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The microRNA miR-10b as a potentially promising biomarker to predict the prognosis of cancer patients: a meta-analysis.

Increased expression of miR-10b is associated with the susceptibility to lymph node metastasis and distant metastasis in various tumors.The results of the meta-analysis revealed that lymph node metastasis occurred more frequently in the patients group with high expression level of miR-10b than in the patients group with low expression level of miR-10b (OR=4.65, 95% CI: 3.40-6.37, P ¡0.00001, fixed-effects model). Additionally, a similar result was observed in the association between miR-10b expression and distant metastasis (OR=2.70, 95% CI: 1.79-4.08, P ¡0.00001, fixed-effects model).In this study, a meta-analysis, including the majority of the relevant articles, was conducted to investigate the association of the miR-10b expression level with metastasis in cancer patients. A total of 962 patients with carcinoma from 9 studies were included in analysis.This meta-analysis demonstrated that the overexpression of miR-10b was significantly correlated with metastasis status, and indicated the potential clinical use of miR-10b as a molecular biomarker, particularly in assessing prognosis for patients with cancers.

mir-10b, metastasis, expression, patients, meta-analysis, level, studies, [1]

Differential Expression Profiles of the Transcriptome in Breast Cancer Cell Lines Revealed by Next Generation Sequencing.

As MCF-7 and MDA-MB-231 cells are the typical cell lines of two clinical breast tumour subtypes, the aim of the present study was to elucidate the transcriptome differences between MCF-7 and MDA-MB-231 breast cancer cell lines.The mRNA, miRNA (MicroRNA) and lncRNA (Long non-coding RNA) expression profiles were examined using NGS (next generation sequencing) instrument Illumina HiSeq-2500. Differentially expressed mRNAs are primarily involved in biological processes of locomotion, biological adhesion, ECM-receptor interaction pathway and focal adhesion. In the targeting regulatory network of differentially expressed RNAs, mRNAs and miRNAs are primarily associated with tumour metastasis, but the functions of lncRNAs remain uncharacterized.These results provide a basis for future studies of breast cancer metastasis and drug resistance.

cells, rna, mcf-7, mda-mb-231, mrna, expressed, [2]

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MiRNAs are Unlikely to be Involved in Retinoid Receptor Gene Regulation in Pancreatic Cancer Cells.

Retinoid receptors and retinoic acid were reported to be down-regulated in pancreatic duct adenocarcinoma (PDAC) compared to normal pancreas. The aim of this study was to find out whether selected dysregulated miRNAs in PDAC are responsible for the decreased level of retinoid receptors.Bioinformatics, real-time PCR, western blot analysis as well as molecular manipulation with miRNA in cells of PDAC were carried out.We first performed bioinformatics research to identify conserved target sequences for deregulated miRNAs within the 3'UTR region of retinoid receptor mRNA. This research revealed binding sites for miR-138, -27a, -27b, -206, -613, -9-5p, -27a/b-3p and -27a.

mirnas, retinoid, cells, pdac, receptors, selected, [3]

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mirnas, retinoid, cells, pdac, receptors, selected, [3]

Prognostic value of microRNA expression levels in pancreatic adenocarcinoma: a review of the literature.

Clinical and pathologic markers of prognosis and patterns of failure help guide clinicians in selecting patients for adjuvant therapy after surgical resection for pancreatic adenocarcinoma (PDAC). Here, we review and summarize the current literature regarding associations between microRNA expression and overall survival in PDAC patients.We conducted a systematic search in the PubMed database to identify all primary research studies reporting prognostic associations between tumor and/or serum microRNA expression and overall survival in PDAC patients. We summarize the preclinical and clinical data implicating these miRNAs in various molecular signaling pathways and cellular functions.There is growing evidence that miRNA expression profiles have the potential to provide tumor-specific prognostic information to assist clinicians in more appropriately selecting patients for adjuvant therapy.

mirnas, pdac, clinical, survival, prognostic, reported, [4]

MicroRNAs in the development and neoplasia of the mammary gland.

Study on the role of microRNAs (miRs) as regulators of gene expression through posttranscriptional gene silencing is currently gaining much interest,due to their wide involvement in different physiological processes. In addition, lactogenic hormones influence miR expression as evidenced by overexpression of miR-148a in cow mammary epithelial cells, leading to enhanced lactation. This review focuses on the recent findings concerning the role of miRs in developmental stages of the mammary gland (mainly lactation and involution stages) and their involvement in breast cancer progression.

mirs, cancer, lactation, breast, mammary, expression, [5]

A BAP1 Mutation-specific MicroRNA Signature Predicts Clinical Outcomes in Clear Cell Renal Cell Carcinoma Patients with Wild-type BAP1.

Background: Clear cell renal cell carcinoma (ccRCC) is the most prevalent histologic subtype of kidney cancers in adults, which could be divided into two distinct subgroups according to the BRCA1 associated protein-1 (BAP1) mutation status. In the current study, we comprehensively analyzed the genome-wide microRNA (miRNA) expression profiles in ccRCC, with the aim to identify the differentially expressed miRNAs between BAP1 mutant and wild-type tumors, and generate a BAP1 mutation-specific miRNA signature for ccRCC patients with wild-type BAP1. Conclusions: In summary, our study identified a total of 33 miRNAs differentially expressed between BAP1 mutant and wild-type tumors, and generated a BAP1 mutation-specific miRNA signature including eleven miRNAs, which could serve as a novel prognostic biomarker for ccRCC patients with wild-type BAP1.

bap1, mirna, wild-type, ccrcc, patients, mutant, [6]

Upregulation of Serum miR-10b Is Associated with Poor Prognosis in Patients with Melanoma.

Aberrant expression of microRNAs (miRNAs) are believed to play a central role in the initiation and development of cancer. Our results showed that the expression level of miR-10b was significantly increased in metastasis melanoma cells and melanoma patients compared to their respective controls. In addition, serum miR-10b expression level was able to discriminate melanoma patients from healthy volunteers as well differentiate melanoma patients at different clinical stage with high accuracy.

melanoma, mir-10b, serum, expression, patients, level, clinical, [7]

Activation of Matrix Hyaluronan-Mediated CD44 Signaling, Epigenetic Regulation and Chemoresistance in Head and Neck Cancer Stem Cells.

Head and neck squamous cell carcinoma (HNSCC) is a solid tumor composed by a genotypically and phenotypically heterogeneous population of neoplastic cells types. Hyaluronan (HA), an important glycosaminoglycan component of the extracellular matrix (ECM), and its major cell surface receptor, CD44, have been suggested to be important cellular mediators influencing tumor progression and treatment resistance in head and neck cancer. Most importantly, the important knowledge obtained from HA/CD44-regulated CSC signaling and functional activation could provide new information regarding the design of novel drug targets to overcome current therapeutic drug resistance which will have significant treatment implications for head and neck cancer patients.

cell, tumor, hnscc, csc, head, neck, cancer, important, [8]

Modeling miRNA-mRNA interactions that cause phenotypic abnormality in breast cancer patients.

The dysregulation of microRNAs (miRNAs) alters expression level of pro-oncogenic or tumor suppressive mRNAs in breast cancer, and in the long run, causes multiple biological abnormalities. However, current

approaches have limitations to consider the regulatory relationship between miRNAs and mRNAs and to implicate the relationship with phenotypic abnormality and cancer pathogenesis.We modeled causal relationships between genomic expression and clinical data using a Bayesian Network (BN), with the goal of discovering miRNA-mRNA interactions that are associated with cancer pathogenesis. We also calculated Bayesian network posterior probability (BNPP) for the models discovered by the MBS algorithm to validate true models with high likelihood.The MBS algorithm successfully learned miRNA and mRNA expression profile data using a BN, and identified miRNA-mRNA interactions that probabilistically affect breast cancer pathogenesis.

interactions, expression, algorithm, mbs, data, mirna-mrna, cancer, [9]

Genetic Variants in the Promoter Region of miR-10b and the Risk of Breast Cancer.

Variants in microRNA genes may affect their expression by interfering with the microRNA maturation process and may substantially contribute to the risk of breast cancer. This case-control study evaluated the associations between variants in the upstream transcription regulation region of miR-10b and the risk of breast cancer among Chinese women. We found that rs4078756, which was located at the promoter region of miR-10b, was significantly associated with breast cancer risk (rs4078756 AG/GG versus AA, adjusted odds ratio: 1.17, 95% confidence interval: 1.02-1.35).

cancer, breast, mir-10b, rs4078756, region, snps, potentially, associations, promoter, risk, [10]

Therapy targeted to the metastatic niche is effective in a model of stage IV breast cancer.

Treatment of stage IV metastatic breast cancer patients is limited to palliative options and represents an unmet clinical need. Here, we demonstrate that pharmacological inhibition of miRNA-10b - a master regulator of metastatic cell viability - leads to elimination of distant metastases in a mouse model of metastatic breast cancer. Intravenous injection of MN-anti-miR10b into mice bearing lung, bone, and brain metastases from breast cancer resulted in selective accumulation of the nanodrug in metastatic tumor cells.

metastatic, cancer, resulted, metastases, breast, mirna-10b, [11]

Colorectal adenoma and carcinoma specific miRNA profiles in biopsy and their expression in plasma specimens.

MiRNA expression markers are well characterized in colorectal cancer (CRC), but less is known about miRNA expression profiles in colorectal adenomas. Microarray data were analyzed using Expression Console and mRNA targets were predicted using miRWALK 2.0.Based on microarray analysis, 447 miRNAs were expressed in tissue and 320 in plasma. Twelve were upregulated (miR-31, 8-fold p¡0.001) and 11 were downregulated (miR-10b 3-fold p¡0.001) in neoplastic lesions compared to normal group.

mirna, expression, plasma, adenomas, tissue, colorectal, [12]

A microRNA signature in circulating exosomes is superior to exosomal glypican-1 levels for diagnosing pancreatic cancer.

Pancreatic ductal adenocarcinoma (PDAC) is a deadly malignancy that often presents clinically at an advanced stage and that may be confused with chronic pancreatitis (CP). We report that exosomal GPC1 is not diagnostic for PDAC, whereas high exosomal levels of microRNA-10b, (miR-10b), miR-21, miR-30c, and miR-181a and low miR-let7a readily differentiate PDAC from normal control and CP samples. All 29 PDAC cases exhibited significantly elevated exosomal miR-10b and miR-30c levels, whereas 8 cases had normal or slightly increased CA 19-9 levels.

pdac, exosomal, levels, cp, gpc1, normal, [13]

Circulating exosomal microRNAs as prognostic biomarkers for non-small-cell lung cancer.

Using a quantitative polymerase chain reaction (qPCR) array panel, we analyzed 84 plasma exosomal miRNAs in 10 lung adenocarcinoma patients and 10 matched healthy controls. Elevated levels of exosomal miR-23b-3p, miR-10b-5p and miR-21-5p were independently associated with poor overall survival (with hazard ratio [95% confidence interval]: 2.42 (1.45 - 4.04), P = 0.001; When compared to the clinical prognostic variables only model, adding the three exosomal miRNA signatures significantly improved survival predictive accuracy with an increase of time-dependent area under the receiver operating characteristic curve from 0.88 to 0.91 (P=0.015).

exosomal, mirnas, prognostic, lung, nsclc, p, =, biomarkers, , plasma, [14]

An Explorative Analysis for the Role of Serum miR-10b-3p Levels in Predicting Response to Sorafenib in Patients with Advanced Hepatocellular Carcinoma.

The prognostic role of aberrant serum miRNA expression for predicting response to sorafenib treatment in advanced hepatocellular carcinoma (HCC) patients has not been well characterized. However, miR-10b-3p levels were significantly higher in the subgroup of HCC patients with worse overall survival (fold change = 5.8, P = 0.008). Although no single serum miRNA was predictive of response to sorafenib treatment, analysis of serum miR-10b-3p levels may be valuable for diagnosis of HCC and prediction of survival of sorafenib-treated patients.

patients, serum, hcc, mirna, survival, significantly, =, mir-10b-3p, treatment, [15]

Ablation of miR-10b Suppresses Oncogene-Induced Mammary Tumorigenesis and Metastasis and Reactivates Tumor-Suppressive Pathways.

The invasive and metastatic properties of many human tumors have been associated with upregulation of the miRNA miR-10b, but its functional contributions in this setting have not been fully unraveled. Mechanistically, miR-10b promotes breast cancer cell proliferation, migration, and invasion through inhibition of the expression of the transcription factor TBX5, leading to repression of the tumor suppressor genes DYRK1A and PTEN In clinical specimens of breast cancer, the expression of TBX5, HOXD10, and DYRK1A correlates with relapse-free survival and overall survival outcomes in patients. Our results establish miR-10b as an oncomiR that drives metastasis, termed a metastamiR, and define the set of critical tumor suppressor mechanisms it overcomes to drive breast cancer progression.

mir-10b, cancer, suppressor, genes, breast, tumors, [16]

Up-regulation of mir-10b predicate advanced clinicopathological features and liver metastasis in colorectal cancer.

Given the emerging role of microRNA in tumor disease progression, we investigated the association between miRNA 10b expression, liver metastasis, and clinicopathological of colorectal cancer (CRC). All samples verified to contain at least 80% tumor cells, and were immediately frozen in liquid nitrogen and stored at -80C or fixed in 10% formalin for paraffin embedding. miR-10b expression was also found correlated with advanced stage (P ¡ 0.0001), lymph node metastasis (P = 0.025), venous infiltration (P = 0.007), poorer differentiation (P = 0.002), and served as an independent prognostic factor of poor overall survival (P ¡ 0.0001).

expression, crc, mir-10b, metastasis, patients, liver, [17]

miR-10b exerts oncogenic activity in human hepatocellular carcinoma cells by targeting expression of CUB and sushi multiple domains 1 (CSMD1).

Hepatocellular carcinoma (HCC) is a lethal disease, while the precise underlying molecular mechanisms of HCC pathogenesis remain to be defined. This study assessed expression and the oncogenic activity of miRNA-10b (miR-10b) in HCC.Forty-five paired human HCC and adjacent non-tumor tissues were collected for qRT-PCR and immunohistochemistry analysis of miR-10b and CUB and Sushi multiple domains 1 (CSMD1), respectively. HCC cell lines were used to assess the effects of miR-10b mimics or inhibitors on cell viability, migration, invasion, cell cycle distribution, and colony formation.

mir-10b, hcc, cell, expression, csmd1, tissues, [18]

The human nucleophosmin 1 mutation A inhibits myeloid differentiation of leukemia cells by modulating miR-10b.

Mutations in the nucleophosmin 1 (NPM1) gene are the most frequent genetic alteration in acute myeloid leukemia (AML). Here, we showed that enforced expression of NPM1 mutation type A (NPM1-mA) inhibits myeloid differentiation of leukemia cells, whereas knockdown of NPM1-mA has the opposite effect. These results demonstrated that miR-10b exerts its effects by repressing the translation of KLF4 and that NPM1-mA inhibits myeloid differentiation through the miR-10b/KLF4 axis.

npm1-ma, aml, effect, mir-10b, myeloid, differentiation, expression, npm1-mutated, npm1, [19]

Correction: Combining miR-10b-Targeted Nanotherapy with Low-Dose Doxorubicin Elicits Durable Regressions of Metastatic Breast Cancer.

[20]

MicroRNA 10b promotes abnormal expression of the proto-oncogene c-Jun in metastatic breast cancer cells.

MicroRNAs have been shown to act as oncogenes or tumor suppressers via various cellular pathways. Here we show that at the receiving end of the miR-10b pathway is the proto-oncogene c-Jun, a transcription factor that plays a critical role in stimulation of cell proliferation and tumor progression. This was supported by analysis of breast cancer cells, which showed that loss of E-cadherin in metastatic cells is accompanied by elevation of miR-10b and interestingly, by a marked increase in accumulation of c-Jun.

cell, mir-10b, c-jun, increase, expression, cancer, pathways, [21]

Regulation of Cell Proliferation and Migration by miR-203 via GAS41/miR-10b Axis in Human Glioblastoma Cells.

Glioma amplified sequence 41(GAS41) is a potent transcription factor that play a crucial role in cell proliferation and survival. In glioblastoma, the expression of GAS41 at both transcriptional and post transcriptional level needs to be tightly maintained in response to cellular signals. Enforced expression of GAS41 produced contradictory effect on miR-203 but was able to enhance p53 tumor suppressor pathway associated protein.

mir-203, gas41, expression, cell, p53, glioma, [22]

Stage-Specific MicroRNAs and Their Role in the Anticancer Effects of Calorie Restriction in a Rat Model of ER-Positive Luminal Breast Cancer.

MicroRNAs have emerged as ubiquitous post-transcriptional regulators that coordinate many fundamental processes within cells, including those commonly linked to cancer when dysregulated. Profiling microRNAs across stages of cancer progression provides focus as to which microRNAs are key players in cancer development and are therefore important to manipulate with interventions to delay cancer onset and progression. We used the dimethylbenz[a]-anthracene-induced model of luminal mammary cancer in Sprague Dawley rats to elucidate which microRNAs are linked to progression in this type of cancer and, subsequently, to study how calorie restriction affects such microRNAs.

micrornas, cancer, progression, restriction, calorie, mammary, mir-200a, [23]

Characterization of the CD49f+/CD44+/CD24- single-cell derived stem cell population in basal-like DCIS cells.

In this study, by applying a novel single-cell clonogenic approach with the CD49f+/CD44+/CD24- surface markers, we characterized the aggressive clones that have enhanced self-renewal, migratory and invasive capacities derived from a human DCIS model cell line MCF10DCIS. The aggressive clones had elevated ALDH1 activity, lower global DNA methylation and increased expression of stem cell related genes, especially concurrent activation of SOX2/OCT4. Finally, we confirmed our in vitro results in vivo, demonstrating that aggressive clones were capable of forming tumors in nude mice, whereas non-aggressive clones were not.

clones, aggressive, non-aggressive, invasive, dcis, molecular, lincrna-ror, expression, increased, cell, self-renewal, enhanced, cd49f+/cd44+/cd24, activity, transition, ductal, carcinoma, [24]

miR-10b expression in breast cancer stem cells supports self-renewal through negative PTEN regulation and sustained AKT activation.

[25]

MiR-10b decreases sensitivity of glioblastoma cells to radiation by targeting AKT.

Glioblastomas are the most aggressive brain tumors with extremely poor prognosis despite advances in treatment techniques. The western blot was used to evaluate protein expression.Altered expression of MiR-10b changed the radiation-induced inhibitory effect on proliferation of glioblastoma cells with dose-dependent manner. In addition, MiR-10b decreased the sensitivity of glioblastoma cells to radiotherapy by activation of p-AKT expression.MiR-10b might be a potential biomarker to predict radiotherapy response and prognosis in glioblastomas.

glioblastomas, cell, mir-10b, examined, radiotherapy, activity, proliferation, [26]

DDX3 Represses Stemness by Epigenetically Modulating Tumor-suppressive miRNAs in Hepatocellular Carcinoma.

Studies indicate that the presence of cancer stem cells (CSCs) is responsible for poor prognosis of hepatocellular carcinoma (HCC) patients. Knockdown of DDX3 in HCC cell line HepG2 induced stemness gene signature followed by occurrence of self-renewal, chemoreisistance, EMT, migration as well as CSC expansion, and most importantly, DDX3 knockdown promotes tumorigenesis. In conclusion, our study suggested that DDX3 prevents generation of CSCs through epigenetically regulating a subset of tumor-suppressive miRNAs expressions, which strengthens tumor suppressor role of DDX3 in HCC.

ddx3, cscs, tumor-suppressive, hcc, promotes, mirnas, studies, cells, [27]

Prognostic significance of microRNA-10b overexpression in breast cancer: a meta-analysis.

Many microRNAs (miRNAs) exhibit altered expression levels in cancers, and they may be considered as valuable prognostic biomarkers for cancers. Here we aimed to summarize the recent advances in miR-10b involvement in human breast cancer and analyze the predicting role of miR-10b for survival. Our results showed that high miR-10b expression in patients with breast cancer was significantly associated with poor disease-free survival (DFS) (RR = 1.53;

mir-10b, expression, =, cancer, survival, studies, breast, [28]

Molecular cystoscopy: Micro-RNAs could be a marker for identifying genotypic changes for transitional cell carcinoma of the urinary bladder.

This study was aimed at exploring the role of the quantitative expression of micro-RNAs (miRNAs) in bladder cancer tissue in comparison with normal mucosa and healthy controls (HCs) as a molecular marker.Between October 2011 to December 2012, tissue from the bladder tumor of 21 patients (cases tumor, CT), normal mucosa (case control, CC) of the same patients (n-21) and normal bladder mucosa from 10 HCs were obtained. Statistical analysis was performed using the Chi square and independent sample T tests by using SPSS version 16.The mean age of the patients and controls were 55.41 11.03 and 52.14 13.04 years. The fold change of miR129, miR205 and miR200a was significantly higher in the normal-looking mucosa of bladder tumor patients than the HC (P ¡ 0.005).Expression of miR129, miR205 and miR200a in the normal-looking mucosa of bladder cancer patients was significantly higher than the normal mucosa of a HC.

mucosa, patients, bladder, tumor, ¡, normal, [29]

miR-10b expression in breast cancer stem cells supports self-renewal through negative PTEN regulation and sustained AKT activation.

To study this issue, we compared the expression of 353 miRNAs in CSCs enriched from breast cancer cell lines using qRT-PCR analysis. Bioinformatics analyses identified several potential miR-10b mRNA targets, including phosphatase and tensin homolog (PTEN), a key regulator of the PI3K/AKT pathway involved in metastasis, cell survival, and self-renewal. Correspondingly, PTEN knockdown increased stem cell markers, whereas AKT inhibitors compromised the self-renewal ability of CSCs and breast cancer cell lines overexpressing miR-10b.

mir-10b, cells, cscs, pten, self-renewal, expression, metastasis, mirnas, [25]

Matrix Hyaluronan Promotes Specific MicroRNA Upregulation Leading to Drug Resistance and Tumor Progression.

Solid tumor invasion, metastasis and therapeutic drug resistance are the common causes for serious morbidity and cancer recurrence in patients. In this article, I have focused on the role of HA interaction with CD44 and several important signaling molecules in the regulation of unique miRNAs (e.g., miR-21, miR-302 and miR-10b) and their downstream targets leading to multiple tumor cell-specific functions (e.g., tumor cell growth, drug resistance and metastasis) and cancer progression. This new knowledge could provide the groundwork necessary for establishing new tumor markers and developing important, novel drugs targeted against HA/CD44-associated tumor progression, which can be utilized in the therapeutic treatment of metastatic cancer patients.

tumor, cancer, cell, ha, drug, cd44, functions, targets, [30]

miR-31 is distinctively overexpressed in primary male extramammary Paget's disease.

MicroRNAs (miRNAs) are small noncoding RNAs involved in cancer development. Using laser capture micro-dissection technique, we collected EMPD tumor cells (ET, n=12), normal epidermal cells (NE, n=12) and normal apocrine glands cells (NA, n=7). The single real-time PCR (RT-PCR) further confirmed that miR-375, miR-31 and miR-31* were upregulated in EMPD cells than those of the normal epidermis and apocrine glands.

empd, mirnas, cells, mir-31, involved, normal, [31]

Up-regulation of Histone Methyltransferase, DOT1L, by Matrix Hyaluronan Promotes MicroRNA-10 Expression Leading to Tumor Cell Invasion and Chemoresistance in Cancer Stem Cells from Head and Neck Squamous Cell Carcinoma.

Human head and neck squamous cell carcinoma is a solid tumor malignancy associated with major morbidity and mortality. In this study, we determined that human head and neck squamous cell carcinoma-derived HSC-3 cells contain a subpopulation of cancer stem cells (CSCs) characterized by a high level of CD44v3 and aldehyde dehydrogenase-1 (ALDH1) expression. Taken together, these findings strongly support the contention that histone methyltransferase, DOT1L-associated epigenetic changes induced by HA play pivotal roles in miR-10 production leading to up-regulation of RhoGTPase and survival proteins.

cell, cscs, expression, tumor, invasion, proteins, [30]

Reactivation of epigenetically silenced miR-124 reverses the epithelial-to-mesenchymal transition and inhibits invasion in endometrial cancer cells via the direct repression of IQGAP1 expression.

Overexpression of IQGAP1 and microRNA (miRNA) dysregulation are frequent in human tumors, but little is known about the role of IQGAP1 and its relationship to miRNA in endometrial carcinogenesis. The overexpression of IQGAP1 stimulates EMT features and enhances migration, invasion and proliferation of EC cells, whereas knocking down IQGAP1 expression reverses EMT and inhibits these malignant properties. Using miRNA microarray profiling, we identified 29 miRNAs (let-7b, let-7f, miR-10b, miR-15b, miR-23a, miR-24, miR-25, miR-27a, miR-29b, miR-30a-5p, miR-34a, miR-124, miR-127, miR-130b, miR-148a, miR-155, miR-191*, miR-194, miR-224, miR-362, miR-409-3p, miR-422b, miR-424, miR-453, miR-497, miR-518d, miR-518f*, miR-526a and miR-656) that are significantly down-regulated in an in vitro-selected highly invasive derivative cell line (HEC-50-HI) relative to the parental HEC-50 cells.

iqgap1, ec, cells, mir-124, expression, mirna, emt, [32]

Therapeutic potential of targeting microRNA-10b in established intracranial glioblastoma: first steps toward the clinic.

MicroRNA-10b (miR-10b) is a unique oncogenic miRNA that is highly expressed in all GBM subtypes, while absent in normal neuroglial cells of the brain. Here, we demonstrate that in heterogeneous GSC, miR-10b regulates cell cycle and alternative splicing, often through the non-canonical targeting via 5'UTRs of its target genes, including MBNL1-3, SART3, and RSRC1. Three delivery routes for the miR-10b antisense oligonucleotide inhibitors (ASO), direct intratumoral injections, continuous osmotic delivery, and systemic intravenous injections, have been explored.

mir-10b, targets, cells, gsc, aso, gbm, systemic, [33]

microRNA-10b is a prognostic biomarker for melanoma.

From a discovery analysis using 40 thick primary melanomas (20 cases with metastasis and 20 controls without metastasis at 5 years), microRNA expression was measured by quantitative RT-PCR (QRT-PCR). In the combined discovery and validation cohorts (n=79), miR-10b expression showed a 3.7-fold increase in expression between cases and controls (P=0.005) and showed a trend of increasing expression between primary melanomas and their matched metastases (P¡0.001). We demonstrated that miR-10b and miR-200b showed independent prognostic value (P=0.002 and 0.047, respectively) in multivariable analysis alongside known clinico-pathological prognostic features (eg, Breslow thickness) using a Cox proportional hazards regression model.

melanoma, micrornas, expression, prognostic, mir-10b, showed, metastasis, discovery, primary, [34]

Differential expression of miRNAs in pancreatobiliary type of periampullary adenocarcinoma and its associated stroma.

The latter is more frequent and aggressive, and characterized by a prominent desmoplastic stroma, which is tightly related to the biology of the cancer, including its poor response to chemotherapy. Whereas miRNAs are known to regulate various cellular processes and interactions between cells, their exact role in periampullary carcinoma remains to be characterized, especially with respect to the prominent stromal component of pancreatobiliary type cancers. Pathway analysis revealed that pathways regulating tumor-stroma interactions such as ECM interaction remodeling, epithelial-mesenchymal transition, focal adhesion pathway, TGF-beta, MAPK signaling, axon guidance and endocytosis were differently regulated.

mirnas, carcinoma, stromal, interactions, cells, component, expression, [35]

Predictive Value of Serum miR-10b, miR-29c, and miR-205 as Promising Biomarkers in Esophageal Squamous Cell Carcinoma Screening.

Esophageal squamous cell carcinoma (ESCC) is a leading cause of cancer-related deaths worldwide. Current detection methods have their own weakness, including high costs and invasive procedures. specificity=64%), respectively, suggesting that miR-10b, miR-29c, and miR-205 have great potential to be non-invasive screening tools for ESCC detection.

escc, microrna, mir-10b, mir-29c, mir-205, ci, controls, level, patients, healthy, 95[36]

Similar Squamous Cell Carcinoma Epithelium microRNA Expression in Never Smokers and Ever Smokers.

The incidence of oral tumors in patients who never used mutagenic agents such as tobacco is increasing. In an effort to better understand these tumors we studied microRNA (miRNA) expression in tumor epithelium of never tobacco users, tumor epithelium of ever tobacco users, and nonpathological control oral epithelium. A comparison of levels among 372 miRNAs in 12 never tobacco users with oral squamous cell carcinoma (OSCC) versus 10 healthy controls was made using the reverse transcription quantitative polymerase chain reaction.

oscc, tobacco, never, tumors, ever, mirna, [37]

Heterogeneity of miR-10b expression in circulating tumor cells.

Circulating tumor cells (CTCs) in the blood of cancer patients are recognized as important potential targets for future anticancer therapies. MicroRNAs (miRNAs) are key regulators of gene expression and have emerged as potentially important diagnostic markers and targets for anti-cancer therapy. Here, we describe a robust in situ hybridization (ISH) protocol, incorporating the CellSearch() CTC detection system, enabling clinical investigation of important miRNAs, such as miR-10b on a cell by cell basis.

ctcs, important, mir-10b, patients, heterogeneity, cells, [38]

Small RNA Sequencing Uncovers New miRNAs and moRNAs Differentially Expressed in Normal and Primary Myelofibrosis CD34+ Cells.

Myeloproliferative neoplasms (MPN) are chronic myeloid cancers thought to arise at the level of CD34+ hematopoietic stem/progenitor cells. To attain deeper knowledge of short RNAs (sRNAs) expression pattern in CD34+ cells and of their possible role in mediating post-transcriptional regulation in PMF, we sequenced with Illumina HiSeq2000 technology CD34+ cells from healthy subjects and PMF patients. As a whole, data obtained in this study deepened the knowledge of miRNAs and moRNAs altered expression in PMF CD34+ cells and allowed to identify and validate a specific small RNA profile that distinguishes PMF granulocytes from those of normal subjects.

pmf, mirnas, cells, cd34+, rnas, new, [39]

Selective Activation of Cancer Stem Cells by Size-Specific Hyaluronan in Head and Neck Cancer.

We determined that human head and neck cancer cells (HSC-3 cell line) contain a subpopulation displaying cancer stem cell (CSC) properties and are very tumorigenic. First, we observed that 200kDa-HA (but not other sizes of HA) preferentially induces certain stem cell marker expression resulting in self-renewal and clonal formation of these cells. Together, our findings suggest that selective activation of oncogenic signaling by certain sizes of HA (e.g., 200kDa-HA) may be instrumental in the formation of CSC functions leading to tumor cell survival and chemoresistance in head and neck cancer progression.

csc, cells, 200kda-ha, survival, expression, protein, ha, sizes, leading, cancer, [40]

Combining miR-10b-Targeted Nanotherapy with Low-Dose Doxorubicin Elicits Durable Regressions of Metastatic Breast Cancer.

In the protocol developed, we combined a miR-10b-inhibitory nanodrug with low-dose anthracycline to achieve complete durable regressions of metastatic disease in a murine model of metastatic breast cancer. Mechanistic investigations suggested a potent antiproliferative, proapoptotic effect of the nanodrug in the metastatic cells, potentiated by a cell-cycle arrest produced by administration of the low-dose anthracycline. Taken together, our results implied the existence of pathways that regulate the viability and proliferation of tumor cells only after they have acquired the ability to grow at distant metastatic sites.

metastatic, cell, target, mir-10b, therapeutic, suggested, nanodrug, pathways, proliferation, viability, tumor, cancer, site, potent, mirna, role, low-dose, anthracycline, [41]

MicroRNA-10b promotes migration and invasion through Hoxd10 in human gastric cancer.

This study aims to investigate the effect of miR-10b overexpression on cancer cell proliferation, migration, invasion, and Hoxd10 expression.The effect of miR-10b on proliferation, migration, and invasion of MKN-28, BGC-823, and SGC-7901 cells and the expression of Hoxd10 protein in SGC-7901 and BGC-823 cells were detected following transfection of miR-10b inhibitor or Negative Control B. Expression of Hoxd10 protein in 436 paraffin-embedded cancer tissues was also investigated.miR-10b was significantly upregulated in AGS, MKN-28, BGC-823, HCG-27, SGC-7901, and MKN-45 cell lines, miR-10b inhibitor significantly inhibited proliferation and migration of MKN-45, BGC-823 and SGC-7901 cells 48 h after transfection, while Hoxd10 protein in these cells lines had increased 72 h after transfection. Hoxd10 was highly expressed in gastric cancer and correlated with size of tumor, Lauren classification, depth of invasion, lymph node and distant metastasis, Tumor-Node-Metastasis (TNM) stage, and prognosis.miR-10b promotes migration and invasion through Hoxd10 in human gastric cancer cell lines and may play an important role in tumorigenesis, progression, and prognosis.

cell, hoxd10, bgc-823, invasion, mir-10b, migration, cancer, sgc-7901, [42]

Non-invasive approaches to monitor EGFR-TKI treatment in non-small-cell lung cancer.

Tyrosine kinase inhibitors of epidermal growth factor receptor (EGFR-TKIs) are standard treatments for advanced non-small-cell lung cancer (NSCLC) patients harboring activating epidermal growth factor receptor (EGFR) mutations. A commercialized serum-based proteomic test, named VeriStrat test, has shown an outstanding ability to predict the clinical outcome of NSCLC patients receiving EGFR-TKIs. These evidences suggested that non-invasive techniques based on serum or plasma samples had a great potential for monitoring EGFR-TKI treatment in NSCLC.

egfr-tkis, nsclc, egfr, tumor, monitor, resistance, treatment, patients, mutations, [43]

Functional role of miR-10b in tamoxifen resistance of ER-positive breast cancer cells through down-regulation of HDAC4.

For breast cancer patients diagnosed with estrogen receptor (ER)-positive tumors, treatment with tamoxifen is the gold standard. The mechanistic role of HDAC4 in miR-10b-mediated tamoxifen resistance was studied using HDAC4 cDNA and HDAC4-specific siRNA in appropriate models.Over-expression of miR-10b in ER-positive MCF-7 and T47D cells led to increased resistance to tamoxifen and an attenuation of tamoxifen-mediated inhibition of migration, whereas down-regulation of miR-10b in MCF7TR cells resulted in increased sensitivity to tamoxifen. HDAC4-specific siRNA-mediated inactivation of HDAC4 in MCF-7 cells led to acquisition of tamoxifen resistance, and, moreover, reduction of HDAC4 in MCF7TR cells by HDAC4-specific siRNA transfection resulted in further enhancement of tamoxifen-resistance.We propose miR-10b-HDAC4 nexus as one of the molecular mechanism of tamoxifen resistance which can potentially be expolited as a novel targeted therapeutic approach for the clinical management of tamoxifen-resistant breast cancers.

cells, mir-10b, tamoxifen, hdac4, mcf7tr, resistance, [44]

MicroRNAs: New Biomarkers for Diagnosis, Prognosis, Therapy Prediction and Therapeutic Tools for Breast Cancer.

Dysregulation of microRNAs (miRNAs) is involved in the initiation and progression of several human cancers, including breast cancer (BC), as strong evidence has been found that miRNAs can act as oncogenes or tumor suppressor genes. Based on the results obtained in the last decade, some miRNAs are emerging as biomarkers of BC for diagnosis (i.e., miR-9, miR-10b, and miR-17-5p), prognosis (i.e., miR-148a and miR-335), and prediction of therapeutic outcomes (i.e., miR-30c, miR-187, and miR-339-5p) and have important roles in the control of BC hallmark functions such as invasion, metastasis, proliferation, resting death, apoptosis, and genomic instability. New miRNA-based drugs are also promising therapy for BC (e.g., miR-9, miR-21, miR34a, miR145, and miR150), and other miRNAs are showing a fundamental role in modulation of the response to other non-miRNA treatments, being able to increase their efficacy (e.g., miR-21, miR34a, miR195, miR200c, and miR203 in combination with chemotherapy).

mirnas, bc, role, i.e., e.g., therapy, prognosis, diagnosis, mir-9, mir-21, mir34a, showing, circulating, better, new, [45]

KRAS-dependent sorting of miRNA to exosomes.

Mutant KRAS colorectal cancer (CRC) cells release protein-laden exosomes that can alter the tumor microenvironment. To test whether exosomal RNAs also contribute to changes in gene expression in recipient cells, and whether mutant KRAS might regulate the composition of secreted microRNAs (miRNAs), we compared small RNAs of cells and matched exosomes from isogenic CRC cell lines differing only in KRAS status. We show that exosomal profiles are distinct from cellular profiles, and mutant exosomes cluster separately from wild-type KRAS exosomes.

cells, mutant, exosomes, kras, crc, mirnas, [46]

Diagnostic and prognostic microRNAs in the serum of breast cancer patients measured by droplet digital PCR.

Breast cancer circulating biomarkers include carcinoembryonic antigen and carbohydrate antigen 15-3, which are used for patient follow-up. To acquire an absolute concentration of circulating miRNAs and reduce the impact of preanalytical and analytical variables, we used the droplet digital PCR (ddPCR) technique.We investigated a panel of five miRNAs in the sera of two independent cohorts of breast cancer patients and disease-free controls. The use of the ddPCR quantitative approach revealed very good agreement between two independent cohorts in terms of comparable absolute miRNA concentrations and consistent trends of dysregulation in breast cancer patients versus controls.

mirnas, cancer, breast, circulating, patient, controls, ddpcr, [47]

Integrated genomic analysis identifies subclasses and prognosis signatures of kidney cancer.

To define robust miRNA-based molecular classifiers for human clear cell renal cell carcinoma (ccRCC) subgrouping and prognostication.Multidimensional data of over 500 clear cell renal cell carcinoma (ccRCC) patients were retrieved from The Cancer Genome Atlas (TCGA) archive. Data analysis was based on a novel computational approach that selectively considers patients with extreme expression values of miRNAs to detect survival-associated molecular signatures.Our in silico analysis unveiled a novel ccRCC-specific 5-miRNA (miR-10b, miR-21, miR-143, miR-183, and miR-192) signature able, when combined with information from conventional TNM staging and the age of the patient, to prognosticate ccRCC outcome more accurately than known ccRCC miRNA signatures or TNM staging alone. It also demonstrated that BAP1 mutations correlate with tumor progression rather than overall survival.Integrated analysis of multidimensional data from the TCGA archive allowed to draw a portrait of distinct molecular subclasses of human ccRCC and to define signatures for prognosticating disease outcome.

ccrcc, cell, data, signature, molecular, tumor, analysis, staging, patients, [48]

Secreted uPAR isoform 2 (uPAR7b) is a novel direct target of miR-221.

miR-221/-222 and components of the urokinase-type plasminogen activator system (uPAS) are associated with metastasis and poor prognosis in breast cancer, including the triple-negative subtype (TNBC). To substantiate direct targeting of miR-221/-222 within 3' UTR of the uPAR isoform 2, in silico analysesand in vitro assays were conducted. These results demonstrate a direct and positive regulation of the secreted uPAR isoform 2 by miR-221, increasing its protein expression, a prerequisite for malignancy, while the other uPAR isoforms (1, 3 and 4) are indirectly regulated through miR-10b and miR-221/-222.

upar, isoform, mir-221/-222, 2, targeted, cancer, breast, [49]

Circulating microRNAs as biomarkers in hepatocellular carcinoma screening: a validation set from China.

All these miRNAs (miR-10b, miR-181a, miR-106b) could well discriminate HCC patients from normal controls, with area under the receiver-operating characteristic curve (AUC) values of 0.85 (95% confidence interval [CI]: 0.76-0.94), 0.82 (95% CI: 0.72-0.91), and 0.89 (95% CI: 0.81-0.97), respectively. Panel of these miRNAs displayed a better performance compared with single miRNA assay, with AUC values of 0.94 (95% CI: 0.89-0.99) in discriminating HCC patients from normal controls and 0.91 (95% CI: 0.80-0.97) in discriminating HCC patients from CLD controls. Results of meta-analysis of previous studies combined with the current study suggested that circulating miRNAs could well differentiate HCC from normal controls, with AUC values of 0.86 (95% CI: 0.82-0.89) for single miRNA assay and 0.94 (95% CI: 0.91-0.96) for miRNA panel assay.

hcc, mirnas, study, patients, 95[50]

MicroRNA-10b inhibition reduces E2F1-mediated transcription and miR-15/16 activity in glioblastoma.

MicroRNA-10b (miR-10b) is commonly elevated in glioblastoma (GBM), while not expressed in normal brain tissues. Targeted inhibition of miR-10b has pleiotropic effects on GBM derived cell lines, it reduces GBM growth in animal models, but does not affect normal neurons and astrocytes. In cells expressing high levels of tumor suppressor p21WAF1/Cip1, it represses E2F1-mediated transcription, leading to down-regulation of multiple E2F1 target genes encoding for S-phase specific proteins, epigenetic modulators, and miRNAs (e.g.

gbm, mir-10b, cell, targeted, expressed, inhibition, glioma, [51]

High expression of miR-214 is associated with a worse disease-specific survival of the triple-negative breast cancer patients.

Hereditary triple-negative breast cancer patients have better recurrence-free survival than triple-negative sporadic ones. The attempt to associate expression level of some miRNA in triple-negative hereditary and sporadic breast cancers to disease specific survival was performed in this study.Study group was made of 18 triple-negative breast cancer patients harboring the BRCA1 gene mutations and 32 triple-negative sporadic breast cancer patients. Triple-negative breast cancer patients with high level of miR-214 showed significantly worse disease-specific survival than patients with low level (p=0.0314).Our finding suggests that miR-214 possibly could be used as a potential prognostic biomarker for triple-negative breast cancer patients.

triple-negative, breast, patients, cancer, level, survival, [52]

Polymer nanoparticles mediated codelivery of antimiR-10b and antimiR-21 for achieving triple negative breast cancer therapy.

The current study shows the therapeutic outcome achieved in triple negative breast cancer (TNBC) by simultaneously antagonizing miR-21-induced antiapoptosis and miR-10b-induced metastasis, using antisense-miR-21-PS and antisense-miR-10b-PS delivered by polymer nanoparticles (NPs). We synthesized the antisense-miR-21 and antisense-miR-10b loaded PLGA-b-PEG polymer NPs and evaluated their cellular uptake, serum stability, release profile, and the subsequent synchronous blocking of endogenous miR-21 and miR-10b function in TNBC cells in culture, and tumor xenografts in living animals using molecular imaging. Targeted delivery of antisense-miR-21 and antisense-miR-10b coloaded urokinase plasminogen activator receptor (uPAR) targeted polymer NPs treated mice showed substantial reduction in tumor growth at very low dose of 0.15 mg/kg, compared to the control NPs treated mice and 40% reduction in tumor growth compared to scramble peptide conjugated NPs treated mice, thus demonstrating a potential new therapeutic option for TNBC.

nps, treatment, tumor, shows, mice, polymer, tnbc, targeting, [53]

The association between abnormal microRNA-10b expression and cancer risk: a meta-analysis.

Several studies have investigated the association between abnormal microRNA-10b expression and the risk of various developing cancers, but the results are inconsistent. Among them, 25 studies were subjected to the meta-analysis with a vote-counting strategy, 13 studies were estimated using odds ratio (OR) and diagnostic accuracy, and 2 studies were assessed by both methods. Of 13 included studies calculated for OR and diagnostic accuracy, it was shown that high-expression of microRNA-10b could be significantly associated with cancer risk (OR = 32.80, 95% CI: 11.90-90.37, P¡0.0001), and the area under the summary receiver operating characteristic (SROC) curve for microRNA-10b high-expression in the diagnosis of cancer is 0.81, which suggested that high-expression of microRNA-10b can predict worse outcomes in some types of cancer and the regular monitoring of miR-10b expression might be useful in the clinical practice.

cancer, microrna-10b, studies, expression, types, high-expression, [54]

Exosome-mediated transfer of miR-10b promotes cell invasion in breast cancer.

Exosomes are 30-100 nm membrane vesicles of endocytic origin, mediating diverse biological functions including tumor cell invasion, cell-cell communication and antigen presentation through transfer of proteins, mRNAs and microRNAs. Thus, the aim of this study was to identify the exosomal microRNAs involved in breast cancer invasion.The expression level of endogenous and exosomal miRNAs were examined by real time PCR and the expression level of target proteins were detected by western blot. Finally, treatment with exosomes derived from MDA-MB-231 cells could induce the invasion ability of non-malignant HMLE cells.Together, our results suggest that a set of specific microRNAs may play an important role in modulating tumor microenvironment through exosomes.

exosomes, cell, micrornas, invasion, mir-10b, breast, [55]

MiR-520d-5p directly targets TWIST1 and downregulates the metastamiR miR-10b.

Some microRNAs are involved in the genesis of tumors and are therefore termed oncomiRs, while others, termed metastamiRs, play a significant role in the formation of cancer metastases. We next show that the miR-520d-5p-mediated decrease of TWIST1 expression results in reduced expression of one of its targets, miR-10b, and in the restoration of E-Cadherin expression, which in turn results in reduced cellular motility and invasiveness. Finally, we show that miR-520d-5p leads to reduced proliferation of tumor cells, and that high levels of miR-520d-5p correlate with higher survival rates of cancer patients.

micrornas, expression, twist1, tumors, show, mir-520d-5p, reduced, target, cancer, [56]

MicroRNA expression profiling and DNA methylation signature for deregulated microRNA in cutaneous T-cell lymphoma.

MicroRNAs usually regulate gene expression negatively, and aberrant expression has been involved in the development of several types of cancers. Microarray profiling of microRNA expression was performed to define a microRNA signature in a series of mycosis fungoides tumor stage (MFt, n=21) and CD30+ primary cutaneous anaplastic large cell lymphoma (CD30+ cALCL, n=11) samples in comparison with inflammatory dermatoses (ID, n=5). DNA methylation in microRNA gene promoters, as expression regulatory mechanism for deregulated microRNAs, was analyzed using Infinium 450K array and approximately one-third of the differentially expressed microRNAs showed significant DNA methylation differences.

micrornas, cd30+, expression, calcl, mft, signature, methylation, [57]

MicroRNAs expression in triple negative vs non triple negative breast cancer in Tunisia: interaction with clinical outcome.

MicroRNAs are small, non coding regulatory molecules containing approximately 21 to 25 nucleotides. The objective of the present study is to evaluate the expression profile of the following micro-RNAs: miR-10b, miR-17, miR-21, miR-34a, miR-146a, miR-148a and miR-182, and to determine their possible interaction in triple-negative and non triple-negative primary breast cancers based on clinical outcome.60 triple-negative and non triple-negative breast cancer cases, along with their corresponding normal samples were investigated in relation to the expression of the seven studied miRNAs using qPCR Syber Green.We observed that miR-21, miR-146a and miR-182 were significantly over expressed in triple negative breast cancer. The additive effect of hormonal factors in triple negative breast cancer cases showed an association with all the studied miRs except for miR-34 and miR-146a.The studied microRNAs are strongly influenced by environmental factors especially with hormonal patients' history.

breast, cancer, negative, non, triple, studied, cases, triple-negative, mir-182, mir-21, mir-10b, micrornas, [58]

The prognostic significance of RUNX2 and miR-10a/10b and their inter-relationship in breast cancer.

It is important to identify genes regulating metastasis and invasion in order to curtail metastatic spread of cancer cells.This study investigated the association between RUNX2 and miR-10a/miR-10b and the risk of breast cancer relapse. Expression levels of RUNX2 and miR-10a/b in 108 pairs of tumor and non-tumor tissue of breast cancer were assayed by quantitative PCR analysis and evaluated for their prognostic implications.The median expression levels of RUNX2 and miR-10b in tumor tissue normalized using adjacent non-tumor tissue were significantly higher in relapsed patients than in relapse-free patients. In a breast cancer cell line, RUNX2 silencing reduced the expression of miR-10a/b and also impaired cell motility, while RUNX2 overexpression elicited opposite effects.These findings indicate that higher expression of RUNX2 and miR-10a/b was associated with adverse outcome of breast cancer.

runx2, cancer, expression, breast, mir-10a/b, higher, , =, ci, 95[59]

miR-10b is overexpressed in hepatocellular carcinoma and promotes cell proliferation, migration and invasion through RhoC, uPAR and MMPs.

Recently, miR-10b is identified as a miRNA highly expressed in many human cancers, promoting cell migration and invasion. However, the specific function of miR-10b in hepatocellular carcinoma (HCC) is unclear at this point.The miR-10b expression levels in 60 paired different TNM Stage HCC tumor tissues compared with adjacent non-tumor (ANT) tissues, normal tissue control (8 benign tumor and 7 normal liver tissues), 3 normal liver and 7 HCC cell lines were measured by real-time quantitative RT-PCR and to evaluate their association with HCC clinicopathologic features. Furthermore, we found that miR-10b induced HCC cell invasion and migration by modulating the HOXD10 target gene RhoC, uPAR, MMP-2 and MMP-9 expression.Our results suggested that miR-10b was overexpressed in HCC and promoted HCC cell migration and invasion through the HOXD10/ RhoC/ uPAR/ MMPs pathway which may provide a novel bio-target for HCC therapy.

hcc, mir-10b, cell, tissues, invasion, normal, assay, [60]

miRNA as potential biomarkers of breast cancer in the Lebanese population and in young women: a pilot study.

Relative to western populations, the percentage of women diagnosed with breast cancer at a young age in Lebanon is high. The objective of this study is to investigate the contribution of miRNAs in this setting through the analysis of the expression of five reported dysregulated miRNAs, miR-148b, miR-10b, miR-21, miR-221, and miR-155 in 20 normal and 57 cancerous breast tissues from Lebanese breast cancer patients. miR-155 was also significantly overexpressed in postmenopausal patients and in those of age at diagnosis greater than 40 years old as well as in PR negative or in human epidermal growth factor 2 (Her2) positive tissues.

breast, mirnas, expression, tissues, cancer, mir-10b, lebanese, mir-155, age, [61]

Hypoxic signature of microRNAs in glioblastoma: insights from small RNA deep sequencing.

Hypoxia is a critical aspect of the glioma microenvironment and has been associated with poor prognosis and resistance to various therapies. We thus hypothesized their prominent role in hypoxia resistance in glioblastoma (GBM) and aimed to identify those.With this study, we present the first detailed analysis of small RNA transcriptome of cell line U87MG, a grade IV glioma cell line, and its alteration under hypoxic condition. Additionally, a total of 139 novel miRNAs were discovered by the analysis of deep sequencing data and three of these were found to be differentially expressed under hypoxia.Overall, our study reveals a novel miRNA signature of hypoxia in GBM and suggests miR-210-3p to be an oncogenic player and a novel potential intrinsic marker of hypoxia in glioblastoma.

hypoxia, gbm, mir-210-3p, mirnas, cells, showing, hypoxic, [62]

The expression and significance of five types of miRNAs in breast cancer.

This study aimed to investigate the expression and significance of 5 types of miRNAs in breast cancer to provide a theoretical and practical foundation for using these miRNAs in the diagnosis and treatment of breast cancer, thereby improving medical services.Stem-loop real-time RT-PCR was used to detect the expression levels of miR-145, miR-21, miR-10b, miR-125a, and miR-206 in 35 cases of breast cancer and adjacent normal breast tissues, and to analyze the relationship of miRNAs expression with clinicopathological features of breast cancer. MiR-206 expression was correlated with negative ER status, negative PR status, and negative HER-2 status (P¡0.05), regardless of age, menstruation, lymph node metastasis, and TOP 2A. MiR-10b expression was positively correlated with breast cancer tumor size, lymph node metastasis, and TOP 2A status (P¡0.05), but had no correlations with age, menstruation, ER, PR, and HER-2.MiR-145, miR-21, miR-10b, miR-125a, and miR-206 may play important roles in breast cancer development and invasion.

expression, breast, cancer, p¡0.05, status, pr, er, negatively, correlated, [63]

Evaluation of microRNA-10b prognostic significance in a prospective cohort of breast cancer patients.

MicroRNA-10b (miR-10b) has a prominent role in regulating tumor invasion and metastasis by targeting the HOXD10 transcriptional repressor and has been found up-regulated in several tumor types.We evaluated the expression of miR-10b in paired tumor and normal specimens obtained from a prospective cohort of breast cancer patients with at least 36 months follow-up enrolled according to the REMARK guidelines (n=150). In the subgroup of patients without synchronous metastases (n=90), higher miR-10b RERs were associated with increased risk of disease progression and death in both univariable (HR 1.16, p=0.021 and HR 1.20, p=0.015 respectively for 0.10 unitary increase of miR-10b RERs levels) and multivariable (HR1.30, p¡0.001, and HR 1.31, p=0.003 respectively for 0.10 unitary increase of miR-10b RERs levels) Cox regression models. Survival C-indices significantly increased from 0.849 to 0.889 (p=0.009) for OS and from 0.735 to 0.767 (p=0.050) for DFS.Our results provide evidences that the addition of miR-10b RERs to the prognostic factors used in clinical routine could improve the prediction abilities for both overall mortality and disease progression in breast cancer patients.

mir-10b, rers, patients, tumor, hr, metastases, [64]

MicroRNA profiling implies new markers of chemoresistance of triple-negative breast cancer.

Triple-negative breast cancer (TNBC) patients with truly chemosensitive disease still represent a minority among all TNBC patients. The aim of the present study is to identify microRNAs (miRNAs) that correlate with TNBC chemoresistance.In this study, we conducted miRNAs profile comparison between triple-negative breast cancer (TNBCs) and normal breast tissues by microRNA array. Cells viability and apoptosis assays were employed to determine the effect of alteration of the specific miRNAs in TNBC cells on the chemosensitivity.We identified 11 specific deregulated miRNAs, including 5 up-regulated miRNAs (miR-155-5p, miR-21-3p, miR-181a-5p, miR-181b-5p, and miR-183-5p) and 6 down-regulated miRNAs (miR-10b-5p, miR-451a, miR-125b-5p, miR-31-5p, miR-195-5p and miR-130a-3p).

mirnas, tnbc, specific, found, cells, deregulated, mir-130a-3p, result, potential, chemotherapy, mir-451a, breast, patients, [65]

TWIST1 expression in breast cancer cells facilitates bone metastasis formation.

The transcription factor TWIST1 induces epithelial-mesenchymal transition and/or escape to the oncogenic-induced failsafe program, facilitating the intravasation of breast cancer cells in the systemic circulation and their dissemination to the lungs. This difference was accompanied by a sharp reduction of the bone volume (indicating a higher bone destruction) and a twofold increase in the tumor volume compared with mice

bearing mock-transfected tumors, as determined by histomorphometry. Additionally, examination of the bone marrow from untreated and dox-treated animals on day 7 after tumor cell inoculation, at which time there was no evidence of radiographic osteolytic lesions, revealed that the number of tumor cell colonies that were recovered from the bone marrow of untreated mice was dramatically increased compared with that of dox-fed animals.

bone, tumors, cells, twist1, breast, cancer, [66]

miR-21 promotes human nucleus pulposus cell proliferation through PTEN/AKT signaling.

The precise role of nucleus pulposus cell proliferation in the pathogenesis of intervertebral disc degeneration remains to be elucidated. Here, we showed that miR-21 was significantly upregulated in degenerative nucleus pulposus tissues when compared with nucleus pulposus tissues that were isolated from patients with idiopathic scoliosis and that miR-10b levels were associated with disc degeneration grade. Taken together, aberrant miR-21 upregulation in intervertebral disc degeneration could target PTEN, which would contribute to abnormal nucleus pulposus cell proliferation through derepressing the Akt pathway.

mir-21, proliferation, target, nucleus, pulposus, cell, disc, degeneration, [67]

Detection of miRNA expression in intact cells using activatable sensor oligonucleotides.

We describe a technology for the profiling of miRNA expression in intact cells. This triggers assembly of the endogenous RNA Induced Silencing Complex (RISC) around the miRNA-sensor duplex and cleavage of the sensor oligonucleotide, resulting in separation between the dye and quencher, and a fluorescence turn-on. Using a human breast adenocarcinoma cell line, we illustrate the application of this technology for miRNA detection with nanomolar sensitivity in both a cell-free system and intact cells.

mirna, cells, technology, sensor, oligonucleotides, dye, quencher, breast, target, complementary, specific, intact, [68]

High serum miR-19a levels are associated with inflammatory breast cancer and are predictive of favorable clinical outcome in patients with metastatic HER2+ inflammatory breast cancer.

Altered serum microRNA (miRNA) levels may be correlated with a dysregulated expression pattern in parental tumor tissue and reflect the clinical evolution of disease. thus, we determined their utility as serum biomarkers for aggressive breast cancer (HER2-overexpressed or -amplified [HER2(+)] and inflammatory breast cancer [IBC]).In this prospective study, we measured miR-21, miR-10b, and miR-19a levels using quantitative reverse transcriptase-polymerase chain reaction in the serum of 113 breast cancer patients and determined their association with clinicopathologic factors and clinical outcome. Thirty healthy donors with no history of cancer were enrolled as controls.Patients with non-metastatic HER2(+) breast cancer had higher serum miR-21 median levels than patients with non-metastatic HER2(-) disease (p=0.044);

serum, levels, patients, metastatic, mir-19a, cancer, [69]

Expression of 19 microRNAs in glioblastoma and comparison with other brain neoplasia of grades I-III.

Several biomarkers have been proposed as useful parameters to better specify the prognosis or to delineate new target therapy strategies for glioblastoma patients. In this work the expression of 19 microRNAs (miR-7, miR-9, miR-9, miR-10a, miR-10b, miR-17, miR-20a, miR-21, miR-26a, miR-27a, miR-31, miR-34a, miR-101, miR-137, miR-182, miR-221, miR-222, miR-330, miR-519d) was evaluated in sixty formalin-fixed and paraffin-embedded glioblastoma samples using a locked nucleic acid real-time PCR. The analysis of 14 validated miRNA expression in the 60 glioblastomas, using three different non-neoplastic references as controls, revealed a putative miRNA signature: mir-10b and miR-21 were up-regulated, while miR-7, miR-31, miR-101, miR-137, miR-222 and miR-330 were down-regulated in glioblastomas.

mirna, glioblastoma, expression, mir-10b, micrornas, grades, [70]

MicroRNA-10b promotes nucleus pulposus cell proliferation through RhoC-Akt pathway by targeting HOXD10 in intervetebral disc degeneration.

Aberrant proliferation of nucleus pulposus cell is implicated in the pathogenesis of intervertebral disc degeneration. Here, we showed that miR-10b was dramatically upregulated in degenerative nucleus pulposus tissues when compared with nucleus pulposus tissues isolated from patients with idiopathic scoliosis. In cultured nucleus pulposus cells, miR-10b overexpression stimulated cell proliferation with concomitant translational inhibition of HOXD10 whereas restored expression of HOXD10 reversed the mitogenic effect of miR-10b.

mir-10b, nucleus, pulposus, cell, proliferation, hoxd10, [71]

MicroRNA-10b overexpression promotes non-small cell lung cancer cell proliferation and invasion.

miRNAs are a class of small non-coding RNA molecules that play an important role in the pathogenesis of human diseases through negative regulation of gene expression. Western blotting was used to predicate the target of miR-10b.The A549 cell line transfected with the miR-10b exhibited significantly increased proliferation, migration, and invasion capacities when compared with the control cells (P ¡0.05). Krppel-like factor 4 (KLF4) may be indirectly targeted by miR-10b during the proliferation increasing of A549 cells.In this study, we found that miR-10b is a tumor enhancer in NSCLC.

cell, mir-10b, nsclc, target, role, a549, [72]

MicroRNA expression profile in head and neck cancer: HOX-cluster embedded microRNA-196a and microRNA-10b dysregulation implicated in cell proliferation.

Some studies have evaluated the potential use of microRNA as biomarkers with clinical application in HNSCC.MicroRNA expression profile of oral squamous cell carcinoma samples was determined by means of DNA microarrays. The effect of the over-expression of these molecules was evaluated by means of global gene expression profiling and cell proliferation assessment.Altered microRNA expression was detected for a total of 72 microRNAs. Our results suggest that both molecules interfere in cell proliferation through distinct processes, possibly targeting a small set of genes involved in cell cycle progression.Functional data on miRNAs in HNSCC is still scarce.

microrna, cell, hnscc, expression, roles, carcinomas, gene, proliferation, molecules, squamous, [73]

Regulation of breast cancer and bone metastasis by microRNAs.

Breast cancer progression including bone metastasis is a complex process involving numerous changes in gene expression and function. MicroRNAs (miRNAs) are small endogenous noncoding RNAs that regulate gene expression by targeting protein-coding mRNAs posttranscriptionally, often affecting a number of gene targets simultaneously. In this review we summarize the experimentally validated targets of up- and down-regulated miRNAs and their regulation in breast cancer and bone metastasis for diagnostic and therapeutic purposes.

breast, cancer, mirnas, expression, targeting, gene, [74]

miR-10b promotes migration and invasion in nasopharyngeal carcinoma cells.

MicroRNA-10b (miR-10b) has been reported to play an important role in some types of cancer, but the effects and possible mechanisms of action of miR-10b in the metastasis of nasopharyngeal carcinoma cells (NPC) have not been explored. Wound healing and transwell migration assays were applied to assess cell migration and invasion, while and expression of E-cadherin and MMP-9 were detected using Western blot analysis. In addition, the expression of genes related to migration and invasion, such as E-cadherin,

vimentin, and MMP-9, were confirmed to be different in the CNE-2Z NPC cell line transfected with miR-10b mimics and with miR-10b inhibitors.

mir-10b, cells, expression, npc, invasion, migration, assay, lines, [**?**]

Prognostic significance of metastasis-related microRNAs in early breast cancer patients with a long follow-up.

Stability of microRNAs (miRNAs) in formalin-fixed paraffin-embedded (FFPE) tissues enables their reliable analysis in archived FFPE tissue samples, which are an invaluable source for the evaluation of novel biomarkers. We investigated the prognostic significance of 6 metastasis-related miRNAs that can critically regulate various stages of migration and invasion and play critical roles in the multistep metastatic process.We quantified the expression of 6 mature miRNAs (namely miR-21, miR-205, miR-10b, miR-210, miR-335, and let-7a) by reverse-transcription quantitative PCR in FFPE tissues of 84 patients with early breast cancer and a long follow-up and 13 cancer-free breast tissue FFPE samples that were used as the control group. Multivariate analysis demonstrated that miR-205 and miR-21 were independent factors associated with early disease relapse, whereas only miR-205 overexpression was associated with OS.Our results clearly indicate that deregulation of metastasis-associated miRNAs in primary tumors is associated with clinical outcome in patients with early breast cancer and can differentiate patients with higher risk in well-characterized subgroups.

mirnas, breast, tissues, mir-205, ffpe, cancer, analysis, associated, [75]

Impact of microRNAs on regulatory networks and pathways in human colorectal carcinogenesis and development of metastasis.

Qualitative alterations or abnormal expression of microRNAs (miRNAs) in colon cancer have mainly been demonstrated in primary tumors. To identify changes in both miRNA and gene expression levels among normal colon mucosa, primary tumor and liver metastasis samples, and to classify miRNAs into functional networks, in this work miRNA and gene expression profiles in 158 samples from 46 patients were analysed.Most changes in miRNA and gene expression levels had already manifested in the primary tumors while these levels were almost stably maintained in the subsequent primary tumor-to-metastasis transition. The suppressor activity of miR-182 on ENTPD5 gene was identified for the first time and confirmed in an independent set of samples.Using a large dataset of CRC miRNA and gene expression profiles, we describe the interplay of miRNA groups in regulating gene expression, which in turn affects modulated pathways that are important for tumor development.

mirnas, tumors, expression, primary, gene, metastasis, [76]

Analysis of microRNAs expressions in chondrosarcoma.

MicroRNAs (miRNAs) are small non-coding RNAs capable of inhibiting gene expression post-transcriptionally and expression profiling can provide therapeutic targets and tools for cancer diagnosis. Here, we profiled miRNA expression of chondrosarcoma, namely clinical samples from human conventional chondrosarcoma tissue, established chondrosarcoma cell lines, and primary non-tumorous adult articular chondrocytes, by miRNA array and quantitative real-time PCR. 27 miRNAs: miR-10b, 23b, 24-1*, 27b, 100, 134, 136, 136*, 138, 181d, 186, 193b, 221*, 222, 335, 337-5p, 376a, 376a*, 376b, 376c, 377, 454, 495, 497, 505, 574-3p, and 660, were significantly downregulated in chondrosarcoma and only 2: miR-96 and 183, were upregulated.

chondrosarcoma, mirnas, expression, downregulated, samples, 222, 335, 376a, pcr, significantly, real-time, quantitative, chondrocytes, articular, non-tumorous, clinical, 100, 136, profiling, mir-181a, provide, [77]

MicroRNAome profiling in benign and malignant neurofibromatosis type 1-associated nerve sheath tumors: evidences of PTEN pathway alterations in early NF1 tumorigenesis.

Neurofibromatosis type 1 (NF1) is a common dominant tumor predisposition syndrome affecting 1 in 3,500 individuals. The hallmarks of NF1 are the development of peripheral nerve sheath tumors either benign (dermal and plexiform neurofibromas) or malignant (MPNSTs).To comprehensively characterize the role of microRNAs in NF1 tumorigenesis, we analyzed 377 miRNAs expression in a large panel of dermal and plexiform neurofibromas, and MPNSTs. In MPNSTs, significant deregulated miRNAs were involved in PTEN repression (miR-301a, miR-19a, and miR-106b), RAS-MAPK pathway regulation (Let-7b, miR-195, and miR-10b), mesenchymal transition (miR-200c, let-7b, miR-135a, miR-135b, and miR-9), HOX genes expression (miR-210, miR-196b, miR-10a, miR-10b, and miR-9), and cell cycle progression (miR-195, let-7b, miR-20a, miR-210, miR-129-3p, miR-449a, and miR-106b).We confirmed the implication of PTEN in genesis of plexiform neurofibromas and MPNSTs in NF1.

nf1, neurofibromas, plexiform, mirnas, tumor, pten, [78]

MicroRNA expression in Epstein-Barr virus-associated post-transplant smooth muscle tumours is related to leiomyomatous phenotype.

Epstein-Barr virus (EBV)-associated post-transplant smooth muscle tumours (PTSMT) are rare complications. Tissue samples from PTSMT and uterine leiomyomas were analysed by quantitative real-time PCR for the expression of 365 mature microRNA. The expression pattern of microRNA in PTSMT is not associated with EBV infection but reflects the leiomyomatous differentiation of the tumour cells.

microrna, expression, ptsmt, ebv-related, mir-146a, mir-10b, leiomyomas, tumours, mir-203, mir-155, analysis, profiles, [79]

Deep Sequencing the MicroRNA Transcriptome in Colorectal Cancer.

Colorectal cancer (CRC) is one of the leading causes of cancer related deaths and the search for prognostic biomarkers that might improve treatment decisions is warranted. Few associations were found between clinical parameters and miRNA expression, among them, low expression of miR-592 and high expression of miR-10b-5p and miR-615-3p were associated with tumors located in the right colon relative to the left colon and rectum. Pathway analysis of the target genes regulated by the five most highly expressed miRNAs uncovered a significant number of genes involved in the CRC pathway, including APC, TGF and PI3K, thus suggesting that these miRNAs are relevant in CRC.

mirnas, expression, crc, tumors, associations, cohort, expressed, high, gene, [80]

Identification of circulating microRNA signatures for breast cancer detection.

The goal of this study is to identify circulating microRNA (miRNA) signatures using a cohort of Asian Chinese patients with breast cancer, and to compare miRNA profiles between tumor and serum samples.miRNA from paired breast cancer tumors, normal tissue, and serum samples derived from 32 patients were comprehensively profiled using microarrays or locked nucleic acid real-time PCR panels. Significant serum miRNAs, identified by logistic regression, were validated in an independent set of serum samples from patients (n = 132) and healthy controls (n = 101).The 20 most significant miRNAs differentially expressed in breast cancer tumors included miRNA (miR)-21, miR-10b, and miR-145, previously shown to be dysregulated in breast cancer. receiver operating characteristic curves derived from combinations of these miRNAs exhibited areas under the curves of 0.90 to 0.91.The clinical use of miRNA signatures as a noninvasive diagnostic strategy is promising, but should be further validated for different subtypes of breast cancers.

mirna, serum, breast, cancer, samples, tumor, [81]

Comprehensive microRNA Profiling of Prostate Cancer.

MicroRNAs are small non-coding RNA molecules that have been shown to regulate the expression of genes linked to cancer. Our study investigated the importance of several microRNAs in cases of prostate cancer from 37 patients that were manually microdissected to obtain pure populations of tumor cells, normal epithelium and adjacent stroma. Loss of 18 miRNAs (e.g.miR-34c, miR-29b, miR-212 and miR-10b) and upregulation of miR-143 and miR-146b were significantly found in all the tumors in comparison with normal epithelium and/or stroma (p 0.001).

tumors, micrornas, prostate, normal, cancer, found, mirnas, epithelium, stroma, [82]

Deregulated serum concentrations of circulating cell-free microRNAs miR-17, miR-34a, miR-155, and miR-373 in human breast cancer development and progression.

In the current study, we investigated the use of circulating miR concentrations as biomarkers in the serum of breast cancer patients.We analyzed serum samples from 120 patients with primary breast cancer after surgery and before chemotherapy (M0, classified into 3 subgroups of 40 patients with progesterone/estrogen-positive, HER2-positive, and triple-negative cancer), 32 patients with overt metastasis (M1), and 40 healthy women. The data were correlated with clinicopathologic risk factors, with particular reference to HER2 and hormone receptor status of the primary tumor and the presence of metastases.The relative serum concentrations of circulating miR-34a [P = 0.013, area under the curve (AUC) 0.636], miR-93 (P = 0.001, AUC 0.699), and miR-373 (P = 0.0001, AUC 0.879) were significantly different between M0 breast cancer patients and healthy women, whereas miR-17 (P = 0.002, AUC 0.679) and miR-155 (P = 0.0001, AUC 0.781) were differently expressed between M0 and M1 patients. Deregulated concentrations of miR-17 (P = 0.019) and miR-34a (P = 0.029) were detected in patients with progesterone/estrogen receptor-positive and -negative status, respectively.Our findings indicate that serum concentrations of deregulated microRNAs may be linked to a particular biology of breast carcinomas favoring progression and metastatic spread.

=, p, patients, concentrations, auc, cancer, breast, serum, micrornas, tumor, [83]

Salivary microRNAs as promising biomarkers for detection of esophageal cancer.

In this study, we investigated the discriminatory power of salivary miRNAs (including whole saliva and saliva supernatant) for detection of esophageal cancer.By Agilent microarray, six deregulated miRNAs from whole saliva samples from seven patients with esophageal cancer and three healthy controls were selected. The six selected miRNAs were subjected to validation of their expression levels by RT-qPCR using both whole saliva and saliva supernatant samples from an independent set of 39 patients with esophageal cancer and 19 healthy controls.Six miRNAs (miR-10b*, miR-144, miR-21, miR-451, miR-486-5p, and miR-634) were identified as targets by Agilent microarray. After validation by RT-qPCR, miR-10b*, miR-144, and miR-451 in whole saliva and miR-10b*, miR-144, miR-21, and miR-451 in saliva supernatant were significantly upregulated in patients, with sensitivities of 89.7, 92.3, 84.6, 79.5, 43.6, 89.7, and 51.3% and specificities of 57.9, 47.4, 57.9%, 57.9, 89.5, 47.4, and 84.2%, respectively.We found distinctive miRNAs for esophageal cancer in both whole saliva and saliva supernatant.

saliva, mirnas, esophageal, cancer, whole, supernatant, [84]

The C-terminal putative nuclear localization sequence of breast cancer metastasis suppressor 1, BRMS1, is necessary for metastasis suppression.

Breast cancer metastasis suppressor 1 (BRMS1) is a predominantly nuclear protein that suppresses metastasis in multiple human and murine carcinoma cell lines. MDA-MB-231 human metastatic breast cancer cells transduced with BRMS1(NLS1,1), BRMS1(NLS2,2) or BRMS1(NLS2,1) were evaluated for metastasis suppression in an experimental xenograft mouse model. Together, these data demonstrate an important role for NLS2 in the cytoplasm that is critical for metastasis suppression and is distinct from nuclear localization.

metastasis, brms1, nuclear, nls2, localization, nls1, suppression, brms1(nls2,1, brms1(nls2,2, brms1(nls1,1, [85]

The High Mobility Group A proteins contribute to thyroid cell transformation by regulating miR-603 and miR-10b expression.

The overexpression of the HMGA1 proteins is a feature of human malignant neoplasias and has a causal role in cell transformation. The aim of our study has been to investigate the microRNAs (miRNAs or miRs) regulated by the HMGA1 proteins in the process of cell transformation analyzing the miRNA expression profile of v-ras-Ki oncogene-transformed thyroid cells expressing or not HMGA1 proteins. Moreover, functional studies showed that miR-10b and miR-603 regulate positively and negatively, respectively, cell proliferation and migration suggesting a role of their dysregulation in thyroid cell transformation.

cell, hmga1, proteins, mir-603, mir-10b, regulated, transformation, [86]

Analysis of miR-205 and miR-155 expression in the blood of breast cancer patients.

The purpose of this study was to identify and validate circulating microRNAs (miRNAs) in human plasma for use as breast cancer (BC) biomarkers and to analyze their relationship to clinicopathologic features and its preliminary biological function. Using real-time PCR (RT-PCR), we analyzed miR-205 and miR-155 in archived serum from 30 participants, 20 with breast cancer and 10 healthy people. Functional analysis showed that ectopic expression of miR-205 significantly inhibits cell proliferation and promotes apoptosis.

bc, mir-205, patients, mir-155, mirnas, serum, expression, [**?**]

Serum circulating microRNA profiling for identification of potential breast cancer biomarkers.

MicroRNAs (miRNAs) are a class of small, non-coding RNA molecules that can regulate gene expression, thereby affecting crucial processes in cancer development. miRNAs offer great potential as biomarkers for cancer detection because of their remarkable stability in blood and their characteristic expression in different diseases. We performed miRNA profiling on serum from breast cancer patients, followed by construction of ROC (Receiver Operating Characteristic) curves to determine the sensitivity and specificity of the assay.

mirnas, cancer, serum, breast, controls, roc, patients, profiling, expression, curves, [87]

Relationship between circulating and tissue microRNAs in a murine model of breast cancer.

MiRNAs are key regulators of tumorigenesis that are aberrantly expressed in the circulation and tissue of patients with cancer. Tumour volume was monitored weekly and blood sampling performed at weeks 1, 3 and 6 following tumour induction (total n=60). Animals were sacrificed at week 6 and tumour tissue (n=15), lungs (n=20) and enlarged lymph nodes (n=3) harvested.

tumour, tissue, circulation, mirnas, p¡0.05, significantly, weekly, expression, [88]

The role of microRNAs in breast cancer migration, invasion and metastasis.

MicroRNAs (miRNAs) are a major class of small, noncoding RNA molecules that regulate gene expression by targeting mRNAs to trigger either translational repression or mRNA degradation. The link between altered miRNA signatures and breast cancer development and metastasis can be observed either through the loss of tumor suppressor miRNAs, such as let-7s, miR-30a/31/34a/125s/200s/203/205/206/342 or the overexpression of oncogenic miRNAs, such as miR-10b/21/135a/155/221/222/224/373/520c in breast cancer cells. Some of these miRNAs have also been validated in tumor specimens of breast cancer patients, underscoring their potential roles in diagnostics, as well as targets for novel therapeutics for breast cancer.

mirnas, cancer, breast, targeting, therapeutics, potential, [89]

Identification of metastamirs as metastasis-associated microRNAs in clear cell renal cell carcinomas.

MicroRNAs (miRNAs) play a pivotal role in cancerogenesis and cancer progression, but their specific role in the metastasis of clear cell renal cell carcinomas (ccRCC) is still limited. Based on microRNA microarray analyses from normal and cancerous samples of ccRCC specimens and from bone metastases of ccRCC patients, we identified a set of 57 differentially expressed microRNAs between these three sample groups of ccRCC. The altered miRNA profiles, comprising newly identified metastasis-associated miRNAs, termed metastamir and the predicted miRNA-target interactions together with the significant correlations of miRNAs that were either lost or newly appeared in the studied sample groups, afford a solid basis for further functional analyses of individual miRNAs in RCC metastatic progression.

mirnas, samples, tissue, ccrcc, metastatic, micrornas, cell, normal, [90]

miR-10b, a master inhibitor of the cell cycle, is down-regulated in human breast tumours.

Here, we show that microRNA-10b* is a master regulator of breast cancer cell proliferation and is downregulated in tumoural samples versus matched peritumoural counterparts. Ectopic delivery of synthetic microRNA-10b* in breast cancer cell lines or into xenograft mouse breast tumours inhibits cell proliferation and impairs tumour growth in vivo, respectively. We identified and validated in vitro and in vivo three novel target mRNAs of miR-10b* (BUB1, PLK1 and CCNA2), which play a remarkable role in cell cycle regulation and whose high expression in breast cancer patients is associated with reduced disease-free survival, relapse-free survival and metastasis-free survival when compared to patients with low expression.

cancer, cells, breast, expression, proliferation, survival, microrna-10b*, [91]

MiR-10b downregulates the stress-induced cell surface molecule MICB, a critical ligand for cancer cell recognition by natural killer cells.

Natural killer cells (NK) are a component of innate immunity well known for their potent ability to kill virus-infected or neoplastically transformed cells following stimulation of the NK cell receptor NKG2D. Notably, antagonizing miR-10b action enhanced NKG2D-mediated killing of tumor cells in vitro and enhanced clearance of tumors in vivo. Together, our results define MICB as a novel immune target of miR-10b, implying a direct link between metastasis capability and immune escape from NK cells.

cells, tumor, mir-10b, immunity, micb, killer, nk, [92]

MicroRNAs regulate tumor angiogenesis modulated by endothelial progenitor cells.

Bone marrow-derived endothelial progenitor cells (EPC) contribute to the angiogenesis-dependent growth of tumors in mice and humans. Here, we show that genetic ablation of miRNA-processing enzyme Dicer, specifically in the bone marrow, decreased the number of circulating EPCs, resulting in angiogenesis suppression and impaired tumor growth. Furthermore, genome-wide deep sequencing of small RNAs revealed tumor EPC-intrinsic miRNAs including miR-10b and miR-196b, which have been previously identified as key regulators of HOX signaling and adult stem cell differentiation.

tumors, growth, angiogenesis, mirnas, bone, epc, mir-196b, mir-10b, [93]

Identification of a 4-microRNA signature for clear cell renal cell carcinoma metastasis and prognosis.

Renal cell carcinoma (RCC) metastasis portends a poor prognosis and cannot be reliably predicted. Using 28 localized and metastatic ccRCC specimens as the training cohort and the univariate logistic regression and risk score methods, we developed a miRNA signature model in which the expression levels of miR-10b, miR-139-5p, miR-130b and miR-199b-5p were used to determine the status of ccRCC metastasis. Using

the most stably expressed miRNA among benign and tumorous kidney tissue as the internal reference for normalization, we successfully converted his signature to be a quantitative PCR (qPCR)-based assay, which showed the same high sensitivity and specificity.

ccrcc, signature, metastasis, mirna, expression, cohort, [94]

Targeting of syndecan-1 by microRNA miR-10b promotes breast cancer cell motility and invasiveness via a Rho-GTPase- and E-cadherin-dependent mechanism.

miR-10b overexpression induced post-transcriptional downregulation of syndecan-1, as demonstrated by quantitative real-time PCR (qPCR), flow cytometry, and 3'UTR luciferase assays, resulting in increased cancer cell migration and matrigel invasiveness. Affymetrix screening and confirmatory qPCR and Western blotting analysis of syndecan-1-deficient cells revealed upregulation of ATF-2, COX-2, cadherin-11, vinculin, actin 2, MYL9, transgelin-1, RhoA/C, matrix metalloproteinase 2 (MMP2) and heparanase, and downregulation of AML1/RUNX1, E-cadherin, CLDN1, p21WAF/CIP, cyclin-dependent kinase 6, TLR-4, PAI1/2, Collagen1alpha1, JHDM1D, Mpp4, MMP9, matrilin-2 and ANXA3/A10. Rho-GTPase-dependent modulation of cytoskeletal function and downregulation of E-cadherin expression are identified as relevant effectors of the miR-10b-syndecan-1 axis, which emerges as a promising target for the development of new therapeutic approaches for breast cancer.

syndecan-1, cells, increased, mir-10b, cancer, target, breast, downregulation, [95]

Genome-wide profiling identified a set of miRNAs that are differentially expressed in glioblastoma stem cells and normal neural stem cells.

A major challenge in cancer research field is to define molecular features that distinguish cancer stem cells from normal stem cells. In this study, we compared microRNA (miRNA) expression profiles in human glioblastoma stem cells and normal neural stem cells using combined microarray and deep sequencing analyses. Moreover, two of the miRNAs with increased expression in glioblastoma stem cells also exhibited elevated expression in glioblastoma patient tissues examined, while two miRNAs with decreased expression in glioblastoma stem cells displayed reduced expression in tumor tissues.

stem, cells, mirna, glioblastoma, expression, normal, [96]

MicroRNAs and metastasis-related gene expression in Egyptian breast cancer patients.

MicroRNAs (miRNAs) are a class of naturally occurring small noncoding RNAs that regulate gene expression, cell growth, differentiation and apoptosis by targeting mRNAs for translational repression or cleavage. The present study was conducted to study miRNAs in Egyptian breast cancer (BC) and their relation to metastasis, tumor invasion and apoptosis in addition to their association with the ER and PR statuses.Real Time RT-PCR was performed to identify the miRNA expression level of eight miRNAs and eight metastatic-related genes in 40 breast cancer samples and their adjacent non-neoplastic tissues. Mir-21 was significantly over-expressed in ER-/PR- cases.Specific miRNAs (mir-10, mir-21, mir-155, mir-373, mir-30b, mir-126, mir-17p, mir-335) are associated with tumor metastasis and other clinical characteristics for BC, facilitating identification of individuals who are at risk.

mirnas, gene, bc, expression, metastasis, mir-21, tissues, tumor, significantly, cancer, mir-155, [**?**]

Downregulation of six microRNAs is associated with advanced stage, lymph node metastasis and poor prognosis in small cell carcinoma of the cervix.

Small cell carcinoma of the cervix (SCCC) is very rare, and due to the long time period required to recruit sufficient numbers of patients, there is a paucity of information regarding the prognostic factors associated with survival. MicroRNAs (miRNAs) have been used as cancer-related biomarkers in a variety of tumor types, and the objective of this study was to determine whether microRNA expression profiles can predict

clinical outcome in SCCC.Forty-four patients with SCCC who underwent radical hysterectomy between January 2000 and October 2009 were enrolled. Kaplan-Meier survival analyses revealed that SCCC patients with low expression of has-miR-100 (P = 0.019) and has-miR-125b (P = 0.020) projected a significant tendency towards poorer prognosis.This study demonstrates that downregulation of 7 miRNA associated with advanced stage, 6 miRNAs with metastasis and 2 with poor prognosis in SCCC.

sccc, mirnas, patients, expression, associated, has-mir-100, has-mir-125b, metastasis, survival, significantly, stage, [97]

Oncogenic function and early detection potential of miRNA-10b in oral cancer as identified by microRNA profiling.

The miRNA participates in a variety of biologic processes, and dysregulation of miRNA is associated with malignant transformation. There were 23 miRNAs found with considerably differential expressions between six oral cancer cell lines and five lines of normal oral keratinocytes, in which, 10 miRNAs showed the highest significant difference after independent examination by reverse transcription quantitative PCR. This upregulation of miR-10b in plasma was further shown in the patients with oral cancer [P ¡ 0.0001, area under curve (AUC) = 0.932] and precancer lesions (P ¡ 0.0001, AUC = 0.967), suggesting that miR-10b possesses a high potential to discriminate the normal subjects.

mir-10b, mirna, cancer, oral, cell, plasma, associated, lines, [98]

Delivery of MicroRNA-10b with Polylysine Nanoparticles for Inhibition of Breast Cancer Cell Wound Healing.

Recent studies revealed that micro RNA-10b (mir-10b) is highly expressed in metastatic breast cancer cells and positively regulates breast cancer cell migration and invasion through inhibition of HOXD10 target synthesis. An RNA molecule sequence exactly matching the mature mir-10b minor antisense showed strong inhibition when mixed with PLL in a wound-healing assay with human breast cell line MDA-MB-231. The resulting PLL-RNA nanoparticles delivered the anti-microRNA molecules into cytoplasm of breast cancer cells in a concentration-dependent manner that displayed sustainable effectiveness.

breast, cells, molecules, cancer, studies, effectiveness, pll, mir-10b, inhibition, [99]

miRNA profiling in metastatic renal cell carcinoma reveals a tumour-suppressor effect for miR-215.

Recently, microRNAs (miRNAs) have been shown to have a role in cancer metastasis and potential as prognostic biomarkers in cancer.We performed a miRNA microarray to identify a miRNA signature characteristic of metastatic compared with primary RCCs. We performed experimental and bioinformatic analyses to explore the involvement of miR-215 in RCC progression and metastasis.We identified 65 miRNAs that were significantly altered in metastatic compared with primary RCCs. In addition, through gene expression profiling, we identified direct and indirect targets of miR-215 that can contribute to tumour metastasis.Our analysis showed that miRNAs are altered in metastatic RCCs and can contribute to kidney cancer metastasis through different biological processes.

rcc, mirnas, metastatic, mir-215, kidney, cancer, [100]

Cysteine-rich 61-connective tissue growth factor-nephroblastoma-overexpressed 5 (CCN5)/Wnt-1-induced signaling protein-2 (WISP-2) regulates microRNA-10b via hypoxia-inducible factor-1-TWIST signaling networks in human breast cancer cells.

MicroRNAs (miRNAs) are naturally occurring single-stranded RNA molecules that post-transcriptionally regulate the expression of target mRNA transcripts. Among the several miRNAs, miRNA-10b (miR-10b) expression is increased in metastatic breast cancer cells and positively regulates cell migration and invasion

through the suppression of the homeobox D10 (HOXD10) tumor suppressor signaling pathway. On the basis of these findings, it is plausible that reactivation of CCN5 in miR-10b-positive invasive/metastatic breast cancers alone or in combination with current therapeutic regimens could provide a unique, alternative strategy to existing breast cancer therapy.

expression, cell, breast, ccn5, cancer, mir-10b, twist1, regulate, metastatic, pathway, [101]

Suppression of breast tumor growth and metastasis by an engineered transcription factor.

Maspin is a tumor and metastasis suppressor playing an essential role as gatekeeper of tumor progression. Genome-wide transcriptional profiles of ATF-induced cells revealed a gene signature that was found over-represented in estrogen receptor positive (ER+) "Normal-like" intrinsic subtype of breast cancer and in poorly aggressive, ER+ luminal A breast cancer cell lines. Our data suggest that Maspin up-regulates downstream tumor and metastasis suppressor genes that are silenced in breast cancers, and are normally expressed in the neural system, including CARNS1, SLC8A2 and DACT3.

tumor, maspin, breast, cells, cancer, atf-126, [102]

Integrated miRNA and mRNA expression profiling of mouse mammary tumor models identifies miRNA signatures associated with mammary tumor lineage.

miRNA expression profiling of human breast cancers has identified miRNAs related to the clinical diversity of the disease and potentially provides novel diagnostic and prognostic tools for breast cancer therapy. In order to further understand the associations between oncogenic drivers and miRNA expression in sub-types of breast cancer, we performed miRNA expression profiling on mammary tumors from eight well-characterized genetically engineered mouse (GEM) models of human breast cancer, including MMTV-H-Ras, -Her2/neu, -c-Myc, -PymT, -Wnt1 and C3(1)/SV40 T/t-antigen transgenic mice, BRCA1(fl/fl);p53(+/-);MMTV-cre knock-out mice and the p53(fl/fl);MMTV-cre transplant model.miRNA expression patterns classified mouse mammary tumors according to luminal or basal tumor subtypes. Integrated miRNA and mRNA gene expression analyses greatly improved the identification of miRNA targets from potential targets identified in silico.This is the first large-scale miRNA gene expression study across a variety of relevant GEM models of human breast cancer demonstrating that miRNA expression is highly associated with mammary tumor lineage, differentiation and oncogenic pathways.

mirnas, tumors, expression, mammary, breast, cancer, human, [103]

microRNA-10b: a new marker or the marker of pancreatic ductal adenocarcinoma?

microRNA-10b (miR-10b) expression in pancreatic ductal adenocarcinoma (PDAC), as identified by in situ hybridization, is highly correlated with cancer diagnosis, therapy response, and prognosis. If these findings are further confirmed in prospective studies, miR-10b could be used to improve the management of PDAC and decrease the mortality rate of this deadly cancer.

mir-10b, pdac, cancer, microrna-10b, mortality, decrease, management, improve, used, studies, prospective, confirmed, further, findings, prognosis, therapy, rate, diagnosis, correlated, highly, hybridization, situ, identified, adenocarcinoma, ductal, pancreatic, expression, response, deadly, [104]

MicroRNA-10b expression correlates with response to neoadjuvant therapy and survival in pancreatic ductal adenocarcinoma.

In this study, we sought to determine whether miR-10b could serve as a biomarker for PDAC.miRNA expression was characterized by fluorescence-based in situ hybridization using locked nucleic acid-modified DNA probes against miR-10b, miR-21, miR-155, miR-196a, and miR-210, followed by codetection of proteins by immunohistochemistry on the same tissue sections. miRNA expression in surgically resected PDAC

tissues and in endoscopic ultrasonography (EUS)-guided fine-needle aspirate (EUS-FNA) samples was analyzed in cytokeratin 19 (CK19)-positive epithelial cells using optical intensity analysis.In 10 resected PDAC samples, miR-10b was the most frequently and consistently overexpressed miRNA among characterized miRNAs, exhibiting a four-fold increase in the cancer cells (P = 0.012). In patients with PDACs, lower levels of miR-10b were associated with improved response to multimodality neoadjuvant therapy, likelihood of surgical resection, delayed time to metastasis, and increased survival.miR-10b is a novel diagnostic biomarker for PDACs when assessing pancreatic lesions.

mir-10b, expression, pdac, cells, mirna, samples, lesions, pancreatic, [105]

Heparin impairs angiogenesis through inhibition of microRNA-10b.

Heparin, which has been used as an anticoagulant drug for decades, inhibits angiogenesis, whereas thrombin promotes tumor-associated angiogenesis. Overexpression of miR-10b induces HMEC-1 cell migration, tube formation, and angiogenesis, and down-regulates homeobox D10 (HoxD10) expression via direct binding of miR-10b to the putative 3' UTR of HoxD10. In addition, HMEC-1 cell migration and tube formation are induced by HoxD10 knockdown, whereas angiogenesis is arrested when HoxD10 expression is increased after anti-miR-10b or heparin treatments.

expression, thrombin, heparin, angiogenesis, mir-10b, hoxd10, [106]

Micro-RNA expression in cisplatin resistant germ cell tumor cell lines.

We compared microRNA expression patterns in three cisplatin resistant sublines derived from paternal cisplatin sensitive germ cell tumor cell lines in order to improve our understanding of the mechanisms of cisplatin resistance.Three cisplatin resistant sublines (NTERA-2-R, NCCIT-R, 2102EP-R) showing 2.7-11.3-fold increase in drug resistance after intermittent exposure to increasing doses of cisplatin were compared to their parental counterparts, three well established relatively cisplatin sensitive germ cell tumor cell lines (NTERA-2, NCCIT, 2102EP). RNA was converted into cDNA and quantitative RT-PCR was run using 384 well low density arrays covering almost all (738) known microRNA species of human origin.Altogether 72 of 738 (9.8%) microRNAs appeared differentially expressed between sensitive and resistant cell line pairs (NTERA-2R/NTERA-2 = 43, NCCIT-R/NCCIT = 53, 2102EP-R/2102EP = 15) of which 46.7-95.3% were up-regulated (NTERA-2R/NTERA-2 = 95.3%, NCCIT-R/NCCIT = 62.3%, 2102EP-R/2102EP = 46.7%). These were hsa-miR-512-3p/-515/-517/-518/-525 (up to 8.1-fold up-regulated) and hsa-miR-99a/-100/-145 (up to 10-fold down-regulated).Examining almost all known human micro-RNA species confirmed the miR-371-373 cluster as a promising target for explaining cisplatin resistance, potentially by counteracting wild-type P53 induced senescence or linking it with the potency to differentiate.

cell, cisplatin, lines, =, three, resistant, [107]

Human glioma growth is controlled by microRNA-10b.

MicroRNA (miRNA) expression profiling studies revealed a number of miRNAs dysregulated in the malignant brain tumor glioblastoma. Analysis of The Cancer Genome Atlas expression data set reveals a strong positive correlation between numerous genes sustaining cellular growth and miR-10b levels in human glioblastomas, while proapoptotic genes anticorrelate with the expression of miR-10b. Furthermore, survival of glioblastoma patients expressing high levels of miR-10 family members is significantly reduced in comparison to patients with low miR-10 levels, indicating that miR-10 may contribute to glioma growth in vivo.

mir-10b, gliomas, growth, mirna, expression, levels, revealed, human, glioblastoma, mir-10, [108]

The small-nucleolar RNAs commonly used for microRNA normalisation correlate with tumour pathology and prognosis.

To investigate small-nucleolar RNAs (snoRNAs) as reference genes when measuring miRNA expression in tumour samples, given emerging evidence for their role in cancer.Four snoRNAs, commonly used for normalisation, RNU44, RNU48, RNU43 and RNU6B, and miRNA known to be associated with pathological factors, were measured by real-time polymerase chain reaction in two patient series: 219 breast cancer and 46 head and neck squamous cell carcinoma (HNSCC). RNU44 is an intronic gene in a cluster of highly conserved snoRNAs in the growth arrest specific 5 (GAS5) transcript, which is normally upregulated to arrest cell growth under stress. RNU48 and RNU43 were also identified as intronic snoRNAs within genes that are dysregulated in cancer.Small-nucleolar RNAs are important in cancer prognosis, and their use as reference genes can introduce bias when determining miRNA expression.

expression, snornas, mirna, associated, genes, rnu44, prognosis, rnas, [109]

MicroRNAs 10a and 10b are potent inducers of neuroblastoma cell differentiation through targeting of nuclear receptor corepressor 2.

MicroRNAs function as negative regulators of posttranscriptional gene expression, having major roles in cellular differentiation. Several neuroblastoma cell lines can be induced to undergo differentiation by all-trans-retinoic acid (ATRA) and are used for modeling signaling pathways involved in this process. We conclude that miR-10a/b has major roles in the process of neural cell differentiation through direct targeting of NCOR2, which in turn induces a cascade of primary and secondary transcriptional alterations, including the downregulation of MYCN.

differentiation, cell, targets, ncor2, mir-10a/b, major, atra, induced, lines, [110]

MicroRNAs involved in neoplastic transformation of liver cancer stem cells.

The existence of cancer stem cells in hepatocellular carcinoma (HCC) has been verified by characterizing side population (SP) cells based on efflux of Hoechst 33342 dye from stem cells. However, it is still unclear which miRNAs participate in the neoplastic transformation of liver cancer stem cells (LCSCs) during hepatocarcinogenesis.To identify the unique set of miRNAs differentially regulated in LCSCs, we applied SP sorting to primary cultures of F344 rat HCC cancer cells treated with diethylnitrosamine (DEN) and normal syngenic fetal liver cells, and the stem-like characteristics of SP cells were verified through detecting expression of CD90.1, AFP and CK-7. Global miRNA expression profiles of two groups of SP cells were screened through microarray platform.A total of 68 miRNAs, including miR-10b, miR-21, miR-470*, miR-34c-3p, and let-7i*, were identified as overexpressed in SP of HCC cells compared to fetal liver cells.

cells, mirna, sp, lcscs, expression, cancer, stem, liver, hcc, [111]

Role of miR-10b in breast cancer metastasis.

Ninety percent of cancer-related mortality is caused by metastasis. In particular, recent studies provide the first functional evidence that overexpression of a specific miRNA, miR-10b, can contribute to the development of metastasis, which can be exploited therapeutically in treating breast cancer metastasis in mice. Further in-depth analysis should provide more precise evaluation of the roles, mechanisms, and therapeutic utility of this miRNA in breast cancer.

metastasis, mirnas, cancer, provide, evidence, breast, [112]

Hyaluronan-CD44 interaction promotes c-Src-mediated twist signaling, microRNA-10b expression, and RhoA/RhoC up-regulation, leading to Rho-kinase-associated cytoskeleton activation and breast tumor cell invasion.

Our results indicate that HA binding to CD44 promotes c-Src kinase activation, which, in turn, increases Twist phosphorylation, leading to the nuclear translocation of Twist and transcriptional activation. Further analyses reveal that miR-10b is controlled by an upstream promoter containing the Twist binding site(s), whereas ChIP assays demonstrate that stimulation of miR-10b expression by HA/CD44-activated c-Src is Twist-dependent in breast tumor cells. Taken together, these findings indicate that the HA-induced CD44 interaction with c-Src-activated Twist plays a pivotal role in miR-10b production, leading to the down-regulation of tumor suppressor protein (HOXD10), RhoGTPase-ROK activation, and tumor cell invasion.

cell, tumor, breast, mir-10b, twist, expression, [113]

Systemic miRNA-195 differentiates breast cancer from other malignancies and is a potential biomarker for detecting noninvasive and early stage disease.

The potential of microRNAs (miRNAs) as novel tumor markers has been the focus of recent scrutiny because of their tissue specificity, stability, and association with clinicopathological parameters. Our aim was to assess a panel of cancer-associated miRNAs in the circulation of patients with various malignancies, to determine whether these "oncomirs" were tumor specific, and thus to establish whether systemic miRNA analysis has utility in cancer diagnosis.Whole blood samples were prospectively collected from preoperative cancer patients (breast, prostate, colon, and renal cancer and melanoma; A combination of three circulating miRNAs, including miR-195, further enhanced the discriminative power of this test for breast cancer to 94%.These findings suggest that individual cancers display specific systemic miRNA profiles, which could aid in discriminating among cancer types.

mirnas, cancer, specificity, systemic, breast, patients, tumor, circulating, whether, cancers, [114]

MicroRNA-10b regulates tumorigenesis in neurofibromatosis type 1.

MicroRNAs (miRNAs) are frequently deregulated in human tumors, and play important roles in tumor development and progression. We demonstrated that miR-10b was up-regulated in primary Schwann cells isolated from NF1 neurofibromas and in cell lines and tumor tissues from malignant peripheral nerve sheath tumors (MPNSTs). Intriguingly, a significantly high level of miR-10b correlated with low neurofibromin expression was found in a neuroectodermal cell line: Ewing's sarcoma SK-ES-1 cells.

cells, mir-10b, nf1, neurofibromin, tumors, roles, mpnsts, signaling, ras, expression, [115]

miR-10b targets Tiam1: implications for Rac activation and carcinoma migration.

Understanding the mechanisms by which specific microRNAs regulate cell migration and invasion is a timely and significant problem in cancer cell biology. We demonstrate, using an miR-10b synthetic precursor, expression vector, and antisense oligonucleotide, that miR-10b represses Tiam1 expression in breast carcinoma cells and that it interacts with the 3'-UTR of Tiam1. These data provide a mechanism for the regulation of Tiam1-mediated Rac activation in breast cancer cells and need to be considered in the context of other reported functions for miR-10b.

mir-10b, cell, breast, tiam1, rac, expression, [116]

MicroRNAs and their target gene networks in breast cancer.

MicroRNAs (miRNAs) are a major class of small endogenous RNA molecules that post-transcriptionally inhibit gene expression. The gene networks orchestrated by these miRNAs are still largely unknown, although key targets have been identified that may contribute to the disease phenotype. Here we report how the

observed perturbations in miRNA expression profiles may lead to disruption of key pathways involved in breast cancer.

mirnas, breast, cancer, key, cancers, expression, gene, here, observed, [117]

hsa-mir-210 is a marker of tumor hypoxia and a prognostic factor in head and neck cancer.

Hypoxia is an important mechanism of treatment resistance in head and neck squamous cell carcinoma (HNSCC). Expression levels were correlated with clinicopathological variables and other markers of hypoxia: a published 99-gene hypoxia metagene, individual hypoxia-related genes such as TWIST1, and immunohistochemical expression of hypoxia-inducible factor 1 and its target gene carbonic anhydrase 9. We then performed survival analyses to investigate the prognostic significance of these microRNAs.Only the level of hsa-miR-210 was significantly correlated with other markers of hypoxia, including the 99-gene hypoxia metagene (rho = 0.67, P ¡ .001).

hypoxia, hsa-mir-210, markers, p, =, hsa-mir-21, hsa-mir-10b, levels, micrornas, correlated, [118]

MicroRNA-10b promotes migration and invasion through KLF4 in human esophageal cancer cell lines.

Recently, microRNAs have emerged as regulators of cancer metastasis through acting on multiple signaling pathways involved in metastasis. Overexpression of miR-10b in KYSE140 cells increased cell motility and invasiveness, whereas inhibition of miR-10b in EC9706 cells reduced cell invasiveness, although it did not alter cell motility. Finally, analyses of the miR-10b level in 40 human esophageal cancer samples and their paired normal adjacent tissues revealed an elevated expression of miR-10b in 95% (38 of 40) of cancer tissues, although no significant correlation of the miR-10b level with clinical metastasis status was observed in these samples.

cell, mir-10b, klf4, motility, cancer, invasiveness, level, [119]

Changes in microRNA expression levels correlate with clinicopathological features and prognoses in endometrial serous adenocarcinomas.

This study aimed to determine the expression profiles of microRNAs (miRNAs) in endometrial serous adenocarcinoma and to examine the association between miRNA expression and clinical outcomes. Univariate analysis revealed that lower expression of miR-101, miR-10b*, miR-139-5p, miR-152, miR-29b, and miR-455-5p was significantly correlated with poor overall survival (P ¡ 0.05), and reduced expression of miR-152, miR-29b, and miR-455-5p was significantly correlated with poor disease-free survival (P ¡ 0.05). Multivariate analysis demonstrated that decreased expression of miR-152 (P = 0.021) was a statistically independent risk factor for overall survival, and decreased expression levels of miR-101 (P = 0.016) and miR-152 (P = 0.010) were statistically independent risk factors for disease-free survival.

p, expression, =, mirnas, mir-152, survival, mir-101, endometrial, serous, correlated, [120]

Breast cancer metastasis suppressor 1 coordinately regulates metastasis-associated microRNA expression.

Breast cancer metastasis suppressor 1 (BRMS1) suppresses metastasis of multiple tumor types without blocking tumorigenesis. BRMS1 forms complexes with SIN3, histone deacetylases and selected transcription factors that modify metastasis-associated gene expression (e.g., EGFR, OPN, PI4P5K1A, PLAU). Collectively, these data show that BRMS1 coordinately regulates expression of multiple metastasis-associated miRNA and suggests that recruitment of BRMS1-containing SIN3:HDAC complexes to, as yet undefined, miRNA promoters might be involved in the regulation of cancer metastasis.

brms1, mirna, expression, metastasis, downstream, mir-10b, e.g., metastasis-associated, rna, involved, complexes, data, microrna, cancer, regulating, multiple, suppresses, [121]

MicroRNA-10b is overexpressed in malignant glioma and associated with tumor invasive factors, uPAR and RhoC.

MicroRNAs (miRNAs) are effective post-transcriptional regulators of gene expression and are important in many biological processes. Here, we performed real-time reverse transcriptase polymerase chain reaction (RT-PCR) assays on 43 glioma samples (17 glioblastoma, 6 anaplastic astrocytoma, 10 low-grade astrocytoma, 6 oligodendroglioma and 4 ependymoma) and 6 glioma cell lines. In addition, mRNA expressions of RhoC and urokinase-type plasminogen activator receptor (uPAR), which were thought to be regulated by miR-10b via HOXD10, were statistically significantly correlated with the expression of miR-10b (p ¡ 0.001, p = 0.001, respectively).

mir-10b, expression, glioma, p, mirnas, levels, =, [122]

Identification of suitable endogenous control genes for microRNA gene expression analysis in human breast cancer.

The discovery of microRNAs (miRNAs) added an extra level of intricacy to the already complex system regulating gene expression. To correct for systematic variables such as amount of starting template, RNA quality and enzymatic efficiencies, RQ-PCR data is commonly normalised to an endogenous control (EC) gene, which ideally, is stably-expressed across the test sample set. A universal endogenous control suitable for every tissue type, treatment and disease stage has not been identified and is unlikely to exist, so, to avoid introducing further error in the quantification of expression data it is necessary that candidate ECs be validated in the samples of interest.

expression, mirnas, gene, tissues, ecs, breast, profiling, rq-pcr, rna, [123]

Breast cancer metastasis: a microRNA story.

MicroRNAs (miRNAs) are small noncoding RNAs with regulatory functions, which play an important role in breast cancer. Altogether, these remarkable findings are important for our understanding of malignant transformation in the breast and may have implications for the management of patients with advanced breast cancer. The use of miRNAs as anticancer therapeutic agents is promising, and such fine molecular studies certainly help in bringing miRNAs closer to clinical practice.

mirnas, breast, cancer, metastasis, tumor, studies, prove, [124]

MicroRNA fingerprints during human megakaryocytopoiesis.

microRNAs are a highly conserved class of noncoding RNAs with important regulatory functions in proliferation, apoptosis, development, and differentiation. To discover novel regulatory pathways during megakaryocytic differentiation, we performed microRNA expression profiling of in vitro-differentiated megakaryocytes derived from CD34(+) hematopoietic progenitors. We confirmed in vitro and in vivo that miR-130a targets the transcription factor MAFB, which is involved in the activation of the GPIIB promoter, a key protein for platelet physiology.

microrna, target, expression, regulatory, megakaryocytes, mir-10a, differentiation, [125]

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