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MicroRNA-409: Molecular functions and clinical applications in cancer

Yasamin Rajabloo [a], Hanieh Latifi [a], Iman Akhlaghipour [a], Negin Taghehchian [b], Meysam Moghbeli [b,*]

[a] Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[b] Department of Medical Genetics and Molecular Medicine, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

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ABSTRACT

Late diagnosis is one of the main reasons for high mortality rates in cancer patients. Therefore, investigating the molecular mechanisms involved in tumor progression can improve the cancer diagnosis in the early stages of the tumor progression. MicroRNAs (miRNAs) have important roles in regulation of cell growth, proliferation, metabolism, and migration. Since, deregulation of miR-409 has been reported in a wide range of cancers, in the present review, we investigated the molecular mechanisms of miR-409 during tumor progression and invasion. It has been shown that miR-409 functions as a tumor suppressor in different tumor types. MiR-409 can reduce tumor cell proliferation, growth, and migration by regulation of signaling pathways, cellular metabolism, transcription factors, and cellular adhesion. This review can be an effective step in introducing miR-409 as a non-invasive marker in cancer patients.

1. Introduction

Cancer is one of the prominent causes of human deaths worldwide [1,2]. It is appraised that there will be over 28 million cancer cases worldwide by the year 2040 [2]. Lack of the efficient screening methods to ascertain cancers in their early stages results in tumor detection in advanced stages with poor prognosis [3]. Despite the recent advances in diagnostic and therapeutic methods, there is still a high tumor recurrence and unfavorable prognosis among these patients [4,5]. Enhanced understanding of the cancer pathophysiology improves early tumor detection and effective treatment [6]. Noncoding RNAs (ncRNAs) have an indispensable role in tumor progression [7]. MicroRNAs (miRNAs) are short ncRNAs that participate in the post-transcriptional regulation [8]. They have a decisive role in regulation of cellular processes such as autophagy, differentiation, proliferation, and migration [9,10]. Deregulation of miRNAs has been observed in various diseases, such as diabetes, autoimmune disorders, and cancer [11–13]. Disease-specific miRNAs could be useful as diagnostic markers and conceivable targets for treatment [14]. Abnormal expression of miRNAs is not only correlated with tumor type, but also is correlated with stage of tumor progression [15,16]. MiRNAs are recognized to function as oncogenes or tumor suppressors in different cancers [17]. They have been also found to be correlated with cancer aggressiveness and prognosis [18]. Accordingly, miRNAs have promising implications for improving cancer diagnosis, prognosis, and treatment outcomes. Due to their high stability in body fluids, they can be used as the suitable molecular indicators for the non-invasive, rapid, and cost-effective diagnosis in different human disorders and cancers [6,19]. MiR-409–3p/-5p is predominantly expressed in embryonic stem cells and is located within the DLK1-DIO3 cluster on chromosome 14 [20]. MiR-409 has a crucial function in cell migration, growth, differentiation, proliferation, and angiogenesis [21–23]. MiR-409–3p has tissue specific function in which it has a tumor suppressive or oncogenic role in different tumor types [24–28]. Accordingly, this review chiefly concentrated on the molecular mechanisms of miR-409 during tumor progression to introduce that as a probable diagnostic and prognostic tumor marker (Table 1).

1.1. Signaling pathways

Various signaling pathways can be regulated by miR-409 during tumor progression (Fig. 1). Growth factors have key roles in tumor progression through the activation of receptor tyrosine kinases (RTKs) that trigger PI3K/AKT axis to regulate cell proliferation and metabolism. Therefore, deregulation of PI3K/AKT can be observed frequently in different tumor types [29]. Akt1 induces cell survival through inhibition of cytochrome *c* release and maintains mitochondrial membrane integrity via elevated hexokinase association with mitochondria [30,31]. MiR-409-3 inhibited breast cancer (BC) progression through Akt1

* Corresponding author.
E-mail addresses: Meysam_moghbeli@yahoo.com, moghbelim@mums.ac.ir (M. Moghbeli).

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Table 1
Role of miR-409 in tumor progression.

STUDY	TYPE	MIR-409 TARGET GENE	SAMPLES	CLINICAL APPLICATION
song [23]	NSCLC	SPIN1	85 NT[a] A549 and H460 cell lines	Diagnosis and prognosis
weng [26]	Sarcoma	ANG	HT1080 and Cos-7 cell lines	Diagnosis
xu [27]	Bladder Cancer	c-MET	10 NT SV-HUC-1, T24, 5637, J82 and UMUC3 cell lines	Diagnosis
zheng [28]	Gastric cancer	RDX	90 NT MKN-45, SGC-7901, HGC-27, AGS, MGC-803, NCI–N87 and HEK293T cell lines	Diagnosis
Zhang [32]	Breast cancer	Akt1	30 NT MCF-7, T47D, MDA-MB-468, MDAMB-231, and HBL-100 cell lines	Diagnosis
wan [37]	Lung Adenocarcinoma	c-MET	128 NT HBE, A549, SPC-A1 and PC9 cell lines	Diagnosis and prognosis
bai [45]	Colorectal cancer	GAB1	82 NT HCT116, RKO, DLD1, SW480 and 293 T/17 cell lines	Diagnosis
long [56]	Osteosarcoma	IGFBP3	30 NT hFOB 1.19, SJSA1 and U2OS cell lines	Diagnosis
zhang [59]	Liver cancer	Stat3 and Jak2	64 NT HepG2, HHCC, HB611 and L-O2 cell lines	Diagnosis and prognosis
zhang [61]	Endometrial carcinoma	SMAD2	16 NT HEC-1A and HEC-1B cell lines	Diagnosis
zhou [64]	Cervical cancer	CDK8	47 NT HcerEpic, SiHa, SW756, CaScki and C-33 A cell lines	Diagnosis and prognosis
yu [66]	Breast cancer	RSU1	113 NT MCF10A, MDA-MB-231, MDA-MB-451, MCF-7, CAMA-1, SK-BR-3, MB-157, HCC1806, UACC-732, UACC-3199, and ZF-75-1 cell lines	Diagnosis
Feng [68]	Gastric cancer	KLF17	94 NT GES-1, MKN45, BGC823, MGC803, HGC27, and SGC7901 cell lines	Diagnosis and prognosis
su [70]	Breast cancer	TWIST1	44 NT MCF-10 A, MCF-7, and SKBR-3 cell lines	Diagnosis and prognosis
ma [73]	Breast cancer	ZEB1	111 NT MDA-MB-231 cell line	Diagnosis and prognosis
wu [74]	Osteosarcoma	ZEB1	49 NT HOS (GDC76), MG63 (GDC074), and hFOB 1.19 CRL-11372 cell lines	Diagnosis
chang [78]	HCC	BRF2	45 NT Huh-7, HMCC-97H, SMMC-7721, HepG2, and Hep3B cell lines	Diagnosis
cui [83]	Cervical cancer	ATF1	55 NT ECT1/E6E7, HeLa, Caski, C33A and Siha cell lines	Diagnosis
zhang [85]	Osteosarcoma	ELF2	36 NT MG63, SaOS-2, U2OS, G292, NHOst, and hFOB 1.19 cell lines	Diagnosis and prognosis
li [89]	Gastric cancer	PHF10	67 NT MKN45, MKN28, SGC-7901, NCI–N87, AGS, and GES-1 cell lines	Diagnosis
wang [90]	Gastric cancer	PHF10	33 NT GES-1, AGS, BGC-823, MGC-803, MKN-28, and SGC-7901 cell lines	Diagnosis
yang [92]	Breast cancer	HMGA2	64 NT MCF7, MDA-MB-231, and MCF10A cell lines	Diagnosis and prognosis
cao [98]	Glioma cancer	HMGN5	20 NT NHAs, A172, SHG44, U251, and U87 cell lines	Diagnosis
wang [106]	NSCLC	SPIN1	61 NT BEAS-2B, A549, SK-MES-1, H1703, H460 and H522 cell lines	Diagnosis and prognosis
Yu [109]	Gastric cancer	MAP7	30 NT XGC-1, MKN45, and GES1 cell lines	Diagnosis
wu [121]	Osteosarcoma	Catenin-δ1	58 NT hFOB, U2OS, MG-63, and SAOS-2 cell lines	Diagnosis
li [123]	Ovarian cancer	DLGAP5	39 NT IOSE80, SKOV-3 and OVCAR3 cell lines	Diagnosis
han [130]	Breast cancer	ERCC1	HCT-116 cell line	Diagnosis
liu [136]	NSCLC	SETDB1	196 NT A549, PC-9, NCI–H1299, NCI–H460, NCI–H1650, NCI–H520 and 16HBE cell lines	Diagnosis and prognosis
yin [141]	Lung cancer	HK2 and LDHA	66 NT BEAS-2B, H1299, A549, H460 and PC-9 cell lines	Diagnosis and prognosis
zhang [142]	Osteosarcoma	LDHA	60 NT U2OS, Saos-2, MG63 and hFOB cell lines	Diagnosis and prognosis
chen [143]	Colorectal cancer	HK2	45 NT HT-29, SW480, LOVO, HCT116, and NCM-460 cell lines	Diagnosis and prognosis
wang [146]	Renal cell carcinoma	PDK1	56 NT A-498 and 769-P cell lines	Diagnosis
ma [149]	Glioma	PDK1	47 NT U-87 MG, U-138 MG, U-118 MG, T98-G, LN-229, and LN-18 cell lines	Diagnosis
tan [152]	Colorectal cancer	Beclin-1	20 T, 10 N FHC, CCD-18Co, LoVo, HCT 116, DLD-1, SW480, HT-29 and RKO cell lines	Diagnosis and prognosis

[a] Tumor (T) tissues and Normal (N) margins.

targeting [32]. c-MET as a RTK, binds with hepatocyte growth factor (HGF) which subsequently activates Akt signaling [33]. c-MET is implicated in migration, invasion, and growth [34,35]. HGF-met autocrine loop induces tumorigenicity in lung adenocarcinoma cells [36]. There was an association between decreased miR-409–3p levels in lung adenocarcinoma (LAD) and poor prognosis. MiR-409–3p induced

LAD apoptosis, while suppressed invasion and growth through the down regulation of Akt signaling via c-Met targeting. MiR-409–3p reduced phosphorylated Akt protein that resulted in Bax up regulation and MMP9, MMP-2 and Bcl-2 down regulations [37]. Increased MMP-9 and MMP-2 levels has crucial roles in metastasis and carcinogenesis that induces penetration of cancer cells through matrix protein barriers [38]. It has been reported that c-Met up regulated MMP-9 and MMP-2 [39, 40]. There were decreased miR-409–3p levels in bladder cancer cells. MiR-409–3p inhibited bladder tumor cell invasion through c-Met targeting. There was also MMP-9 and MMP-2 down regulations in miR-409–3p transfected bladder tumor cells [27]. GAB1 is a member of Grb2-associtated binder (Gab) family that are adapter proteins involved in cell growth in response to the growth factors and cytokines [41–43]. It is an adapter protein, which recruits PI3K to the RTK in response to the growth factors [44]. miR-409–3p had anti-metastatic activity via targeting GAB1 in colorectal tumor cells [45]. IGFBP3 as a regulator of IGF is involved in cell proliferation, metabolism, and survival [46–49]. Circular RNAs (CircRNAs) are closed-loop structure ncRNAs that exert their function through miRNA sponging via binding to miRNAs and subsequent regulation of target genes in several cancers [50–54]. They have pivotal roles in modulation of biological processes [55]. There was circ_0000285 up regulation in osteosarcoma (OS) cells. circ_0000285 induced OS cell progression through sponging miR-409–3p and subsequent IGFBP3 up regulation [56].

JAK/STAT signaling is activated through cytokines interacting with receptors that subsequently translocates STAT to the nucleus and promotes expression of target gene. JAK/STAT signaling is implicated in physiological processes including cell differentiation and organ formation [57]. JAK-STAT signal transduction has oncogenic roles in tumor cell proliferation and angiogenesis via up regulation of bFGF and VEGF [58]. There was significant miR-409 down regulation while STAT3 and JAK2 up regulations in hepatocellular carcinoma (HCC) cells. MiR-409 suppressed HCC cell viability by STAT3 and JAK2 targeting [59]. Transforming growth factor-β (TGF-β) activates the receptor kinases that mediate SMAD proteins to regulate expression of target genes associated with cell proliferation, migration, and apoptosis [60]. MiR-409 reduced endometrial tumor cell growth while induced apoptosis by SMAD2 targeting [61].

Mitogen-activated protein kinase (MAPK) pathway has critical functions in regulation of cellular response toward the extracellular signals. It triggers a cascade of cytoplasmic serine/threonine kinases that finally activate the ERK, p38, and JNK effectors [62]. MAPK is a major pathway implicated in cell proliferation and apoptosis [63]. There was an association between increased circFAT1 levels in CC tissues and advanced stage, vascular invasion, and lymph node involvement. Patients with circFAT1 up regulation had reduced overall survival. Suppression of circFAT1 inhibited CC cell proliferation and invasion while increased apoptosis. There was an association between circFAT1 down regulation and decreased phosphorylated p38 MAPK and ERK1/2. Inhibition of circFAT1 also suppressed ERK1/2 and p38 MAPK signaling and had tumor suppressive roles. CircFAT1/miR-409–3p axis induced CC progression through the regulation of p38 and ERK1/2 signaling. There was CDK8 up regulation in CC cells. Suppression of CDK8 had tumor suppressive roles via the negative modulation of p38 MAPK and ERK1/2. CircFAT1 up regulated CDK8 through direct binding to miR-409–3p. CircFAT1 increased CC cell motility and survival through miR-409–3p/CDK8 axis, which subsequently activated ERK1/2 and p38 signaling [64]. RSU1 was originally characterized as an inhibitor of Ras-dependent oncogenic transformation. RSU1 inhibits cell migration via stabilization of Rsu1-PINCH1-ILK-parvin complex [65]. There were increased miR-409–5p levels in BC tissues. Inhibition of miR-409–5p suppressed BC development via RSU1 regulation [66].

1.2. Chromatin architecture and transcription factors

MiR-409 has a key role in tumor progression by regulation of transcription factors and chromatin remodelers (Fig. 2). KLF17 is a zinc-finger transcription factor that is involved in cell differentiation, proliferation, apoptosis, and migration [67]. Hyperthermia inhibited EMT through miR-409–3p up regulation and KLF17 targeting in GC [68]. TWIST1 is an EMT-related transcription factor that has a pivotal role in cancer metastasis [69]. CircCNOT2 promoted BC cell migration, proliferation, and EMT process through the modulation of miR-409–3p/TWIST1 pathway. There was also an association between increased circCNOT2 levels and poor prognosis in BC patients [70]. ZEB1 is a crucial transcription factor that promotes EMT process [71, 72]. There was miR-409–3p down regulation in BC tissues and cells that was correlated with stage and tumor size. MiR-409–3p had tumor suppressive roles via ZEB1 targeting in BC [73]. There was significant miR-409–3p down regulation in OS tissues that was associated with metastasis and advanced clinical stage. MiR-409–3p repressed OS cell proliferation through ZEB1 targeting [74]. RNA polymerase III (RNA Pol III) transcribes short non-coding RNAs that have crucial roles in cellular processes [75]. BRF1 and BRF2 have critical role in function of RNA Pol III. Up regulation of BRF2 was reported in numerous malignancies and has oncogenic roles [76,77]. BRF2 was found to be up regulated in HCC that was correlated with HCC cell migration and invasion. However, decreased miR-409–3p levels were reported in HCC cells. MiR-409–3p reduced HCC invasion by targeting BRF2 and suppressing Wnt/β-catenin axis. Decreased BRF2 levels down regulated *N*-cadherin while up regulated *E*-cadherin [78].

Activating transcription factor 1 (ATF1) modulates the transcription of target genes [79]. ATF1 had metastatic activity via MMP-2 and EGFR up regulations [80]. Warburg effect is characterized by induction of cell glycolysis that results in cancer metastasis and proliferation [81]. GLUT1 is a glucose transporter that has crucial roles as a biomarker in anaerobic glycolysis [82]. Circ_0000745 induced CC cell glycolysis, metastasis, and proliferation through the modulation of the miR-409–3p/ATF1 axis [83]. ETS transcription factors are involved in cell apoptosis, proliferation, invasion, and angiogenesis [84]. MiR-409–3p suppressed osteosarcoma cell proliferation via ELF2 targeting [85]. Plant homeodomain finger 10 (PHF10) is a zinc finger protein that induces tumor growth through caspase-3 down regulation [86]. PHF10 is also implicated in the regulation of transcription through chromatin remodeling [87]. Increased PHF10 levels have been reported in CRC and GC tissues [86,88]. Down regulation of miR-409–3p was observed in gastric cancer (GC) tissues that were correlated with invasion and tumor size. MiR-409–3p repressed SGC-7901 cell growth while induced apoptosis via targeting PHF10 [89]. There was increased circ_0001023 levels in GC cells that induced GC cell proliferation, invasion and migration while inhibited apoptosis through miR-409–3p/PHF10 axis [90].

HMGA2 is a member of high-mobility group (HMG) protein family that is implicated in cell differentiation, angiogenesis, and carcinogenesis [91]. Increased circTRIM28 levels were observed in tamoxifen-resistant BC tissues. There was an inverse correlation between up regulation of circTRIM28 and poor prognosis in BC patients. Inhibition of circTRIM28 induced tamoxifen sensitivity and BC cell apoptosis, while suppressed invasion through miR-409–3p/HMGA2 axis [92]. HMGN5 has oncogenic roles in several malignancies [93]. HMGN5 is a ubiquitous protein implicated in transcription, recombination, replication, and DNA repair [94–96]. HMGN5 is involved in tumorigenesis through the regulation of Bcl-2, CCND1, cyclin B1, and MMP2/9 [97]. There was miR-409–3p down regulation in glioma tissues and cells. MiR-409–3p suppressed glioma cell proliferation and invasion via HMGN5 regulation. miR-409–3p also modulated CCND1 and MMP2 that were correlated with cancer metastasis [98]. SATB1 binds to base-unpairing regions (BURs) and organizes chromatin into spatial loops. SATB1 bound to BUR subsequently creates a ‘docking site’ essential for binding of chromatin modifiers and transcription factors. SATB1 modulates chromatin structure and regulates gene expression [99]. MiR-409 suppressed breast tumor cell invasion and proliferation

via targeting SATB1 [100].

Spindlin 1 (SPIN1) as a chromatin reader that recognizes histone H3 (H3K4me3 and H3R8me2a) is aberrantly expressed in unfertilized oocytes and embryos in mice during gametogenesis [101]. SPIN1 also forms a ribonucleoprotein complex and modulates meiotic resumption in oocytes during meiotic maturation [102]. Moreover, increased SPIN1 level negatively regulates somatic cell cycle progression during metaphase [102]. SPIN1 induces ovarian tumor cell proliferation via WNT/TCF-4 axis [101]. MiR-409 reduced NSCLC cell proliferation and migration through targeting SPIN1. MiR-409 down regulation was reported in NSCLC tissues. There was an association between miR-409 up regulation and longer overall survival among NSCLC patients [23]. LncRNAs regulate transcription, translation, epigenetics, and genome structure [103,104]. They have vital functions in the tumorigenesis of various cancers [105]. PSMA3-AS1 up regulation was correlated with lymph node invasion, TNM stage, and shorter survival in NSCLC tissues. Inhibition of PSMA3-AS1 induced NSCLC apoptosis while reduced cell proliferation, invasion, and migration. PSMA3-AS1 had oncogenic roles in NSCLC via sponging miR-409–3p and SPIN1 up regulation [106].

1.3. Structural proteins

MiR-409 has a pivotal role in tumor progression by regulation of structural proteins (Fig. 3). Microtubule associated protein (MAP7) has a key role in microtubule reorganization during cellular polarization and differentiation. It facilitates the transportation of cytoplasmic cargoes by kinesin-1 [107]. MAP7 increased cervical cancer cell metastasis via regulation of autophagy [108]. MiR-409–3p had anti-metastatic activity via targeting MAP7. There was circNEK9 up regulation in GC cancer patients that promoted GC cell metastasis and proliferation by miR-409–3p sponging and subsequent MAP7 up regulation [109]. RDX is a cytoskeletal protein that functions as a cross-linker between actin and plasma membrane [110]. RDX regulates cell adhesion, polarity, microvilli formation and cell shape [111,112]. RDX is also implicated in tumor metastasis [113]. There was a correlation between decreased miR-409–3p levels in GC and cancer stage and lymph node involvement. MiR-409-3 inhibited GC invasion through targeting RDX [28]. Catenin-δ1 (CTNND1) is a key regulator of cell-cell adhesion [114]. Catenin-δ1 binds to juxtamembrane domain of *E*-cadherin, which subsequently stabilizes *E*-cadherin. It also regulates Rho GTPase, which modulates actin dynamics in the cytosol. Catenin-δ1 translocates to the nucleus to regulate transcription of Kaiso target genes [115]. Catenin-δ1 has oncogenic and tumor suppressor roles in different cancers. CTNND1 gene amplification is implicated in tumorigenesis [116,117]. Catenin-δ1 has an oncogenic role by modulation of Rho GTPases and oncogenic genes in the cytosol. Loss of cytoplasmic Catenin-δ1 has been also reported in cancers [118–120]. There was decreased miR-409–3p levels in osteosarcoma tissue compared to para-cancer tissues. MiR-409–3p inhibited osteosarcoma cell invasion and migration via targeting Catenin-δ1 [121]. Discs large-associated protein 5 (DLGAP5) is involved in

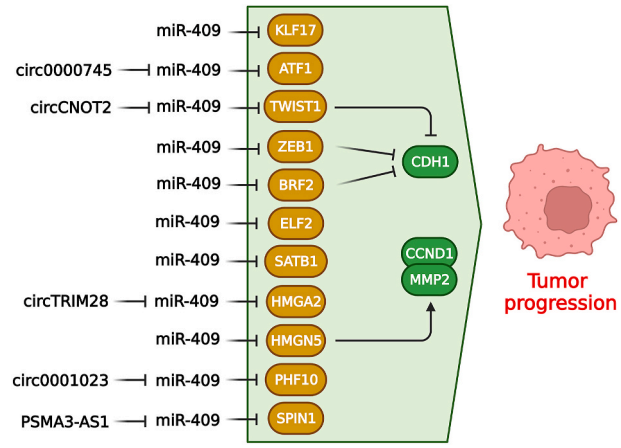

Fig. 2. Role of miR-409 during tumor progression by regulation of transcription factors and chromatin remodelers. (Created with BioRender.com).

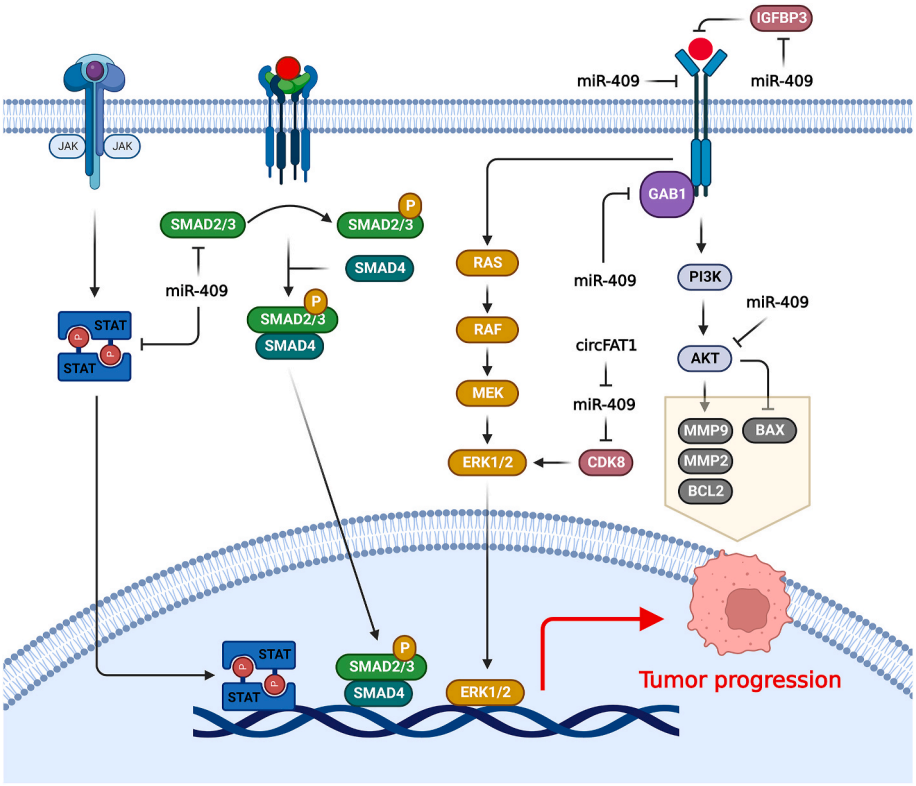

Fig. 1. Role of miR-409 during tumor progression by regulation of signaling pathways. (Created with BioRender.com).

cellular integrity and differentiation by regulation of CDH1-mediated adhesion [122]. There was miR-409–5p down regulation in OC cells that was correlated with FIGO stage and tumor size. miR-409–5p inhibited OC cell proliferation through apoptosis and G2/M arrest via DLGAP5 targeting [123]. Angiogenin (ANG) is a member of the RNAse superfamily that is implicated in activation of endothelial cells and subsequent cell proliferation, invasion, and tubular structure formation [124]. ANG promotes proteolytic mechanisms to up regulate proteases and plasmin for degradation of fibronectin and laminin in basement membrane through binding with actin in smooth muscle and endothelial cells [124]. Angiogenic factors including EGF, VEGF, aFGF, and bFGF require ANG-induced rRNA transcription for angiogenesis [125]. ANG is implicated in induction of angiogenesis and tumor cell proliferation [124]. MiR-409-3 inhibited cell proliferation, vascularization, and tumor growth via targeting ANG [26].

L-OHP is one of the main platinum-based therapeutic drugs in CRC, however long-term L-OHP use induces chemotherapy resistance [126,127]. Nucleotide excision repair (NER) has pivotal roles in promoting the DNA repair ability of tumor cells. ERCC1 promotes DNA repair ability while reduces platinum drug sensitivity through NER mechanism [128]. 5FU combined with curcumin induces chemo sensitivity of 5FU in CRC cells through reduction of mismatch repair ability [129]. Increased ERCC1, survivin, Bcl-2, MRP, GST-π and P-gp were observed in HCT-116/LOHP cells demonstrating that ERCC1 induced L-OHP resistance in CRC cells. Decreased miR-409–3p levels induced ERCC1 expression, that subsequently promoted proteins involved in drug resistance including survivin, Bcl-2, P-gp, GST-π, and MRP. Decreased ERCC1, survivin, Bcl-2, MRP, GST-π and P-gp levels were occurred after curcumin treatment [130]. Superoxide dismutases (SODs) catalyze oxygen and hydrogen peroxide production [131]. SOD1 responds to oxidative stress through suppression of apoptosis via down regulation of superoxide [132]. SETDB1 is a histone methyltransferase that participates in methylation and inhibition of various genes [133–135]. Increased SOD1 level was observed in NSCLC tissues that was correlated with poorer overall survival. SOD1 induced NSCLC cell metastasis and proliferation, whereas miR-409–3p suppressed SOD1. SETDB1 is involved in the interaction between SOD1 and miR-409–3p. SETDB1 induced methylation of miR-409–3p promoter region and miR-409–3p can target the SETDB1 in a negative feedback loop. SETDB1 regulated SOD1 and miR-409–3p in NSCLC cells, and SOD1 exerted its function through miR-409–3p/SETDB1/SOD1 loop [136].

1.4. Autophagy and cellular metabolism

Aerobic glycolysis is a typical characteristic of cancer cells that promotes tumor growth by increased glucose uptake and lactate synthesis [137,138]. It has been shown that miR-409 has a key role in tumor progression by regulation of cellular metabolism and autophagy (Fig. 3). HK2 and LDHA are crucial enzymes in glycolysis. HK2 is an enzyme that participates in glycolysis through glucose phosphorylation. LDHA catalyzes pyruvate into lactate conversion [139,140]. There was an association between elevated DUXAP8 levels in NSCLC tissues and lymph node involvement and TNM stage. DUXAP8 down regulation suppressed H1299 and A549 cell migration and growth. Meanwhile, DUXAP8 inhibition up regulated CDH1 while down regulated MMP9, c-myc, and CCND1 in NSCLC cells. DUXAP8 had oncogenic roles in NSCLC through miR-409–3p sponging and LDHA and HK2 up regulations [141]. There was circATRNL1 up regulation in OS tissue that was associated with poor prognosis. CircATRNL1 induced aerobic glycolysis through miR-409–3p sponging that resulted in LDHA up regulation [142]. There were increased LINC00630 levels in CRC tissues that had tumor suppressor roles through glycolysis inhibition via targeting miR-409–3p/HK2 axis [143]. Phosphoinositide-dependent kinase 1 (PDK1) has a key role in cellular metabolism via pyruvate dehydrogenase phosphorylation and inhibition that regulates metabolite flux by down regulation of acetyl-coenzyme A. It has also an important function in cell proliferation under hypoxia and protects cells toward apoptosis [144,145]. There were decreased miR-409–3p levels in ccRCC cells that suppressed glycolysis via PDK1 targeting. Hypoxia and HIF-1α reduced miR-409–3p levels. Hypoxia/HIF-1α increased ccRCC cell survival and glycolysis [146]. PDK1 is up regulated in glioma tissues and inhibition of PDK1 suppressed glioma colony formation [147,148]. Increased circ_0000418 level was observed in glioma cells that promoted cell cycle progression through miR-409–3p/PDK1 axis [149]. Autophagy is implicated in the development of chemo resistance [150]. Autophagy is an important cellular process that sequestered dysfunctional organelles and protein in autophagosomes to be degraded via lysosomal machinery. Autophagy acts as a response to nutrient deficiency or metabolic stress. Beclin-1 and class III PI3K promote autophagosome formation [151]. MiR-409–3p suppressed chemotherapy-induced autophagy in CRC cells by Beclin-1 targeting [152].

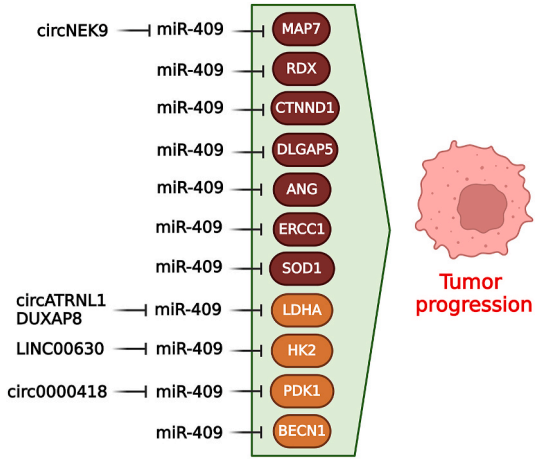

Fig. 3. Role of miR-409 during tumor progression by regulation of structural factors, autophagy, and cellular metabolism. (Created with BioRender.com).

2. Conclusions

According to the numerous reports of miR-409 deregulation in various cancers, in this review we discussed the molecular mechanisms of miR-409 during tumor progression. It was shown that miR-409 has a tumor suppressor role in which it reduces the tumor cell proliferation, growth, and migration through the regulation of signaling pathways, cellular metabolism, transcription factors, and cellular adhesion. This review can be a valuable step in suggesting miR-409 as a diagnostic biomarker and therapeutic target among cancer patients. Considering the role of miR-409 as a tumor suppressor, miR-409 mimic strategy can be used to reduce the tumor cell proliferation and growth. However, more animal studies and clinical trials are needed to use miR-409 mimic as a reliable therapeutic strategy in cancer patients.

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CRediT authorship contribution statement

Yasamin Rajabloo: Writing – original draft, Methodology. **Hanieh Latifi:** Writing – original draft. **Iman Akhlaghipour:** Writing – original draft. **Negin Taghehchian:** Writing – original draft. **Meysam Moghbeli:** Writing – review & editing, Visualization, Validation, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] Global, Collaborators GBDCoD, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017, Lancet 392 (2018) 1736–1788.
[2] H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, F. Bray, Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA A Cancer J. Clin. 71 (2021) 209–249.
[3] D.M. Parkin, S.M. Moss, Lung cancer screening: improved survival but no reduction in deaths–the role of "overdiagnosis", Cancer 89 (2000) 2369–2376.
[4] K.D. Miller, L. Nogueira, A.B. Mariotto, J.H. Rowland, K.R. Yabroff, C.M. Alfano, A. Jemal, J.L. Kramer, R.L. Siegel, Cancer treatment and survivorship statistics, 2019, CA A Cancer J. Clin. 69 (2019) 363–385.
[5] S. Simard, B. Thewes, G. Humphris, M. Dixon, C. Hayden, S. Mireskandari, G. Ozakinci, Fear of cancer recurrence in adult cancer survivors: a systematic review of quantitative studies, J Cancer Surviv 7 (2013) 300–322.
[6] R.B. Fu, X. Chen, Y. Chen, Q.H. Ye, B. Yang, Q. Shao, J.H. Zhu, Research progress on microRNAs as molecular markers in pancreatic cancer: a narrative review, J. Gastrointest. Oncol. 13 (2022) 2048–2056.
[7] R.A. Mahmoudian, I. Akhlaghipour, M. Lotfi, S. Shahidsales, M. Moghbeli, Circular RNAs as the pivotal regulators of epithelial-mesenchymal transition in gastrointestinal tumor cells, Pathol. Res. Pract. 245 (2023) 154472.
[8] A. Nasimi Shad, A. Fanoodi, A. Maharati, I. Akhlaghipour, M. Moghbeli, Molecular mechanisms of microRNA-301a during tumor progression and metastasis, Pathol. Res. Pract. 247 (2023) 154538.
[9] F. Tolue Ghasaban, I. Akhlaghipour, N. Taghehchian, A. Maharati, B. Memar, M. Moghbeli, MicroRNA-185: a non-invasive diagnostic and prognostic tumor marker, Process Biochem. 130 (2023) 645–658.
[10] F. Tolue Ghasaban, A. Maharati, I. Akhlaghipour, M. Moghbeli, MicroRNAs as the critical regulators of autophagy-mediated cisplatin response in tumor cells, Cancer Cell Int. 23 (2023) 80.
[11] I. Akhlaghipour, A.R. Bina, M.R. Mogharrabi, A. Fanoodi, A.R. Ebrahimian, S. Khojasteh Kaffash, A. Babazadeh Baghan, M.E. Khorashadizadeh, N. Taghehchian, M. Moghbeli, Single-nucleotide polymorphisms as important risk factors of diabetes among Middle East population, Hum. Genom. 16 (2022) 11.
[12] M. Gachpazan, I. Akhlaghipour, H.R. Rahimi, E. Saburi, M. Mojarrad, M. R. Abbaszadegan, M. Moghbeli, Genetic and Molecular Biology of Systemic Lupus Erythematosus Among Iranian Patients: an Overview, Autoimmunity Highlights, vol. 12, 2021, p. 2.
[13] I. Akhlaghipour, A. Fanoodi, A.S. Zangouei, N. Taghehchian, G. Khalili-Tanha, M. Moghbeli, MicroRNAs as the critical regulators of forkhead box protein family in pancreatic, thyroid, and liver cancers, Biochem. Genet. 61 (2023) 1645–1674.
[14] S. Dwivedi, P. Purohit, P. Sharma, MicroRNAs and diseases: promising biomarkers for diagnosis and therapeutics, Indian J. Clin. Biochem. 34 (2019) 243–245.
[15] B. Smolarz, A. Durczynski, H. Romanowicz, P. Hogendorf, The role of microRNA in pancreatic cancer, Biomedicines 9 (2021).
[16] A. Fanoodi, A. Maharati, I. Akhlaghipour, H.R. Rahimi, M. Moghbeli, MicroRNAs as the critical regulators of tumor angiogenesis in liver cancer, Pathol. Res. Pract. 251 (2023) 154913.
[17] I. Akhlaghipour, N. Taghehchian, A.S. Zangouei, A. Maharati, R.A. Mahmoudian, E. Saburi, M. Moghbeli, MicroRNA-377: a therapeutic and diagnostic tumor marker, Int. J. Biol. Macromol. 226 (2023) 1226–1235.
[18] A. Maharati, F. Tolue Ghasaban, I. Akhlaghipour, N. Taghehchian, A.S. Zangouei, M. Moghbeli, MicroRNA-495: a therapeutic and diagnostic tumor marker, J. Mol. Histol. 54 (2023) 559–578.
[19] N. Taghehchian, M. Lotfi, A.S. Zangouei, I. Akhlaghipour, M. Moghbeli, MicroRNAs as the Critical Regulators of Forkhead Box Protein Family during Gynecological and Breast Tumor Progression and Metastasis, vol. 28, European Journal of Medical Research, 2023, p. 330.
[20] S. Josson, M. Gururajan, P. Hu, C. Shao, G.Y. Chu, H.E. Zhau, C. Liu, K. Lao, C. L. Lu, Y.T. Lu, J. Lichterman, S. Nandana, Q. Li, A. Rogatko, D. Berel, E. M. Posadas, L. Fazli, D. Sareen, L.W. Chung, miR-409-3p/-5p promotes tumorigenesis, epithelial-to-mesenchymal transition, and bone metastasis of human prostate cancer, Clin. Cancer Res. 20 (2014) 4636–4646.
[21] S.R. Baglio, V. Devescovi, D. Granchi, N. Baldini, MicroRNA expression profiling of human bone marrow mesenchymal stem cells during osteogenic differentiation reveals Osterix regulation by miR-31, Gene 527 (2013) 321–331.
[22] D. Becker-Greene, H. Li, D. Perez-Cremades, W. Wu, F. Bestepe, D. Ozdemir, C. E. Niosi, C. Aydogan, D.P. Orgill, M.W. Feinberg, B. Icli, MiR-409-3p targets a MAP4K3-ZEB1-PLGF signaling axis and controls brown adipose tissue angiogenesis and insulin resistance, Cell. Mol. Life Sci. 78 (2021) 7663–7679.
[23] Q. Song, Q. Ji, J. Xiao, F. Li, L. Wang, Y. Chen, Y. Xu, S. Jiao, miR-409 inhibits human non-small-cell lung cancer progression by directly targeting SPIN1, molecular therapy, Nucleic acids 13 (2018) 154–163.
[24] G.H. Cao, X.L. Sun, F. Wu, W.F. Chen, J.Q. Li, W.C. Hu, Low expression of miR-409-3p is a prognostic marker for breast cancer, Eur. Rev. Med. Pharmacol. Sci. 20 (2016) 3825–3829.
[25] H.C. Nguyen, W. Xie, M. Yang, C.L. Hsieh, S. Drouin, G.S. Lee, P.W. Kantoff, Expression differences of circulating microRNAs in metastatic castration resistant prostate cancer and low-risk, localized prostate cancer, Prostate 73 (2013) 346–354.
[26] C. Weng, H. Dong, G. Chen, Y. Zhai, R. Bai, H. Hu, L. Lu, Z. Xu, miR-409-3p inhibits HT1080 cell proliferation, vascularization and metastasis by targeting angiogenin, Cancer Lett. 323 (2012) 171–179.
[27] X. Xu, H. Chen, Y. Lin, Z. Hu, Y. Mao, J. Wu, X. Xu, Y. Zhu, S. Li, X. Zheng, L. Xie, MicroRNA-409-3p inhibits migration and invasion of bladder cancer cells via targeting c-Met, Mol. Cell. 36 (2013) 62–68.
[28] B. Zheng, L. Liang, S. Huang, R. Zha, L. Liu, D. Jia, Q. Tian, Q. Wang, C. Wang, Z. Long, Y. Zhou, X. Cao, C. Du, Y. Shi, X. He, MicroRNA-409 suppresses tumour cell invasion and metastasis by directly targeting radixin in gastric cancers, Oncogene 31 (2012) 4509–4516.
[29] A. Maharati, M. Moghbeli, PI3K/AKT signaling pathway as a critical regulator of epithelial-mesenchymal transition in colorectal tumor cells, Cell Commun. Signal. : CCS 21 (2023) 201.
[30] S.G. Kennedy, E.S. Kandel, T.K. Cross, N. Hay, Akt/Protein kinase B inhibits cell death by preventing the release of cytochrome c from mitochondria, Mol. Cell Biol. 19 (1999) 5800–5810.
[31] N. Majewski, V. Nogueira, P. Bhaskar, P.E. Coy, J.E. Skeen, K. Gottlob, N. S. Chandel, C.B. Thompson, R.B. Robey, N. Hay, Hexokinase-mitochondria interaction mediated by Akt is required to inhibit apoptosis in the presence or absence of Bax and Bak, Mol. Cell 16 (2004) 819–830.
[32] G. Zhang, Z. Liu, H. Xu, Q. Yang, miR-409-3p suppresses breast cancer cell growth and invasion by targeting Akt1, Biochem. Biophys. Res. Commun. 469 (2016) 189–195.
[33] A.C. Porter, R.R. Vaillancourt, Tyrosine kinase receptor-activated signal transduction pathways which lead to oncogenesis, Oncogene 17 (1998) 1343–1352.
[34] F.J. Lowery, D. Yu, Growth factor signaling in metastasis: current understanding and future opportunities, Cancer Metastasis Rev. 31 (2012) 479–491.
[35] B. Grzelakowska-Sztabert, M. Dudkowska, Paradoxical action of growth factors: antiproliferative and proapoptotic signaling by HGF/c-MET, Growth Factors 29 (2011) 105–118.
[36] S. Yi, M.-S. Tsao, Activation of hepatocyte growth factor-met autocrine loop enhances tumorigenicity in a human lung adenocarcinoma cell line, Neoplasia 2 (2000) 226–234.
[37] L. Wan, L. Zhu, J. Xu, B. Lu, Y. Yang, F. Liu, Z. Wang, MicroRNA-409-3p functions as a tumor suppressor in human lung adenocarcinoma by targeting c-Met, Cell. Physiol. Biochem. : international journal of experimental cellular physiology, biochemistry, and pharmacology 34 (2014) 1273–1290.
[38] R.B. Hazan, G.R. Phillips, R.F. Qiao, L. Norton, S.A. Aaronson, Exogenous expression of N-cadherin in breast cancer cells induces cell migration, invasion, and metastasis, J. Cell Biol. 148 (2000) 779–790.
[39] J.-H. Baek, C. Birchmeier, M. Zenke, T. Hieronymus, The HGF receptor/Met tyrosine kinase is a key regulator of dendritic cell migration in skin immunity, J. Immunol. 189 (2012) 1699–1707.
[40] C. Birchmeier, W. Birchmeier, E. Gherardi, G.F. Vande Woude, Met, metastasis, motility and more, Nat. Rev. Mol. Cell Biol. 4 (2003) 915–925.
[41] K. Nishida, T. Hirano, The role of Gab family scaffolding adapter proteins in the signal transduction of cytokine and growth factor receptors, Cancer Sci. 94 (2003) 1029–1033.
[42] S. Yamasaki, K. Nishida, Y. Yoshida, M. Itoh, M. Hibi, T. Hirano, Gab1 is required for EGF receptor signaling and the transformation by activated ErbB2, Oncogene 22 (2003) 1546–1556.
[43] H. Gu, B.G. Neel, The 'Gab'in signal transduction, Trends Cell Biol. 13 (2003) 122–130.
[44] D. Su, Y. Zhou, S. Hu, L. Guan, C. Shi, Q. Wang, Y. Chen, C. Lu, Q. Li, X. Ma, Role of GAB1/PI3K/AKT signaling high glucose-induced cardiomyocyte apoptosis, Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 93 (2017) 1197–1204.
[45] R. Bai, C. Weng, H. Dong, S. Li, G. Chen, Z. Xu, Micro RNA-409-3p suppresses colorectal cancer invasion and metastasis partly by targeting GAB1 expression, Int. J. Cancer 137 (2015) 2310–2322.
[46] S. Deivendran, H. Marzook, T. Santhoshkumar, R. Kumar, M.R. Pillai, Metastasis-associated protein 1 is an upstream regulator of DNMT3a and stimulator of insulin-growth factor binding protein-3 in breast cancer, Sci. Rep. 7 (2017) 44225.
[47] L. Bao, H. Liu, B. You, M. Gu, S. Shi, Y. Shan, L. Li, J. Chen, Y. You, Overexpression of IGFBP3 is associated with poor prognosis and tumor metastasis in nasopharyngeal carcinoma, Tumor Biol. 37 (2016) 15043–15052.
[48] M. Canel, A. Byron, A.H. Sims, J. Cartier, H. Patel, M.C. Frame, V.G. Brunton, B. Serrels, A. Serrels, Nuclear FAK and Runx1 cooperate to regulate IGFBP3, cell-cycle progression, and tumor growth, Cancer Res. 77 (2017) 5301–5312.
[49] L.J. Schedlich, V.M. Yenson, R.C. Baxter, TGF-β-induced expression of IGFBP-3 regulates IGF1R signaling in human osteosarcoma cells, Mol. Cell. Endocrinol. 377 (2013) 56–64.

[50] R. Ashwal-Fluss, M. Meyer, N.R. Pamudurti, A. Ivanov, O. Bartok, M. Hanan, N. Evantal, S. Memczak, N. Rajewsky, S. Kadener, circRNA biogenesis competes with pre-mRNA splicing, Mol. Cell 56 (2014) 55–66.
[51] L.-L. Chen, L. Yang, Regulation of circRNA biogenesis, RNA Biol. 12 (2015) 381–388.
[52] S. Meng, H. Zhou, Z. Feng, Z. Xu, Y. Tang, P. Li, M. Wu, CircRNA: functions and properties of a novel potential biomarker for cancer, Mol. Cancer 16 (2017) 1–8.
[53] X. Jin, C.-y. Feng, Z. Xiang, Y.-p. Chen, Y.-m. Li, CircRNA expression pattern and circRNA-miRNA-mRNA network in the pathogenesis of nonalcoholic steatohepatitis, Oncotarget 7 (2016) 66455.
[54] E. Andrés-León, R. Núñez-Torres, A.M. Rojas, miARma-Seq: a comprehensive tool for miRNA, mRNA and circRNA analysis, Sci. Rep. 6 (2016) 25749.
[55] B. Han, J. Chao, H. Yao, Circular RNA and its mechanisms in disease: from the bench to the clinic, Pharmacol. Therapeut. 187 (2018) 31–44.
[56] Z. Long, F. Gong, Y. Li, Z. Fan, J. Li, Circ_0000285 regulates proliferation, migration, invasion and apoptosis of osteosarcoma by miR-409-3p/IGFBP3 axis, Cancer Cell Int. 20 (2020) 481.
[57] J.G. Williams, STAT signalling in cell proliferation and in development, Curr. Opin. Genet. Dev. 10 (2000) 503–507.
[58] M. Zhao, F.-H. Gao, J.-Y. Wang, F. Liu, H.-H. Yuan, W.-Y. Zhang, B. Jiang, JAK2/STAT3 signaling pathway activation mediates tumor angiogenesis by upregulation of VEGF and bFGF in non-small-cell lung cancer, Lung Cancer 73 (2011) 366–374.
[59] C.S. Zhang, Y. Lin, F.B. Sun, J. Gao, B. Han, S.J. Li, miR-409 down-regulates Jak-Stat pathway to inhibit progression of liver cancer, Eur. Rev. Med. Pharmacol. Sci. 23 (2019) 146–154.
[60] K. Tzavlaki, A. Moustakas, TGF-Beta signaling, Biomolecules 10 (2020).
[61] C. Zhang, B. Wang, L. Wu, MicroRNA-409 may function as a tumor suppressor in endometrial carcinoma cells by targeting Smad2, Mol. Med. Rep. 19 (2019) 622–628.
[62] A. Maharati, M. Moghbeli, Long non-coding RNAs as the critical regulators of PI3K/AKT, TGF-beta, and MAPK signaling pathways during breast tumor progression, J. Transl. Med. 21 (2023) 556.
[63] M. Cargnello, P.P. Roux, Activation and function of the MAPKs and their substrates, the MAPK-activated protein kinases, Microbiol. Mol. Biol. Rev. 75 (2011) 50–83.
[64] B. Zhou, T. Li, R. Xie, J. Zhou, J. Liu, Y. Luo, X. Zhang, CircFAT1 facilitates cervical cancer malignant progression by regulating ERK1/2 and p38 MAPK pathway through miR-409-3p/CDK8 axis, Drug Dev. Res. 82 (2021) 1131–1143.
[65] G.W. Dougherty, C. Jose, M. Gimona, M.L. Cutler, The Rsu-1-PINCH1-ILK complex is regulated by Ras activation in tumor cells, Eur. J. Cell Biol. 87 (2008) 721–734.
[66] H. Yu, H. Xing, W. Han, Y. Wang, T. Qi, C. Song, Z. Xu, H. Li, Y. Huang, MicroRNA-409-5p is upregulated in breast cancer and its downregulation inhibits cancer development through downstream target of RSU1, Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine 39 (2017) 1010428317701647.
[67] J. Van Vliet, L.A. Crofts, K.G. Quinlan, R. Czolij, A.C. Perkins, M. Crossley, Human KLF17 is a new member of the Sp/KLF family of transcription factors, Genomics 87 (2006) 474–482.
[68] J. Feng, K. Li, G. Liu, Y. Feng, H. Shi, X. Zhang, Precision hyperthermia-induced miRNA-409-3p upregulation inhibits migration, invasion, and EMT of gastric cancer cells by targeting KLF17, Biochem. Biophys. Res. Commun. 549 (2021) 113–119.
[69] T. Liu, X. Zhao, X. Zheng, Y. Zheng, X. Dong, N. Zhao, S. Liao, B. Sun, The EMT transcription factor, Twist1, as a novel therapeutic target for pulmonary sarcomatoid carcinomas, Int. J. Oncol. 56 (2020) 750–760.
[70] Q. Su, H. Shen, B. Gu, N. Zhu, Circular RNA CNOT2 knockdown regulates twist family BHLH transcription factor via targeting microRNA 409-3p to prevent breast cancer invasion, migration and epithelial-mesenchymal transition, Bioengineered 12 (2021) 9058–9069.
[71] S. Josson, M. Gururajan, P. Hu, C. Shao, G.C.-Y. Chu, H.E. Zhau, C. Liu, K. Lao, C.-L. Lu, Y.-T. Lu, miR-409-3p/-5p promotes tumorigenesis, epithelial-to-mesenchymal transition, and bone metastasis of human prostate cancer, Clin. Cancer Res. 20 (2014) 4636–4646.
[72] C. Vandewalle, F. Van Roy, G. Berx, The role of the ZEB family of transcription factors in development and disease, Cell. Mol. Life Sci. 66 (2009) 773–787.
[73] Z. Ma, Y. Li, J. Xu, Q. Ren, J. Yao, X. Tian, MicroRNA-409-3p regulates cell invasion and metastasis by targeting ZEB1 in breast cancer, IUBMB Life 68 (2016) 394–402.
[74] L. Wu, Y. Zhang, Z. Huang, H. Gu, K. Zhou, X. Yin, J. Xu, MiR-409-3p inhibits cell proliferation and invasion of osteosarcoma by targeting zinc-finger E-box-binding homeobox-1, Front. Pharmacol. 10 (2019) 137.
[75] L. Li, Z. Yu, D. Zhao, Y. Ren, H. Hou, Y. Xu, Structure of human RNA polymerase III elongation complex, Cell Res. 31 (2021) 791–800.
[76] C. Henique, G. Bollée, X. Loyer, F. Grahammer, N. Dhaun, M. Camus, J. Vernerey, L. Guyonnet, F. Gaillard, H. Lazareth, Genetic and pharmacological inhibition of microRNA-92a maintains podocyte cell cycle quiescence and limits crescentic glomerulonephritis, Nat. Commun. 8 (2017) 1829.
[77] G. Zhang, Z. Liu, H. Xu, Q. Yang, miR-409-3p suppresses breast cancer cell growth and invasion by targeting Akt1, Biochem. Biophys. Res. Commun. 469 (2016) 189–195.
[78] J.-H. Chang, B.-W. Xu, D. Shen, W. Zhao, Y. Wang, J.-l. Liu, G.-X. Meng, G.-Z. Li, Z.-L. Zhang, BRF2 is mediated by microRNA-409-3p and promotes invasion and metastasis of HCC through the Wnt/β-catenin pathway, Cancer Cell Int. 23 (2023) 1–12.
[79] Q. Hao, X. Zhao, Y. Zhang, Z. Dong, T. Hu, P. Chen, Targeting overexpressed activating transcription factor 1 (ATF1) inhibits proliferation and migration and enhances sensitivity to paclitaxel in esophageal cancer cells, Medical Science Monitor Basic Research 23 (2017) 304.
[80] J. Cui, Z. Yin, G. Liu, X. Chen, X. Gao, H. Lu, W. Li, D. Lin, Activating transcription factor 1 promoted migration and invasion in lung cancer cells through regulating EGFR and MMP-2, Mol. Carcinog. 58 (2019) 1919–1924.
[81] P. Icard, S. Shulman, D. Farhat, J.-M. Steyaert, M. Alifano, H. Lincet, How the Warburg effect supports aggressiveness and drug resistance of cancer cells? Drug Resist. Updates 38 (2018) 1–11.
[82] T. Amann, C. Hellerbrand, GLUT1 as a therapeutic target in hepatocellular carcinoma, Expert Opin. Ther. Targets 13 (2009) 1411–1427.
[83] X. Cui, J. Chen, Y. Zheng, H. Shen, Circ_0000745 promotes the progression of cervical cancer by regulating miR-409-3p/ATF1 Axis, Cancer Biother. Rad. 37 (2022) 766–778.
[84] A.D. Sharrocks, The ETS-domain transcription factor family, Nat. Rev. Mol. Cell Biol. 2 (2001) 827–837.
[85] J. Zhang, W. Hou, J. Jia, Y. Zhao, B. Zhao, MiR-409-3p regulates cell proliferation and tumor growth by targeting E74-like factor 2 in osteosarcoma, FEBS open bio 7 (2017) 348–357.
[86] M. Wei, B. Liu, L. Su, J. Li, J. Zhang, Y. Yu, M. Yan, Z. Yang, X. Chen, J. Liu, A novel plant homeodomain finger 10–mediated antiapoptotic mechanism involving repression of caspase-3 in gastric cancer cells, Mol. Cancer Therapeut. 9 (2010) 1764–1774.
[87] R. Aasland, T.J. Gibson, A.F. Stewart, The PHD finger: implications for chromatin-mediated transcriptional regulation, Trends Biochem. Sci. 20 (1995) 56–59.
[88] D. Cavalieri, P. Dolara, E. Mini, C. Luceri, C. Castagnini, S. Toti, K. Maciag, C. De Filippo, S. Nobili, M. Morganti, Analysis of gene expression profiles reveals novel correlations with the clinical course of colorectal cancer, Oncol. Res. 16 (2007) 535–548.
[89] C. Li, H. Nie, M. Wang, L. Su, J. Li, B. Yu, M. Wei, J. Ju, Y. Yu, M. Yan, Q. Gu, Z. Zhu, B. Liu, MicroRNA-409-3p regulates cell proliferation and apoptosis by targeting PHF10 in gastric cancer, Cancer Lett. 320 (2012) 189–197.
[90] Y. Wang, J. Zhang, X. Chen, L. Gao, Circ_0001023 promotes proliferation and metastasis of gastric cancer cells through miR-409-3p/PHF10 Axis, OncoTargets Ther. 13 (2020) 4533–4544.
[91] N. Krahn, M. Meier, V. To, E.P. Booy, K. McEleney, J.D. O'Neil, S.A. McKenna, T. R. Patel, J. Stetefeld, Nanoscale assembly of high-mobility group AT-Hook 2 protein with DNA replication fork, Biophys. J. 113 (2017) 2609–2620.
[92] S. Yang, C. Zou, Y. Li, X. Yang, W. Liu, G. Zhang, N. Lu, Knockdown circTRIM28 enhances tamoxifen sensitivity via the miR-409-3p/HMGA2 axis in breast cancer, Reprod. Biol. Endocrinol. : RB Elektron. 20 (2022) 146.
[93] Z. Shi, R. Tang, D. Wu, X. Sun, Research advances in HMGN5 and cancer, Tumor Biol. 37 (2016) 1531–1539.
[94] H. Shirakawa, D. Landsman, Y.V. Postnikov, M. Bustin, NBP-45, a novel nucleosomal binding protein with a tissue-specific and developmentally regulated expression, J. Biol. Chem. 275 (2000) 6368–6374.
[95] L.M. King, C.A. Francomano, Characterization of a human gene encoding nucleosomal binding protein NSBP1, Genomics 71 (2001) 163–173.
[96] R. Hock, T. Furusawa, T. Ueda, M. Bustin, HMG chromosomal proteins in development and disease, Trends Cell Biol. 17 (2007) 72–79.
[97] S.-Q. Ji, L. Yao, X.-Y. Zhang, X.-S. Li, L.-Q. Zhou, Knockdown of the nucleosome binding protein 1 inhibits the growth and invasion of clear cell renal cell carcinoma cells in vitro and in vivo, J. Exp. Clin. Cancer Res. 31 (2012) 1–8.
[98] Y. Cao, L. Zhang, M. Wei, X. Jiang, D. Jia, MicroRNA-409-3p represses glioma cell invasion and proliferation by targeting high-mobility group nucleosome-binding domain 5, Oncology research 25 (2017) 1097–1107.
[99] Z. Pan, W. Jing, K. He, L. Zhang, X. Long, SATB1 Is Correlated with Progression and Metastasis of Breast Cancers: A Meta-Analysis, S. Karger AG, Basel, Switzerland, 2016, pp. 1975–1983.
[100] Z. Chen, M.X. Sang, C.Z. Geng, H.Q. Jia, MicroRNA-409 regulates the proliferation and invasion of breast cancer cell lines by targeting special AT-rich sequence-binding protein 1 (SATB1), Bioengineered 13 (2022) 13045–13054.
[101] J.-X. Wang, Q. Zeng, L. Chen, J.-C. Du, X.-L. Yan, H.-F. Yuan, C. Zhai, J.-N. Zhou, Y.-L. Jia, W. Yue, SPINDLIN1 promotes cancer cell proliferation through activation of WNT/TCF-4 signaling, Mol. Cancer Res. 10 (2012) 326–335.
[102] J.-W. Choi, M.-H. Zhao, S. Liang, J. Guo, Z.-L. Lin, Y.-H. Li, Y.-J. Jo, N.-H. Kim, X.-S. Cui, Spindlin 1 is essential for metaphase II stage maintenance and chromosomal stability in porcine oocytes, MHR: Basic science of reproductive medicine 23 (2017) 166–176.
[103] U.P.R. Soci, S.F.S. Melo, J.L.P. Gomes, A.C. Silveira, C. Nóbrega, E.M. de Oliveira, Exercise training and epigenetic regulation: multilevel modification and regulation of gene expression, Exercise for Cardiovascular Disease Prevention and Treatment: from Molecular to Clinical, Partisans 2 (2017) 281–322.
[104] E. Cusanelli, P. Chartrand, Telomeric repeat-containing RNA TERRA: a noncoding RNA connecting telomere biology to genome integrity, Front. Genet. 6 (2015) 143.
[105] L. Benetatos, E. Voulgaris, G. Vartholomatos, The crosstalk between long non-coding RNAs and PI3K in cancer, Med. Oncol. 34 (2017) 1–13.
[106] L. Wang, L. Wu, J. Pang, Long noncoding RNA PSMA3-AS1 functions as a microRNA-409-3p sponge to promote the progression of non-small cell lung carcinoma by targeting spindlin 1, Oncol. Rep. 44 (2020) 1550–1560.
[107] L.S. Ferro, Q. Fang, L. Eshun-Wilson, J. Fernandes, A. Jack, D.P. Farrell, M. Golcuk, T. Huijben, K. Costa, M. Gur, F. DiMaio, E. Nogales, A. Yildiz, Structural and functional insight into regulation of kinesin-1 by microtubule-associated protein MAP7, Science (New York, N.Y.) 375 (2022) 326–331.

[108] L. Zhang, X. Liu, L. Song, H. Zhai, C. Chang, MAP7 promotes migration and invasion and progression of human cervical cancer through modulating the autophagy, Cancer Cell Int. 20 (2020) 1–8.
[109] L. Yu, J. Xie, X. Liu, Y. Yu, S. Wang, Plasma exosomal CircNEK9 accelerates the progression of gastric cancer via miR-409-3p/MAP7 Axis, Dig. Dis. Sci. 66 (2021) 4274–4289.
[110] K.P. Hoeflich, M. Ikura, Radixin: cytoskeletal adopter and signaling protein, Int. J. Biochem. Cell Biol. 36 (2004) 2131–2136.
[111] M. Arpin, D. Chirivino, A. Naba, I. Zwaenepoel, Emerging role for ERM proteins in cell adhesion and migration, Cell Adhes. Migrat. 5 (2011) 199–206.
[112] G. Liu, T.A. Voyno-Yasenetskaya, Radixin stimulates Rac1 and Ca2+/calmodulin-dependent kinase, CaMKII: cross-talk with Gα13 signaling, J. Biol. Chem. 280 (2005) 39042–39049.
[113] H. Yu, Y. Zhang, L. Ye, W.G. Jiang, The FERM family proteins in cancer invasion and metastasis, Frontiers in Bioscience-Landmark 16 (2011) 1536–1550.
[114] N. Ishiyama, S.-H. Lee, S. Liu, G.-Y. Li, M.J. Smith, L.F. Reichardt, M. Ikura, Dynamic and static interactions between p120 catenin and E-cadherin regulate the stability of cell-cell adhesion, Cell 141 (2010) 117–128.
[115] R.C. Schackmann, M. Tenhagen, R.A. van de Ven, P.W. Derksen, p120-catenin in cancer–mechanisms, models and opportunities for intervention, J. Cell Sci. 126 (2013) 3515–3525.
[116] Y. Liu, Y. Wang, Y. Zhang, Y. Miao, Y. Zhao, P.-X. Zhang, G.-Y. Jiang, J.-Y. Zhang, Y. Han, X.-Y. Lin, Abnormal expression of p120-catenin, E-cadherin, and small GTPases is significantly associated with malignant phenotype of human lung cancer, Lung Cancer 63 (2009) 375–382.
[117] S.D. Castillo, B. Angulo, A. Suarez-Gauthier, L. Melchor, P.P. Medina, L. Sanchez-Verde, J. Torres-Lanzas, G. Pita, J. Benitez, M. Sanchez-Cespedes, Gene amplification of the transcription factor DP1 and CTNND1 in human lung cancer, J. Pathol. 222 (2010) 89–98.
[118] K. Syrigos, A. Karayiannakis, E. Syrigou, K. Harrington, M. Pignatelli, Abnormal expression of p120 correlates with poor survival in patients with bladder cancer, Eur. J. Cancer 34 (1998) 2037–2040.
[119] D.I. Bellovin, R.C. Bates, A. Muzikansky, D.L. Rimm, A.M. Mercurio, Altered localization of p120 catenin during epithelial to mesenchymal transition of colon carcinoma is prognostic for aggressive disease, Cancer Res. 65 (2005) 10938–10945.
[120] K.M. Mann, J.M. Ward, C.C.K. Yew, A. Kovochich, D.W. Dawson, M.A. Black, B. T. Brett, T.E. Sheetz, A.J. Dupuy, A.P.C.G. Initiative, Sleeping Beauty mutagenesis reveals cooperating mutations and pathways in pancreatic adenocarcinoma, Proc. Natl. Acad. Sci. USA 109 (2012) 5934–5941.
[121] S. Wu, X. Du, M. Wu, H. Du, X. Shi, T. Zhang, MicroRNA-409-3p inhibits osteosarcoma cell migration and invasion by targeting catenin-δ1, Gene 584 (2016) 83–89.
[122] P. Laprise, A. Viel, N. Rivard, Human homolog of disc-large is required for adherens junction assembly and differentiation of human intestinal epithelial cells, J. Biol. Chem. 279 (2004) 10157–10166.
[123] W. Li, J. Lin, J. Huang, Z. Chen, Q. Sheng, F. Yang, X. Yang, X. Cui, MicroRNA-409-5p inhibits cell proliferation, and induces G(2)/M phase arrest and apoptosis by targeting DLGAP5 in ovarian cancer cells, Oncol. Lett. 24 (2022) 261.
[124] X. Gao, Z. Xu, Mechanisms of action of angiogenin, Acta Biochim. Biophys. Sin. 40 (2008) 619–624.
[125] K. Kishimoto, S. Liu, T. Tsuji, K.A. Olson, G.-f. Hu, Endogenous angiogenin in endothelial cells is a general requirement for cell proliferation and angiogenesis, Oncogene 24 (2005) 445–456.
[126] J. Yin, L. Wang, Y. Wang, H. Shen, X. Wang, L. Wu, Curcumin reverses oxaliplatin resistance in human colorectal cancer via regulation of TGF-β/Smad2/3 signaling pathway, OncoTargets Ther. 12 (2019) 3893.
[127] X. Ying, Y. Qi, C. Center, Targeted therapy of colorectal cancer and its drug resistance mechanism, World Clinical Drugs 38 (2017) 721–726.
[128] L. Gossage, S. Madhusudan, Current status of excision repair cross complementing-group 1 (ERCC1) in cancer, Cancer Treat Rev. 33 (2007) 565–577.
[129] M. Shakibaei, C. Buhrmann, P. Kraehe, P. Shayan, C. Lueders, A. Goel, Curcumin chemosensitizes 5-fluorouracil resistant MMR-deficient human colon cancer cells in high density cultures, PLoS One 9 (2014) e85397.
[130] W. Han, H. Yin, H. Ma, Y. Wang, D. Kong, Z. Fan, Curcumin regulates ERCC1 expression and enhances oxaliplatin sensitivity in resistant colorectal cancer cells through its effects on miR-409-3p, evidence-based complementary and alternative medicine, eCAM 2020 (2020) 8394574.
[131] K. Watanabe, S. Shibuya, Y. Ozawa, H. Nojiri, N. Izuo, K. Yokote, T. Shimizu, Superoxide dismutase 1 loss disturbs intracellular redox signaling, resulting in global age-related pathological changes, BioMed Res. Int. 2014 (2014).
[132] C.K. Tsang, Y. Liu, J. Thomas, Y. Zhang, X.S. Zheng, Superoxide dismutase 1 acts as a nuclear transcription factor to regulate oxidative stress resistance, Nat. Commun. 5 (2014) 3446.
[133] Q. Fei, K. Shang, J. Zhang, S. Chuai, D. Kong, T. Zhou, S. Fu, Y. Liang, C. Li, Z. Chen, Histone methyltransferase SETDB1 regulates liver cancer cell growth through methylation of p53, Nat. Commun. 6 (2015) 8651.
[134] L. Rivière, L. Gérossier, O. Hantz, C. Neuveut, Hepatitis B virus and chromatin remodeling: HBx counteracts SETDB1/HP1/H3K9me3 transcriptional silencing, M-S (Med. Sci.): Méd./Sci. 32 (2016) 455–458.
[135] A.V. Karanth, R.R. Maniswami, S. Prashanth, H. Govindaraj, R. Padmavathy, S. K. Jegatheesan, R. Mullangi, S. Rajagopal, Emerging role of SETDB1 as a therapeutic target, Expert Opin. Ther. Targets 21 (2017) 319–331.
[136] S. Liu, B. Li, J. Xu, S. Hu, N. Zhan, H. Wang, C. Gao, J. Li, X. Xu, SOD1 promotes cell proliferation and metastasis in non-small cell lung cancer via an miR-409-3p/SOD1/SETDB1 epigenetic regulatory feedforward loop, Front. Cell Dev. Biol. 8 (2020) 213.
[137] D. Hanahan, R.A. Weinberg, Hallmarks of cancer: the next generation, Cell 144 (2011) 646–674.
[138] M.G. Vander Heiden, L.C. Cantley, C.B. Thompson, Understanding the Warburg effect: the metabolic requirements of cell proliferation, Science (New York, N.Y.) 324 (2009) 1029–1033.
[139] D. Mirebeau-Prunier, S. Le Pennec, C. Jacques, J.-F. Fontaine, N. Gueguen, N. Boutet-Bouzamondo, A. Donnart, Y. Malthièry, F. Savagner, Estrogen-related receptor alpha modulates lactate dehydrogenase activity in thyroid tumors, PLoS One 8 (2013) e58683.
[140] L. Jiao, H.-L. Zhang, D.-D. Li, K.-L. Yang, J. Tang, X. Li, J. Ji, Y. Yu, R.-Y. Wu, S. Ravichandran, Regulation of glycolytic metabolism by autophagy in liver cancer involves selective autophagic degradation of HK2 (hexokinase 2), Autophagy 14 (2018) 671–684.
[141] D. Yin, L. Hua, J. Wang, Y. Liu, X. Li, Long non-coding RNA DUXAP8 facilitates cell viability, migration, and glycolysis in non-small-cell lung cancer via regulating HK2 and LDHA by inhibition of miR-409-3p, OncoTargets Ther. 13 (2020) 7111–7123.
[142] Q. Zhang, L. Wang, L. Cao, T. Wei, Novel circular RNA circATRNL1 accelerates the osteosarcoma aerobic glycolysis through targeting miR-409-3p/LDHA, Bioengineered 12 (2021) 9965–9975.
[143] J. Chen, R. Wang, E. Lu, S. Song, Y. Zhu, LINC00630 as a miR-409-3p sponge promotes apoptosis and glycolysis of colon carcinoma cells via regulating HK2, Am. J. Tourism Res. 14 (2022) 863–875.
[144] M. Kato, J. Li, J.L. Chuang, D.T. Chuang, Distinct structural mechanisms for inhibition of pyruvate dehydrogenase kinase isoforms by AZD7545, dichloroacetate, and radicicol, Structure 15 (2007) 992–1004.
[145] T. McFate, A. Mohyeldin, H. Lu, J. Thakar, J. Henriques, N.D. Halim, H. Wu, M. J. Schell, T.M. Tsang, O. Teahan, S. Zhou, J.A. Califano, N.H. Jeoung, R.A. Harris, A. Verma, Pyruvate dehydrogenase complex activity controls metabolic and malignant phenotype in cancer cells, J. Biol. Chem. 283 (2008) 22700–22708.
[146] Y. Wang, Y. He, H. Bai, Y. Dang, J. Gao, P. Lv, Phosphoinositide-dependent kinase 1-associated glycolysis is regulated by miR-409-3p in clear cell renal cell carcinoma, J. Cell. Biochem. 120 (2019) 126–134.
[147] Z. Wang, X. Xu, N. Liu, Y. Cheng, W. Jin, P. Zhang, X. Wang, H. Yang, H. Liu, Y. Tu, SOX9-PDK1 axis is essential for glioma stem cell self-renewal and temozolomide resistance, Oncotarget 9 (2018) 192.
[148] P.A. Gagliardi, A. Puliafito, L. Primo, PDK1: at the crossroad of cancer signaling pathways, in: Seminars in Cancer Biology, Elsevier, 2018, pp. 27–35.
[149] Z. Ma, Z. Chen, Y. Zhou, Y. Li, S. Li, H. Wang, J. Feng, Hsa_circ_0000418 promotes the progression of glioma by regulating microRNA-409-3p/pyruvate dehydrogenase kinase 1 axis, Bioengineered 13 (2022) 7541–7552.
[150] Y. Zhou, K. Sun, Y. Ma, H. Yang, Y. Zhang, X. Kong, L. Wei, Autophagy inhibits chemotherapy-induced apoptosis through downregulating Bad and Bim in hepatocellular carcinoma cells, Sci. Rep. 4 (2014) 5382.
[151] G.V. Helgason, T.L. Holyoake, K.M. Ryan, Role of autophagy in cancer prevention, development and therapy, Essays Biochem. 55 (2013) 133–151.
[152] S. Tan, H. Shi, M. Ba, S. Lin, H. Tang, X. Zeng, X. Zhang, miR-409-3p sensitizes colon cancer cells to oxaliplatin by inhibiting Beclin-1-mediated autophagy, Int. J. Mol. Med. 37 (2016) 1030–1038.