

lncRNA影响乳腺癌化疗耐药性的研究进展

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摘要

目前lncRNA对乳腺癌化疗耐药的相关研究越来越多, 本文重点就lncRNA对乳腺癌常见化疗药耐药的发生和发展中起的重要作用进行总结, 并对lncRNA与乳腺癌化疗耐药之间的作用进行分析综合, 讨论lncRNA作为乳腺癌化疗耐药的潜在靶点的治疗意义。本文总结国内外文献对lncRNA与乳腺癌一线化疗药物紫杉醇、多西他赛、阿霉素和顺铂的耐药相关研究进行综述。lncRNA介导乳腺癌化疗耐药的耐药机制包括: (1) 影响化疗药物靶基因的lncRNA及其影响效应。(2) lncRNAs通过调节乳腺癌细胞周期和细胞凋亡。(3) lncRNAs靶向PTE、NF- κ B等信号通路。(4) lncRNAs影响多重耐药基因。lncRNA有望是改善乳腺癌患者化疗耐药的新靶点。以lncRNA为靶点可能是未来改善乳腺癌患者化疗效果的一种新策略。

关键词

lncRNA, 乳腺癌, 化疗, 耐药性

Research Progress on the Effect of lncRNA on Chemoresistance of Breast Cancer

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Abstract

At present, there are more and more researches on lncRNA in breast cancer chemotherapy resistance. This article focuses on the important role of lncRNA in the occurrence and development of

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common chemotherapy drug resistance in breast cancer, and analyzes and synthesizes the role between lncRNA and breast cancer chemotherapy resistance to discuss the therapeutic significance of lncRNA as a potential target for chemoresistance in breast cancer. In this paper, the domestic and foreign literature on the relationship between lncRNA and the resistance of first-line chemotherapy drugs paclitaxel, docetaxel, doxorubicin and cisplatin in breast cancer is reviewed. The mechanisms of lncRNA-mediated chemoresistance in breast cancer include: (1) lncRNA affects the target genes of chemotherapy drugs and its effect, (2) lncRNAs regulate breast cancer cell cycle and apoptosis, (3) lncRNAs target PTE and NF- κ B signaling pathways, (4) lncRNAs affect multidrug resistance genes. lncRNA is expected to be a new target for improving chemotherapy resistance in breast cancer patients. Targeting lncRNA may be a new strategy to improve the efficacy of chemotherapy in breast cancer patients in the future.

Keywords

lncRNA, Breast Cancer, Chemotherapy, Drug Resistance

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1. 引言

乳腺癌(breast cancer, BC)是全球第二常见的癌症,也是女性最常见的癌症[1],乳腺癌的肿瘤异质性将乳腺癌区分为四种分子亚型:Luminal A、Luminal B、HER 2 阳性和三阴性。

化疗是目前乳腺癌重要临床治疗方法之一,乳腺癌常用化疗药物包括:(1) 紫杉类:如白蛋白紫杉醇、多西他赛等;(2) 蒽环类:如表柔比星、阿霉素等;(3) 氟尿嘧啶类:如卡培他滨;(4) 植物碱类:如长春瑞滨;(5) 铂类:顺铂、卡铂等。虽然研究表明化疗显著降低了乳腺癌患者的转移和复发风险。并延长了晚期乳腺癌患者的生存时间,但由于部分患者对化疗药物产生耐药导致疾病进展,导致肿瘤治疗失败[2],因此耐药性是乳腺癌治疗中的一个严峻挑战。

长链非编码 RNA (lncRNA)是不编码功能蛋白的非编码 RNA 的一个亚类。它们由 200 多个核苷酸组成,通常根据其相对于相邻蛋白质编码基因的位置分为 5 类,包括双向、反义、基因间、内含子和正义 lncRNA [3]。已被证明在许多关键的细胞过程中发挥着重要作用,如转录、翻译、干细胞分化、细胞自噬、细胞凋亡和表观遗传控制[4]。越来越多的证据表明 lncRNA 在乳腺癌的发生发展及化疗耐药中起着关键作用[5] [6]。因此本文重点针对 lncRNA 对乳腺癌常见化疗药物耐药性的影响进行综述。

2. lncRNA 与乳腺癌化疗耐药

2.1. lncRNA 与紫杉醇耐药

lncRNA 在调节 BC 细胞紫杉醇耐药的机制中,其关键因素包括 ATP 结合盒转运蛋白(ABC)家族及其衍生物, P-糖蛋白(P-gp)、多药耐药相关蛋白(MRP)的过度表达。一些 lncRNA 可以通过影响乳腺癌细胞中的 ABC 外排转运蛋白来介导紫杉醇耐药性。例如,据报道, lncRNABC032585 可能通过顺式或反式调节机制调节 MDR1 表达[7],在 ER 阴性乳腺癌细胞中,发现 lncRNA MAPT-AS1 通过与 tau 蛋白(MAPT)的反义配对与细胞生长、侵袭性和紫杉醇耐药性相关[8]。相比之下, lncRNA FTH1P3 通过靶向 miR-206/ABCB1 轴来增加 ABCB1 蛋白的产生,从而诱导乳腺癌细胞对紫杉醇的耐药性[9]。研究发现,

Linc00518 通过 miR-199a/MRP1 轴减少紫杉醇诱导的细胞凋亡,从而增加 MCF-7 细胞对紫杉醇的耐药性, linc00518 通过调节乳腺癌中的 miR-199a/MRP1 轴来降低多药耐药性[10]。在紫杉醇耐药的 MCF-7 细胞中, lncRNA RP11-770J1.3 和 TMEM25 高表达, lncRNA RP11-770J1.3 和 TMEM25 的下调可通过抑制 MRP、BCRP 和 P-gp 的表达来增加这些细胞中的紫杉醇敏感性[11]。

在多项研究中, 与细胞周期和细胞凋亡途径相关的 lncRNA 与乳腺癌的紫杉醇耐药性有关[12]。linc00511 通过作为 ceRNA (内源性 RNA)在乳腺癌细胞中诱导紫杉醇耐药性, 以海绵化 miR-29c 并增加 CDK6 的表达[13]。研究人员发现, 在紫杉醇耐药的临床乳腺癌样本和细胞系中, lncRNA CASC2 的表达增加。紫杉醇以浓度依赖性方式诱导 CASC2 表达, CASC2 的下调增加紫杉醇毒性并降低 IC50 值。研究人员进一步阐明, miR-18a-5p/CDK19 是 CASC2 功能的下游靶点[14]。同样, lncRNA UCA1 在紫杉醇耐药乳腺癌组织和 MCF-7 细胞中高表达, 并进一步证实 UCA1 通过调节 miR-613/CDK12 轴介导紫杉醇耐药性[15]。与亲本细胞相比, lncRNA NEAT1 在顺铂耐药和紫杉醇耐药 MDA-MB-231 细胞中的表达上调, 并且敲除 NEAT1 会让细胞对化疗重新致敏。功能研究表明, NEAT1 通过调节三阴性乳腺癌(TNBC)细胞的凋亡和细胞周期进程而发挥致癌作用[16]。研究发现, lncRNA NONHSAT141924 通过抑制 p-CREB/Bcl-2 凋亡途径促进紫杉醇耐药, lncRNA NONHSAT141924 过表达可增加乳腺癌中 Bcl-2 和 p-CREB 蛋白水平[17]。另一项研究还表明, lncRNA H19 可以通过灭活两个关键的促凋亡基因(BIK/NOXA)来降低乳腺癌对紫杉醇的敏感性[18]。Li 等人[19]发现 lncRNA OTUD6B-AS1 调控下游的 miR-26a-5p, 后者表达上调促进了紫杉醇的细胞毒性。lncRNA AF178030.2 可直接与乳腺癌中的致癌基因 TRPS1 结合, 并下调其在紫杉醇耐药 TNBC 细胞中的表达, TRPS1 过表达有效提高了紫杉醇耐药 TNBC 细胞对紫杉醇的敏感性[20]。

2.2. lncRNA 与多西他赛耐药

有多种 lncRNAs 在乳腺癌细胞多西他赛耐药中起着重要作用。多西紫杉醇是一种半合成紫杉烷, 结构与紫杉醇相似, 具有与紫杉醇相同或重叠的结合位点。多西紫杉醇衍生的微管蛋白聚合物在结构上与紫杉醇衍生的微管蛋白聚合物不同, 并且由于其对 β -微管蛋白的结合亲和力更高, 因此在微管蛋白组装中更有效, 此外, 多西他赛在癌细胞中的停留时间比紫杉醇长[21]。

尽管多西紫杉醇已被证明可有效治疗乳腺癌, 但患者经常出现耐药性。lncRNA 在多西紫杉醇耐药性中也起着重要作用。对两种多西紫杉醇耐药乳腺癌细胞系(MCF7-RES 和 MDA-RES)及其多西紫杉醇敏感亲本细胞系进行了全面的 RNA 测序和分析。结果显示, lncRNA EPB41L4A-AS2 在亲本乳腺癌细胞系中表达, 但在多西紫杉醇耐药细胞株后代中缺失; EPB41L4A-AS2 水平的降低也与 ABCB1 mRNA 水平的增加显著相关[22]。在多西紫杉醇耐药乳腺癌细胞中, lncRNA LINC00680 表达水平上调, LINC00680 发现通过 miR-320b/CDKL5 轴促进多西紫杉醇耐药[23]。同样, 研究发现, 多西紫杉醇耐药 TNBC 细胞来源的外泌体中 LINC00667 的表达水平明显高于多西他赛敏感的 TNBC 细胞来源的外泌体。研究发现, 外泌体 LINC00667 通过调节 miR-200b-3p/Bcl-2 轴来促进 TNBC 细胞对多西他赛的耐药性[24]。此外, 在乳腺癌中, LINC00461 可以通过直接与 miR-411-5p 相互作用来充当 ceRNA, 并通过充当 miR-411-5p 分子的海绵来促进多西紫杉醇耐药性[25]。lncRNA TMPO-AS1 已被确定为肺癌患者的预后指标。然而, 最近的研究表明, 它还可以通过调节 miR-1179/TRIM37 轴来促进多西紫杉醇耐药性和乳腺癌侵袭[26]。

2.3. lncRNA 与蒽环类药物耐药

蒽环类药物最初被称为抗生素, 包括柔红霉素(daunorubicin, DAU)、多柔比星(dox)、表柔比星(epirubicin, EPI)和伊达比星(idarubicin, IDA), 是目前抗癌化疗中疗效较强的一类重要药物, 主要用于 BC

[27]。尽管其作用机制仍存在争议,但蒽环类药物的抗癌活性可能涉及通过 DNA 插层、自由基生成和抑制拓扑异构酶 II 抑制大分子合成(引起 DNA 损伤、结合、烷基化和交联)以及诱导细胞凋亡[28]。

有研究报道 Yao 等人[29]发现 lncRNA NONHSAT101069 与 miR-129-5p 一起作为 ceRNA 并靶向 BC 细胞中的 Twist1。lncRNA 的表达 NONHSAT101069 促进 BC 细胞对表柔比星的抗性,并通过 lncRNA NONHSAT101069/miR-129-5p/Twist1 轴诱导细胞 EMT 和迁移过程。Gooding 等人[30]报道,lncRNABORG 通过激活 NF- κ B 信号通路促进了三阴性 BC (TNBC)细胞对多柔比星的化疗耐药性。Chen 等[31]发现,LncRNAGAS5 通过 miR-221-3p/DKK2 轴抑制 Wnt/ β -catenin 信号通路,显著逆转了 BC 细胞对 ADR 耐药性。近年来有微阵列分析鉴定 lncRNA 作为蒽环类药物耐药 BC 的关键参与者。然而,当前数据库中大多数失调的 lncRNA 尚未进行功能注释;出于这个原因,作者根据其相关的 mRNA 和实验验证预测了它们的功能。在这项工作中,他们展示了 lncRNA 和基因之间的特定相互作用,以及 lncRNA 和转录因子之间的特定相互作用。基于此,他们验证了 lncRNA NONHSAT028712 调节附近的细胞周期蛋白依赖性激酶 2 (CDK2),干扰细胞周期和化疗耐药性。此外,作者还鉴定了另一组 lncRNA (NONHSAT057282 和 NONHSAG023333),它们与化疗耐药调节转录因子(如 ELF1 和 E2F1)相互作用[32]。如上所述,与蒽环类药物耐药相关的 lncRNA 研究仍不明朗。

2.4. lncRNA 与顺铂耐药

顺铂(DDP)是乳腺癌治疗过程中广泛应用的强效化疗药物,主要通过破坏 DNA 以及诱导细胞凋亡发挥作用,但因其具有快速获得性耐药性或固有耐药性,从而导致乳腺癌治疗失败。顺铂对三阴性 BC (triple-negative BC, TNBC)特别有用,TNBC 是一组基因组不稳定性高的肿瘤,通常与 HR 缺陷有关,约占所有 BC 病例的 15%~20% [33]。Adriaens 等人发现,NEAT1 能够通过 p53 再激活使 MCF7 BC 细胞系对不同的化疗药物和 PARP 抑制剂敏感[34]。Zhang 等人[35]发现 SNHG1 沉默通过表观遗传抑制 miR-381 表达抑制肿瘤进展并克服乳腺癌细胞对顺铂的耐药性。DU 等人[36]发现 lncRNA DLX6-AS1 在体外和体内通过 TNBC 中的 miR-199b-5p/PXN 信号转导促进细胞增殖、EMT 和顺铂耐药性。还有研究表明 lncRNA HCP5 通过调节 PTEN 表达促进人三阴性乳腺癌的顺铂耐药性[37]。

3. 总结与展望

化疗耐药是临床上乳腺癌治疗失败的主要原因之一,这也是一个涉及多因素、多通路和多基因的复杂过程。在这篇文章中,我们总结了 lncRNAs 在乳腺癌化疗耐药中的机制。根据报道,lncRNAs 参与乳腺癌耐药的分子生物机制包括:(1) 影响化疗药物靶基因的 lncRNA 及其影响效应,(2) lncRNAs 通过调节乳腺癌细胞周期和细胞凋亡,(3) lncRNAs 靶向 PTEN、NF- κ B 等信号通路,(4) lncRNAs 影响多重耐药基因。

lncRNAs 与乳腺癌发展之间的关系已被广泛研究。许多研究已经确定了 lncRNAs 在乳腺癌化疗耐药性中的重要性,下一代测序技术的进步为耐药性肿瘤中发生的分子变化提供了更好的理解,从而丰富了对耐药机制的理解。众所周知,lncRNAs 通过不同的机制参与化疗耐药性的发展,包括调节药物外排代谢、抑制细胞死亡、增强增殖信号通路和 EMT。确定 lncRNA 在乳腺癌化疗耐药性中作用的分子机制可能有助于开发有效的治疗方式。因此,除了用作肿瘤的早期诊断和预后生物标志物外,lncRNA 还可能具有作为耐药性乳腺癌潜在治疗靶点的临床用途。然而,尽管沉默 lncRNA 可能是克服化疗耐药性的有效策略,但作为所有形式的癌症基因治疗的常见问题,缺乏合适和特异性的递送载体是一个主要障碍。因此,在将 lncRNA 用作真正的治疗策略之前,需要对 lncRNA 的生物学效应进行更广泛和完整的研究。总体而言,全面而透彻地了解 lncRNA 介导的乳腺癌化疗耐药机制对于未来癌症治疗的临床转化至关重要。

尽管本文综述了 lncRNA 在乳腺癌化疗耐药中的大部分研究,但其生物学机制的细节仍需进一步探

讨。随着技术的发展和研究的阐明, 我们相信以 lncRNA 为靶点可能是未来改善乳腺癌患者化疗结果的一种新策略。

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参考文献

- [1] Loibl, S., Poortmans, P., Morrow, M., Denkert, C. and Curigliano, G. (2021) Breast Cancer. *Lancet*, **397**, 1750-1769. [https://doi.org/10.1016/S0140-6736\(20\)32381-3](https://doi.org/10.1016/S0140-6736(20)32381-3)
- [2] Dan, V.M., Raveendran, R.S. and Baby, S. (2021) Resistance to Intervention: Paclitaxel in Breast Cancer. *Mini-Reviews in Medicinal Chemistry*, **21**, 1237-1268. <https://doi.org/10.2174/1389557520999201214234421>
- [3] Lin, W., Zhou, Q., Wang, C.Q., Zhu, L., Bi, C., Zhang, S., Wang, X. and Jin, H. (2020) lncRNAs Regulate Metabolism in Cancer. *International Journal of Biological Sciences*, **16**, 1194-1206. <https://doi.org/10.7150/ijbs.40769>
- [4] Qian, X., Zhao, J., Yeung, P.Y., Zhang, Q.C. and Kwok, C.K. (2019) Revealing lncRNA Structures and Interactions by Sequencing-Based Approaches. *Trends in Biochemical Sciences*, **44**, 33-52. <https://doi.org/10.1016/j.tibs.2018.09.012>
- [5] Peng, L., Jiang, J., Tang, B., Nice, E.C., Zhang, Y.Y. and Xie, N. (2020) Managing Therapeutic Resistance in Breast Cancer: From the lncRNAs Perspective. *Theranostics*, **10**, 10360-10377. <https://doi.org/10.7150/thno.49922>
- [6] Zhang, X. and Yang, H. (2020) Research Progress on Long Non-Coding RNAs and Drug Resistance of Breast Cancer. *Clinical Breast Cancer*, **20**, 275-282. <https://doi.org/10.1016/j.clbc.2019.11.001>
- [7] Zeng, Y., Wang, G., Zhou, C.F., Zhang, H.B., Sun, H., Zhang, W., Zhou, H.H., Liu, R. and Zhu, Y.S. (2019) lncRNA Profile Study Reveals a Three-lncRNA Signature Associated with the Pathological Complete Response Following Neoadjuvant Chemotherapy in Breast Cancer. *Frontiers in Pharmacology*, **10**, Article 574. <https://doi.org/10.3389/fphar.2019.00574>
- [8] Pan, Y., Pan, Y., Cheng, Y., Yang, F., Yao, Z. and Wang, O. (2018) Knockdown of lncRNA MAPT-AS1 Inhibits Proliferation and Migration and Sensitizes Cancer Cells to Paclitaxel by Regulating MAPT Expression in ER-Negative Breast Cancers. *Cell & Bioscience*, **8**, Article No. 7. <https://doi.org/10.1186/s13578-018-0207-5>
- [9] Wang, R., Zhang, T., Yang, Z., Jiang, C. and Seng, J. (2018) Long Non-Coding RNA FTH1P3 Activates Paclitaxel Resistance in Breast Cancer through MiR-206/ABCB1. *Journal of Cellular and Molecular Medicine*, **22**, 4068-4075. <https://doi.org/10.1111/jcmm.13679>
- [10] Chang, L., Hu, Z., Zhou, Z. and Zhang, H. (2018) Linc00518 Contributes to Multidrug Resistance Through Regulating the MiR-199a/MRP1 Axis in Breast Cancer. *Cellular Physiology and Biochemistry*, **48**, 16-28. <https://doi.org/10.1159/000491659>
- [11] Li, Y., Wang, Y., Wang, H., Zhang, L., Ding, Y., Chen, S., Yang, Q. and Chen, C. (2017) [Effects of lncRNA RP11-770J1.3 and TMEM25 Expression on Paclitaxel Resistance in Human Breast Cancer Cells]. *Journal of Zhejiang University*, **46**, 364-370.
- [12] Zheng, S., Fu, W., Huang, Q., Zhou, J., Lu, K., Gu, J., Ma, R. and Guo, G. (2023) lncRNA PRKCQ-AS1 Regulates Paclitaxel Resistance in Triple-Negative Breast Cancer Cells Through MiR-361-5p/PIK3C3 Mediated Autophagy. *Clinical and Experimental Pharmacology and Physiology*, **50**, 431-442. <https://doi.org/10.1111/1440-1681.13758>
- [13] Zhang, H., Zhao, B., Wang, X., Zhang, F. and Yu, W. (2019) LINC00511 Knockdown Enhances Paclitaxel Cytotoxicity in Breast Cancer via Regulating MiR-29c/CDK6 Axis. *Life Sciences*, **228**, 135-144. <https://doi.org/10.1016/j.lfs.2019.04.063>
- [14] Zheng, P., Dong, L., Zhang, B., Dai, J., Zhang, Y., Wang, Y. and Qin, S. (2019) Long Noncoding RNA CASC2 Promotes Paclitaxel Resistance in Breast Cancer through Regulation of MiR-18a-5p/CDK19. *Histochemistry and Cell Biology*, **152**, 281-291. <https://doi.org/10.1007/s00418-019-01794-4>
- [15] Liu, C., Jiang, F., Zhang, X. and Xu, X. (2020) Long Non-Coding RNA UCA1 Modulates Paclitaxel Resistance in Breast Cancer via MiR-613/CDK12 Axis. *Cancer Management and Research*, **12**, 2777-2788. <https://doi.org/10.2147/CMAR.S241969>
- [16] Shin, V.Y., Chen, J., Cheuk, I.W., Siu, M.T., Ho, C.W., Wang, X., Jin, H. and Kwong, A. (2019) Long Non-Coding RNA NEAT1 Confers Oncogenic Role in Triple-Negative Breast Cancer through Modulating Chemoresistance and Cancer Stemness. *Cell Death & Disease*, **10**, Article No. 270. <https://doi.org/10.1038/s41419-019-1513-5>
- [17] Gu, M., Zheng, W., Zhang, M., Dong, X., Zhao, Y., Wang, S., Jiang, H. and Zheng, X. (2020) lncRNA

- NONHSAT141924 Promotes Paclitaxel Chemotherapy Resistance through P-CREB/Bcl-2 Apoptosis Signaling Pathway in Breast Cancer. *Journal of Cancer*, **11**, 3645-3654. <https://doi.org/10.7150/jca.39463>
- [18] Si, X., Zang, R., Zhang, E., Liu, Y., Shi, X., Zhang, E., Shao, L., Li, A., Yang, N., Han, X., *et al.* (2016) lncRNA H19 Confers Chemoresistance in ERalpha-Positive Breast Cancer through Epigenetic Silencing of the Pro-Apoptotic Gene BIK. *Oncotarget*, **7**, 81452-81462. <https://doi.org/10.18632/oncotarget.13263>
- [19] Li, P.P., Li, R.G., Huang, Y.Q., Lu, J.P., Zhang, W.J. and Wang, Z.Y. (2021) lncRNA OTUD6B-AS1 Promotes Paclitaxel Resistance in Triple Negative Breast Cancer by Regulation of MiR-26a-5p/MTDH Pathway-Mediated Autophagy and Genomic Instability. *Aging*, **13**, 24171-24191. <https://doi.org/10.18632/aging.203672>
- [20] Zhao, T., Zhang, T., Zhang, Y., Zhou, B. and Lu, X. (2022) Paclitaxel Resistance Modulated by the Interaction between TRPS1 and AF178030.2 in Triple-Negative Breast Cancer. *Evidence-Based Complementary and Alternative Medicine*, **2022**, Article ID: 6019975. <https://doi.org/10.1155/2022/6019975>
- [21] Gligorov, J. and Lotz, J.P. (2004) Preclinical Pharmacology of the Taxanes: Implications of the Differences. *Oncologist*, **9**, 3-8. https://doi.org/10.1634/theoncologist.9-suppl_2-3
- [22] Huang, P., Li, F., Li, L., You, Y., Luo, S., Dong, Z., Gao, Q., Wu, S., Brunner, N. and Stenvang, J. (2018) lncRNA Profile Study Reveals the MRNAs and lncRNAs Associated with Docetaxel Resistance in Breast Cancer Cells. *Scientific Reports*, **8**, Article No. 17970. <https://doi.org/10.1038/s41598-018-36231-4>
- [23] Li, J., Ke, J., Qin, C.L. and Zhu, X. (2022) LINC00680 Modulates Docetaxel Resistance in Breast Cancer via the MiR-320b/CDKL5 Axis. *International Journal of Immunopathology and Pharmacology*, **36**, 1-9. <https://doi.org/10.1177/03946320221105608>
- [24] Li, J., Kang, J., Liu, W., Liu, J., Pan, G., Mao, A., Zhang, Q., Lu, J., Ding, J. and Li, H. (2022) Docetaxel-Resistant Triple-Negative Breast Cancer Cell-Derived Exosomal lncRNA LINC00667 Reduces the Chemosensitivity of Breast Cancer Cells to Docetaxel via Targeting MiR-200b-3p/Bcl-2 Axis. *European Journal of Histochemistry*, **66**, 3592. <https://doi.org/10.4081/ejh.2022.3529>
- [25] Zhang, C., Wang, J., Zhang, J., Qu, H. and Tang, X. (2020) LINC00461 Overexpression Can Induce Docetaxel Resistance in Breast Cancer by Interacting with MiR-411-5p. *OncoTargets and Therapy*, **13**, 5551-5562. <https://doi.org/10.2147/OTT.S247776>
- [26] Ning, X., Zhao, J., He, F., Yuan, Y., Li, B. and Ruan, J. (2021) Long Non-Coding RNA TMPO-AS1 Facilitates Chemoresistance and Invasion in Breast Cancer by Modulating the MiR-1179/TRIM37 Axis. *Oncology Letters*, **22**, Article No. 500. <https://doi.org/10.3892/ol.2021.12761>
- [27] Zhang, Z., Yu, X., Yu, X., Wang, Z., Wu, P. and Huang, J. (2015) Anthracyclines Potentiate Anti-Tumor Immunity: A New Opportunity for Chemoimmunotherapy. *Cancer Letters*, **369**, 331-335. <https://doi.org/10.1016/j.canlet.2015.10.002>
- [28] Minotti, G., Menna, P., Salvatorelli, E., Cairo, G. and Gianni, L. (2004) Anthracyclines: Molecular Advances and Pharmacologic Developments in Antitumor Activity and Cardiotoxicity. *Pharmacological Reviews*, **56**, 185-229. <https://doi.org/10.1124/pr.56.2.6>
- [29] Yao, N., Fu, Y., Chen, L., Liu, Z., He, J., Zhu, Y., *et al.* (2019) Long Non-Coding RNA NONHSAT101069 Promotes Epirubicin Resistance, Migration, and Invasion of Breast Cancer Cells through NONHSAT101069/MiR-129-5p/Twist1 Axis. *Oncogene*, **38**, 7216-7233. <https://doi.org/10.1038/s41388-019-0904-5>
- [30] Gooding, A.J., Zhang, B., Gunawardane, L., Beard, A., Valadkhan, S. and Schiemann, W.P. (2019) The lncRNA BORG Facilitates the Survival and Chemoresistance of Triple-Negative Breast Cancers. *Oncogene*, **38**, 2020-2041. <https://doi.org/10.1038/s41388-018-0586-4>
- [31] Chen, Z., Pan, T., Jiang, D., Jin, L., Geng, Y., Feng, X., *et al.* (2020) The lncRNA-GAS5/MiR-221-3p/DKK2 Axis Modulates ABCB1-Mediated Adriamycin Resistance of Breast Cancer via the Wnt/ β -Catenin Signaling Pathway. *Nucleic Acids*, **19**, 1434-1448. <https://doi.org/10.1016/j.omtn.2020.01.030>
- [32] He, D.X., Zhang, G.Y., Gu, X.T., Mao, A.Q., Lu, C.X., Jin, J., Liu, D.Q. and Ma, X. (2016) Genome-Wide Profiling of Long Non-Coding RNA Expression Patterns in Anthracycline-Resistant Breast Cancer Cells. *International Journal of Oncology*, **49**, 1695-1703. <https://doi.org/10.3892/ijo.2016.3665>
- [33] O'Brien, K.M., Cole, S.R., Tse, C.K., Perou, C.M., Carey, L.A., Foulkes, W.D., Dressler, L.G., Geradts, J. and Millikan, R.C. (2010) Intrinsic Breast Tumor Subtypes, Race, and Long-Term Survival in the Carolina Breast Cancer Study. *Clinical Cancer Research*, **16**, 6100-6110. <https://doi.org/10.1158/1078-0432.CCR-10-1533>
- [34] Adriaens, C., Standaert, L., Barra, J., Latil, M., Verfaillie, A., Kalev, P., Boeckx, B., Wijnhovwn, P.W., Radaelli, E., Vwemi, W., *et al.* (2016) P53 Induces Formation of NEAT1 lncRNA-Containing Paraspeckles That Modulate Replication Stress Response and Chemosensitivity. *Nature Medicine*, **22**, 861-868. <https://doi.org/10.1038/nm.4135>
- [35] Zhang, M., Yang, L., Hou, L. and Tang, X. (2021) lncRNA SNHG1 Promotes Tumor Progression and Cisplatin Resistance through Epigenetically Silencing MiR-381 in Breast Cancer. *Bioengineered*, **12**, 9239-9250.

<https://doi.org/10.1080/21655979.2021.1996305>

- [36] Du, C., Wang, Y., Zhang, Y., Zhang, J., Zhang, L. and Li, J. (2020) lncRNA DLX6-AS1 Contributes to Epithelial-Mesenchymal Transition and Cisplatin Resistance in Triple-Negative Breast Cancer via Modulating Mir-199b-5p/Paxillin Axis. *Cell Transplantation*, **29**, 1-11. <https://doi.org/10.1177/0963689720929983>
- [37] Wu, J., Chen, H., Ye, M., Wang, B., Zhang, Y., Sheng, J., Meng, T. and Chen, H. (2019) Long Noncoding RNA HCP5 Contributes to Cisplatin Resistance in Human Triple-Negative Breast Cancer via Regulation of PTEN Expression. *Biomedicine & Pharmacotherapy*, **115**, Article ID: 108869. <https://doi.org/10.1016/j.biopha.2019.108869>