

MiR-622 Expression and Role in Multiple Tumors

Jason Hopkins¹, Mohammad Ali², and Safar Zadeh²

¹Department of Molecular Genetics, University of Kansas

²Affiliation not available

November 22, 2023

MiR-622 Expression and Role in Multiple Tumors

Jason Hopkins 1* Mohammad Ali Safar Zadeh

1. Department of Molecular Genetics, University of Kansas , Kansas, USA
2. Department of Molecular Genetics, University of Kansas , Kansas, USA

* Corresponding Author: Email: gpvvrfk@telegmail.com

Abstract

Worldwide, cancer causes a lot of suffering and death. Both surgical and nonsurgical methods are used in modern cancer therapy. The most recent development is molecularly targeted treatment. MicroRNAs (miRNAs) are a class of short, non-coding RNAs that may be found in plants and animals and play an important role in cancer and other disorders by modulating a wide range of cellular and organismal functions. It has been revealed that the miRNA miR-622 regulates many pathways that have an impact on illness. Tumors including glioma, as well as those of the liver, colon, and breast, may benefit or suffer from aberrant miR-622 expression. In this article, we outlined the processes and linked molecules of miR-622 and analyzed its expression levels and clinical consequences in different types of cancers.

Keywords: Cancer, microRNAs, mechanisms, and molecules; specifically, miR-622

1. Introduction

Regardless of where one lives or one's economic status, cancer is the top cause of mortality. From 2008 to 2030, the global cancer burden is projected to rise by 100% in low- and middle-income countries [1]. Early identification and treatment are crucial for improved health management and effective cancer screening. For example, mutations in genes in the EGFR signaling pathway may be a negative predictor of anti-EGFR monoclonal antibody therapeutic efficacy in colorectal cancer (CRC) [2]. In addition, the most widely used biomarkers for detecting gastric cancer are carcinoembryonic antigen (CEA) and Glucoprotein antigen 199 (CA19-9). Treatment options for cancer nowadays range from surgery and radiation to hormone and targeted therapies [4]. Breast cancer, leukemia, and colorectal cancer have all been successfully treated using molecular targeted treatment. Many additional cancers, such as lung cancer and ovarian cancer, have shown promising clinical results [5]. In order to effectively diagnose and treat cancer, research into molecular markers and molecularly targeted therapies is crucial.

MicroRNAs (miRNAs) are a kind of tiny noncoding RNA found in the genomes of almost all eukaryotic organisms [6]. MicroRNAs (miRNAs) control how much a gene is expressed by interfering with transcription, translation, or epigenetic processes based on the recognition of homologous sequences [7]. Inhibiting transcription by complementary base pairing with target mRNA, miRNAs regulate the expression of several downstream target genes [8, 9]. Disease progression is affected by miRNAs in several ways [10], [11], including cell proliferation, cell death, the immunological response, and the manufacture of neurotransmitters. In addition, new research investigating miRNAs' roles in malignancies have shown that aberrant miRNA expression is a common feature of the disease. For example, miR-106b-5p increases breast cancer lung metastasis via modulating the Rho/ROCK1 pathway [12]. Several types of cancer have miR-146a-5p as a potential noninvasive biomarker and therapeutic target [13]. More research is needed to completely elucidate the roles of miRNAs in the development of various malignancies. There is mounting evidence that the

microRNA miR-622 plays a role in cancer progression or suppression in a wide variety of malignancies, including breast, glioma, CRC, HCC, lung, gastric, melanoma, ovarian, prostatic, and pancreatic cancers [14, 15], [16], [17], [18], [19], [20], [21], [22], [23]. MiR-622 regulates molecular pathways such as EGF/ERK signaling and K-Ras signaling, and its expression is linked to the clinical characteristics of these cancers [17], [18], [19], [24], [25]. miR-622 is a possible target for the treatment of cancer and is linked to medication resistance [26]. In addition, miR-622 may affect other disorders by, for instance, binding to circ_ANRIL in cerebral ischemia-reperfusion to regulate the NF-kappaB pathway and reducing vascular endothelial damage due to oxygen-glucose deprivation and reoxygenation [27]. In this review, we compile information on miR-622's expression in malignancies and its effect on tumor characteristics, oncogenes, and anti-oncogenes. The potential of miR-622 as a biomarker in a number of tumors is discussed, along with its biological activities, target genes, and interacting molecules.

2. Methods for a Search

To do this, we queried PubMed for papers published as recently as April 2011. MicroRNA-622, miR-622, and cancer are some related terms. Titles and abstracts were used to identify articles that were relevant to this review's subject. Literature, case reports, meeting minutes, correspondence, publications whose entire text is unavailable, retractions, and revisions that are not related to the topic at hand should be disregarded. Finally, the two writers conduct their own, separate analyses of the complete texts of the chosen scholarly works.

4.1. HCC

Hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC) are the two most common histological subtypes of primary liver cancer, both of which are etiologically and physiologically diverse [29, 30]. It has been observed that miR-622 expression is dramatically downregulated in HCC tissues and cells. MiR-622 has been shown to induce cell apoptosis [17] and suppress cell growth and invasion. The proliferation and migratory abilities of HCC cells are greatly aided by miR-622 inhibition [31]. Serum HBsAg positivity, cirrhosis, tumor stage, vascular invasion, and intrahepatic metastases were all linked with low miR-622 expression [24]. According to Kaplan-Meier analysis, patients whose miR-622 levels were low had a lower median overall survival time compared to those whose miR-622 levels were high. MiR-622 expression was shown to be an independent survival predictor for patients with HCC in a multivariate survival study [24]. Furthermore, as shown by Dietrich [25] and Gaza [32], miR-622 is linked to sorafenib resistance.

4.2. Glioma

Most malignant tumors found within the skull are gliomas [33]. Half of all gliomas are glioblastoma, a highly invasive kind [34]. MiR-622 is known to be severely downregulated in glioma tissues and cell lines, according to a plethora of research. Increased expression of miR-622 inhibits glioma cell invasion and migration, according to functional studies [35]. Furthermore, miR-622 promotes cell cycle arrest in the G0/G1 phase in glioma cells and suppresses cell growth [15]. Downregulation of miR-622 was substantially connected with advanced pathological grades and poor Karnofsky scores in a study examining the association between miR-622 and the clinical characteristics of glioma. Kaplan-Meier analysis demonstrated that decreased miR-622 expression is strongly linked to poor overall survival. Downregulation of miR-622 was shown to be an independent indication of poor prognosis in glioma patients using Cox regression analysis [36]. Overexpression of miR-622 suppresses tumor cell proliferation, migration, and invasion in glioblastoma [37]. miR-622 expression is low in glioblastoma tumor tissues and cells.

4.3. CRC

CRC is a contemporary illness that kills around 700,000 people a year [38]. MiR-622 levels in CRC are often found to be much lower than those in normal tissues or cell lines. The miR-622 level was observed to be decreased in metastatic

CRC tissues compared to nonmetastatic CRC tissues. Furthermore, miR-622 was shown to influence tumor growth and migration in a functional study [39]. Experiments in both vitro and in vivo have shown that miR-622 may act as an angiogenesis inhibitor by reducing cell proliferation, migration, and tumor development [16]. In contrast, another study reported that miR-622 expression was elevated in CRC tissues and cell lines, and that downregulating miR-622 expression reduced cell motility and invasion [40].

Surgery, in conjunction with adjuvant chemotherapy, radiation, and immunotherapy, is the gold standard for treating CRC [41]. Increased success in developing tailored drugs may potentially help CRC patients live longer [42]. Recent studies have shown that miR-622 is upregulated in CRC cells exposed to ionizing radiation, leading to radioresistance [43]. There has also been research into the mechanisms of miR-622 in relation to sevoflurane medication [44].

4.4. GC

Gastric cancer is the fifth most prevalent form of the illness overall [45], although it is also one of the most diverse. In GC cells and tissues, miR-622 expression was shown to be rather low. Regulation of invasion, migration, tumorigenesis, and metastasis by miR-622 is linked to cell differentiation and lymphatic metastasis [19]. Another study confirmed that miR-622 inhibited cell invasion by lowering levels of Laminin gamma-2 subunit (LAMC2) [46]. Thus, miR-622 acts as a tumor suppressor in GC and may be a therapeutic target for GC that has spread.

4.5. Carcinoma of the Breast

In addition to being the largest cause of cancer-related mortality among women, breast cancer is the most common malignancy globally. Individuals in industrialized nations account for half of all breast cancer cases [47]. Patients with breast cancer had lower levels of miR-622 in their plasma and tissues [14]. The ability of breast cancer cells to migrate and invade, as well as higher grades, are all linked to low miR-622 expression [14]. Overexpression of miR-622 is linked to poor prognosis, tumor mesenchymal transition, cell viability, and invasion, according to a database bioinformatics analysis and in vitro experiment-based research [48]. More research is needed on miR-622's expression and roles.

In Mojdeh Mahmoudian and colleagues' study, it was discovered that certain microRNAs showed increased expression in BC tumor compared to the adjacent tissues. Specifically, hsa-miR-25-3p, -29a-5p, -105-3p, and -181b1-5p were upregulated, while hsa-miR-335-5p and -339-5p were downregulated. The upregulation or downregulation of these candidate microRNAs was found to be associated with TNM stages, except for hsa-miR-339-5p. Additionally, with the exception of hsa-miR-105-3p, each candidate microRNA correlated with HER-2 status. Furthermore, the analysis of ROC curves revealed that the combination of these six microRNAs could potentially serve as a biomarker to differentiate between tumor and non-tumor breast tissue samples.

4.6. Melanoma

Melanoma is a primary cause of cancer-related mortality and has the potential to spread [49]. For this reason, precise melanoma staging is essential. When comparing primary and metastatic tumors, miR-622 expression was shown to be considerably downregulated in melanoma tissues and cells. miR-622 is related with disease-specific survival outcomes, according to a study of The Cancer Genome Atlas (TCGA) database [50]. MiR-622 has been linked to both cell proliferation and angiogenesis [20], according to another research.

4.7. Variant cancers

Cholangiocarcinoma (CCA) tissues and cell lines have been discovered to have reduced levels of the microRNA miR-622. miR-622 expression may influence cell proliferation, migration, and invasion and is related with T stage and lymph node metastases [18], [51]. The expression of miR-622 is downregulated in lung cancer [52], and it regulates cell migration and invasion, epithelial-mesenchymal transition, and tumor metastasis. Concerning therapy, miR-622 has

been shown to be an independent predictive biomarker for the response of patients with high-grade serous ovarian cancer (HGSOC) to platinum-based chemotherapy [21]. In addition, miR-622 overexpression is related with lower patient survival outcomes following platinum treatment in BRCA1-mutant ovarian cancer [53]. In esophageal squamous cell carcinoma (ESCC), miR-622 also has a tumor-suppressive function. miR-622 is correlated with tumor subtype, tumor size, invasion depth, TNM stage, and lymph node metastasis, making it an independent risk factor for ESCC prognosis. Also, miR-622's function is linked to cell division, cell death, metastasis, and invasion [54]. Similar miR-622 functions and an association with RCC metastasis [55] have been identified in renal cell carcinoma (RCC). Both prostate [22] and pancreatic [23] cancers have been linked to reduced miR-622 expression.

5. MiR-622's role and associated mechanism in tumorigenesis.

It is widely known that miRNAs detect target mRNAs via complementary base pairing to limit protein production [56], [57]. We described the role of miR-622 in tumor regulation and the associated signaling pathways to better comprehend its impact on malignancies. In addition, Fig. displays the functions of miR-622 in HCC and the ways by which it does so. 2.

5.1. Cell division and cell death

The continual expansion and evasion of cell death characteristic of tumors necessitates a cascade of abnormalities [58]. Reduced miR-622 expression in CCA cells increases cell proliferation by modulating c-Myc expression directly [51]. To increase MAPK1 mRNA expression, stimulate proliferation, and suppress apoptosis in HCC, hsa_circ_0101432 can target miR-622 [17]. Researchers have shown that miR-622 has anticancer effects via reducing phosphorylation of JNK and NF-B [24], which in turn inhibits JNK and NF-B signaling. Targeting K-Ras [50] or interacting with circ_0119872 to control the target gene G3BP1 and downstream Wnt/-catenin and mTOR signaling pathways [20] are two methods in which miR-622 suppresses clonogenicity and proliferation in melanoma. In a similar vein, miR-622 may restrain the growth of CRC cells by lowering their expression of K-Ras [39]. Intriguingly, Sev administration controls hsa_circ_0000231 expression while simultaneously reducing miR-622 expression, resulting in a decrease in cell proliferation and an increase in apoptosis induction [44]. Targeting E2F1 and controlling cell proliferation and apoptosis [54] are two ways in which miR-622 functions as a tumor suppressor in ESCC.

DNA methylation is an important mechanism for controlling chromatin structure and gene expression [58, 59], and alterations in DNA methylation status may serve as diagnostic biomarkers for cancer. Methylation of the miR-622 promoter and EZH2-dependent H3K27 trimethylation govern miR-622 downregulation in liver cancer cells. When miR-622 expression is downregulated, CXCR4 is activated, which promotes tumor growth [31]. DNA methylation has also been shown to repress miR-622 expression in HCC [55], which inhibits cell proliferation via the CCL18/MAPK signaling pathway. Both apoptosis and proliferation rely on properly functioning cell cycle control [60]. MiR-622 targets K-Ras, and studies have shown that increasing miR-622 expression in HCC improves the G1/G0 cell cycle ratio and reduces the G2 cell cycle percentage [25]. Furthermore, miR-622 targets YAP1 in glioma cells to suppress cell growth and cause G0/G1 cell cycle arrest [15]. In conclusion, miR-622 controls cell growth and death via many signaling mechanisms.

5.2. Metastasis

To a lesser extent, miR-622 can control cell invasion and migration. miR-622 suppresses migration and invasion via the hsa_circ_0000211/miR-622/HIF1- α axis in lung adenocarcinoma [18], whereas in HCC, miR-622 restricts invasion ability via the hsa_circ_0101432/miR-622/MAPK1 axis [17]. In gliomas, miR-622 has been found to target ATF2 [35], ZEB2 [36], and K-Ras [37], therefore inhibiting cell migration and invasion. Targeting genes involved in metastasis [22] is one way in which miR-622 influences prostate cancer. The metastasis of tumors caused by HCC [31], CCA [51], and glioblastoma [37] have all been shown to be influenced by the first three genes listed. Furthermore, miR-622 may restrict GC cell

invasion by focusing on ING1 [19]. Droscha reduces production of miR-622, which in turn upregulates LAMC2 expression, activates EGFR-ERK1/2 signaling, and promotes GC cell invasion [46].

A biological process known as epithelial-mesenchymal transition (EMT) occurs when quiescent epithelial cells acquire an invasive mesenchymal phenotype [61]. Inhibiting Snail, -catenin, and vimentin and lowering HIF-1 levels increases E-cadherin and impedes the EMT axis, preventing lung cancer cells from metastasizing [52]. Overexpression of miR-622 may be facilitated by ERK activation, which in turn suppresses FOXO3a [52]. miR-622 aims for HULC in pancreatic cancer. By downregulating miR-622, TGF- facilitates EMT signaling via EVs by decreasing E-cadherin expression and raising levels of Snail, N-cadherin, and Vimentin [23]. In breast cancer, miR-622 suppresses EMT and cell migration by directly regulating RNF8 [48]. Furthermore, the miR-622/NUAK1 axis has been identified to influence the motility characteristic of breast cancer cells [14].

Important to the metastatic route is angiogenesis, which is how tumor cells get into the bloodstream after escaping the initial location [62]. MiR-622 can suppress angiogenesis in CRC by targeting the CXCR4-VEGFA axis [16]. In addition to being controlled by circ_GLG1 [63], miR-622 works directly on K-Ras to reduce tumor invasion and migration [39], [63]. The opposite is true for miR-622, which targets DYRK2 and has been shown to encourage migration and invasion [40]. Tumor metastasis prevention has been shown to reduce cancer-related mortality [64]. As a result, miR-622 shows promise as a tumor biomarker for early detection and intervention, ultimately leading to better outcomes for cancer patients.

5.3. Resistance

Drug resistance is a major obstacle in the treatment of malignancies [65]. Targeting the Ku complex and rescuing homologous recombination (HR)-mediated double-strand break (DSB) repair [21], miR-622 develops drug resistance to Poly ADP-ribose polymerase inhibitors (PARPis) and platinum-based therapies in HGSOEs. Tumor resistance to sorafenib has been linked to the RAS-RAF-ERK axis [66], and a recently discovered mechanism involves the RAS pathway axis MAPK14-ATF2. Reduced expression of miR-622 mediates disinhibition of the MAPK14-ATF2 axis, which controls chemical resistance of HCC cells to sorafenib [25], and results in a lack of control of the RAS-RAF-ERK and PI3K/AKT signaling pathways. Overexpression of LIN28A, which promotes chemotherapy resistance in HCC, has been linked to loss of miR-622 [26] (Table 1), as has the targeting of LIN28A and its collaborator, ZCCHC11.

Adjuvant radioimmunotherapy for colorectal cancer shows promise [67]. Overexpression of miR-622 might enhance radiation resistance by suppressing RB expression, while miR-622 expression is dramatically upregulated in CRC cells exposed to ionizing radiation. High levels of miR-622 expression have been seen in individuals whose tumors do not regress with chemotherapy [43], suggesting that this biomarker may be used to predict the response of patients with rectal cancer to radiation. More research is needed to determine how well miR-622 expression can predict radiation resistance.

6. Conclusion

Based on our analysis, we know that miR-622 is overexpressed in many different types of cancer, and that it generally functions as a tumor suppressor by preventing the initiation and progression of malignancies. On the other hand, miR-622 has been shown to promote carcinogenesis in HGSOEs, whereas contradictory results have been reported in breast and CRC. This discrepancy calls for more research into the molecular processes of miR-622, since it reveals the importance of cell type and environment. Tumor proliferation, apoptosis, migration, invasion, and resistance are all influenced by miR-622 via distinct molecular pathways. To affect gene expression, miR-622 may either directly target mRNAs or regulate signaling pathway axis. Here, we addressed how miR-622 is tightly linked to JNK and NF- κ B signaling, ERK signaling, and the K-Ras pathway, all of which indicate that it is a promising target for tumor prevention. In conclusion, miR-622 has been the subject of substantial research into its clinical features and molecular

processes in relation to malignancies. The results highlight the importance of miR-622 as a potential biomarker for different cancers. The relevance of miR-622 in clinical treatment, notably radiation, is of increased significance because of its involvement in cell function, metastasis, and resistance.

Funding: N/A

Conflicts of Interest: The authors declare that they have no competing interests

References

- 1) Mahmoudian M, Razmara E, Mahmud Hussien B, Simiyari M, Lotfizadeh N, Motaghd H, Khazraei Monfared A, Montazeri M, Babashah S. Identification of a six-microRNA signature as a potential diagnostic biomarker in breast cancer tissues. *J Clin Lab Anal.* 2021 Nov;35(11):e24010. <https://doi.org/10.1002/jcla.24010> PMID: 34528314; PMCID: PMC8605139.
- 2) Adams BD, Wali VB, Cheng CJ, et al., 2016. miR-34a silences c-SRC to attenuate tumor growth in triple-negative breast cancer. *Cancer Res*, 76(4):927-939. <https://doi.org/10.1158/0008-5472.CAN-15-2321>
- 3) Amorim M, Salta S, Henrique R, et al., 2016. Decoding the usefulness of non-coding RNAs as breast cancer markers. *J Transl Med*, 14:265. <https://doi.org/10.1186/s12967-016-1025-3>
- 4) Anfossi S, Fu X, Nagvekar R, et al., 2018. MicroRNAs, regulatory messengers inside and outside cancer cells. In: Mettinger KL, Rameshwar P, Kumar V (Eds.), *Exosomes, Stem Cells and MicroRNA*. Springer, Cham, p.87-108. https://doi.org/10.1007/978-3-319-74470-4_6
- 5) Atkinson SR, Marguerat S, Bähler J, 2012. Exploring long non-coding RNAs through sequencing. *Semin Cell Dev Biol*, 23(2):200-205. <https://doi.org/10.1016/j.semcdb.2011.12.003>
- 6) Bai XD, Han GH, Liu Y, et al., 2018. MiRNA-20a-5p promotes the growth of triple-negative breast cancer cells through targeting RUNX3. *Biomed Pharmacother*, 103: 1482-1489. <https://doi.org/10.1016/j.biopha.2018.04.165>
- 7) Bayraktar R, Pichler M, Kanlikilicer P, et al., 2017. MicroRNA 603 acts as a tumor suppressor and inhibits triple-negative breast cancer tumorigenesis by targeting elongation factor 2 kinase. *Oncotarget*, 8(7):11641-11658. <https://doi.org/10.18632/oncotarget.14264>
- 8) Bhardwaj A, Singh H, Rajapakshe K, et al., 2017. Regulation of miRNA-29c and its downstream pathways in preneoplastic progression of triple-negative breast cancer. *Oncotarget*, 8(12):19645-19660. <https://doi.org/10.18632/oncotarget.14902>
- 9) Biswas T, Efird JT, Prasad S, et al., 2017. The survival benefit of neoadjuvant chemotherapy and PCR among patients with advanced stage triple negative breast cancer. *Oncotarget*, 8(68):112712-112719. <https://doi.org/10.18632/oncotarget.22521>
- 10) Boon RA, Jaé N, Holdt L, et al., 2016. Long noncoding RNAs: from clinical genetics to therapeutic targets? *J Am Coll Cardiol*, 67(10):1214-1226. <https://doi.org/10.1016/j.jacc.2015.12.051>
- 11) Browne G, Dragon JA, Hong DL, et al., 2016. MicroRNA- 378-mediated suppression of Runx1 alleviates the aggressive phenotype of triple-negative MDA-MB-231 human breast cancer cells. *Tumour Biol*, 37(7):8825-8839. <https://doi.org/10.1007/s13277-015-4710-6>
- 12) Catalanotto C, Cogoni C, Zardo G, 2016. MicroRNA in control of gene expression: an overview of nuclear functions. *Int J Mol Sci*, 17(10):1712. <https://doi.org/10.3390/ijms17101712>

- 13) Chadwick BP, Scott KC, 2013. Molecular versatility: the many faces and functions of noncoding RNA. *Chromosome Res*, 21(6-7):555-559. <https://doi.org/10.1007/s10577-013-9397-1>
- 14) Chen H, Pan H, Qian Y, et al., 2018. MiR-25-3p promotes the proliferation of triple negative breast cancer by targeting BTG2. *Mol Cancer*, 17:4. <https://doi.org/10.1186/s12943-017-0754-0>
- 15) Chen J, Wang BC, Tang JH, 2012. Clinical significance of microRNA-155 expression in human breast cancer. *J Surg Oncol*, 106(3):260-266. <https://doi.org/10.1002/jso.22153>
- 16) Chen JW, Shin VY, Siu MT, et al., 2016. miR-199a-5p confers tumor-suppressive role in triple-negative breast cancer. *BMC Cancer*, 16:887. <https://doi.org/10.1186/s12885-016-2916-7>
- 17) Chen QN, Wei CC, Wang ZX, et al., 2017. Long non-coding RNAs in anti-cancer drug resistance. *Oncotarget*, 8(1): 1925-1936. <https://doi.org/10.18632/oncotarget.12461>
- 18) Chen XW, Zhao M, Huang J, et al., 2018. microRNA-130a suppresses breast cancer cell migration and invasion by targeting FOSL1 and upregulating ZO-1. *J Cell Biochem*, 119(6):4945-4956. <https://doi.org/10.1002/jcb.26739>
- 19) Collignon J, Lousberg L, Schroeder H, et al., 2016. Triple- negative breast cancer: treatment challenges and solutions. *Breast Cancer* (Dove Med Press), 8:93-107. <https://doi.org/10.2147/BCTT.S69488>
- 20) Costa FF, 2005. Non-coding RNAs: new players in eukaryotic biology. *Gene*, 357(2):83-94. <https://doi.org/10.1016/j.gene.2005.06.019>
- 21) De S, Das S, Mukherjee S, et al., 2017. Establishment of twist-1 and TGFBR2 as direct targets of microRNA-20a in mesenchymal to epithelial transition of breast cancer cell-line MDA-MB-231. *Exp Cell Res*, 361(1):85-92. <https://doi.org/10.1016/j.yexcr.2017.10.005>
- 22) Delás MJ, Hannon GJ, 2017. lncRNAs in development and disease: from functions to mechanisms. *Open Biol*, 7(7): 170121. <https://doi.org/10.1098/rsob.170121>
- 23) Deng H, Zhang J, Shi JJ, et al., 2016. Role of long non-coding RNA in tumor drug resistance. *Tumor Biol*, 37(9):11623- 11631. <https://doi.org/10.1007/s13277-016-5125-8>
- 24) Eades G, Wolfson B, Zhang YS, et al., 2015. lincRNA-RoR and miR-145 regulate invasion in triple-negative breast cancer via targeting ARF6. *Mol Cancer Res*, 13(2):330- 338. <https://doi.org/10.1158/1541-7786.MCR-14-0251>
- 25) Eades GL, Zhou Q, 2014. Abstract 1463: long non-coding RNA RoR and microRNA-145 regulate tumor cell invasion in triple-negative breast cancer via targeting of ADP- ribosylation factor 6. *Cancer Res*, 74(S19):1463. <https://doi.org/10.1158/1538-7445.AM2014-1463>
- 26) Evans JR, Feng FY, Chinnaiyan AM, 2016. The bright side of dark matter: lncRNAs in cancer. *J Clin Invest*, 126(8): 2775-2782. <https://doi.org/10.1172/JCI84421>
- 27) Fang H, Xie JP, Zhang M, et al., 2017. miRNA-21 promotes proliferation and invasion of triple-negative breast cancer cells through targeting PTEN. *Am J Transl Res*, 9(3): 953-961.
- 28) Ferlay J, Héry C, Autier P, et al., 2010. Global burden of breast cancer. In: Li C (Ed.), *Breast Cancer Epidemiology*. Springer, New York, p.1-19. https://doi.org/10.1007/978-1-4419-0685-4_1
- 29) Fu PF, Zheng X, Fan X, et al., 2019. Role of cytoplasmic lncRNAs in regulating cancer signaling pathways. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 20(1):1-8. <https://doi.org/10.1631/jzus.B1800254>
- 30) Gebert LFR, MacRae IJ, 2019. Regulation of microRNA function in animals. *Nat Rev Mol Cell Biol*, 20(1):21-37. <https://doi.org/10.1038/s41580-018-0045-7>
- 31) Gilam A, Conde J, Weissglas-Volkov D, et al., 2016. Local microRNA delivery targets Palladin and prevents metastatic breast cancer. *Nat Commun*, 7:12868. <https://doi.org/10.1038/ncomms12868>
- 32) Gu J, Wang YP, Wang XD, et al., 2018. Downregulation of lncRNA GAS5 confers tamoxifen resistance by activating miR-222 in breast cancer. *Cancer Lett*, 434:1-10. <https://doi.org/10.1016/j.canlet.2018.06.039>
- 33) Gülsen K, Berberoglu U, Kinaş V, et al., 2014. Breast cancer subtypes can be a predictor of pathologic complete response and survival in the neoadjuvant setting for T4 noninflammatory breast cancer. *Acta Chir Belg*, 114(3): 153-159. <https://doi.org/10.1080/00015458.2014.11681001>
- 34) Gupta RA, Shah N, Wang KC, et al., 2010. Long non-coding RNA HOTAIR reprograms chromatin state to promote cancer metastasis. *Nature*, 464(7291):1071-1076. <https://doi.org/10.1038/nature08975>

- 35) Han JG, Han BJ, Wu XY, et al., 2018. Knockdown of lncRNA H19 restores chemo-sensitivity in paclitaxel-resistant triple-negative breast cancer through triggering apoptosis and regulating Akt signaling pathway. *Toxicol Appl Pharmacol*, 359:55-61. <https://doi.org/10.1016/j.taap.2018.09.018>
- 36) Han JJ, Yu JJ, Dai YN, et al., 2018. Overexpression of miR- 361-5p in triple-negative breast cancer (TNBC) inhibits migration and invasion by targeting RQCD1 and inhibiting the EGFR/PI3K/Akt pathway. *Bosn J Basic Med Sci*, 19(1):52-59. <https://doi.org/10.17305/bjbms.2018.3399>
- 37) Harrow J, Frankish A, Gonzalez JM, et al., 2012. GENCODE: the reference human genome annotation for the encode project. *Genome Res*, 22(9):1760-1774. <https://doi.org/10.1101/gr.135350.111>
- 38) Hata A, Kashima R, 2016. Dysregulation of microRNA biogenesis machinery in cancer. *Crit Rev Biochem Mol Biol*, 51(3):121-134. <https://doi.org/10.3109/10409238.2015.1117054>
- 39) Hiatt RA, Brody JG, 2018. Environmental determinants of breast cancer. *Annu Rev Public Health*, 39:113-133. <https://doi.org/10.1146/annurev-publhealth-040617-014101>
- 40) Hong LQ, Pan F, Jiang HF, et al., 2016. MiR-125b inhibited epithelial-mesenchymal transition of triple-negative breast cancer by targeting MAP2K7. *Onco Targets Ther*, 9: 2639-2648. <https://doi.org/10.2147/OTT.S102713>
- 41) Hu JH, Xu J, Wu YQ, et al., 2015. Identification of microRNA- 93 as a functional dysregulated miRNA in triple-negative breast cancer. *Tumour Biol*, 36(1):251-258. <https://doi.org/10.1007/s13277-014-2611-8>
- 42) Huang J, Zhou N, Watabe K, et al., 2014. Long non-coding RNA UCA1 promotes breast tumor growth by suppression of p27 (Kip1). *Cell Death Dis*, 5:e1008. <https://doi.org/10.1038/cddis.2013.541>
- 43) Huarte M, 2015. The emerging role of lncRNAs in cancer. *Nat Med*, 21(11):1253-1261. <https://doi.org/10.1038/nm.3981>
- 44) Jia ZM, Liu Y, Gao Q, et al., 2016. miR-490-3p inhibits the growth and invasiveness in triple-negative breast cancer by repressing the expression of TNKS2. *Gene*, 593(1):41-47. <https://doi.org/10.1016/j.gene.2016.08.014>
- 45) Karagoz K, Sinha R, Arga KY, 2015. Triple negative breast cancer: a multi-omics network discovery strategy for candidate targets and driving pathways. *OMICS*, 19(2):115- 130. <https://doi.org/10.1089/omi.2014.0135>
- 46) Khaled N, Bidet Y, 2019. New insights into the implication of epigenetic alterations in the EMT of triple negative breast cancer. *Cancers (Basel)*, 11(4):559. <https://doi.org/10.3390/cancers11040559>
- 47) Kim SY, Kawaguchi T, Yan L, et al., 2017. Clinical relevance of microRNA expressions in breast cancer validated using The Cancer Genome Atlas (TCGA). *Ann Surg Oncol*, 24(10):2943-2949. <https://doi.org/10.1245/s10434-017-5984-2>
- 48) Kolesnikov NN, Vetyaskina YA, Titov SE, et al., 2019. Expression of microRNAs in molecular genetic breast cancer subtypes. *Cancer Treat Res Commun*, 20:100026. <https://doi.org/10.1016/j.ctarc.2016.08.006>
- 49) Kunej T, Obsteter J, Pogacar Z, et al., 2014. The decalog of long non-coding RNA involvement in cancer diagnosis and monitoring. *Crit Rev Clin Lab Sci*, 51(6):344-357. <https://doi.org/10.3109/10408363.2014.944299>
- 50) Lee J, Jung JH, Chae YS, et al., 2016. Long noncoding RNA snaR regulates proliferation, migration and invasion of triple-negative breast cancer cells. *Anticancer Res*, 36(12): 6289-6295. <https://doi.org/10.21873/anticancer.11224>
- 51) Lehmann BD, Bauer JA, Chen X, et al., 2011. Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. *J Clin Invest*, 121(7):2750-2767. <https://doi.org/10.1172/JCI45014>
- 52) Li HY, Liang JL, Kuo YL, et al., 2017. miR-105/93-3p promotes chemoresistance and circulating miR-105/93-3p acts as a diagnostic biomarker for triple negative breast cancer. *Breast Cancer Res*, 19:133. <https://doi.org/10.1186/s13058-017-0918-2>
- 53) Li J, Chen CC, Ma XC, et al., 2016. Long noncoding RNA NRON contributes to HIV-1 latency by specifically inducing TAT protein degradation. *Nat Commun*, 7:11730. <https://doi.org/10.1038/ncomms11730>
- 54) Li J, Cui ZG, Li H, et al., 2018. Clinicopathological and prognostic significance of long noncoding RNA MALAT1 in human cancers: a review and meta-analysis. *Cancer Cell Int*, 18:109. <https://doi.org/10.1186/s12935-018-0606-z>

- 55) Li N, Deng YJ, Zhou LH, et al., 2019. Global burden of breast cancer and attributable risk factors in 195 countries and territories, from 1990 to 2017: results from the global burden of disease study 2017. *J Hematol Oncol*, 12:140. <https://doi.org/10.1186/s13045-019-0828-0>
- 56) Li SQ, Zhou J, Wang ZX, et al., 2018. Long noncoding RNA GAS5 suppresses triple negative breast cancer progression through inhibition of proliferation and invasion by competitively binding miR-196a-5p. *Biomed Pharmacother*, 104:451-457. <https://doi.org/10.1016/j.biopha.2018.05.056>
- 57) Li WT, Liu CL, Zhao CL, et al., 2016. Downregulation of $\beta 3$ integrin by miR-30a-5p modulates cell adhesion and invasion by interrupting Erk/Ets-1 network in triple- negative breast cancer. *Int J Mol Sci*, 48(3):1155-1164. <https://doi.org/10.3892/ijo.2016.3319>
- 58) Li XH, Hou LL, Yin L, et al., 2020. LncRNA XIST interacts with miR-454 to inhibit cells proliferation, epithelial mesenchymal transition and induces apoptosis in triple- negative breast cancer. *J Biosci*, 45:45. <https://doi.org/10.1007/s12038-020-9999-7>
- 59) Li XN, Wu YM, Liu AH, et al., 2016. Long non-coding RNA UCA1 enhances tamoxifen resistance in breast cancer cells through a miR-18a-HIF1 α feedback regulatory loop. *Tumor Biol*, 37(11):14733-14743. <https://doi.org/10.1007/s13277-016-5348-8>
- 60) Li Z, Li Y, Li Y, et al., 2017. Long non-coding RNA H19 promotes the proliferation and invasion of breast cancer through upregulating DNMT1 expression by sponging miR-152. *J Biochem Mol Toxicol*, 31(9):e21933. <https://doi.org/10.1002/jbt.21933>
- 61) Li ZS, Meng QY, Pan AF, et al., 2017. MicroRNA-455-3p promotes invasion and migration in triple negative breast cancer by targeting tumor suppressor EI24. *Oncotarget*, 8(12):19455-19466. <https://doi.org/10.18632/oncotarget.14307>
- 62) Li ZX, Qian J, Li J, et al., 2019. Knockdown of lncRNA- HOTAIR downregulates the drug-resistance of breast cancer cells to doxorubicin via the PI3K/AKT/mTOR signaling pathway. *Exp Ther Med*, 18(1):435-442. <https://doi.org/10.3892/etm.2019.7629>
- 63) Liang YJ, Hu J, Li JT, et al., 2015. Epigenetic activation of TWIST1 by MTDH promotes cancer stem-like cell traits in breast cancer. *Cancer Res*, 75(17):3672-3680. <https://doi.org/10.1158/0008-5472.CAN-15-0930>
- 64) Liedtke C, Mazouni C, Hess K, et al., 2008. Response to neoadjuvant therapy and long-term survival in patients with triple-negative breast cancer. *J Clin Oncol*, 26(8):1275- 1281. <https://doi.org/10.1200/JCO.2007.14.4147>
- 65) Lin AF, Li CL, Xing Z, et al., 2016. The LINK-A lncRNA activates normoxic HIF1 α signalling in triple-negative breast cancer. *Nat Cell Biol*, 18(2):213-224. <https://doi.org/10.1038/ncb3295>
- 66) Liu AN, Qu HJ, Gong WJ, et al., 2019. LncRNA AWPPH and miRNA-21 regulates cancer cell proliferation and chemosensitivity in triple-negative breast cancer by interacting with each other. *J Cell Biochem*, 120(9):14860-14866. <https://doi.org/10.1002/jcb.28747>
- 67) Liu HY, Wang G, Yang LL, et al., 2016. Knockdown of long non-coding RNA UCA1 increases the tamoxifen sensitivity of breast cancer cells through inhibition of Wnt/ β -catenin pathway. *PLoS ONE*, 11(12):e0168406. <https://doi.org/10.1371/journal.pone.0168406>
- 68) Liu L, He J, Wei X, et al., 2017a. MicroRNA-20a-mediated loss of autophagy contributes to breast tumorigenesis by promoting genomic damage and instability. *Oncogene*, 36(42):5874-5884. <https://doi.org/10.1038/onc.2017.193>
- 69) Liu L, Yu DH, Shi H, et al., 2017b. Reduced lncRNA Aim enhances the malignant invasion of triple-negative breast cancer cells mainly by activating Wnt/ β -catenin/mTOR/ PI3K signaling. *Pharmazie*, 72(10):599-603. <https://doi.org/10.1691/ph.2017.7547>
- 70) Liu M, Xing LQ, Liu YJ, 2017. A three-long noncoding RNA signature as a diagnostic biomarker for differentiating between triple-negative and non-triple-negative breast cancers. *Medicine (Baltimore)*, 96(9):e6222. <https://doi.org/10.1097/MD.00000000000006222>
- 71) Liu XP, Tang HL, Chen JP, et al., 2015. MicroRNA-101 inhibits cell progression and increases paclitaxel sensitivity by suppressing MCL-1 expression in human triple- negative breast cancer. *Oncotarget*, 6(24):20070-20083. <https://doi.org/10.18632/oncotarget.4039>

- 72) Luan T, Zhang XM, Wang SY, et al., 2017. Long non-coding RNA MIAT promotes breast cancer progression and functions as ceRNA to regulate DUSP7 expression by sponging miR-155-5p. *Oncotarget*, 8(44):76153-76164. <https://doi.org/10.18632/oncotarget.19190>
- 73) Luo LY, Tang HL, Ling L, et al., 2018. LINC01638 lncRNA activates MTDH-Twist1 signaling by preventing SPOP-mediated c-Myc degradation in triple-negative breast cancer. *Oncogene*, 37(47):6166-6179. <https://doi.org/10.1038/s41388-018-0396-8>
- 74) Luo N, Zhang KJ, Li X, et al., 2020. ZEB1 induced-upregulation of long noncoding RNA ZEB1-AS1 facilitates the progression of triple negative breast cancer by binding with ELAVL1 to maintain the stability of ZEB1 mRNA. *J Cell Biochem*, online. <https://doi.org/10.1002/jcb.29572>
- 75) Lv ZD, Kong B, Liu XP, et al., 2016. miR-655 suppresses epithelial-to-mesenchymal transition by targeting Prrx1 in triple-negative breast cancer. *J Cell Mol Med*, 20(5): 864-873. <https://doi.org/10.1111/jcmm.12770>
- 76) Ma DC, Chen C, Wu J, et al., 2019. Up-regulated lncRNA AFAP1-AS1 indicates a poor prognosis and promotes carcinogenesis of breast cancer. *Breast Cancer*, 26(1):74-83. <https://doi.org/10.1007/s12282-018-0891-3>
- 77) Matamala N, Vargas MT, González-Cámpora R, et al., 2015. Tumor microRNA expression profiling identifies circulating microRNAs for early breast cancer detection. *Clin Chem*, 61(8):1098-1106. <https://doi.org/10.1373/clinchem.2015.238691>
- 78) Mathe A, Scott RJ, Avery-Kiejda K, 2015. miRNAs and other epigenetic changes as biomarkers in triple negative breast cancer. *Int J Mol Sci*, 16(12):28347-28376. <https://doi.org/10.3390/ijms161226090>
- 79) Mattick JS, 2011. The central role of RNA in human development and cognition. *FEBS Lett*, 585(11):1600-1616. <https://doi.org/10.1016/j.febslet.2011.05.001>
- 80) Mattick JS, Makunin IV, 2006. Non-coding RNA. *Hum Mol Genet*, 15(1):R17-R29. <https://doi.org/10.1093/hmg/ddl046>
- Mattick JS, Amaral PP, Dinger ME, et al., 2009. RNA regulation of epigenetic processes. *BioEssays*, 31(1):51-59. <https://doi.org/10.1002/bies.080099>
- 81) Mayer IA, Abramson VG, Lehmann BD, et al., 2014. New strategies for triple-negative breast cancer—deciphering the heterogeneity. *Clin Cancer Res*, 20(4):782-790. <https://doi.org/10.1158/1078-0432.CCR-13-0583>
- 82) Miao YF, Fan RG, Chen LG, et al., 2016. Clinical significance of long non-coding RNA MALAT1 expression in tissue and serum of breast cancer. *Ann Clin Lab Sci*, 46(4):418-424.
- 83) Mou EX, Wang H, 2019. lncRNA LUCAT1 facilitates tumorigenesis and metastasis of triple-negative breast cancer through modulating miR-5702. *Biosci Rep*, 39(9): BSR20190489. <https://doi.org/10.1042/BSR20190489>
- 84) Niu LM, Fan QX, Yan M, et al., 2019. lncRNA NRON down-regulates lncRNA snaR and inhibits cancer cell proliferation in TNBC. *Biosci Rep*, 39(5):BSR20190468. <https://doi.org/10.1042/BSR20190468>
- 85) O'Brien K, Lowry MC, Corcoran C, et al., 2015. MiR-134 in extracellular vesicles reduces triple-negative breast cancer aggression and increases drug sensitivity. *Oncotarget*, 6(32):32774-32789. <https://doi.org/10.18632/oncotarget.5192>
- 86) Onyeagucha B, Rajamanickam S, Subbarayalu P, et al., 2016. Abstract P2-03-04: down-regulation of Bcl2-related ovarian killer (BOK) by miR-296-5p protects breast cancer cells from paclitaxel-induced apoptosis. *Cancer Res*, 76(S4): P2-03-04. <https://doi.org/10.1158/1538-7445.SABCS15-P2-03-04>
- 87) Paraskevopoulou MD, Hatzigeorgiou AG, 2016. Analyzing miRNA-lncRNA interactions. In: Feng Y, Zhang L (Eds.), *Long Non-Coding RNAs: Methods and Protocols*. Humana Press, New York, p.271-286. https://doi.org/10.1007/978-1-4939-3378-5_21
- 88) Phan B, Majid S, Ursu S, et al., 2016. Tumor suppressor role of microRNA-1296 in triple-negative breast cancer. *Oncotarget*, 7(15):19519-19530. <https://doi.org/10.18632/oncotarget.6961>
- 89) Piasecka D, Braun M, Kordek R, et al., 2018. MicroRNAs in regulation of triple-negative breast cancer progression. *J Cancer Res Clin Oncol*, 144(8):1401-1411. <https://doi.org/10.1007/s00432-018-2689-2>
- 90) Prensner JR, Chinnaiyan AM, 2011. The emergence of lncRNAs in cancer biology. *Cancer Discov*, 1(5):391-407. <https://doi.org/10.1158/2159-8290.CD-11-0209>

- 91) Razaviyan J, Hadavi R, Tavakoli R, et al., 2018. Expression of miRNAs targeting mTOR and S6K1 genes of mTOR signaling pathway including miR-96, miR-557, and miR-3182 in triple-negative breast cancer. *Appl Biochem Biotechnol*, 186(4):1074-1089. <https://doi.org/10.1007/s12010-018-2773-8>
- 92) Ren Y, Han XD, Yu K, et al., 2014. microRNA-200c downregulates XIAP expression to suppress proliferation and promote apoptosis of triple-negative breast cancer cells. *Mol Med Rep*, 10(1):315-321. <https://doi.org/10.3892/mmr.2014.2222>
- 93) Reshetnikova G, Troyanovsky S, Rimm DL, 2007. Definition of a direct extracellular interaction between Met and E- cadherin. *Cell Biol Int*, 31(4):366-373. <https://doi.org/10.1016/j.cellbi.2007.01.022>
- 94) Rhodes LV, Martin EC, Segar HC, et al., 2015. Dual regulation by microRNA-200b-3p and microRNA-200b-5p in the inhibition of epithelial-to-mesenchymal transition in triple- negative breast cancer. *Oncotarget*, 6(18):16638-16652. <https://doi.org/10.18632/oncotarget.3184>
- 95) Romero-Cordoba SL, Rodriguez-Cuevas S, Rebollar-Vega R, et al., 2016. A microRNA signature identifies subtypes of triple-negative breast cancer and reveals miR-342-3p as regulator of a lactate metabolic pathway through silencing monocarboxylate transporter 1. *Cancer Res*, 76(6):A47. <https://doi.org/10.1158/1538-7445.NONRNA15-A47>
- 96) Sha S, Yuan DY, Liu YJ, et al., 2017. Targeting long non- coding RNA DANCR inhibits triple negative breast cancer progression. *Biol Open*, 6(9):1310-1316. <https://doi.org/10.1242/bio.023135>
- 97) Shen X, Zhong JX, Yu P, et al., 2019. YY1-regulated LINC00152 promotes triple negative breast cancer progression by affecting on stability of PTEN protein. *Biochem Biophys Res Commun*, 509(2):448-454. <https://doi.org/10.1016/j.bbrc.2018.12.074>
- 98) Shin VY, Siu MT, Ho JC, et al., 2014. Abstract 531: miR- 199a-5p is a biomarker for and regulator of epithelial- mesenchymal transition in triple-negative breast cancer patients. *Cancer Res*, 74(S19):531. <https://doi.org/10.1158/1538-7445.AM2014-531>
- 99) Shin VY, Chen JW, Cheuk IWY, et al., 2019. Long non-coding RNA NEAT1 confers oncogenic role in triple-negative breast cancer through modulating chemoresistance and cancer stemness. *Cell Death Dis*, 10(4):270. <https://doi.org/10.1038/s41419-019-1513-5>
- 100) Shukla GC, Singh J, Barik S, 2011. MicroRNAs: processing, maturation, target recognition and regulatory functions. *Mol Cell Pharmacol*, 3(3):83-92. Siegel RL, Miller KD, Jemal A, 2019. Cancer statistics, 2019. *CA Cancer J Clin*, 69(1):7-34. <https://doi.org/10.3322/caac.21551>
- 101) Smith MA, Mattick JS, 2017. Structural and functional annotation of long noncoding RNAs. In: Keith JM (Ed.), *Bioinformatics: Volume II: Structure, Function, and Applications*. Humana Press, New York, p.65-85. https://doi.org/10.1007/978-1-4939-6613-4_4
- 102) Song GQ, Zhao Y, 2015. MicroRNA-211, a direct negative regulator of CDC25B expression, inhibits triple-negative breast cancer cells' growth and migration. *Tumor Biol*, 36(7):5001-5009. <https://doi.org/10.1007/s13277-015-3151-6>
- 103) Song X, Liu ZY, Yu ZY, 2019. LncRNA NEF is downregulated in triple negative breast cancer and correlated with poor prognosis. *Acta Biochim Biophys Sin (Shanghai)*, 51(4):386-392. <https://doi.org/10.1093/abbs/gmz021>
- 104) Sørlie T, 2004. Molecular portraits of breast cancer: tumour subtypes as distinct disease entities. *Eur J Cancer*, 40(18): 2667-2675. <https://doi.org/10.1016/j.ejca.2004.08.021>
- 105) St. Laurent G, Wahlestedt C, Kapranov P, 2015. The landscape of long noncoding RNA classification. *Trends Genet*, 31(5):239-251. <https://doi.org/10.1016/j.tig.2015.03.007>
- 106) Sun WL, Yang YB, Xu CJ, et al., 2017. Regulatory mechanisms of long noncoding RNAs on gene expression in cancers. *Cancer Genet*, 216-217:105-110. <https://doi.org/10.1016/j.cancergen.2017.06.003>
- 107) Sun X, Li YQ, Zheng MZ, et al., 2016. MicroRNA-223 increases the sensitivity of triple-negative breast cancer stem cells to TRAIL-induced apoptosis by targeting HAX-1. *PLoS ONE*, 11(9):e0162754. <https://doi.org/10.1371/journal.pone.0162754>
- 108) Taft RJ, Pang KC, Mercer TR, et al., 2010. Non-coding RNAs: regulators of disease. *J Pathol*, 220(2):126-139. <https://doi.org/10.1002/path.2638>

- 109) Tian T, Wang M, Lin S, et al., 2018. The impact of lncRNA dysregulation on clinicopathology and survival of breast cancer: a systematic review and meta-analysis. *Mol Ther Nucleic Acids*, 12:359-369. <https://doi.org/10.1016/j.omtn.2018.05.018>
- 110) Tse JC, Kalluri R, 2007. Mechanisms of metastasis: epithelial- to-mesenchymal transition and contribution of tumor microenvironment. *J Cell Biochem*, 101(4):816-829. <https://doi.org/10.1002/jcb.21215>
- 111) Tsouko E, Wang J, Frigo DE, et al., 2015. miR-200a inhibits migration of triple-negative breast cancer cells through direct repression of the EPHA2 oncogene. *Carcinogenesis*, 36(9):1051-1060. <https://doi.org/10.1093/carcin/bgv087>
- 112) Verma A, Kaur J, Mehta K, 2019. Molecular oncology update: breast cancer gene expression profiling. *Asian J Oncol*, 1(2):65-72. <https://doi.org/10.4103/2454-6798.173282>
- 113) Wang B, Zhang QY, 2012. The expression and clinical significance of circulating microRNA-21 in serum of five solid tumors. *J Cancer Res Clin Oncol*, 138(10):1659- 1666. <https://doi.org/10.1007/s00432-012-1244-9>
- 114) Wang C, Zheng XQ, Shen CY, et al., 2012. MicroRNA-203 suppresses cell proliferation and migration by targeting BIRC5 and LASP1 in human triple-negative breast cancer cells. *J Exp Clin Cancer Res*, 31:58. <https://doi.org/10.1186/1756-9966-31-58>
- 115) Wang H, Tan ZQ, Hu H, et al., 2019. microRNA-21 promotes breast cancer proliferation and metastasis by targeting LZTFL1. *BMC Cancer*, 19:738. <https://doi.org/10.1186/s12885-019-5951-3>
- 116) Wang J, Tsouko E, Jonsson P, et al., 2014. miR-206 inhibits cell migration through direct targeting of the actin- binding protein Coronin 1C in triple-negative breast cancer. *Mol Oncol*, 8(8):1690-1702. <https://doi.org/10.1016/j.molonc.2014.07.006>
- 117) Wang L, Liu DQ, Wu XR, et al., 2018. Long non-coding RNA (lncRNA) RMST in triple-negative breast cancer (TNBC): expression analysis and biological roles research. *J Cell Physiol*, 233(10):6603-6612. <https://doi.org/10.1002/jcp.26311>
- 118) Wang LH, Luan T, Zhou SH, et al., 2019. LncRNA HCP5 promotes triple negative breast cancer progression as a ceRNA to regulate BIRC3 by sponging miR-219a-5p. *Cancer Med*, 8(9):4389-4403. <https://doi.org/10.1002/cam4.2335>
- 119) Wang N, Hou MS, Zhan Y, et al., 2019a. LncRNA PTCSC3 inhibits triple-negative breast cancer cell proliferation by downregulating lncRNA H19. *J Cell Biochem*, 120(9): 15083-15088. <https://doi.org/10.1002/jcb.28769>
- 120) Wang N, Zhong CC, Fu MT, et al., 2019b. Long non-coding RNA HULC promotes the development of breast cancer through regulating LYPD1 expression by sponging miR- 6754-5p. *Onco Targets Ther*, 12:10671-10679. <https://doi.org/10.2147/OTT.S226040>
- 121) Wang OC, Yang F, Liu YH, et al., 2017. C-MYC-induced upregulation of lncRNA SNHG12 regulates cell proliferation, apoptosis and migration in triple-negative breast cancer. *Am J Transl Res*, 9(2):533-545.
- 122) Wang PS, Chou CH, Lin CH, et al., 2018. A novel long non-coding RNA linc-ZNF469-3 promotes lung metastasis through miR-574-5p-ZEB1 axis in triple negative breast cancer. *Oncogene*, 37(34):4662-4678. <https://doi.org/10.1038/s41388-018-0293-1>
- 123) Wang SW, Ke H, Zhang HL, et al., 2018. LncRNA MIR100HG promotes cell proliferation in triple-negative breast cancer through triplex formation with p27 loci. *Cell Death Dis*, 9(8):805. <https://doi.org/10.1038/s41419-018-0869-2>
- 124) Wang XL, Chen T, Zhang Y, et al., 2019. Long noncoding RNA Linc00339 promotes triple-negative breast cancer progression through miR-377-3p/HOXC6 signaling pathway. *J Cell Physiol*, 234(8):13303-13317. <https://doi.org/10.1002/jcp.28007>
- 125) Wang XS, Zhang Z, Wang HC, et al., 2006. Rapid identification of UCA1 as a very sensitive and specific unique marker for human bladder carcinoma. *Clin Cancer Res*, 12(16):4851-4858. <https://doi.org/10.1158/1078-0432.CCR-06-0134>
- 126) Wang YX, Zhang ZY, Wang JQ, 2018. MicroRNA-384 inhibits the progression of breast cancer by targeting ACVR1. *Oncol Rep*, 39(6):2563-2574. <https://doi.org/10.3892/or.2018.6385>

- 127) Winton MJ, Igaz LM, Wong MM, et al., 2008. Disturbance of nuclear and cytoplasmic TAR DNA-binding protein (TDP-43) induces disease-like redistribution, sequestration, and aggregate formation. *J Biol Chem*, 283(19): 13302-13309. <https://doi.org/10.1074/jbc.M800342200>
- 128) Wu CH, Luo J, 2016. Long non-coding RNA (lncRNA) urothelial carcinoma-associated 1 (UCA1) enhances tamoxifen resistance in breast cancer cells via inhibiting mtor signaling pathway. *Med Sci Monit*, 22:3860-3867. <https://doi.org/10.12659/msm.900689>
- 129) Wu JL, Shuang ZY, Zhao JF, et al., 2018. Linc00152 promotes tumorigenesis by regulating DNMTs in triple-negative breast cancer. *Biomed Pharmacother*, 97:1275-1281. <https://doi.org/10.1016/j.biopha.2017.11.055>
- 130) Xiong HP, Yan T, Zhang WJ, et al., 2018. miR-613 inhibits cell migration and invasion by downregulating Daam1 in triple-negative breast cancer. *Cell Signal*, 44:33-42. <https://doi.org/10.1016/j.cellsig.2018.01.013>
- 131) Xu ST, Xu JH, Zheng ZR, et al., 2017. Long non-coding RNA ANRIL promotes carcinogenesis via sponging miR-199a in triple-negative breast cancer. *Biomed Pharmacother*, 96:14-21. <https://doi.org/10.1016/j.biopha.2017.09.107>
- 132) Yang CF, Humphries B, Li YF, et al., 2017. Abstract 1468: miR-200b targets ARHGAP18 and suppresses triple negative breast cancer metastasis. *Cancer Res*, 77(S13):1468. <https://doi.org/10.1158/1538-7445.AM2017-1468>
- 133) Yang F, Liu YH, Dong SY, et al., 2016a. Co-expression networks revealed potential core lncRNAs in the triple-negative breast cancer. *Gene*, 591(2):471-477. <https://doi.org/10.1016/j.gene.2016.07.002>
- 134) Yang F, Dong SY, Lv L, et al., 2016b. Long non-coding RNA AFAP1-AS1 was up-regulated in triple-negative breast cancer and regulated proliferation and invasion. *Int J Clin Exp Pathol*, 9(6):6378-6384.
- 135) Yang J, Meng XL, Yu Y, et al., 2019. LncRNA POU3F3 promotes proliferation and inhibits apoptosis of cancer cells in triple-negative breast cancer by inactivating caspase 9. *Biosci Biotechnol Biochem*, 83(6):1117-1123. <https://doi.org/10.1080/09168451.2019.1588097>
- 136) Yoon MK, Mitrea DM, Ou L, et al., 2012. Cell cycle regulation by the intrinsically disordered proteins p21 and p27. *Biochem Soc Trans*, 40(5):981-988. <https://doi.org/10.1042/bst20120092>
- 137) Youness RA, Hafez HM, Khallaf E, et al., 2019. The long noncoding RNA sONE represses triple-negative breast cancer aggressiveness through inducing the expression of miR-34a, miR-15a, miR-16, and let-7a. *J Cell Physiol*, 234(11):20286-20297. <https://doi.org/10.1002/jcp.28629>
- 138) Yu FS, Wang L, Zhang BW, 2019. Long non-coding RNA DRHC inhibits the proliferation of cancer cells in triple negative breast cancer by downregulating long non-coding RNA HOTAIR. *Oncol Lett*, 18(4):3817-3822. <https://doi.org/10.3892/ol.2019.10683>
- 139) Zhang H, Li BW, Zhao HB, et al., 2015. The expression and clinical significance of serum miR-205 for breast cancer and its role in detection of human cancers. *Int J Clin Exp Med*, 8(2):3034-3043.
- 140) Zhang KJ, Luo ZL, Zhang Y, et al., 2016. Circulating lncRNA H19 in plasma as a novel biomarker for breast cancer. *Cancer Biomark*, 17(2):187-194. <https://doi.org/10.3233/CBM-160630>
- 141) Zhang KM, Liu P, Tang HL, et al., 2018. AFAP1-AS1 promotes epithelial-mesenchymal transition and tumorigenesis through Wnt/ β -catenin signaling pathway in triple-negative breast cancer. *Front Pharmacol*, 9:1248. <https://doi.org/10.3389/fphar.2018.01248>
- 142) Zhang R, Xia LQ, Lu WW, et al., 2016. LncRNAs and cancer. *Oncol Lett*, 12(2):1233-1239. <https://doi.org/10.3892/ol.2016.4770>
- 143) Zhang YY, He Q, Hu ZY, et al., 2016. Long noncoding RNA LINP1 regulates repair of DNA double-strand breaks in triple-negative breast cancer. *Nat Struct Mol Biol*, 23(6): 522-530. <https://doi.org/10.1038/nsmb.3211>
- 144) Zhao D, Besser AH, Wander SA, et al., 2015. Cytoplasmic p27 promotes epithelial-mesenchymal transition and tumor metastasis via STAT3-mediated TWIST1 upregulation. *Oncogene*, 34(43):5447-5459. <https://doi.org/10.1038/onc.2014.473>
- 145) Zhao M, Ding XF, Shen JY, et al., 2017. Use of liposomal doxorubicin for adjuvant chemotherapy of breast cancer in clinical practice. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 18(1):15-26. <https://doi.org/10.1631/jzus.B1600303>

- 146) Zhao ZT, Li L, Du PN, et al., 2019. Transcriptional downregulation of miR-4306 serves as a new therapeutic target for triple negative breast cancer. *Theranostics*, 9(5):1401-1416. <https://doi.org/10.7150/thno.30701>
- 147) Zheng LH, Zhang YH, Fu YJ, et al., 2019. Long non-coding RNA MALAT1 regulates BLCAP mRNA expression through binding to miR-339-5p and promotes poor prognosis in breast cancer. *Biosci Rep*, 39(2):BSR20181284. <https://doi.org/10.1042/BSR20181284>
- 148) Zuo YG, Li Y, Zhou ZY, et al., 2017. Long non-coding RNA MALAT1 promotes proliferation and invasion via targeting miR-129-5p in triple-negative breast cancer. *Biomed Pharmacother*, 95:922-928. <https://doi.org/10.1016/j.biopha.2017.09.005>