and metastasis of tumor cells through modulation of inflammatory pathways by nutraceuticals. Cancer Metastasis Rev 2010;29(3):405-34.
12. Gupta SC, Awasthee N, Rai V, Chava S, Gunda V, Challagundla KB. Long non-coding RNAs and nuclear factor-kappaB crosstalk in cancer and other human diseases. Biochim Biophys Acta Rev Cancer 2020;1873(1): 188316.
13. Abdollahzadeh R, Mansoori Y, Azarnezhad A, Daraei A, Paknahad S, Mehrabi S, et al. Expression and clinicopathological significance of AOC4P, PRNCR1, and PCAT1 lncRNAs in breast cancer. Pathol Res Pract 2020;216(10):153131.

14. Cao MX, Jiang YP, Tang YL, Liang XH. The crosstalk between lncRNA and microRNA in cancer metastasis: orchestrating the epithelial-mesenchymal plasticity. Oncotarget 2017;8(7):12472-83.
15. Liu B, Sun L, Liu Q, Gong C, Yao Y, Lv X, et al. A cytoplasmic NF-kappaB interacting long noncoding RNA blocks IkappaB phosphorylation and suppresses breast cancer metastasis. Cancer Cell 2015;27(3):370-81.
16. Martello G, Rosato A, Ferrari F, Manfrin A, Cordenonsi M, Dupont S, et al. A MicroRNA targeting dicer for metastasis control. Cell 2010;141(7):1195-207.
17. Bian D, Gao C, Bao K, Song G. The long non-coding RNA NKILA inhibits the invasion-metastasis cascade of malignant melanoma via the regulation of NF-kB. Am J Cancer Res 2017;7(1):28-40.
18. Lu Z, Chen Z, Li Y, Wang J, Zhang Z, Che Y, et al. TGF-beta-induced NKILA inhibits ESCC cell migration and invasion through NF-kappaB/MMP14 signaling. J Mol Med (Berl) 2018;96(3-4):301-13.
19. Jafari D, Noorbakhsh F, Delavari A, Tavakkoli-Bazzaz J, Farashi-Bonab S, Abdollahzadeh R, Rezaei N. Expression level of long noncoding RNA NKILAmiR103-miR107 inflammatory axis and its clinical significance as potential biomarker in patients with colorectal cancer. J Res Med Sci 2020 Apr 13;25:41.
20. Chandra Gupta S, Nandan Tripathi Y. Potential of long non-coding RNAs in cancer patients: From biomarkers to therapeutic targets. Int J Cancer 2017;140(9):1955-67.
21. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71(3):209-49.
22. Min H, Lee H-Y. Mechanisms of resistance to chemotherapy in non-small cell lung cancer. Arch Pharm Res 2021 Feb;44(2):146-164.
23. Zhang J, Li Y, Guo S, Zhang W, Fang B, Wang S. Moving beyond traditional therapies: the role of nanomedicines in lung cancer. Front Pharmacol 2024 Feb 8;15:1363346.
24. Shao J, Wang C, Ren P, Jiang Y, Tian P, Li W-M. Treatment-and immune-related adverse events of immune checkpoint inhibitors in advanced lung cancer. Biosci Rep 2020 May 29;40(5):BSR20192347.
25. Pellegrino B, Facchinetti F, Bordi P, Silva M, Gnetti L, Tiseo M. Lung Toxicity in Non-Small-Cell Lung Cancer Patients Exposed to ALK Inhibitors: Report of a Peculiar Case and Systematic Review of the Literature. Clin Lung Cancer 2018;19(2):e151-e61.
26. Li Q, Lin J, Hao G, Xie A, Liu S, Tang B. Nephrotoxicity of targeted therapy used to treat lung cancer. Front Immunol 2024 Jul 4;15:1369118.
27. Kandra P, Nandigama R, Eul B, Huber M, Kobold S, Seeger W, et al. Utility and Drawbacks of Chimeric Antigen Receptor T Cell (CAR-T) Therapy in Lung Cancer. Front Immunol 2022 Jun 2;13:903562.
28. Pal I, Safari M, Jovanović M, Bates S, Deng C. Targeting Translation of mRNA as a Therapeutic Strategy in Cancer. Curr Hematol Malig Rep 2019 Aug;14(4):219-227.
29. Menon A, Abd-Aziz N, Khalid K, Poh C, Naidu R. miRNA: A Promising Therapeutic Target in Cancer. Int J Mol Sci 2022 Sep 29;23(19):11502.
30. Castro-Oropeza R, Meléndez-Zajgla J, Maldonado V, Vazquez-Santillan K. The emerging role of lncRNAs in the regulation of cancer stem cells. Cell Oncol (Dordr) 2018 Dec;41(6):585-603.
31. Marelli G, Sica A, Vannucci L, Allavena P. Inflammation as target in cancer therapy. Curr Opin Pharmacol 2017 Aug;35:57-65.
32. Hou J, Karin M, Sun B. Targeting cancer-promoting inflammation — have anti-inflammatory therapies come of age? Nat Rev Clin Oncol 2021 May;18(5):261-279.
33. Dolan R, McMillan D. The prevalence of cancer associated systemic inflammation: Implications of prognostic studies using the Glasgow Prognostic Score. Crit Rev Oncol Hematol 2020 Jun;150:102962.
34. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature 2008 Jul 24;454(7203):436-44.
35. Murata M. Inflammation and cancer. Environ Health Prev Med 2018 Oct 20;23(1):50.
36. Tan Z, Xue H, Sun Y, Zhang C, Song Y, Qi Y-F. The Role of Tumor Inflammatory Microenvironment in Lung Cancer. Front Pharmacol 2021 May 17;12:688625.
37. Zhao H, Wu L, Yan G, Chen Y, Zhou M, Wu Y, et al. Inflammation and tumor progression: signaling pathways and targeted intervention. Signal Transduct Target Ther 2021 Jul 12;6(1):263.
38. Yeganeh P, Forghani S, Pouresmaeil L, Parhizkar F, Jafari D. Targeted cytokine delivery for cancer therapy through engineered mesenchymal stem cells. Gene Reports 2025;39:102199.
39. Meylan E, Dooley A, Feldser D, Shen L, Turk E, Ouyang C, Jacks T. Requirement for NF-κB signalling in a mouse model of lung adenocarcinoma. Nature 2009 Nov 5; 462(7269):104-7.
40. Blakely C, Pazarentzos E, Olivas V, Asthana S, Yan J, Tan I, et al. NF-κB-activating complex engaged in response to EGFR oncogene inhibition drives tumor cell survival and residual disease in lung cancer. Cell Rep 2015 Apr 7;11(1):98-110.
41. Yang L, Zhou Y, Li Y, Zhou J, Wu Y, Cui Y, et al. Mutations of p53 and KRAS activate NF-κB to promote chemoresistance and tumorigenesis via dysregulation of cell cycle and suppression of apoptosis in lung cancer cells. Cancer Lett 2015;357(2):520-6.
42. Jones DR, Broad RM, Madrid LV, Baldwin AS Jr, Mayo MW. Inhibition of NF-kappaB sensitizes non-small cell lung cancer cells to chemotherapy-induced apoptosis. Ann Thorac Surg 2000 Sep;70(3):930-6; discussion 936-7.

43. Mi J, Zhang X, Rabbani ZN, Liu Y, Reddy SK, Su Z, et al. RNA aptamer-targeted inhibition of NF-kappa B suppresses non-small cell lung cancer resistance to doxorubicin. Mol Ther 2008 Jan;16(1):66-73.

44. Rasmi RR, Sakthivel KM, Guruvayoorappan C. NF-κB inhibitors in treatment and prevention of lung cancer. Biomed Pharmacother 2020 Oct;130:110569.

45. Lu Z, Li Y, Wang J, Che Y, Sun S, Huang J, et al. Long non-coding RNA NKILA inhibits migration and invasion of non-small cell lung cancer via NF-κB/Snail pathway. J Exp Clin Cancer Res 2017 Apr 17;36(1):54.

46. Liu D-H, Shi X. Long non-coding RNA NKILA inhibits proliferation and migration of lung cancer via IL-11/STAT3 signaling. Int J Clin Exp Pathol 2019 Jul 1;12(7):2595-2603.

47. Huang D, Chen J, Yang L, Qian O, Li J, Lao L, et al. NKILA lncRNA promotes tumor immune evasion by sensitizing T cells to activation-induced cell death. Nat Immunol 2018 Oct;19(10):1112-1125.

48. Chen HY, Lin YM, Chung HC, Lang Y, Lin CJ, Huang J, et al. miR-103/107 promote metastasis of colorectal cancer by targeting the metastasis suppressors DAPK and KLF4. Cancer Res 2012 Jul 15;72(14):3631-41.

49. Zheng J, Liu Y, Qiao Y, Zhang L, Lu S. miR-103 Promotes Proliferation and Metastasis by Targeting KLF4 in Gastric Cancer. Int J Mol Sci 2017 Apr 26;18(5):910.

50. Wang S, Gaoxiang, Zhu H, Lv C, Chu H, Tong N, et al. miR-107 regulates tumor progression by targeting NF1 in gastric cancer. Sci Rep 2016 Nov 9;6:36531.

51. Chen HY, Lang Y, Lin H, Liu YR, Liao CC, Nana AW, et al. miR-103/107 prolong Wnt/β-catenin signaling and colorectal cancer stemness by targeting Axin2. Sci Rep 2019 Jul 4;9(1):9687.

52. Xiong B, Lei X, Zhang L, Fu JY. miR-103 regulates triple negative breast cancer cells migration and invasion through targeting olfactomedin 4. Biomed Pharmacother 2017;89:1401-8.