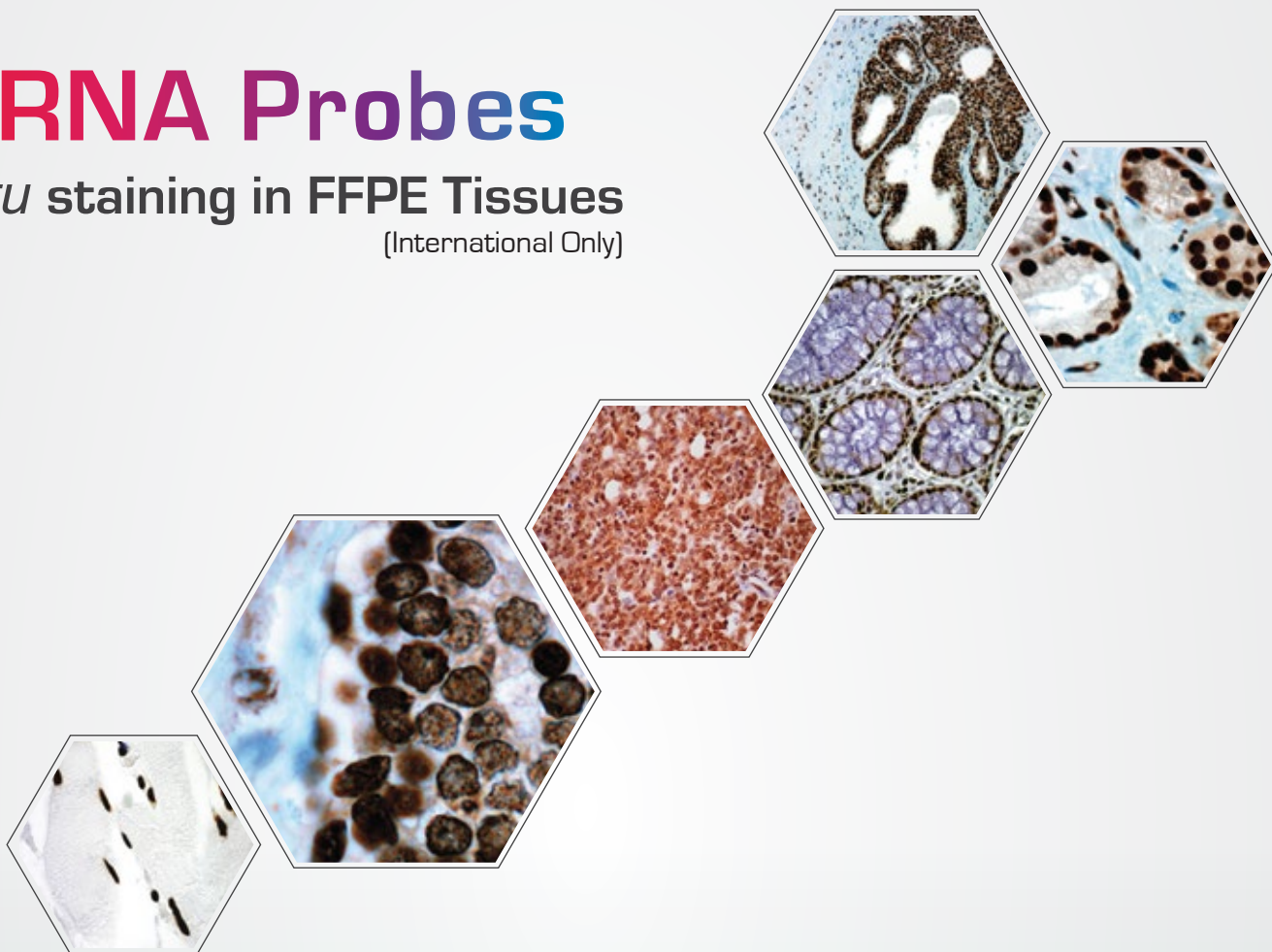


**NEW**

# miRNA Probes

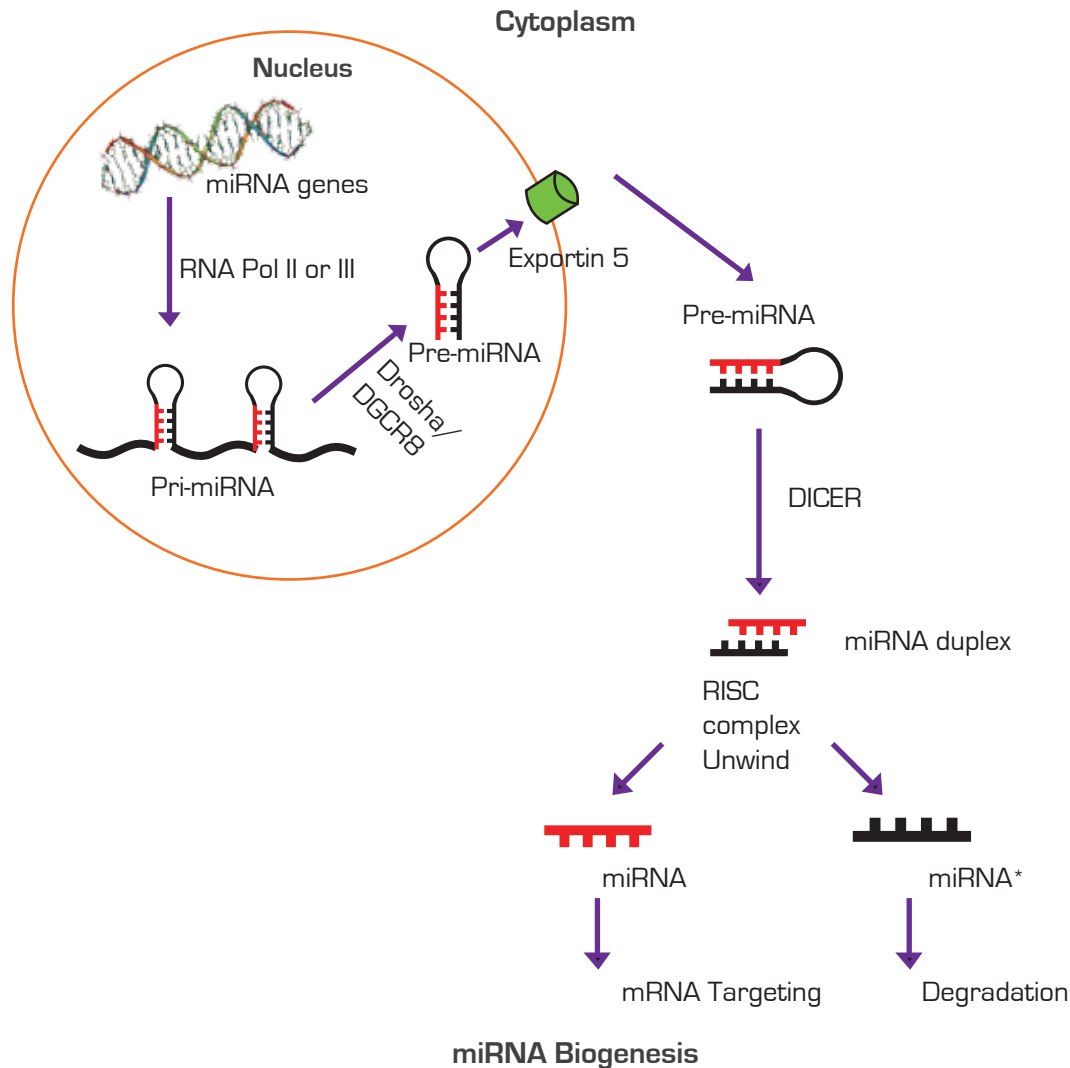
*in situ* staining in FFPE Tissues  
(International Only)



**Next-Gen *in situ* Tissue Signature Markers**  
**Potential Tool for Characterization of CUP**

# miRNA Processing

MicroRNAs (miRNAs) are endogenous, non-coding RNAs known to regulate gene expression by translational repression or RNA cleavage. The figure below shows the steps in which the miRNA genes are processed into the RNA induced silencing complex (RISC). Since miRNA has been observed to deregulate during progression of different cancer stages from normal to malignant and metastasis, the expression profile as a result of this deregulation can be exploited as a potential biomarker for cancer characterization.



## BioGenex MicroRNA Probes

### Highly Specific and Sensitive Probes

- Proprietary technology for clean intense stains
- *in situ* context of tissue morphology

### Manual Protocols

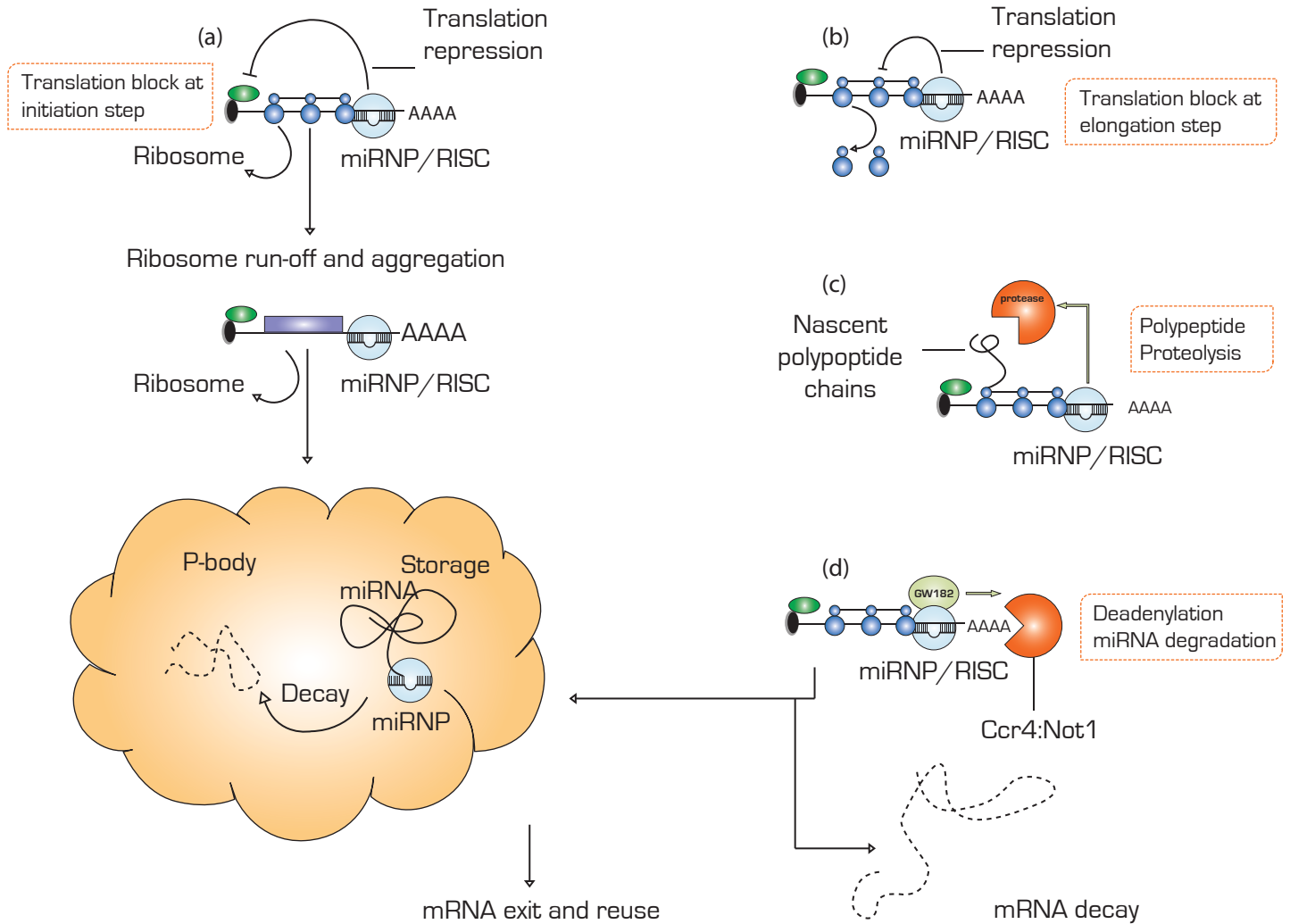
- Optimized for standardized manual ISH staining
- Ready-to-use reagents for FFPE tissues

## miRNA Potential Clinical Applications

Carcinoma of unknown primary (CUP) accounts for an estimated 3% to 5% of all metastatic cancers and one of the ten most frequent cancer diagnosed worldwide. Recent studies on tissue specific tumor markers indicated that miRNA expression is correlated with tumor signature and miRNA is frequently regulated in cancer. This fact indicated a differential expression pattern of miRNA in normal, neoplastic, pre-malignant and malignant tissues. Therefore, *in situ* detection of miRNA differential expression in different stages of cancer makes the expression profiling a potential tool not only for cancer characterization but also for accurate CUP characterization and disease management.

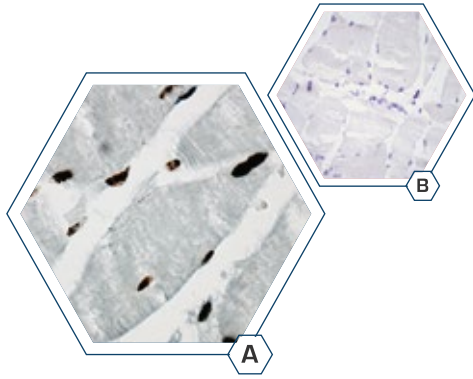
# Role of miRNA in Gene Regulation

miRNA regulates gene expression either by blocking the translation or destabilizing the targeted mRNA transcripts. miRNA as part of RISC complex targets the mRNA to inhibit its translation thus brings about the necessary regulatory control. On the other hand miRNA-RISC complex binds to 3'-UTRs of mRNA to induce mRNA degradation or destabilization by decapping and de-adenylation of mRNA there by inhibiting translation. The targeted mRNA along with the miRNA-RISC complex is often sequestered to P-bodies for further regulation by degradation or subsequent use.



## Translation regulated by miRNA

## miRNA Probes



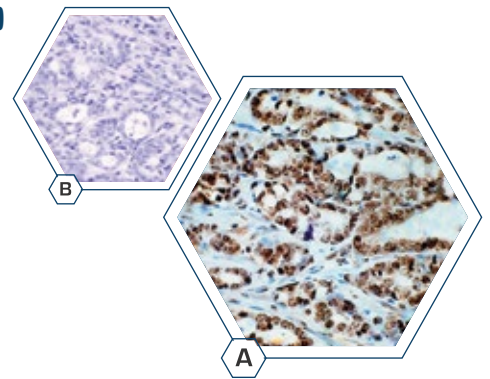
### Hsa-miR-1

miR-1 is believed to be specifically expressed in adult cardiac and skeletal muscle tissues. It plays a key role in the development and differentiation of smooth and skeletal muscles. miR-1 has been found down-regulated in lung, colon and prostate cancers.

- A. miR-1 stained in skeletal muscle tissue
- B. Scramble stained in skeletal muscle tissue

### Hsa-miR-9

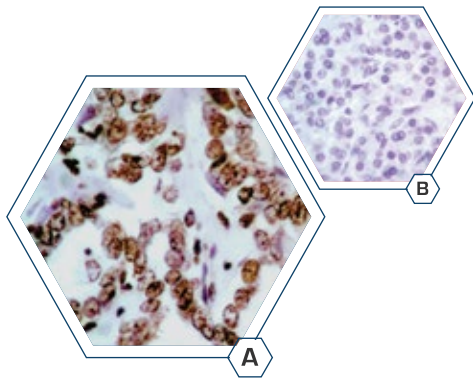
miR-9, a MYC/MYCN-activated microRNA, regulates E-Cadherin and cancer metastasis. A study showed that miR-9, which is specifically up-regulated in MIBC (muscle invasive bladder cancer), is a new promising prognostic marker as a three-microRNA signature (miR-9, miR-182 and miR-200b) was found to be related to MIBC tumor aggressiveness and was associated with both recurrence-free and overall survival.



- A. miR-9 stained in stomach cancer tissue
- B. Scramble stained in stomach cancer tissue

### Hsa-miR-10b

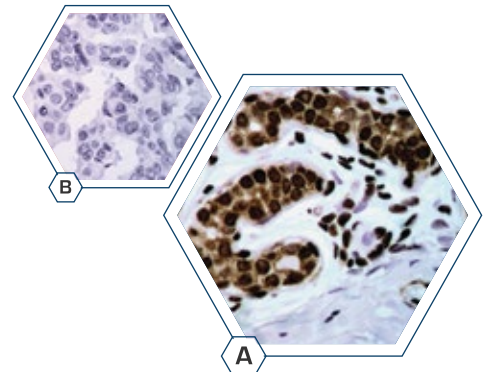
miR-10b is highly expressed in metastatic breast cancer cells and positively regulates cell migration and invasion. Overexpression of miR-10b in non-metastatic breast tumors initiates robust invasion and metastasis. miR-10b is also shown to involve in transforming growth factor- $\beta$ 1 induced epithelial-mesenchymal transition in breast cancer and increase its metastatic potential.



- A. miR-10b stained in cholangiocarcinoma tissue
- B. Scramble stained in cholangiocarcinoma tissue

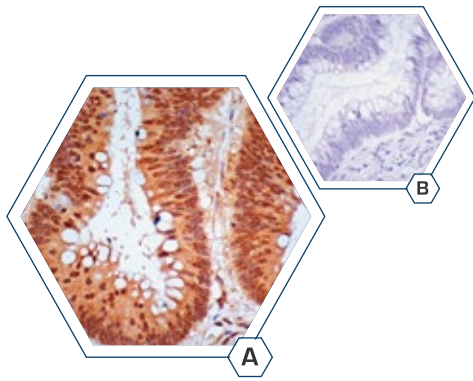
### Hsa-miR-17

miR-17-92 is a polycistronic microRNA cluster that contains multiple microRNA components, each of which has a potential to regulate hundreds of target mRNAs. Genomic amplification and elevated expression of miR-17-92 were both found in several human B-cell lymphomas, and its enforced expression exhibits strong tumorigenic activity in multiple mouse tumor models.



- A. miR-17 stained in sporadic breast cancer tissue
- B. Scramble stained in sporadic breast cancer tissue

# miRNA Probes



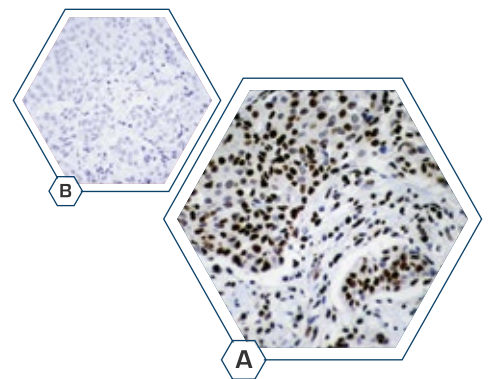
## Hsa-miR-21

miR-21 is one of the markers that have been associated with breast tumorigenesis. Our studies showed that its expression is down-regulated in BRCA-related breast cancer (BC) when comparing to sporadic BC. The cases in the BRCA group for this marker are Luminal A, suggesting an estrogen receptor linkage.

- A. miR-21 stained in adenocarcinoma tissue
- B. Scramble stained in adenocarcinoma tissue

## Hsa-miR-21-3p

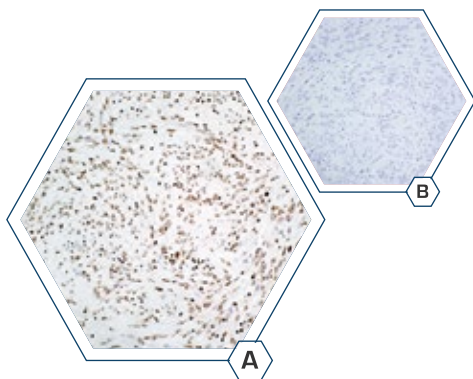
miR-21-3p has been shown to directly reduce the expression of two methionine adenosyltransferase genes by targeting their 3' UTRs. The overexpression of miR-21-3p increases intracellular S-adenosylmethionine contents, which have been proven to be a growth disadvantage for hepatoma cells, suppresses tumor growth and induces apoptosis in HepG2 cells, indicating the therapeutic potential of this marker in hepatocellular carcinoma.



- A. miR-21-3p stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue

## Hsa-miR-27a

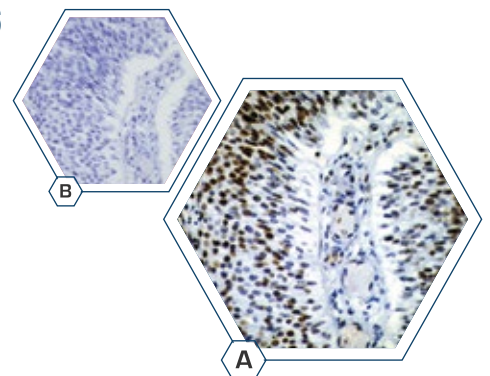
Studies have shown that miR-27a exhibits oncogenic activity by directly suppressing ZBTB10/RINZF expression which, in turn, results in over-expression of transcription factor specificity protein (Sp) and Sp-dependent genes which are important for cell survival and angiogenesis. miR-27a is located at chromosome 19 and has been reported to be expressed in breast cancer, gastric adenocarcinoma and cervical cancer.



- A. miR-27a stained in gastrointestinal stromal tumor tissue
- B. Scramble stained in gastrointestinal stromal tumor tissue

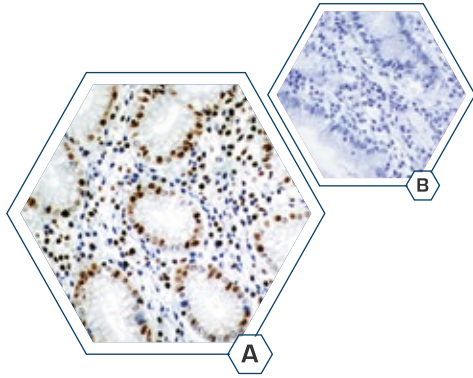
## Hsa-miR-96

miR-96 is shown to act as an oncomiR, regulating proliferation and DNA repair, but also as a tumor suppressor inducing apoptosis in pancreatic cells. miR-96 is highly expressed in lymphoma, liver, breast, ovarian, lung and colorectal cancers. In breast cancer, miR-96 promotes cell proliferation through targeting the tumor suppressor gene Forkhead box O transcription factor (FOXO3a) and the cyclin-dependent kinase inhibitors p27<sup>Kip1</sup> and p21<sup>Cip1</sup>.



- A. miR-96 stained in transitional cell carcinoma tissue
- B. Scramble stained in transitional cell carcinoma tissue

## miRNA Probes



### Hsa-miR-101-3p

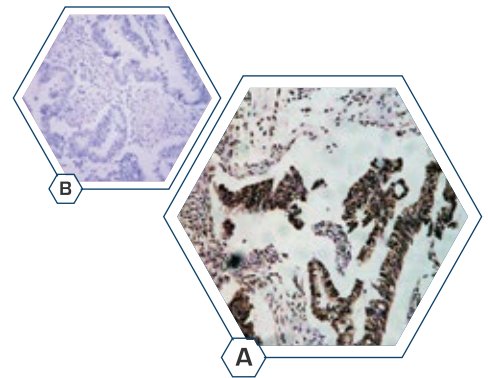
It was reported that Hepatitis B Virus (HBV), a major risk factor in the development and progression of hepatocellular carcinoma (HCC), down-regulates the miR-101-3p expression by inhibiting its promoter activity which results in up-regulation of Rap1b. Down-regulation of miR-101-3p or up-regulation of Rap1b was shown to promote the proliferation and migration of HCC cells. This provides a new understanding of the mechanism of HBV-related HCC pathogenesis and the potential application of miR-101-3p in cancer therapy.

- A. miR-101-3p stained in stomach cancer tissue
- B. Scramble stained in stomach cancer tissue

### Hsa-miR-106a

Sp1 and Egr1 are found to have an important role in miR-106a transcription and thus indirectly regulate the expression of IL-10 post-transcriptionally. Several reports demonstrated that miR-106a is up-regulated in gastric and colorectal cancers and promotes tumor progression. In contrast, in glioma miR-106a plays the role of a tumor suppressor gene rather than an oncogene.

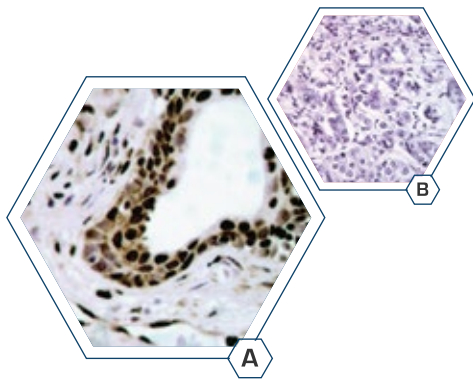
- A. miR-106a stained in colon cancer tissue
- B. Scramble stained in colon cancer tissue



### Hsa-miR-125b

miR-125b, the most down-regulated microRNA in breast tumors, represents a paradoxical microRNA because its phenotypic effects differ considerably, depending on cell type. Thus, miR-125b can function as a tumor suppressor microRNA in many tumor types, including ovarian cancer, hepatocellular carcinoma, melanoma, bladder, colorectal and breast cancers. However, miR-125b may have a tumor-promoting function in other types of cancer, including prostate cancer and leukemia.

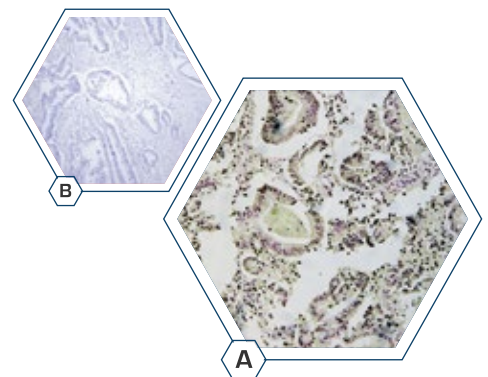
- A. miR-125b stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue



### Hsa-miR-126

Endogenous miR-126, a microRNA silenced in a variety of common human cancers, non-cell-autonomously regulates endothelial cell recruitment to metastatic breast cancer cells, in vitro and in vivo. It suppresses metastatic endothelial recruitment, metastatic angiogenesis and metastatic colonization through coordinate targeting of IGFBP2, PITPNC1 and MERTK-novel pro-angiogenic genes and biomarkers of human metastasis.

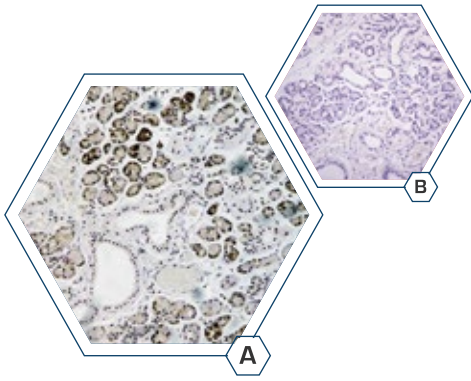
- A. miR-126 stained in colon cancer tissue
- B. Scramble stained in colon cancer tissue



# miRNA Probes

## Hsa-miR-141

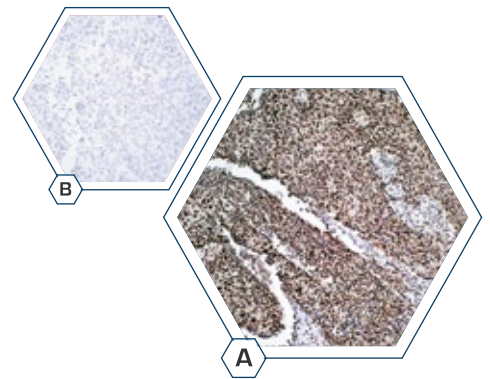
miR-141, along with miR-200c, is an important member of the miR-200 family for regulating the epithelial to mesenchymal transition. The mechanism responsible for the control of miR-200c expression in both normal and cancer cells is not fully understood. However, the epigenetic state is shown to be closely linked to normal cell type specific expression of miR-141 and miR-200c, and this epigenetic state is dysregulated in carcinoma cells, where loss of miR-141/200c expression is linked to aberrant DNA methylation and histone modifications.



- A. miR-141 stained in pancreatic normal and cancer tissue
- B. Scramble stained in pancreatic normal and cancer tissue

## Hsa-miR-143

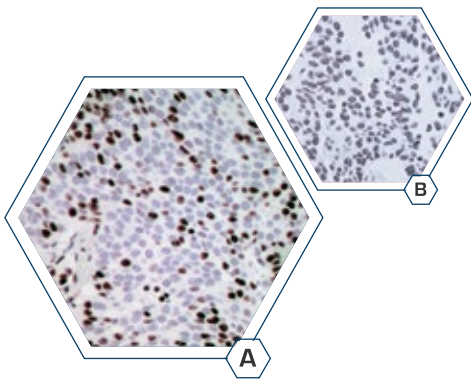
miR-143 specifically targets PKCε and regulates its expression. Anti-miR-143 promotes cell proliferation, decreases apoptosis and up-regulates PKCε expression. Down-regulation of the miR-143/145 microRNA (microRNA) cluster has also been repeatedly reported in colon cancer and other epithelial tumors. overexpression of these microRNAs inhibits tumorigenesis, leading to broad consensus that they function as cell-autonomous epithelial tumor suppressors.



- A. miR-143 stained in cervical carcinoma tissue
- B. Scramble stained in cervical carcinoma tissue

## Hsa-miR-144

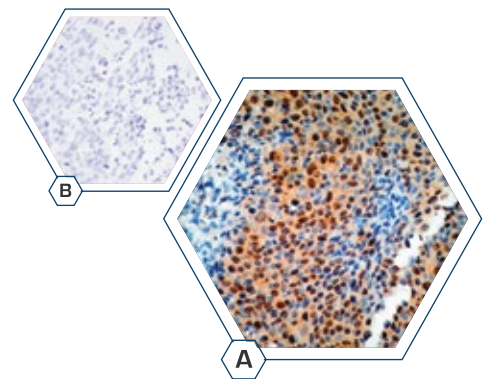
The function of miR-144 in tumorigenesis and cancer development is complicated and highly tissue-specific. Down-regulation of miR-144 in different types of cancers is reported to imply miR-144 is a potential tumor suppressor. This marker is also shown to promote cell proliferation, migration and invasion in nasopharyngeal carcinoma through repression of PTEN and targeted by zinc finger X-chromosomal protein to exert regulatory effects on tumor growth.



- A. miR-144 stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue

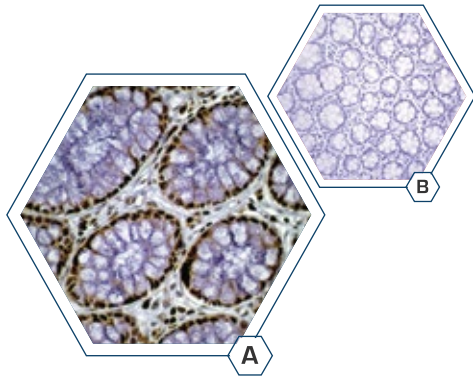
## Hsa-miR-146a

Lower miR-146a expression has been associated with more extensive lymph node metastasis and venous invasion in gastric and breast carcinoma. Up-regulation of miR-146a has also been demonstrated in the majority of cervical squamous cell carcinoma (SCC-Cx) cases with a trend towards increased expression in moderately to poorly differentiated SCC-Cx.



- A. miR-146a stained in cervical carcinoma tissue
- B. Scramble stained in cervical carcinoma tissue

## miRNA Probes



### Hsa-miR-147b

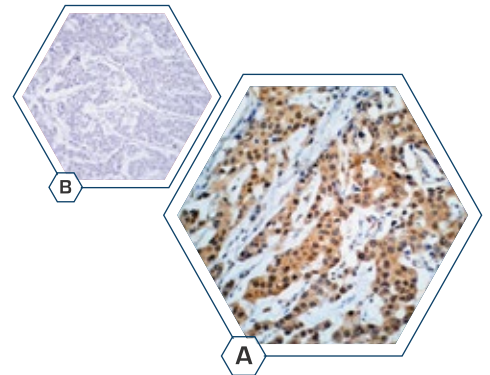
miR-147b is involved in post-transcriptional regulation of gene expression by affecting both stability and translation of target mRNAs. Studies demonstrated the participation of miR-147 in a negative feedback loop that is able to inhibit the pro-inflammatory response of macrophages to multiple TLR ligands. Few studies have been performed on the expression of this microRNA but some of them have reported a down-regulation of miR-147 in colorectal cancer tissue.

- A. miR-147b stained in rectal cancer tissue
- B. Scramble stained in rectal cancer tissue

miR-150 is mainly expressed in the lymph nodes and spleen and is highly up-regulated during the development of mature T and B cells. miR-150 also promotes growth of human breast and lung cancers by targeting the pro-apoptotic purinergic P2X7 receptor and pro-apoptotic gene p53, respectively.

- A. miR-150 stained in lung cancer tissue
- B. Scramble stained in lung cancer tissue

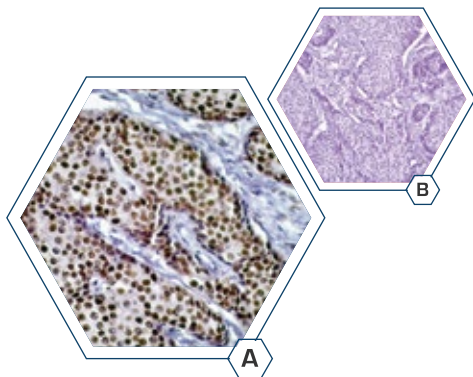
### Hsa-miR-150



### Hsa-miR-151a-3p

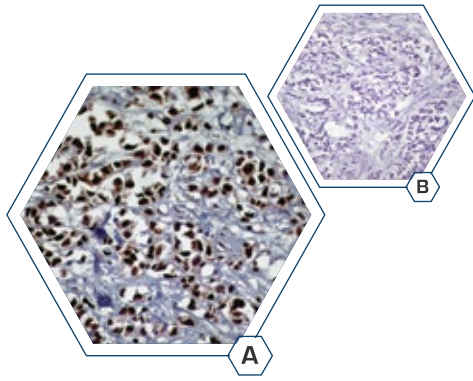
miR-151a has been demonstrated to be directly regulated by the p53-family of transcription factors and contributes to the tuning of p53-induced responses. miR-151 is also correlated with intrahepatic metastasis of hepatocellular carcinoma (HCC) and shown to significantly increase HCC cell migration and invasion in vitro and in vivo, mainly through miR-151-5p, but not through miR-151-3p. In addition, miR-151 can function synergistically with FAK to enhance HCC cell motility and spreading, thus indicating that chromosome gain of miR-151 is a crucial stimulus for tumor invasion and metastasis of HCC.

- A. miR-151a-3p stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue





## miRNA Probes



### Hsa-miR-152-3p

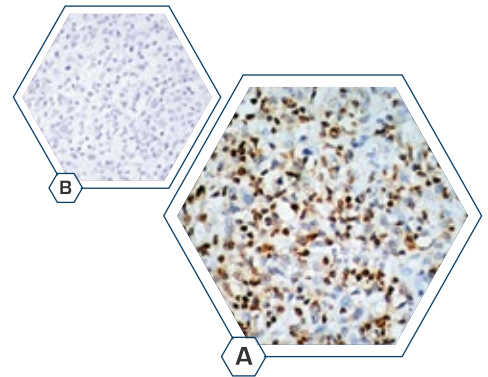
miR-152 controls migration and invasive potential by targeting transforming growth factor-alpha (TGF $\alpha$ ) in prostate cancer cell lines. miR-152 is also found to be a tumor suppressor microRNA that is silenced by DNA hypermethylation in endometrial cancer. E2F3, MET, and Rictor are identified as novel candidate targets of miR-152, suggesting how its epigenetic silencing can drive endometrial carcinogenesis.

- A. miR-152-3p stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue

miR-155 has emerged as a critical regulator of immune cell development, function, and disease. It is expressed in a variety of immune cell types, including B cells, T cells, macrophages, dendritic cells, and progenitor/stem cell populations. miR-155 is present at low levels in most of these cells until their activation by immune stimuli, such as antigen, toll-like receptor ligands, and inflammatory cytokines.

### Hsa-miR-155

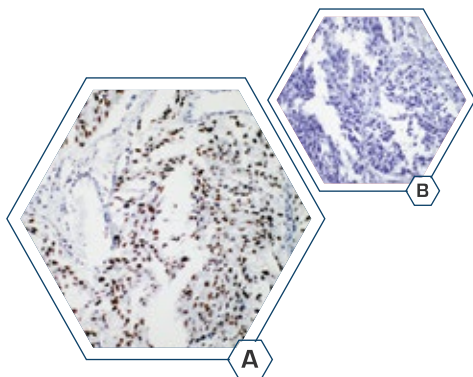
- A. miR-155 stained in Hodgkin lymphoma tissue
- B. Scramble stained in Hodgkin lymphoma tissue



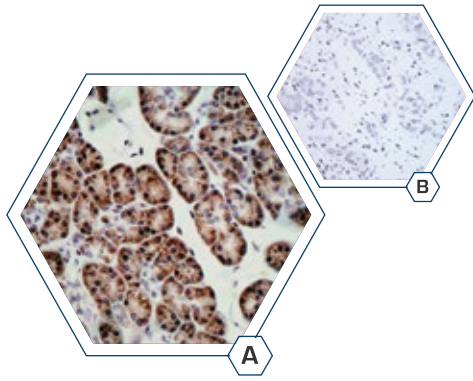
### Hsa-miR-187

miR-187 has been identified as the principal miRNA associated with poor response to anti-estrogen therapy. High miR-187 expression was demonstrated to significantly associate with poor outcome in ER+ breast cancer patients and correlate with increased tumor size, higher grade and PR negativity. Low mRNA expression of both miR-187 target genes OCA2 and HIPK3 was also found to be significantly associated with poor outcome. Therefore, miR-187 is a potential biomarker to aid treatment options and serve as potential drug targets to restore tamoxifen sensitivity in resistant patients.

- A. miR-187 stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue



## miRNA Probes



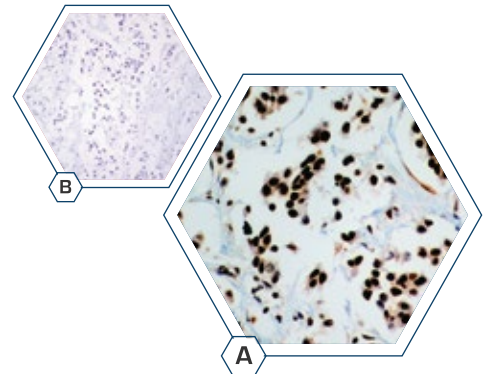
### Hsa-miR-196a

High levels of miR-196a, a microRNA suppressing the expression of specific homeobox genes that are of high relevance for the development of human embryos, activate oncogenic pathways inside human tumor cells and induce tumor cell dissemination. Up-regulated in gastric cancer, miR-196a promotes cell proliferation by down-regulating p27kip1, an enzyme inhibitor encoded by the CDKN1B gene. miR-196a expression is also up-regulated in cholangiocarcinoma when comparing to pancreatic ductal adenocarcinoma.

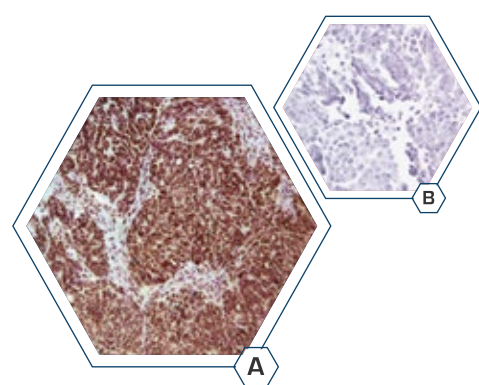
- A. miR-196a stained in pancreatic cancer tissue
- B. Scramble stained in pancreatic cancer tissue

miR-199a, which is encoded from the opposite strand of DNMT2 (Dynamin 2 is a key component of endocytic machinery that is transcriptionally suppressed by HIF-1), is shown to exert reciprocal negative regulation upon HIF-1 $\alpha$  and HIF-2 $\alpha$ . Overexpression of miR-199a decreases HIF-1 $\alpha$  and HIF-2 $\alpha$ , cell migration, and metastasis of ovarian cancer cells, suggesting a regulatory loop between the endocytic pathway and hypoxic response in tumor cells. miR-199a is also found to regulate the tumor suppressor mitogen-activated protein kinase kinase 11 (MAP3K11) in gastric cancer.

- A. miR-199a stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue



### Hsa-miR-199a



### Hsa-miR-200a

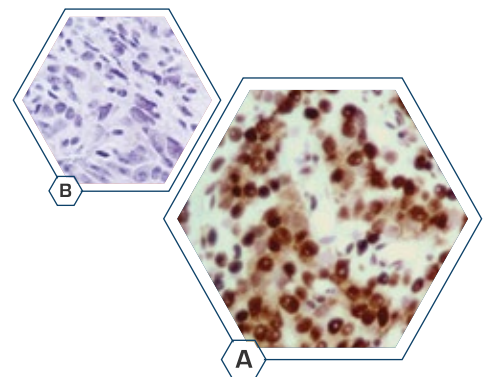
Down-regulation of miR-200a is shown to induce epithelial mesenchymal transition (EMT) phenotypes and colorectal cancer (CRC)-like signatures through targeting the  $\beta$ -catenin pathway in hepatic oval cells. Gain and loss of function assays for miR-200a *in vitro* led to a significant differential and converse expression of EMT-related genes. *In situ* hybridization specifically localized miR-200a in CRC cells, and low miR-200a expression is associated with poor prognosis in CRC patients.

- A. miR-200a stained in high-grade ovarian cancer tissue
- B. Scramble stained in high-grade ovarian cancer tissue

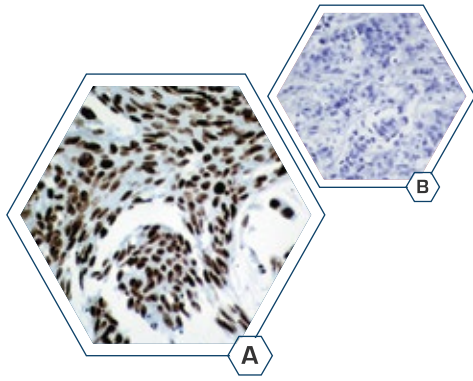
miR-200b targets v-ets erythroblastosis virus E26 oncogene homolog 1 (Ets-1) and is down-regulated by hypoxia to induce angiogenic response of endothelial cells. A study showed that miR-200b is a new promising prognostic marker as a three-microRNA signature (miR-9, miR-182 and miR-200b) was found to be related to muscle invasive bladder cancer (MIBC) tumor aggressiveness and was associated with both recurrence-free and overall survival.

- A. miR-200b stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue

### Hsa-miR-200b



## miRNA Probes



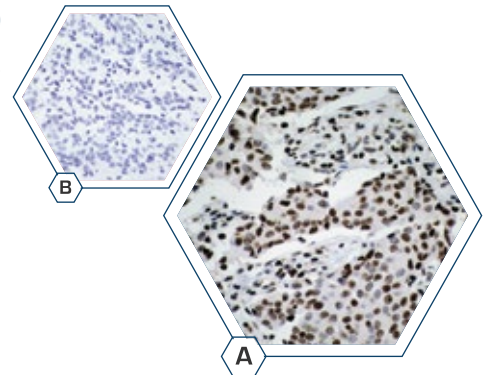
### Hsa-miR-200c

Auto-regulatory feedback loop of EZH2/miR-200c/E2F3 has been shown as a driving force for prostate cancer (PCa) development. In particular, miR-200c serves as an important mediator between EZH2 and E2F3 and inversely modulates E2F3 by directly targeting the binding site within 3'-UTR. Decreased miR-200c expression also largely abrogates the effect of sh-EZH2 on E2F3 expression and E2F3-induced cell cycle progression. Immunohistochemistry and *in situ* hybridization have revealed a significant correlation among EZH2, miR-200c, and E2F3 expression in human PCa tissues in this study.

- A. miR-200c stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue

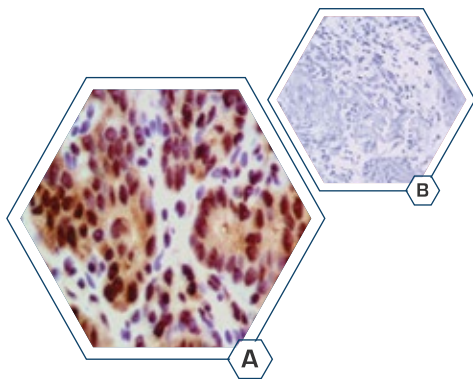
### Hsa-miR-203a-3p

miR-203 is a tumor suppressor microRNA often silenced in different malignancies. Its expression has been shown to repress following epithelial mesenchymal transition (EMT) induced by multiple different stimuli and in established claudin-low cell lines as well as the CD44<sup>hi</sup>/CD24<sup>lo</sup> stem cell-enriched fraction. It is also suggested that restoring miR-203 expression levels may inhibit metastasis and combat deregulated Wnt signaling. Further, miRNA-203 is found to suppress cell proliferation and migration by targeting BIRC5 and LASP1 in human triple-negative breast cancer cells.



- A. miR-203a-3p stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue

### Hsa-miR-204

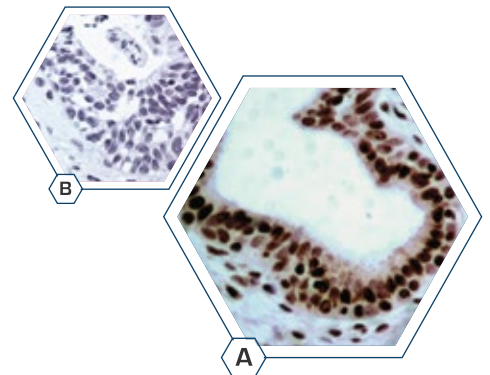


miR-204 is reported to show important roles in tumorigenesis, including regulation of carcinogenesis in peripheral nerve sheath tumors as well as migration and invasion of endometrial cancer cell lines. This marker acts as a tumor suppressor by targeting the function of genes associated with tumorigenesis such as brain-derived neurotrophic factor (BDNF). Chromosomal loci containing miR-204 is frequently lost which results in its lower expression in multiple cancers. Research showed that miR-204 can be targeted therapeutically as systemic delivery of miR-204 inhibited breast cancer lung metastasis without causing any hepatotoxicity.

- A. miR-204 stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue

### Hsa-miR-205

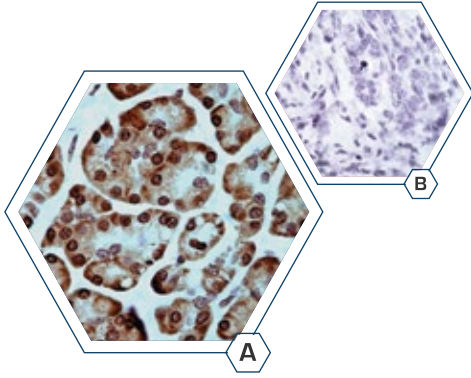
As a member of the miR-200 family, miR-205 is capable of suppressing epithelial to mesenchymal transition by targeting the transcriptional factors ZEB1 and SIP1. miR-205 has also been shown to regulate E-Cadherin and possibly target PTEN, and this have a role in tumor suppressor function. In addition, miR-205 is a well-characterized microRNA marker that is highly expressed in lung squamous cell carcinoma as compared to adenocarcinoma.



- A. miR-205 stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue

# miRNA Probes

## Hsa-miR-216a

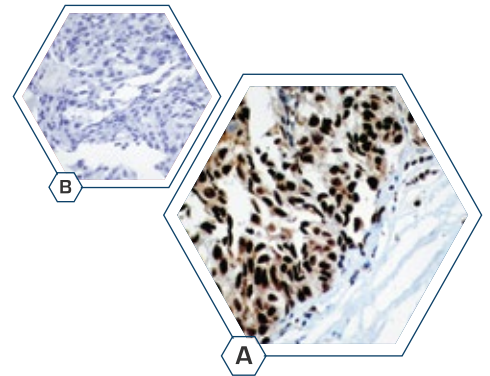


Although the mechanisms of Akt activation by TGF- $\beta$  are not fully understood, it was shown that TGF- $\beta$  activates Akt in glomerular mesangial cells by inducing the miR-216a and miR-217, both of which target PTEN (phosphatase and tensin homologue), an inhibitor of Akt activation. For cancers, miR-216a expression is found to be up-regulated in cholangiocarcinoma compared to pancreatic ductal adenocarcinoma while decreased expression of miR-216a contributes to non-small cell lung cancer progression.

- A. miR-216a stained in pancreatic cancer tissue
- B. Scramble stained in pancreatic cancer tissue

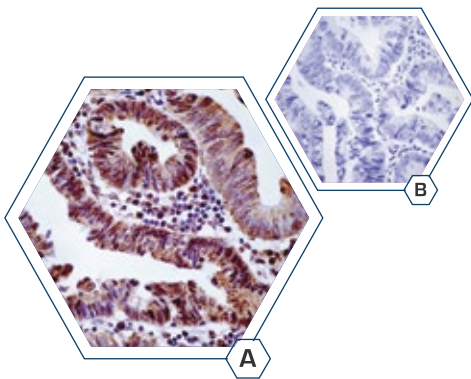
## Hsa-miR-218

The expression levels of miR-218, along with those from miR-7, are strongly and reversely associated with HoxB3 expression. Stable overexpression of these two miRNAs is accompanied by reactivation of tumor suppressor genes such as RASSF1A and Claudin-6 by epigenetic switches in DNA methylation and histone modification. This gives rise to inhibition of the cell cycle and clone formation of breast cancer cells.



- A. miR-218 stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue

## Hsa-miR-221-3p

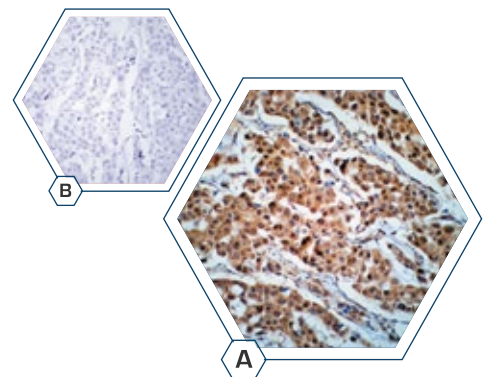


miR-221 and miR-222 are found to involve in the promotion of an aggressive basal-like phenotype in breast cancer, functioning downstream of the oncogenic RAS-RAF-MEK pathway and triggering epithelial-to-mesenchymal transition (EMT). miR-221 is also shown to be a potential novel biomarker for differential diagnosis and prognosis of certain non-small cell lung cancer subtypes or be new targets of histology-specific treatments. Compared to adjacent non-neoplastic lung tissues, increased expression of miR-221 was observed in squamous cell carcinoma and not adenocarcinoma samples.

- A. miR-221-3p stained in colon cancer tissue
- B. Scramble stained in colon cancer tissue

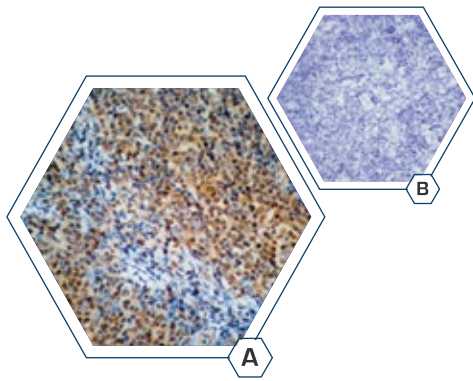
## Hsa-miR-222

Accumulating evidence has demonstrated that miR-222 plays a crucial role in cancer cell proliferation, and overexpression of miR-222 has been found in several types of cancers such as breast cancer, bladder cancer, colorectal carcinoma, glioblastoma, and pancreatic cancer. miR-222 overexpression also confers cell migratory advantages in hepatocellular carcinoma through enhancing AKT signaling.



- A. miR-222 stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue

## miRNA Probes



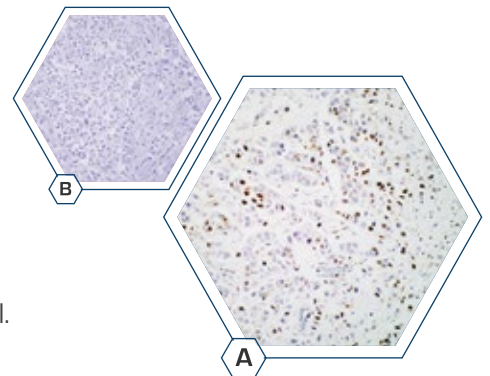
### Hsa-miR-328

miR-328 is differentially expressed in malignant tumors and may have a role in carcinogenesis, including thyroid cancer. It has been shown to be up-regulated in thyroid carcinoma antigen, toll-like receptor ligands and inflammatory cytokines.

- A. miR-328 stained in tonsil
- B. Scramble stained in tonsil

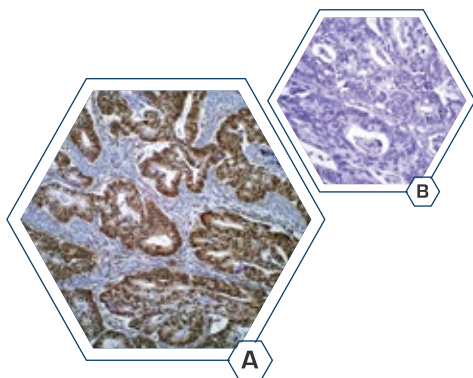
### Hsa-miR-335

Resided on chromosome 7q32, miR-335 is deregulated in many cancers and reported to act as a tumor promoter in conferring tumorigenic features such as growth and invasion on malignant astrocytoma. Differential microRNA expression analyses also reveal that miR-335 is significantly down-regulated upon differentiation of human mesenchymal stem cells (hMSCs). In addition, hMSCs derived from a variety of tissues express miR-335 at a higher level than human skin fibroblasts, and overexpression of miR-335 in hMSCs inhibited their proliferation and migration, as well as their osteogenic and adipogenic potential.



- A. miR-335 stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue

### Hsa-miR-375

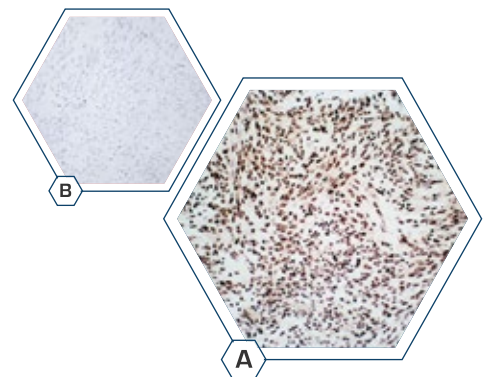


miR-375 has been found significantly down-regulated in multiple types of cancer, and suppresses core hallmarks of cancer by targeting several important oncogenes such as AEG-1, YAP1, IGF1R and PDK1. The alteration of miR-375 in cancer is caused by a variety of mechanisms, including the dysregulation of transcription factors and aberrant promoter methylation. A recent study also suggested that epigenetic silencing of miR-375 induces trastuzumab resistance in HER2-positive breast cancer by targeting IGF1R.

- A. miR-375 stained in rectal cancer tissue
- B. Scramble stained in rectal cancer tissue

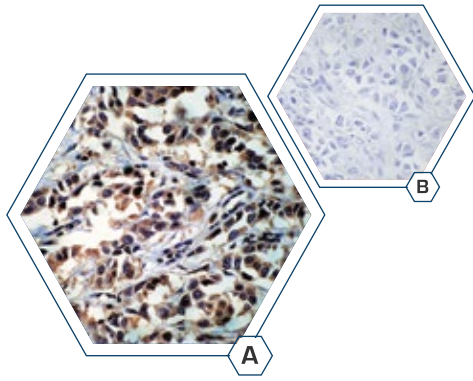
### Hsa-miR-378a

miR-378 transfection is suggested to enhance cell survival, tumor growth and angiogenesis through repression of the expression of two tumor suppressors, Sufu and Fus-1. miR-378 is also shown to overexpress in ovarian cancer cells and tumors vs. normal ovarian epithelial cells. Overexpressing miR-378 in ovarian cancer cells alters expression of genes associated with angiogenesis (ALCAM, EHD1, ELK3, TLN1), apoptosis (RPN2, HIPK3), and cell cycle regulation (SWAP-70, LSM14A, RDX).



- A. miR-378a stained in gastrointestinal stromal tumor tissue
- B. Scramble stained in gastrointestinal stromal tumor tissue

## miRNA Probes



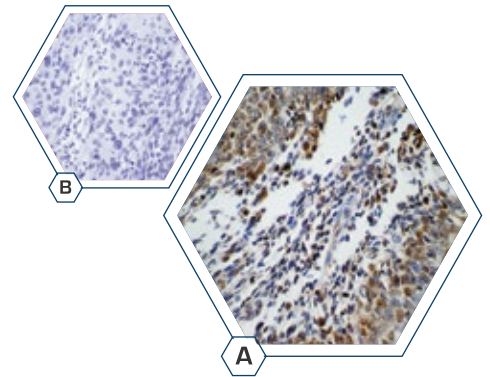
### Hsa-miR-423-3p

miR-423-3p was originally detected in 2004 in untreated HL-60 leukemia cells during 2-O-tetra-decanoylphorbol-13-acetate induced differentiation experiments, indicating that the mature microRNA is involved in differentiation processes. Localized to the frequently amplified region of chromosome 17q11, miRNA-423 has been shown to up-regulate in hepatocellular carcinoma (HCC) and promote cell growth as well as cell cycle progression at the G1/S transition in HCC cells. In particular, miR-423-3p contributes to these effects. Altered expression of both of the mature microRNAs [-3p and -5p] produced from miR-423 has also been reported in multiple cancer types, including mesothelioma, head and neck cancer, and breast cancer, as well as in psoriasis lesions.

- A. miR-423-3p stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue

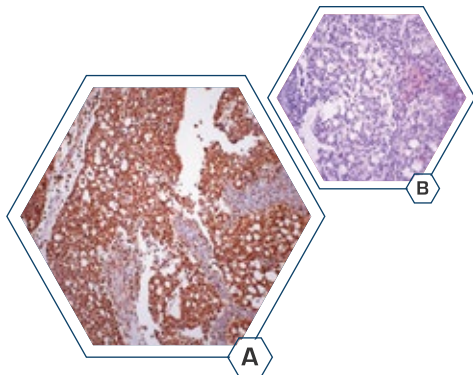
### Hsa-miR-641

miR-641 is an uncharacterized microRNA that locates at intron-1 of the AKT2 gene and is reported to function as an oncomiR that co-regulates and cooperates with AKT2 in human cancer. miR-641 activation of the MAPK pathway is also identified by targeting tumor suppressor NF1, a GTPase-activating protein that inhibits RAS. Upon ectopic expression of miR-641, NF1 expression is reduced. As a result, pERK is elevated whereas knockdown of miR-641 exhibits opposite effects. In addition, depletion of miR-641 sensitizes tumor cells to cisplatin-induced apoptosis. Knockdown of miR-641 synergizes with AKT2 inhibition to induce cell death.



- A. miR-641 stained in cervical carcinoma tissue
- B. Scramble stained in cervical carcinoma tissue

### Hsa-miR-1285

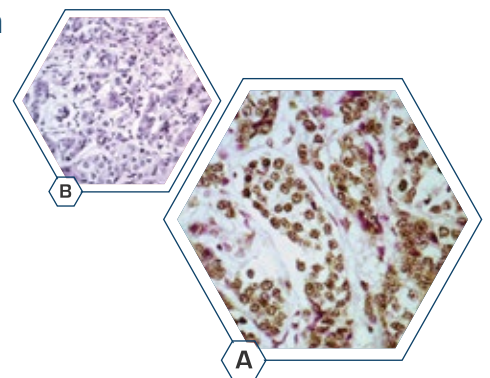


miR-1285 is found to significantly inhibit cancer cell proliferation, invasion, and migration following its transfection. Genome-wide gene expression analysis data show that transglutaminase 2 (TGM2) is directly regulated by miR-1285. Silencing of the target gene demonstrates significant inhibition of cell proliferation and invasion in the renal cell carcinoma (RCC) cells. Down-regulation of tumor suppressive miR-1285, which targets oncogenic genes including TGM2, may contribute to RCC development.

- A. miR-1285 stained in ovarian cancer tissue
- B. Scramble stained in ovarian cancer tissue

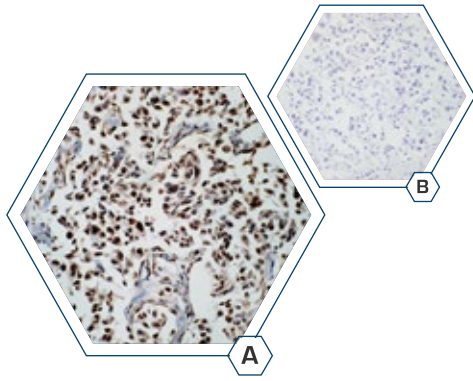
### Hsa-miR-let-7a

Within the miR-let-7 family, let-7a expression increases after differentiation and in mature tissue, but is barely detectable in the embryonic stage. Let-7a has been found to act as a tumor suppressor directly regulating RAS and HMGA2 oncogenes by interacting with the 3'UTR. Reduced levels of let-7a correlate with elevated RAS expression in lung squamous carcinoma. Let-7a is involved in cell proliferation and influences cancer metastasis in various tumors, including breast cancer. Recent studies show that let-7a expression is down-regulated in BRCA-related breast cancer (BC) when comparing to sporadic BC. The cases in the BRCA group for this marker are Luminal A, suggesting an estrogen receptor linkage.



- A. miR-let-7a stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue

## miRNA Probes



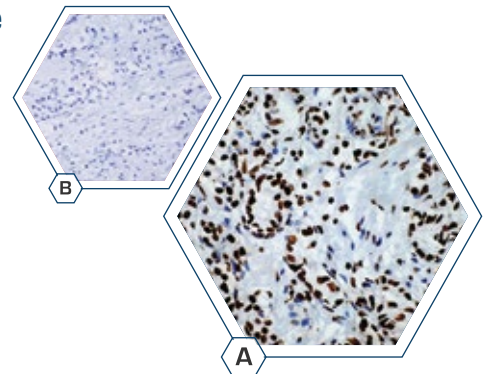
### Hsa-miR-let-7c

miR-let-7c has been identified as a potential tumor suppressor in prostate cancer (PCa). Expression of let-7c is down-regulated in castration-resistant prostate cancer cells. Overexpression of let-7c decreases while down-regulation of let-7c increases cell proliferation, clonogenicity and anchorage-independent growth of PCa cells *in vitro*. Reconstitution of let-7c by lenti-viral-mediated intra-tumoral delivery significantly reduced tumor burden in xenografts of human PCa cells. A separate study also shows that let-7c is among a panel of five circulating microRNAs that help discriminate prostate cancer from benign prostatic hyperplasia and healthy controls.

- A. miR-let-7c stained in breast cancer tissue
- B. Scramble stained in breast cancer tissue

### Hsa-miR-let-7e

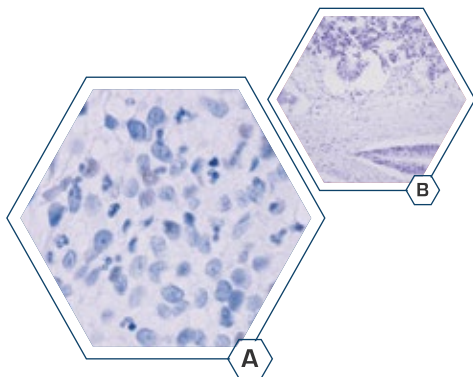
miR-let-7e plays a pivotal role in stem cell differentiation and its loss results in reversion of embryogenesis and dedifferentiation. Decreased levels of miR-let-7e have also been associated with metastasis and poor prognosis in renal cell carcinoma, possibly because of its effects on matrix metalloproteinases (MMPs). Lower let-7e expression is also found to be associated with lymph node metastasis, >3 cm tumor size, and differentiation of the adenocarcinoma subtype in non-small cell lung cancer. In addition, a separate study shows that let-7c is among a panel of five circulating microRNAs that help discriminate prostate cancer from benign prostatic hyperplasia and healthy controls.



- A. miR-let-7e stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue

### Scramble

Bearing no homology to any known microRNA sequences in the miRBase database and having minimal self-annealing properties, a fluoresceinated scramble probe is developed as the negative control to confirm the specificity of the staining signal for a particular FFPE or frozen tissue by *in situ* hybridization technique.

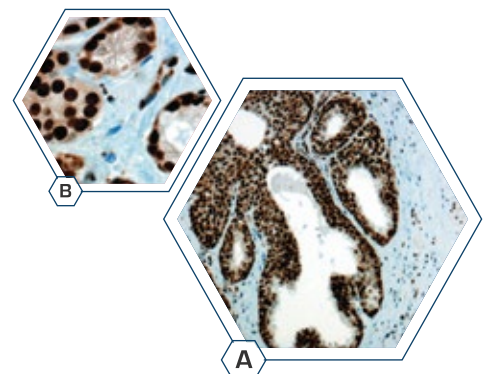


- A. Scramble stained in breast cancer tissue
- B. Scramble stained in lung cancer tissue

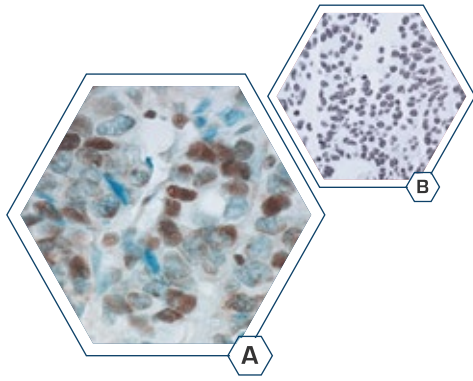
Bearing no homology to any known microRNA sequences in the miRBase database and having minimal self-annealing properties, a small nuclear RNA U6 fluoresceinated probe is used as the positive control, which is a good tool to optimize the sensitivity of the microRNA detection protocol initially for a particular FFPE or frozen tissue by *in situ* hybridization technique.

- A. U6 stained in breast cancer tissue (10x)
- B. U6 stained in breast cancer tissue (40x)

### U6



## miRNA Probes

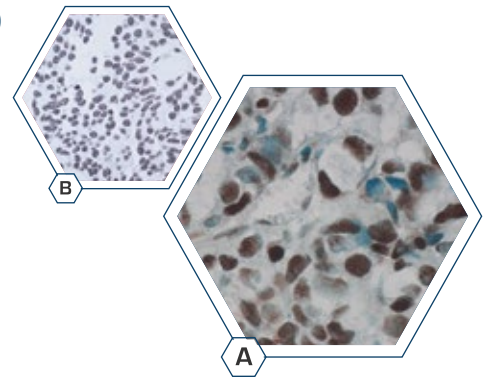


### Hsa-miR-18a

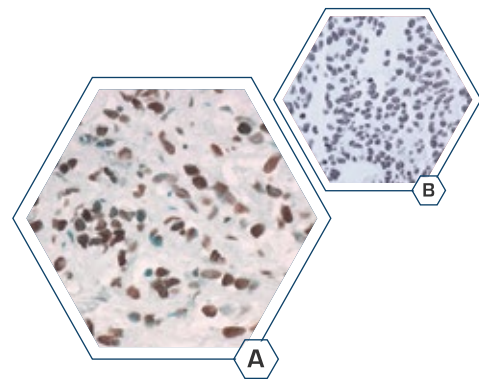
Hsa-miR-18a is located in the miR-17 – 92 cluster and reported to be highly expressed in pancreatic, gastric and colorectal cancer tissues. miR-18a was confirmed to directly target ERα and showed higher levels of expression in ERα-negative clinical tumours. miR-18a had a pro-proliferation effect on hepatocellular carcinoma cells, but an inhibitory effect on breast cancer cells. The fluorescinated hsa-miR-18a probe is designed to localize this miRNA in FFPE tissue by in situ hybridization

- A. miR-18a stained in prostate cancer tissue
- B. Scramble stained in Prostate Cancer Tissue

miR-19 regulates tissue factor expression at a post-transcriptional level in breast cancer cells, providing a molecular basis for the selective expression of the tissue factor gene. Over-expression of miR-19 downregulates tissue factor expression in Human breast cancer cell lines. The main function of miR-19 seems to inhibit protein translation of the tissue factor gene in less invasive breast cancer cells. MiR-19b coordinates a PI3K pathway acting on cell survival in lymphocytes contributing to leukaemogenesis. The fluorescinated hsa-miR-19b-3p probe is designed to localize this miRNA in FFPE tissue by *in situ* hybridization.



- A. miR-19b-3p stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue

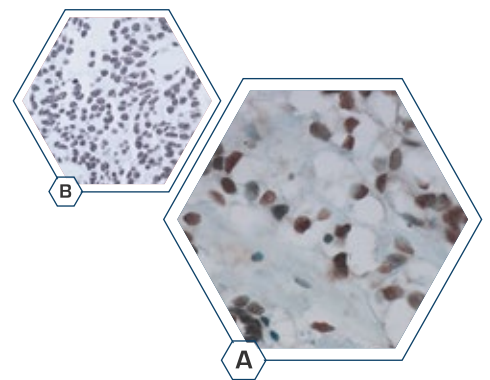


### Hsa-miR-23b

miR-23b miRNAs that is highly up-regulated in human breast cancer. MiR-23b directly targets RUNX2 in EOC tissues. Ectopic expression of miR-23b inhibits EOC cell proliferation and tumorigenicity by regulating the expression of RUNX2. MiR-23b downregulation may be associated with EOC progression and poor prognosis. The fluorescinated hsa-miR-23b probe is designed to localize this miRNA in FFPE tissue by in situ hybridization.

- A. miR-23b stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue

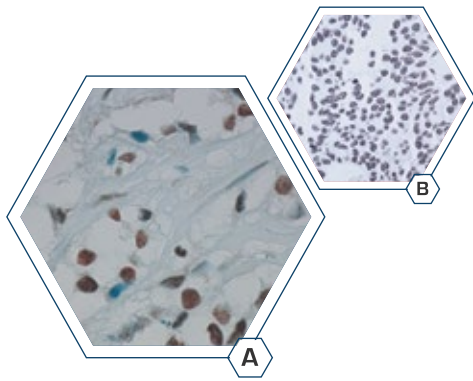
miR-27 is one which was implicated in cholesterol homeostasis and fatty acid metabolism. miR-27 gene family has been shown to be downregulated during the differentiation of adipocytes. miR-27b has been identified as oncogenic microRNA and is highly expressed in breast cancer cells. Inhibition of miR-27 by antisense molecules decreases cell proliferation. miR-27b as miRNAs that are highly up-regulated in human breast cancer. The fluorescinated hsa-miR-27b probe is designed to localize this miRNA in FFPE tissue by in situ hybridization.



- A. miR-27b stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue



## miRNA Probes



### Hsa-miR-383

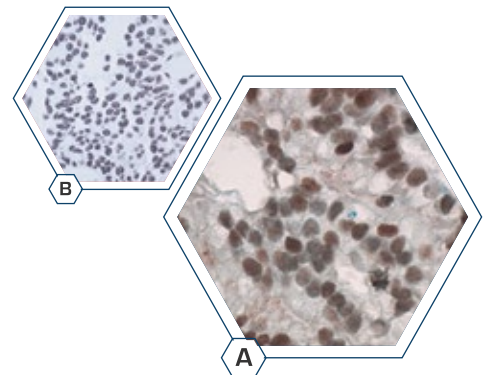
Downregulation of miR-383 promotes glioma cell invasion by targeting IGF1R. miR-383 promoted the expression of miR-320 and enhanced miR-320-mediated suppression of GC proliferation. miR-383 was up-regulated in the follicular fluid of polycystic ovarian syndrome (PCOS) patients, while the expression of E2F1 and SF-1 was down-regulated in GCs. The fluorescinated hsa-miR-383 probe is designed to localize this miRNA in FFPE tissue by in situ hybridization.

- A. miR-383 stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue

### Hsa-miR-505

Hsa-miR-505 is a tumor suppressive microRNA which was significantly elevated in hypertensive patients. FGF18, a proangiogenic factor, is directly regulated by hsa-miR-505. miR-505 is a novel tumor suppressive miRNA and inhibits cell proliferation by inducing apoptosis. The fluorescinated hsa-miR-505 probe is designed to localize this miRNA in FFPE tissue by in situ hybridization.

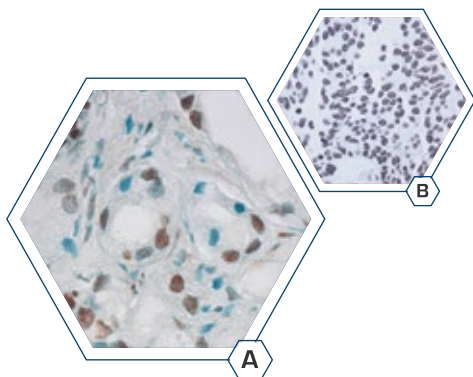
- A. miR-505 stained in prostate cancer tissue
- B. Scramble stained in prostate cancer tissue



### Hsa-miR-629

miR-629 is upregulated in many tissues. miR-629 activate IL-6-JAK-STAT3 signalling in tumour cells, which in turn upregulates miR-629 expression. miR-629 as potent regulators of HNF4 $\alpha$  expression and confirmed the feedback loop by demonstrating increased miR-629 after HNF4 $\alpha$  knockdown in Hepato cellular carcinoma. The fluorescinated hsa-miR-629 probe is designed to localize this miRNA in FFPE tissue by in situ hybridization.

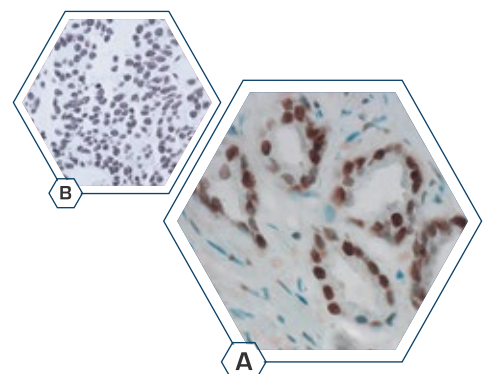
- A. miR-629 stained in Prostate Cancer Tissues
- B. Scramble stained in Prostate Cancer Tissues



### Hsa-miR-101-3p

MicroRNA 101 has been shown to be down-regulated in hepatocellular carcinoma (HCC). Downregulation of miR-101-3p promoted cancer cell growth and migration, and a specific miR-101-3p inhibitor was able to enhance proliferation and migration. Rab5a was one of the target genes of miR-101-3p in HBV-related HCC. The fluorescinated hsa-miR-101-3p probe is designed to localize this miRNA in FFPE tissue by in situ hybridization.

- A. miR-101-3p stained in Prostate Cancer Tissues
- B. Scramble stained in Prostate Cancer Tissues



# Ordering Information

micro RNA probes †	Pack Size	Cat. No.
Hsa-miR-1	25 slides	HMO01-100E
Hsa-miR-let-7a	25 slides	HMO07A-100E
Hsa-miR-let-7b	25 slides	HMO07B-100E
Hsa-miR-let-7c	25 slides	HMO07C-100E
Hsa-miR-let-7d	25 slides	HMO07D-100E
Hsa-miR-let-7e	25 slides	HMO07E-100E
Hsa-miR-let-7g	25 slides	HMO07G-100E
Hsa-miR-9	25 slides	HMO09-100E
Hsa-miR-10b	25 slides	HMO10B-100E
Hsa-miR-15a	25 slides	HMO15A-100E
Hsa-miR-15b	25 slides	HMO15B-100E
Hsa-miR-17	25 slides	HMO17-100E
Hsa-miR-17-3p	25 slides	HMO17-3P-100E
Hsa-miR-18a	25 slides	HMO18A-100E
Hsa-miR-19b-3p	25 slides	HMO19B-3P-100E
Hsa-miR-20a	25 slides	HMO20A-100E
Hsa-miR-21	25 slides	HMO21-100E
Hsa-miR-21-3p	25 slides	HMO21-3P-100E
Hsa-miR-22	25 slides	HMO22-100E
Hsa-miR-23b	25 slides	HMO23B-100E
Hsa-miR-26a	25 slides	HMO26A-100E
Hsa-miR-26b	25 slides	HMO26B-100E
Hsa-miR-27a	25 slides	HMO27A-100E
Hsa-miR-27b	25 slides	HMO27B-100E
Hsa-miR-28-3p	25 slides	HMO28-3P-100E
Hsa-miR-28-5p	25 slides	HMO28-5P-100E
Hsa-miR-29c	25 slides	HMO29C-100E
Hsa-miR-30b	25 slides	HMO30B-100E
Hsa-miR-30c	25 slides	HMO30C-100E
Hsa-miR-30e	25 slides	HMO30E-100E
Hsa-miR-31	25 slides	HMO31-100E
Hsa-miR-34a	25 slides	HMO34A-100E
Hsa-miR-92a	25 slides	HMO92A-100E
Hsa-miR-95	25 slides	HMO95-100E
Hsa-miR-96	25 slides	HMO96-100E
Hsa-miR-99a	25 slides	HMO99A-100E
Hsa-miR-99b	25 slides	HMO99B-100E

micro RNA probes †	Pack Size	Cat. No.
Hsa-miR-100	25 slides	HM100-100E
Hsa-miR-101-3p	25 slides	HM101-3P-100E
Hsa-miR-106a	25 slides	HM106A-100E
Hsa-miR-107	25 slides	HM107-100E
Hsa-miR-122	25 slides	HM122-100E
Hsa-miR-124	25 slides	HM124-100E
Hsa-miR-125a	25 slides	HM125A-100E
Hsa-miR-125b	25 slides	HM125B-100E
Hsa-miR-126	25 slides	HM126-100E
Hsa-miR-127-3p	25 slides	HM127-3P-100E
Hsa-miR-130a	25 slides	HM130A-100E
Hsa-miR-133a	25 slides	HM133A-100E
Hsa-miR-133b	25 slides	HM133B-100E
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Hsa-miR-135b	25 slides	HM135B-100E
Hsa-miR-141	25 slides	HM141-100E
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Hsa-miR-192	25 slides	HM192-100E
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Hsa-miR-195	25 slides	HM195-100E

## Ordering Information

micro RNA probes †	Pack Size	Cat. No.
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Hsa-miR-199a	25 slides	HM199A-100E
Hsa-miR-200a	25 slides	HM200A-100E
Hsa-miR-200b	25 slides	HM200B-100E
Hsa-miR-200c	25 slides	HM200C-100E
Hsa-miR-203a-3p	25 slides	HM203A-3P-100E
Hsa-miR-204	25 slides	HM204-100E
Hsa-miR-205	25 slides	HM205-100E
Hsa-miR-206	25 slides	HM216-100E
Hsa-miR-210	25 slides	HM210-100E
Hsa-miR-212	25 slides	HM212-100E
Hsa-miR-214	25 slides	HM214-100E
Hsa-miR-215	25 slides	HM215-100E
Hsa-miR-216a	25 slides	HM216A-100E
Hsa-miR-218	25 slides	HM218-100E
Hsa-miR-222	25 slides	HM222-100E
Hsa-miR-224	25 slides	HM224-100E
Hsa-miR-328	25 slides	HM328-100E
Hsa-miR-329	25 slides	HM329-100E
Hsa-miR-331-3p	25 slides	HM331-3P-100E
Hsa-miR-335	25 slides	HM335-100EE
Hsa-miR-361	25 slides	HM361-100E
Hsa-miR-362	25 slides	HM362-100E
Hsa-miR-373	25 slides	HM373-100E
Hsa-miR-375	25 slides	HM375-100E
Hsa-miR-378a	25 slides	HM378A-100E
Hsa-miR-383	25 slides	HM383-100E
Hsa-miR-409-3p	25 slides	HM409-3P-100E
Hsa-miR-410	25 slides	HM410-100E
Hsa-miR-412	25 slides	HM412-100E

micro RNA probes †	Pack Size	Cat. No.
Hsa-miR-422a	25 slides	HM422A-100E
Hsa-miR-423-3P	25 slides	HM423-3P-100E
Hsa-miR-424	25 slides	HM424-100E
Hsa-miR-429	25 slides	HM429-100E
Hsa-miR-449a	25 slides	HM449A-100E
Hsa-miR-451	25 slides	HM451-100E
Hsa-miR-483	25 slides	HM483-100E
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Hsa-miR-628	25 slides	HM628-100E
Hsa-miR-629	25 slides	HM629-100E
Hsa-miR-641	25 slides	HM641-100E
Hsa-miR-648	25 slides	HM648-100E
Hsa-miR-650	25 slides	HM650-100E
Hsa-miR-663a	25 slides	HM663A-100E
Hsa-miR-708	25 slides	HM708-100E
Hsa-miR-718	25 slides	HM718-100E
Hsa-miR-1247	25 slides	HM1247-100E
Hsa-miR-1285	25 slides	HM1285-100E
Hsa-miR-1826	25 slides	HM1826-100E
Scramble	25 slides	PRO32-100E
U6	25 slides	PRO31-100E

ISH Detection Kit (Manual staining)	Pack Size	Cat. No.
Super Sensitive One-Step Polymer-HRP ISH Detection Kit	50 Slides	DF400-50KE

†miRNA listed above are either miRNA-5p origin or there is no 3p sequence available for that particular miRNA unless specified otherwise. miRNA-3p sequences are specified in the list separately if available.

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