MiR-29a: a potential therapeutic target and promising biomarker in tumors

Jin-yan Wang1,∗, Qian Zhang1,∗, Dan-dan Wang1, Wei Yan1, Huan-huan Sha2, Jian-hua Zhao3, Su-jin Yang1, He-da Zhang4, Jun-chen Hou1, Han-zi Xu5, Yun-jie He1, Jia-hua Hu2, Shan-liang Zhong3 and Jin-hai Tang6

1Department of General Surgery, The Affiliated Cancer Hospital of Nanjing Medical University & Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research, Nanjing 210009, P.R. China; 2The Fourth Clinical School, Nanjing Medical University, Nanjing 210029, P.R. China; 3Center of Clinical Laboratory Science, Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research & The Affiliated Cancer Hospital of Nanjing Medical University, Nanjing 210009, P.R. China; 4Department of Radiation Oncology, Jiangsu Cancer Hospital, Nanjing, Jiangsu, P.R. China; 5Department of General Surgery, Southeast University Medical School, Nanjing, Jiangsu, P.R. China; 6Department of General Surgery, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, P.R. China

Correspondence: Shan-liang Zhong (slzhong@foxmail.com) or Jin-hai Tang (tangjh@njmu.edu.cn)

Introduction

Mortality caused by cancer is soaring globally, which urgently requests us to figure out a safe and effective way to further improve overall survival of tumor patients [1]. Then, molecular targetting treatment of cancer entered our sight and brought cancer patients a ray of dawn. Based on massive researches, miRNAs appeared to modulate various pathways in malignant neoplasms, which might offer a brand new and effective way in future molecular targetting cancer treatment [2,3]. MiRNAs are a class of small, highly conserved, time sequencing, and non-coding RNAs, including 18–25 nts, that regulate gene expression at both transcriptional and post-transcriptional levels. They are involved in different biological and metabolic processes, through binding to the 3′-UTRs of mRNAs [4]. Additionally, miRNAs are disclosed that they are related to many biological processes including cell proliferation, apoptosis, angiogenesis, drug-resistance, invasion, and metastasis [5]. Cho [6] had summarized miRNAs as a potential biomarker for diagnosis, prognosis, and therapy with ample evidence in cancers. Liu et al. [7] highlighted multifarious miRNAs participated in the regulation of chemoresistance, cell cycle, and apoptosis in the process of epithelial-to-mesenchymal transition (EMT), cell cycle, and apoptosis in colorectal cancer (CRC) cells. For instance, miR-139-5p inhibited cell proliferation of breast cancer (BCa) [8]. MiR-335 promoted gastric cancer (GC) cell apoptosis by targetting CT10 oncogene homolog-like (CRKL) [9]. MiR-222 mediated adriamycin resistance to BCa cells [10]. MiR-22 decreased migration due to down-regulating CD147 expression in tongue squamous cell carcinoma (TSCC) [11].
MiR-29 family (miR-29a, miR-29b, and miR-29c) was connected with aggressiveness and prognosis of malignant neoplasms and might act as a considerable biomarker for forecasting the recurrence and progression of cancers [12-15]. Nonetheless, from articles we have learnt that miR-29a and miR-29b appeared to be more effective than miR-29c in targeting genes and signaling pathways [16,17]. The role of miR-29b in cancers had been fully discussed by Yan et al. [18] in 2015 and the new progression of miR-29b was less. Yet, the function of miR-29a had not been sufficiently summarized. On account of available researches, miR-29a had been found to be associated with kinds of neoplasms. For instance, it was down-regulated in metastatic prostate cancer (PCa) [19], myeloid leukemias [20], endocrine-sensitive BCa [21], lung cancer [22], ALK-positive anaplastic large cell lymphomas (ALCLs) [23], oral squamous carcinoma (OSCC) [24], glioblastoma [25]. Interestingly, other findings proclaimed that miR-29a was up-regulated in cholangiocarcinoma [26], CRC [27], and so on. Apart from its role in cancer, miRNAs were also involved in a variety of non-malignant diseases. According to Wei et al. [28], miRNAs served as a potential biological role in the initiation of pulmonary inflammation. Without exception, miR-29a was correlated with kinds of non-malignant diseases, like Alzheimer’s disease [29], cholestatic pediatric liver disease [30], atherosclerosis [31], atrial fibrillation [32], active pulmonary tuberculosis [33], thoracic aneurysms [34], tendon disease [35], hepatic fibrosis [36], ankylosing spondylitis [37], diabetes [38], scleroderma [39], and fatty liver disease [40]. Besides, evidence had proved that miR-29a greatly participated in multifarious cell processes, such as cell proliferation, apoptosis, angiogenesis, invasion, and metastasis and drug-resistance [41-43]. Thus it could been seen that miR-29a might play a considerable role in the adjustment of kinds of diseases, especially cancers. In this review, we will focus on the action of miR-29a in the processes of cell proliferation, apoptosis, angiogenesis, invasion, metastasis, and drug resistance, and work out the network of genes modulating its functions, and predict the potential role of miR-29a in the diagnosis and molecular targetted therapy of human cancers.

**MiR-29a in cell proliferation**

An increasing number of studies showed that miR-29a was correlated with proliferation to a great extent. TUT1, a nucleotidyl transferase, could increase the expression of miR-29a, then inhibiting PARP and SREBP-1c expression, which suppressed cell proliferation in osteosarcoma (OS) [44]. Li et al. [41] discovered that miR-29a repressed PCa cell proliferation and development of PCa through targeting lysine demethylation 5B (KDM5B). KDM5B could specifically reduce the methylation levels of histone H3 at lysine 4 (H3K4). Additionally, Cui et al. [45] confirmed that, in GC, miR-29a could suppress the expression level of p42.3 which had been proved to be associated with cell proliferation. Consequently, miR-29a might act as an inhibitor in the modulation of cell proliferation. Lately, Zhao et al. [46] also found that, in vitro, enhancing the expression of miR-29a could decrease cell proliferation in GC via diluting the level of Cyclin-dependent kinase (CDK) 2 (CDK2), CDK4, and CDK6. Furthermore, cell proliferation could also be directly refrained by miR-29a through suppressing the expression of Mucin 1 (MUC1). MUC1 was a membrane-bound glycoprotein, interacting with the epidermal growth factor receptor (EGFR) [47]. Besides, MUC1, targeted by miR-29a, was also lately confirmed to accommodate in pancreatic ductal adenocarcinoma (PDAC) cell proliferation through p42-44 MAPK and β-catenin pathways [48]. Moreover, according to Xi et al. [25], miR-29a repressed the level of Wilms’ tumor 1-associating protein (WTAP), phosphoinositide 3-kinase (PI3K)/protein kinase B (PKB)/AKT and extracellular signal-related kinase pathways through targeting Quaking gene isoform 6 (QKI-6) in glioblastoma stem cells (GSCs), accordingly inhibiting cell proliferation. Zhu et al. [49] recognized that osteonectin (SPARC) restrain the phosphorylation of AKT/mTOR, via the overexpression of miR-29a, thus controlling cancer cell proliferation in hepatocellular carcinoma (HCC). MiR-29a was claimed to have the ability to decreased proliferation in non-small-cell lung cancer (NSCLC), via negatively correlating with LIM and SH3 domain protein 1 (LASP1), a cAMP- and cGMP-dependent signaling protein and a member of the nebulin family of actin-binding proteins [50]. At the same time, the suppression of proliferation caused by miR-29a was also affirmed by Li et al. [51] partly via targeting cell division control protein 42 homolog (CDC42) in NSCLC. In addition, Pei et al. [52] demonstrated that, in BCa cells, miR-29a could induce cell proliferation by directly targeting ten eleven translocation (TET) 1 (TET1). TET1 was a member of the TET family and able to alter 5-methylcytosine (5mC) to 5-hydroxymethylcytosine (5hmC), which could induce CpG island demethylation in specific gene promoter [53]. Nonetheless, the newest research acknowledged miR-29a remarkably weakened cell proliferation in MCF-7 cells, one BCa cells, partly through tumor necrosis factor (TNF) receptor (TNFR) associated factor 1 (TNFR1), the prime receptor that commanded TNF-α-induced cellular events [54]. The absolutely opposite standpoint might be worthy of further discovery.
### Table 1 Target genes and dysregulation of miR-29a in proliferation, apoptosis, angiogenesis, and drug resistance

<table>
<thead>
<tr>
<th>hsa-miR-29a</th>
<th>Diseases</th>
<th>Target genes</th>
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<td>Pei et al. [52]</td>
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</table>

Abbreviations: ALCL, anaplastic large cell lymphoma; HSP, heat shock protein; MCL-1, myeloid cell leukemia 1; MMP2, matrix metalloproteinase 2; VASH2, vasohibin 2; VEGF, vascular endothelial growth factor.

![miR-29a regulation diagram](image)

**Figure 1. miR-29a targeted p42.3, CDK2, CDK4, CDK6, MUC1, QKI-6, SPARC, CDC42, TNFR1 and thus inhibited proliferation**

However, miR-29a could also induce proliferation though KDM5B, TET1, PPARγ, SREBP-1c, LASP1.
Figure 2. MCL-1, KDM5B, QKI-6, MMP2, TNFR1 are the five target genes of miR-29a and miR-29a inhibited their functions and promoted apoptosis

On the other hand, miR-29a decreased apoptosis by refraining HSP60 and motivating HSP27, HSP40, HSP70, HSP90. Abbreviations: HSP, heat shock protein; MCL-1, myeloid cell leukemia 1; MMP2, matrix metalloproteinase 2.

Figure 3. VASH2 and VEGF, inhibited by miR-29a, acted in a stimulative role in angiogenesis

But, HBP1 and PTEN, which were also restrained by miR-29a, lessened angiogenesis. Abbreviations: HBP1, HMG box-containing protein-1; PTEN, phosphatase and tensin homolog; VASH2, vasohibin 2; VEGF, vascular endothelial growth factor.

Figure 4. MiR-29a magnified drug resistance via targetting PREN/AKT/GSK3β and Wnt/β-catenin and reduced drug resistance by binding to MUC1

MiR-29a in cell apoptosis

Apoptosis was recognized as a highly regulated and controlled process of cell death that occurred in multicellular organisms. It was activated through two pathways, including the intrinsic pathway and the extrinsic pathway, both of which induced cell death by activating caspases, such as proteases or enzymes that degraded proteins [55]. An increasing number of researches had demonstrated that miR-29a played a significant role in promoting apoptosis via targetting several relevant effectors in human cancer. Desjobert et al. [23] claimed that the expression of miR-29a was...
critically decreased by an active NPM-ALK kinase in ALK-positive (ALK+) ALCCL cells, partly through methylation regulation. And this kind of modulation played a fundamental role in the high expression of myeloid cell leukemia 1 (MCL-1). MCL-1, a major anti-apoptotic BCL-2 family member localized to the mitochondrial membrane of ALK+ ALCCL cells, acted as a protector in tumor cell survival through suppressing apoptosis. Moreover, miR-29a in PCa cell lines (PC-3 and LNCaP cells) induced apoptosis by affecting the methylation status of H3K4 through restraining the expression of KDM5B, which was mentioned elsewhere [41]. MiR-29a also largely inhibited the anti-apoptotic ability of OSCC cell via directly targeting matrix metalloproteinase 2 (MMP2) gene, thus negatively regulating the expression of MMP2, a well-known oncogenic gene [24]. The apoptosis of GSCs was promoted by miR-29a via targeting QKI-6, and the detailed pathway had been mentioned earlier [25]. Similarly, in BCa cells, miR-29a showed a great potential in inducing apoptosis partly though targeting TNRF1 [54]. However, Choghaei et al. [56] found that the absence of miR-29a promoted apoptosis in breast carcinoma through modulating members of heat shock proteins (HSPs), such as up-regulating HSP60 level and down-regulating HSP27, HSP40, HSP70, and HSP90 levels.

**MiR-29a in angiogenesis**

Angiogenesis was generally accepted as a consequential characteristic of varied malignant neoplasm, which was a complex process modulated by a sequential pro-angiogenic and anti-angiogenic factors [57]. Generous researches illustrated that miR-29a might be relevant with angiogenesis in the development and progression of cancers.

Jia et al. [58] found that miR-29a functioned as a suppressor in the expression of vaso-inhibin 2 (VASH2), via the knockdown of H19, one of the long non-coding RNAs (lncRNAs). VASH2 was normally accepted as an angiogenic factor, which could adjust the angiogenesis in glioma. Except VASH2, miR-29a apparently repressed the expression and secretion of vascular endothelial growth factor (VEGF), one of the most common proteins liberated from cancer.
Table 2 Target genes and dysregulation of miR-29a in metastasis

<table>
<thead>
<tr>
<th>hsa-miR-29a</th>
<th>Diseases</th>
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Abbreviations: BMP, bone morphogenetic protein; CEACAM6, carcinoembryonic antigen-related cell adhesion molecule 6; HNSCC, head and neck squamous cell carcinoma; HSP, heat shock protein; ITGB1, integrin β1; MMP2, matrix metalloproteinase 2; PTC, papillary thyroid carcinoma; PTEN, phosphatase and tensin homolog; Robo, roundabout 1; TTP, tristetraprolin; VEGF, vascular endothelial growth factor.

Table 3 The role of miR-29a in the diagnosis, treatment, and stages of carcinoma

<table>
<thead>
<tr>
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Abbreviations: ALCL, anaplastic large cell lymphoma; HNSCC, head and neck squamous cell carcinoma; PTC, papillary thyroid carcinoma.
cells that could promote angiogenesis in GC cells [42]. Nevertheless, it was revealed by Wang et al. [59] that miR-29a, modulated by TGF-β in a Smad4-dependent way, served as a promoter in angiogenesis, since miR-29a stimulated the AKT signaling in endothelial cells, by targeting phosphatase and tensin homolog (PTEN). Furthermore, miR-29a, mediated by HMG box-containing protein-1 (HBPI), might regulate the angiogenic properties of human endothelial cells [60]. HBPI, a tumor suppressor protein, was recognized to inhibit Wnt signaling and modulate cell proliferation in BCa cells [61]. As a result, it still remained to explore whether miR-29a functioned as a suppressor or an enhancer in the angiogenesis of tumors.

MiR-29a in drug-resistance

Nowadays, in malignancy, mortality caused by chemotherapy resistance keeps increasing and Sin et al. [62] and Zhang and Yuan [63] speculated that miRNAs might be involved in the therapy of EGFR-tyrosine kinase inhibitors (EGFR-TKIs) resistance in NSCLC. Besides, agilent miRNA microarrays were carried out to examine the miRNA expression profiles of gefitinib-resistant human HCC827/GR-8-1 cell line and the parental HCC827 cell line. Interestingly, miR-149-5p was up-regulated in the gefitinib-resistant human HCC827/GR-8-1 cells and associated with acquired gefitinib resistance [64]. Based on the above researches, we learned that miRNAs had showed a great potential in the drug resistance of tumor and a daring hypothesis was made that miR-29a took a considerable part in the regulation of chemotherapy resistance.

Cai et al. [65] disclosed previously that miR-29a induced the resistance to gemcitabine (GEM) in pancreatic cancer cells, mediated significantly by the activation the Wnt/β-catenin signaling pathway. The Wnt/β-catenin signaling was widely recognized to participate in the chemotherapy resistance of a variety of malignant tumors such as HCC, head and neck tumor, and PCa [66]. Nevertheless, it was confirmed that Trehoux et al. [47] reported that miR-29a sensitized pancreatic cancer cells to GEM in vitro by targeting MUC1. Additionally, Kwon et al. [67] found that miR-29a sensitized chemotherapeutic resistant pancreatic cancer cells to GEM and increased cytotoxicity. Furthermore, miR-29a played an essential role in ADR resistance via inhibiting the PTEN/AKT/GSK3β pathway in BCa cell lines [68]. Zhong et al. [43] also proved that miR-29a was correlated with drug-resistant ADR and docetaxel (Doc), at least partly by targeting PTEN, which was generally acknowledged as a cancer-depressing gene, and it could also regulate kinds of cell processes, like growth, apoptosis, migration, and invasion [69]. Besides, miR-29a could enhance the chemosensitivity in OSCC, particularly cys-Diaminedichloroplatinum (CDDP) [24].

MiR-29a in invasion and metastasis

Metastasis was the most important sequelae in the progression of cancer. Therefore, the mechanism of tumorigenesis and development were urgently needed for the prevention.

It was hypothesized in the ‘seed and soil’ for metastasis that migratory tumor cells leave the primary tumor via intravasation, disseminating throughout the body by the bloodstream, and eventually implantation in a distant organ. These consecutive steps require close interplay between miRNA and its various targets [70].

Initially, Gebeshuber et al. [71] detected that the down-regulation of miR-29a impaired the expression of tristetraprolin (TTP). TTP was recognized as a protein that was relevant with EMT and negatively modulated AU-rich elements (AREs) containing targets, such as tumor interleukin (IL)-3, IL-8, cyclooxygenase 2 (COX2), VEGF, c-Myc, cyclin D1, and TNF-a, known as the promoters of tumorigenesis. As a result, the high expression of miR-29a induced invasion and metastasis of tumor in co-operation with oncogenic Ras signaling in human BCa. Moreover, it was also clarified by Kong et al. [72] that miR-29a promoted migration of hepatoma cell mediated by hepatitis B virus X protein (HBx), as it directly inhibited the expression of PTEN and thus regulated Akt phosphorylation. MiR-29a was concerned with the aberrant TTP-HuR axis and promoted the invasiveness of BCa cells [73]. Pei et al. [52] presumed the overexpressed miR-29a facilitated cell growth and migration through down-regulating TET1. And it was discovered by Lu et al. [24] that the enhanced ability to invade and metastasize resulted partly from the excessive expression of miR-29a by directly targeting MMP2 gene in OSCC. Tang et al. [74] also claimed that miR-29a/MMP2 signaling pathway largely contributed to the invasion and metastasis of CRC. They found that miR-29a promoted CRC metastasis through modulating KLF4/MMP2/E-cad. In addition, miR-29a took a great part in the TGF-β1/miR-29a/HDAC4 pathway, which promoted metastasis of cholangiocarcinoma [75]. It was unbelievable that others found miR-29a could also serve as a completely adverse role in the metastasis of tumors. For example Li et al. [76] announced that the up-regulation of miR-29a, mediated by isoflavone inhibited cell growth and invasion. Because of its ability to down-regulate its target genes TRIM68 and PGK-1 in PCa, Ahmed et al. [19] elucidated in 2013 that the up-regulation of miR-29a decreased the expression of the TRAF4. TRAF4 was positively related with the expression of bone morphogenetic proteins (BMPs), which belong to converting growth factor-β (TGF-β) superfamily and are well known to take a
grave part in the bone metastasis of Pca. Accordingly, miR-29a might produce a marked effect on the bone metastasis of Pca through decreasing the expression of BMP via targeting TRAF4. At the same time, there was also a pathway about c-Myc, Hedgehog, NF-κB/miR-29a/TRA4 in promoting the invasion and metastasis of Pca, as miR-29a was inhibited by c-Myc, which was overexpressed in Pca. Also, miR-29a diminished cell migration partly by directly targeting MCL1 in Pca [77]. MiR-29a functioned as an inhibition role in NSCLC via negatively modulating expression of LASP1 [50] and CDC42 [51], LASP1 functioned as a CAMP- and cGMP-dependent signaling protein and CDC42 was a protein involved in the adjustment of the cell cycle. MiR-29a, directly under-regulating VEGF-A, was identified to inhibit the tumor microvessel density, and then suppressing the invasion and metastasis of GC cells [78]. MiR-29a, accompanied with other tumor-suppressive miRNAs, such as miR-26a/b, miR-29b/c, and miR-218, apparently inhibited the migration and invasion of head and neck squamous cell carcinoma (HNSCC), via directly up-regulating LOXL2 [98]. MiR-29a, through targeting carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6), also inhibited the metastatic behavior of lung adenocarcinoma cells, as CEACAM6 was involved in the adhesion, migration, invasion, and metastasis of tumor cells by integrin receptors [79]. Wound healing and transwell assays conducted by Zhao et al. [46] revealed that miR-29a decreased the metastasis of GC. He et al. [80] further explored that the expression of miR-29a, inhibited by the up-regulation of hTERT, enhanced the expression of integrin B1 (ITGB1) in GC cells, thus leading to the augmented invasive capacity of GC cells. On the other side, restoration of miR-29a restrained the expression of ITGB1 and inhibited GC cell metastasis [80]. MiR-29a reduced the migration and invasion of PDAC cancer cell by the way of blocking autophagy flux, as indicated by an augmentation of autophagosomes and autophagy markers, p62 and LC3B, a reduction in autophagosome-lysosome fusion, as well as the decreased expression of autophagy proteins, TFEB and ATG9A, which are critical for autophagy [67]. The role of miR-29a in inhibiting the metastasis of BCA, at least in part, lied in its negative regulation of Roundabout 1 (Robo1) in MCF-7 BCA cells, through both the expression of Robo1 mRNA and protein [81]. Similarly, Liu et al. [82] acknowledged, in the same year, the same signaling pathway as Li et al. [81] in GC. The up-regulation of miR-29a obviously decreased AKT3 expression, via directly binding to the 3’-UTR of AKT3, thereby suppressing PI3K/AKT pathway activation, which were involved in multiple cellular functions in papillary thyroid carcinoma (PTC) [83]. MiR-29a refrained from glioma tumor growth and invasion through decreasing the expression of HSP47, also known as SERPINH1. HSP47 was a product of CBP2 gene, located at chromosome 11q13.5, a region frequently amplified in human cancers [84].

**MiR-29a in potential clinical application**

In clinical application, a desirable biomarker that could facilitate disease detection, stages, and prediction of outcome, and provided appropriate treatment for kinds of cancers. There was emerging evidence for the prognostic role of various miRNAs in cancers. Luckily, the abnormality of miR-29a had been found in several types of tumors and might provide novel cancer biomarkers. Exempli gratia, the level of miR-29a in serum was significantly correlated with the clinical stage [85]. And the serum levels of miR-29a were obviously higher in stage III CRC, compared with levels in the healthy individuals [27]. In stage II CRC, high expression of miR-29a was associated with a longer disease-free survival (DFS) [86]. Additionally, higher miR-29a levels were significantly related to longer overall survival in metastatic high-grade serous carcinoma [87]. On the other hand, miR-29a was also lower in the early-recurrence patients, compared with levels in non-early recurrence group [4], and the same in feces from CRC patients, compared with those from normality [88]. Meta-analysis of 281 CRC patients and 299 healthy controls [89] revealed that miR-29a may be a novel potential biomarker for CRC diagnosis.

**Discussion and conclusion**

In this review, we focussed on the function of miR-29a in the progression of cancers, such as Pca, BCA, lung cancer, GC, PDAC, GSCs, HCC, OSCC, glioma, and so on. Consequently, it regulated a variety of biological processes, including proliferation, apoptosis, angiogenesis, invasion, metastasis, and drug resistance. In opposite, miR-29a was discovered to be oncogenically neutral in the pancreatic acinar carcinoma by Dooley et al. [90], no matter the development, nor the growth of pancreatic tumor. In particularly, miR-29a exhibited its tissue specificity in BCA, as its up-regulation in the progression of proliferation and metastasis. This phenomenon was quite different from that in other malignant tissue. Commonly, miR-29a was down-regulated in kinds of cancers regardless of proliferation, apoptosis, drug resistance, and metastasis. The distinct tissue specificity deserved further researches and might disclose a brand new mechanism in the therapy of malignancy.

In detail, miR-29a was associated with various target genes, like CDK2, MMP2, Wnt/β-catenin, VEGF, and so on. MMP2, a type IV collagenase, is widely recognized to promote tumor metastasis by decreasing the basement
membrane [91]. CDK2, a member of protein kinase family, significantly modulated abundant events of eukaryotic cell division cycle [92]. VEGF was known to take a great part in the progression and metastasis of cancers through inducing angiogenesis [93]. Thus it can be seen that miR-29a adjusted these biological and significant genes and participated in tumorigenesis. However the adjustment of miRNAs is a complex network, which means that an miRNA could regulate multiple target genes, meanwhile, a single gene could be influenced by a variety of miRNAs, including miR-29a.

With the development of the depth of the sequencing and the recognition of tumor development, miRNAs were confirmed the relationship with materials which had never caught our eyes, such as extracellular vesicles (EVs), circu-lar RNA, IncRNAs, and autophagy. For example, cell-derived EVs, loaded with functional miRNAs were delivered to the therapeutic targets, which might provide a novel therapies for cancers [94]. In addition, circular RNA modulated the proliferation and invasion of tumors though targeting miRNAs, which provided a novel insight for cancer biology [95-97]. All these potential mechanisms optimized the function of miRNAs. However, no one claimed that miR-29a was involved in the above mechanism and whether there were some mysteries about the tumorigenesis and tumor development. We considered that the connection, amongst miRNAs, EVs, circular RNA, IncRNAs, and autophagy, was interesting and urged us for further exploration.

In conclusion, miR-29a participated in cell proliferation, differentiation, apoptosis, angiogenesis, tumorigenicity, metastasis, drug-resistance, and so on. Increasing researches were involved in the function of miR-29a and the new findings or mechanism might also be related with miR-29a. We suggested that miR-29a serve as a potential therapeutic target and promising biomarker in various tumors, in future miR-29a requires further exploration.

**Author contribution**
S.-I.Z., D.-d.W. and H.-h.S. were responsible for the useful discussions and helped in revision of the present paper. All authors were responsible for the content and writing of the paper.

**Competing interests**
The authors declare that there are no competing interests associated with the manuscript.

**Funding**
This work was supported by the National Natural Science Foundation of China [grant number 81602551]; the Key Research Program for the Social Development of Jiangsu Province, China [grant number BE2015718]; the National Program on Key Research Project [grant number 2016YFC0905900]; the Medical Training Programme Foundation for the Talents by Jiangsu Provincial Department of Health [grant number 17 [2016]]; the 333 Talent Project of Jiangsu Province, top-level [grant number 4 [2016]]; the National Key Clinical Specialist Construction Programs of China [grant number 544 [2013]]; the Major Program of Natural Science Foundation of Jiangsu Province [grant number BL2014090]; the Natural Science Foundation of Jiangsu Province [grant number BK20151579]; a project funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD) [grant number JX10231802]; and the Postgraduate Research and Practice Innovation Program of Jiangsu Province [grant number SJCX17_0387].

**Abbreviations**
BCA, breast cancer; BMP, bone morphogenetic protein; CDC42, cell division control protein 42 homolog; CDK, cyclin-dependent kinase; CEACAM6, carcinoembryonic antigen-related cell adhesion molecule 6; CRC, colorectal cancer; EGFR, epidermal growth factor receptor; EMT, epithelial-to-mesenchymal transition; EV, extracellular vesicle; GC, gastric cancer; GEM, gemcitabine; GSC, glioblastoma stem cell; HBP1, HMG box-containing protein-1; HCC, hepatocellular carcinoma; HSP, heat shock protein; ITGB1, integrin β1; LASP1, LIM and SH3 domain protein 1; lncRNA, long non-coding RNA; MCL-1, myeloid cell leukemia 1; MUC1, mucin 1; MMP2, matrix metalloproteinase 2; NSCLC, non-small-cell lung cancer; OSCC, oral squamous carcinoma; PCA, prostate cancer; PDAC, pancreatic ductal adenocarcinoma; PI3K, phosphoinositide 3-kinase; PTEN, phosphatase and tensin homolog; QKI-6, quaking gene isofrom 6; Robo1, roundabout 1; TET1, ten eleven transloca-tion 1; TNF, tumor necrosis factor; TNFR, TNF receptor; TTP, tristetraprolin; VASH2, vasohibin 2; VEGF, vascular endothelial growth factor.

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LARP4 inhibits cell proliferation and invasion of gastric cancer by sponging miR-424-5p and regulating LATS1.

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