Role of lncRNA in Cancer

Subjects: Cell Biology

Contributor: Meng Gu

Here, we summarize several studies of lncRNAs SNPs relevant to chemotherapy responses to further clarify the potential of lncRNAs as potential biomarkers of cancer risk and predictors of drug resistance as well as toxicity.

Keywords: gene polymorphisms ; cancer chemotherapy ; drug response ; drug toxicity ; personalized oncology

1.Introduction

Table 1. Known lncRNA polymorphisms affecting drug response in cancer therapy.

LncRNA	Polymorphisms	Cancer Type	Patient Population	Drug	Effect	Reference
***MIR2052 Host Gene* (*MIR2052HG*)**	**rs4476990 and rs3802201**	**Breast cancer**	**4658 women with breast cancer, including 252 women experiencing a breast cancer recurrence**	**Aromatase Inhibitor (AIs)**	**Regulated ERα expression in the presence of AIs**	**[1]**
			4406 controls without recurrence of breast cancer and 252 cases with recurrence			**[2]**
***Maternally Expressed 3*(*MEG3*)**	**rs10132552**	**Breast cancer**	**144 women with locally advanced invasive breast cancer**	**Paclitaxel and cisplatin**	**Associated with good DFS and PCR rate**	**[3]**
		Nasopharyngeal carcinoma	**505 newly diagnosed nasopharyngeal carcinoma patients**	**Platinum-based chemotherapy drug**	**Associated with treatment response and risk of developing anemia**	**[4]**
	rs941576	**Breast cancer**	**144 women with locally advanced invasive breast cancer**	**Paclitaxel and cisplatin**	**Associated with good DFS**	**[3]**
	rs116907618	**Lung cancer**	**467 lung cancer patients**	**Platinum-based chemotherapy drug**	**Associated with severe gastrointestinal toxicity**	**[5]**

LncRNA	Polymorphisms	Cancer Type	Patient Population	Drug	Effect	Reference
H19 Imprinted Maternally Expressed Transcript(*H19*)	rs2839698, rs3842761, rs4244809, rs7924316, rs4244809	Epithelial ovarian cancer (EOC)	43 platinum-resistant and 138 platinum-sensitive EOC patients	Platinum-based chemotherapy drug	Associated with platinum-based chemoresistance	[6]
	rs2104725	Lung cancer	467 lung cancer patients	Platinum-based chemotherapy drug	Associated with severe gastrointestinal toxicity	[5]
	rs2839698				Associated with severe gastrointestinal or hematologic toxicities	
antisense non-coding RNA in the INK4 locus (*ANRIL*)	rs1333049	Lung cancer	467 lung cancer patients	Platinum-based chemotherapy drug	Associated with the incidence of severe gastrointestinal toxicity	[5]
	rs10120688				Associated with severe hematologic toxicity	
HOX Transcript Antisense RNA (*HOTAIR*)	rs7958904	Lung cancer	467 lung cancer patients	Platinum-based chemotherapy drug	Associated with the incidence of severe gastrointestinal toxicity	[5]
	rs1899663				Associated with severe gastrointestinal toxicity in age ≥ 57	
metastasis-associated with lung adenocarcinoma transcript-1 (*MALAT1*)	rs619586	Lung cancer	467 lung cancer patients	Platinum-based chemotherapy drug	Associated with gastrointestinal toxicity	[5]
	rs3200401	Metastatic colorectal cancer	98 colorectal cancer patients	Irinotecan	Associated with Pb derived toxicity and tumor resistance to irinotecan	[7]
cancer susceptibility candidate 8 (*CASC8*)	rs10505477	Lung Cancer	498 lung cancer patients and healthy controls	Platinum-based chemotherapy drug	Associated with platinum-based chemotherapy response and toxicity	[8]
Long Intergenic Non-Protein Coding RNA 1139(*LINK-A*)	rs12095274	Breast cancer	Breast cancer patients	AKT inhibitors	Leading to resistance to AKT inhibitors	[9]
Long intergenic non-protein coding RNA-regulator of reprogramming (*Linc-ROR*)	rs2027701	Nasopharyngeal carcinoma	505 newly diagnosed nasopharyngeal carcinoma patients	Platinum-based chemotherapy drug	Associated with chemoresistance and toxicity	[4]1.

2. Background

Transcriptomic studies have implicated that up to 90% of eukaryotic genomes are transcribed [10], and the Human Genome Project revealed that only about 1.2% of the human genome encoded proteins, suggesting that a large number of transcripts were non-coding [10]. Non-coding RNAs with more than 200 nucleotides are defined as long non-coding

RNAs (lncRNAs). Recent studies have shown that lncRNAs seem to regulate their expression levels in a polymorphism-dependent manner and that they participate in different signal pathways, such as PI3K/AKT/NF-κB, thereby achieving the purpose of influencing the chemotherapy response. In this review, we focus on the role of lncRNAs in cancers, particularly the role of lncRNA polymorphisms in response to anti-cancer therapies.

3. lncRNA Polymorphisms in Cancer Chemotherapeutic Response

Notably, lncRNAs SNPs can significantly affect gene expression and function, leading to alterations in cancer susceptibility, chemotoxicity, and sensitivity. was thought to be associated with the risk of toxicity to platinum-based chemotherapeutic drugs in lung cancer patients [5]. Chemotherapy, as one of the important methods of cancer treatment, is of great significance for prolonging the life of patients, but chemotherapy resistance that affects the effectiveness of chemotherapy is still inevitable. Here, we summarize several studies of lncRNAs SNPs relevant to chemotherapy responses to further clarify the potential of lncRNAs as potential biomarkers of cancer risk and predictors of drug resistance as well as toxicity (Table 1).

Compared with 4406 healthy people, it was found that the level of MIR2052HG in 253 breast cancer patients increased, and this change in expression level was regulated by MIR2052HG SNPs [1]. LMTK3 is related to new-onset and intrinsic endocrine resistance in breast cancer [11]. In conclusion, the expression level of MIR2052HG was influenced by its genetic polymorphisms. Furthermore, different expression levels of MIR2052HG regulate the expression of ERα through transcription and protein degradation mode, which is related to the resistance of ERα-positive breast cancer patients to AIs.

14q32.3 has an inhibitory effect in a variety of cancers, such as bladder cancer, gastric cancer, and non-small cell lung cancer [12][13][14]. In non-small cell lung cancer, up-regulation of MEG3 led to an increase in the apoptosis rate of cancer cells. However, cancer cells with MEG3 knockout have a decreased rate of cisplatin-induced apoptosis, and the result is that lung cancer cells enhance cisplatin resistance by activating the WNT/β-catenin signaling pathway [15]. Likewise, the results of the study by Bayarmaa et al. proved that MEG3 rs10132552 was also related to chemotherapy response in breast cancer patients treated with paclitaxel or cisplatin [3].

In recent years, the impact of H19 on cancer risk and prognosis has attracted researchers' interest [5][16][17][18]. For instance, H19 rs217727 was found to be associated with oral squamous cell carcinoma [19], osteosarcoma [20], bladder cancer [21], and gastric cancer [22] risk; H19 rs2839698 has been shown to be associated with hepatocellular cancer risk and prognosis [23]. Further, studies substantiated that H19 knockdown could reduce drug resistance in cells and promote drug-induced apoptosis in resistant choriocarcinoma cells. These results corroborated that H19 polymorphisms were related to the drug reaction and toxicity reaction of platinum chemotherapeutic drugs, but its molecular mechanism needs further study.

According to a recent study comparing TC and CC genotypes, gastric cancer patients carrying the rs1562430 TT genotype had a higher risk of death [24]. OCT3/4 has been confirmed to be involved in the chemotherapy resistance of glioblastoma cell lines by affecting the expression of the drug efflux pump gene ABCG2, which encodes breast cancer resistance protein (BCRP) [25]. Moreover, in non-small cell lung cancer cells, through Western blotting, researchers found that when CASC8 was knockdown, the level of FOXM1 protein decreased [26]. These findings not only provide new insights for the clinical application of CASC8 polymorphisms in predicting cancer risk and chemotherapy response but also provide new directions for exploring the effect of CASC8 SNPs on chemotherapy.

By analyzing genetic mutations within or adjacent to the LINK-A gene locus in breast cancer patients, Lin et al. found that a SNP mutation located downstream of the LINK-A transcriptional region in breast cancer was associated with LINK-A expression and outcome [9]. According to previous studies, lncRNA LINK-A can specifically interact with AKT and PIP3 in breast cancer cells [9]. A allele carriers are more likely than G allele carriers to develop resistance to AKT inhibitors in breast cancer patients. Moreover, stratifying breast cancer according to the expression level of LINK-

The dysfunction of p53 function has been shown to relate to the occurrence and development of breast cancer [27]. Previous studies have suggested that Linc-ROR significantly inhibited p53 in the process of DNA damage, thereby affecting the arrest and apoptosis of cancer cells, which is believed to be the cause of resistance to platinum chemotherapy in cancer patients [4]. In addition, Linc-ROR has also been found to interact with miR-124 and to participate in the resistance of pancreatic cancer to gemcitabine by regulating the miR-124/PTBP1/PKM2 axis [28]. These findings provide new insights into the function of Linc-ROR polymorphisms in cancer development and chemotherapy.

In recent years, lncRNA MALAT1 has been proved to be a metastasis and prognosis marker of some cancers, and it was involved in the proliferation, invasion, and apoptosis of cancer cells [7][29]. The increased expression is positively correlated with cancer susceptibility and poor cancer prognosis. Previous studies revealed that miR-218 could significantly suppress the EMT process and enhance 5-FU–based chemosensitivity in colorectal cancer cells by targeting BIRC5, a key member of the inhibitors of apoptosis gene (IAP) family [30][31]. To sum up, the regulatory role of MALAT1 polymorphisms in cancer chemotherapy is interesting, and its potential as a biomarker to predict the chemotherapy response of cancer patients is promising.

Past studies have shown that ANRIL was involved in the occurrence and development of a variety of cancers, including cancer susceptibility and the proliferation and migration process of cancer cells [32][33]. Studies have confirmed the importance of p16 as a regulator in cancer cells caused by cisplatin. Another study explained the role of ANRIL in cisplatin resistance in ovarian cancer by down-regulating the expression of let-7a and then up-regulating the expression of HMGA2 [34]. In lung cancer, the development of drug resistance is achieved by inhibiting the expression of miR-98 [35].

HOTAIR is a lncRNA overexpressed in a variety of cancer cells, including lung cancer, hepatocellular carcinoma, and colorectal cancer. It is related to the prognosis of cancer patients [5][36]. It promoted cell growth and inhibited apoptosis by regulating H3K27me3 and activating the PI3K/AKT/NF-κB pathway, which was thought to be the mechanism by which HOTAIR regulates the resistance of large B-cell lymphoma to diffuse prednisone [37]. In addition, squamous cell carcinoma patients with HOTAIR rs7958904 were more likely to develop severe hematological toxicity after platinum-based chemotherapy.

In addition to the above, some other important lncRNAs have also been found to play an interesting role in chemotherapy resistance, and their expression levels are regulated by their polymorphisms. Further studies confirmed that the up-regulation of TP73-AS1 promotes resistance of glioblastoma cancer stem cells to temozolomide by regulating the expression of metabolism-related genes and aldehyde dehydrogenase 1 family member A1 (ALDH1A1). Similarly, lncRNA Nuclear Paraspeckle Assembly Transcript 1 (NEAT1) was indicated to be lowly expressed in nasopharyngeal carcinoma cells that are resistant to histone deacetylase inhibitors and could improve the resistance of nasopharyngeal carcinoma to histone deacetylase inhibitors by regulating the miR-129/Bcl-2 axis [38]. Although there is no direct conclusion to prove the direct effect of these lncRNAs polymorphisms on chemotherapy response, based on the existing evidence, we speculate that the above three lncRNAs polymorphisms also affect chemotherapy resistance and deserve further exploration.

4. Conclusions

In this review, we analyzed recently identified gene polymorphisms of lncRNAs affecting the response of chemotherapeutic drugs. The studies of MIR2052HG, LINK-A, MEG3, and ANRIL have revealed that their polymorphisms may regulate either the expression or the structure of functional lncRNAs, thereby exerting biological effects; however, more mechanisms are expected to be discovered based on detailed studies of RNA-protein and RNA–DNA interactions. In conclusion, the polymorphisms of lncRNAs may serve as a biomarker for predicting the response of cancer patients to chemotherapy. Clinically, suitable chemotherapy drugs can be selected according to the polymorphisms of different patients.

References

1. Ingle, J.N.; Xie, F.; Ellis, M.J.; Goss, P.E.; Shepherd, L.E.; Chapman, J.-A.W.; Chen, B.E.; Kubo, M.; Furukawa, Y.; Mo mozawa, Y.; et al. Genetic Polymorphisms in the Long Noncoding RNA miR2052HG Offer a Pharmacogenomic Basis f or the Response of Breast Cancer Patients to Aromatase Inhibitor Therapy. Cancer Res. 2016, 23, 7012.
2. Cairns, J.; Ingle, J.N.; Kalari, K.R.; Shepherd, L.E.; Kubo, M.; Goetz, M.P.; Weinshilboum, R.M.; Wang, L. The LncRNA miR2052HG Regulates Eralpha Levels and Aromatase Inhibitor Resistance through LMTK3 by Recruiting EGR1. Breas t Cancer Res. 2019, 21, 47.
3. Bayarmaa, B.; Wu, Z.; Peng, J.; Wang, Y.; Xu, S.; Yan, T.; Yin, W.; Lu, J.; Zhou, L. Association of LncRNA MEG3 Polym orphisms with Efficacy of Neoadjuvant Chemotherapy in Breast Cancer. BMC Cancer 2019, 19, 877.
4. Wang, Y.; Guo, Z.; Zhao, Y.; Jin, Y.; An, L.; Wu, B.; Liu, Z.; Chen, X.; Chen, X.; Zhou, H.; et al. Genetic Polymorphisms of LncRNA-P53 Regulatory Network Genes Are Associated with Concurrent Chemoradiotherapy Toxicities and Efficacy in Nasopharyngeal Carcinoma Patients. Sci. Rep. 2017, 7, 8320.
5. Gong, W.-J.; Peng, J.-B.; Yin, J.-Y.; Li, X.-P.; Zheng, W.; Xiao, L.; Tan, L.-M.; Xiao, D.; Chen, Y.-X.; Li, X.; et al. Associati on between Well-Characterized Lung Cancer LncRNA Polymorphisms and Platinum-Based Chemotherapy Toxicity in C hinese Patients with Lung Cancer. Acta Pharmacol. Sin. 2017, 38, 581–590.

6. Zeng, Y.; Li, T.-L.; Zhang, H.-B.; Deng, J.-L.; Zhang, R.; Sun, H.; Wan, Z.-R.; Liu, Y.-Z.; Zhu, Y.-S.; Wang, G. Polymorphisms in IGF2/H19 Gene Locus Are Associated with Platinum-Based Chemotherapeutic Response in Chinese Patients with Epithelial Ovarian Cancer. Pharmacogenomics 2019, 20, 179–188.
7. Lampropoulou, D.-I.; Aravantinos, G.; Katifelis, H.; Lazaris, F.; Laschos, K.; Theodosopoulos, T.; Papadimitriou, C.; Gazouli, M. Long Non-Coding RNA Polymorphisms and Prediction of Response to Chemotherapy Based on Irinotecan in Patients with Metastatic Colorectal Cancer. Cancer Biomarks 2019, 25, 213–221.
8. Hu, L.; Chen, S.-H.; Lv, Q.-L.; Sun, B.; Qu, Q.; Qin, C.-Z.; Fan, L.; Guo, Y.; Cheng, L.; Zhou, H.-H. Clinical Significance of Long Non-Coding RNA Casc8 Rs10505477 Polymorphism in Lung Cancer Susceptibility, Platinum-Based Chemotherapy Response, and Toxicity. Int. J. Environ. Res. Public Health 2016, 13, 545.
9. Lin, A.; Hu, Q.; Li, C.; Xing, Z.; Ma, G.; Wang, C.; Li, J.; Ye, Y.; Yao, J.; Liang, K.; et al. The Link—A LncRNA Interacts with Ptdins(3,4,5)P3 to Hyperactivate AKT and Confer Resistance to AKT Inhibitors. Nat. Cell Biol. 2017, 19, 238–251.
10. Costa, F.F. Non-Coding RNAs, Meet Thy Masters. BioEssays 2010, 32, 599–608.
11. Stebbing, J.; Filipovic, A.; Lit, L.C.; Blighe, K.; Grothey, A.; Xu, Y.; Miki, Y.; Chow, L.W.; Coombes, R.C.; Sasano, H.; et al. LMTK3 Is Implicated in Endocrine Resistance Via Multiple Signaling Pathways. Oncogene 2013, 32, 3371–3380.
12. Feng, S.Q.; Zhang, X.Y.; Fan, H.T.; Sun, Q.J.; Zhang, M. Up-Regulation of LncRNA MEG3 Inhibits Cell Migration and Invasion and Enhances Cisplatin Chemosensitivity in Bladder Cancer Cells. Neoplasma 2018, 65, 925–932.
13. Wei, G.H.; Wang, X. LncRNA MEG3 Inhibit Proliferation and Metastasis of Gastric Cancer via P53 Signaling Pathway. Eur. Rev. Med. Pharmacol. Sci. 2017, 21, 3850–3856.
14. Wang, C.; Nie, H.; Li, Y.; Liu, G.; Wang, X.; Xing, S.; Zhang, L.; Chen, X.; Chen, Y.; Li, Y. The Study of the Relation of DNA Repair Pathway Genes SNPS and the Sensitivity to Radiotherapy and Chemotherapy of NSCLC. Sci. Rep. 2016, 6, 26526.
15. Xia, Y.; He, Z.; Liu, B.; Wang, P.; Chen, Y. Downregulation of MEG3 Enhances Cisplatin Resistance of Lung Cancer Cells through Activation of the Wnt/Beta-Catenin Signaling Pathway. Mol. Med. Rep. 2015, 12, 4530–4537.
16. Lottin, S.; Adriaenssens, E.; Dupressoir, T.; Berteaux, N.; Montpellier, C.; Coll, J.; Dugimont, T.; Curgy, J.J. Overexpression of an Ectopic H19 Gene Enhances the Tumorigenic Properties of Breast Cancer Cells. Carcinogenesis 2002, 23, 1885–1895.
17. Yang, F.; Bi, J.; Xue, X.; Zheng, L.; Zhi, K.; Hua, J.; Fang, G. Up-Regulated Long Non-Coding RNA H19 Contributes to Proliferation of Gastric Cancer Cells. FEBS J. 2012, 279, 3159–3165.
18. Tsang, W.P.; Kwok, T.T. Riboregulator H19 Induction of Mdr1-Associated Drug Resistance in Human Hepatocellular Carcinoma Cells. Oncogene 2007, 26, 4877–4881.
19. Guo, Q.-Y.; Wang, H.; Wang, Y. LncRNA H19 Polymorphisms Associated with the Risk of Oscc in Chinese Population. Eur. Rev. Med. Pharmacol. Sci. 2017, 21, 3770–3774.
20. He, T.-D.; Xu, D.; Sui, T.; Zhu, J.-K.; Wei, Z.-X.; Wang, Y.-M. Association between H19 Polymorphisms and Osteosarcoma Risk. Eur. Rev. Med. Pharmacol. Sci. 2017, 21, 3775–3780.
21. Hua, Q.; Lv, X.; Gu, X.; Chen, Y.; Chu, H.; Du, M.; Gong, W.; Wang, M.; Zhang, Z. Genetic Variants in LncRNA H19 Are Associated with the Risk of Bladder Cancer in a Chinese Population. Mutagenesis 2016, 31, 531–538.
22. Yang, C.; Tang, R.; Ma, X.; Wang, Y.; Luo, D.; Xu, Z.; Zhu, Y.; Yang, L. Tag SNPs in Long Non-Coding RNA H19 Contribute to Susceptibility to Gastric Cancer in the Chinese Han Population. Oncotarget 2015, 6, 15311–15320.
23. Yang, M.L.; Huang, Z.; Wang, Q.; Chen, H.H.; Ma, S.N.; Wu, R.; Cai, W.S. The Association of Polymorphisms in LncRNA-H19 with Hepatocellular Cancer Risk and Prognosis. Biosci. Rep. 2018, 38.
24. Zhang, Y.; Wu, Y.; Jia, Z.; Cao, D.; Yang, N.; Wang, Y.; Cao, X.; Jiang, J. Long Non-Coding RNA Polymorphisms on 8q24 Are Associated with the Prognosis of Gastric Cancer in a Chinese Population. PeerJ 2020, 8, e8600.
25. Hosokawa, Y.; Takahashi, H.; Inoue, A.; Kawabe, Y.; Funahashi, Y.; Kameda, K.; Sugimoto, K.; Yano, H.; Harada, H.; Kohno, S.; et al. Oct-3/4 Modulates the Drug-Resistant Phenotype of Glioblastoma Cells through Expression of ATP Binding Cassette Transporter G2. Biochim. Biophys. Acta 2015, 1850, 1197–1205.
26. Jiang, X.; Guan, J.; Xu, Y.; Ren, H.; Jiang, J.; Wudu, M.; Wang, Q.; Su, H.; Zhang, Y.; Zhang, B.; et al. Silencing of CASC8 Inhibits Non-Small Cell Lung Cancer Cells Function and Promotes Sensitivity to Osimertinib Via FOXM1. J. Cancer 2021, 12, 387–396.
27. Duffy, M.J.; Synnott, N.C.; Crown, J. Mutant P53 in Breast Cancer, Potential as a Therapeutic Target and Biomarker. Breast Cancer Res. Treat 2018, 170, 213–219.
28. Li, C.; Zhao, Z.; Zhou, Z.; Liu, R. Linc-ROR Confers Gemcitabine Resistance to Pancreatic Cancer Cells Via Inducing Autophagy and Modulating the miR-124/PTBP1/PKM2 Axis. Cancer Chemother. Pharmacol. 2016, 78, 1199–1207.

29. Ji, P.; Diederichs, S.; Wang, W.; Boing, S.; Metzger, R.; Schneider, P.M.; Tidow, N.; Brandt, B.; Buerger, H.; Bulk, E.; et al. MALAT-1, a Novel Noncoding RNA, and Thymosin Beta4 Predict Metastasis and Survival in Early-Stage Non-Small Cell Lung Cancer. Oncogene 2003, 22, 8031–8041.
30. Yamasaki, T.; Seki, N.; Yoshino, H.; Itesako, T.; Hidaka, H.; Yamada, Y.; Tatarano, S.; Yonezawa, T.; Kinoshita, T.; Nakagawa, M.; et al. MicroRNA-218 Inhibits Cell Migration and Invasion in Renal Cell Carcinoma through Targeting Caveolin-2 Involved in Focal Adhesion Pathway. J. Urol. 2013, 190, 1059–1068.
31. Li, P.L.; Zhang, X.; Wang, L.L.; Du, L.T.; Yang, Y.M.; Li, J.; Wang, C.X. MicroRNA-218 is a Prognostic Indicator in Colorectal Cancer and Enhances 5-Fluorouracil-Induced Apoptosis by Targeting Birc5. Carcinogenesis 2015, 36, 1484–1493.
32. Nie, F.-Q.; Sun, M.; Yang, J.-S.; Xie, M.; Xu, T.-P.; Xia, R.; Liu, Y.-W.; Liu, X.-H.; Zhang, E.-B.; Lu, K.-H.; et al. Long Noncoding RNA Anril Promotes Non-Small Cell Lung Cancer Cell Proliferation and Inhibits Apoptosis by Silencing KLF2 and P21 Expression. Mol. Cancer Ther. 2015, 14, 268–277.
33. Lin, L.; Gu, Z.-T.; Chen, W.-H.; Cao, K.-J. Increased Expression of the Long Non-Coding RNA ANRIL Promotes Lung Cancer Cell Metastasis and Correlates with Poor Prognosis. Diagn. Pathol. 2015, 10, 14.
34. Miao, J.-T.; Gao, J.-H.; Chen, Y.-Q.; Chen, H.; Meng, H.-Y.; Lou, G. LncRNA Anril Affects the Sensitivity of Ovarian Cancer to Cisplatin Via Regulation of Let-7a/HMGA2 Axis. Biosci. Rep. 2019, 39, BSR20182101.
35. Wang, X.; Zhang, G.; Cheng, Z.; Dai, L.; Jia, L.; Jing, X.; Wang, H.; Zhang, R.; Liu, M.; Jiang, T.; et al. Knockdown of LncRNA Anril Inhibits the Development of Cisplatin Resistance by Upregulating miR98 in Lung Cancer Cells. Oncol. Rep. 2020, 44, 1025–1036.
36. Nakagawa, T.; Endo, H.; Yokoyama, M.; Abe, J.; Tamai, K.; Tanaka, N.; Sato, I.; Takahashi, S.; Kondo, T.; Satoh, K. Large Noncoding RNA Hotair Enhances Aggressive Biological Behavior and is Associated with Short Disease-Free Survival in Human Non-Small Cell Lung Cancer. Biochem. Biophys. Res. Commun. 2013, 436, 319–324.
37. Huang, X.; Qian, W.; Ye, X. Long Noncoding RNAS in Diffuse Large B-Cell Lymphoma, Current Advances and Perspectives. Onco Targets Ther. 2020, 13, 4295–4303.
38. Xue, F.; Cheng, Y.; Xu, L.; Tian, C.; Jiao, H.; Wang, R.; Gao, X. LncRNA Neat1/miR-129/Bcl-2 Signaling Axis Contributes to Hdac Inhibitor Tolerance in Nasopharyngeal Cancer. Aging 2020, 12, 1417–1488.