Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

# Gene Section
## Review

# MIR200C (microRNA 200c)

**Sarah Jurmeister, Stefan Uhlmann, Özgür Sahin**

Division of Molecular Genome Analysis, German Cancer Research Center (DKFZ), Division of Molecular Genome Analysis, Im Neuenheimer Feld 580, Heidelberg, Germany (SJ, SU, ÖS)

Published in Atlas Database: August 2011

Online updated version : http://AtlasGeneticsOncology.org/Genes/MIR200CID51054ch12p13.html
DOI: 10.4267/2042/46935



## Identity

**Other names:** hsa-mir-200c, MIRN200C, mir-200c

**HGNC (Hugo):** MIR200C

**Location:** 12p13.31

**Local order:** Based on Mapviewer Genes on Sequence, genes flanking MIRN200C oriented from centromere to telomere on 12q13.31 are:
- ATN1; Atrophin 1, 12q13.31
- U7; U7 small nuclear 1, 12q13.31
- C12orf57; Chromosome 12 open reading frame 57, 12q13.31
- PTPN6; Protein tyrosine phosphatase, non-receptor type 6, 12q13.31
- **MIRN200C**; microRNA 200c, 12q13.31
- MIRN141; microRNA 141, 12q13.31
- snoU89; small nucleolar RNA U89, 12q31.1
- PHB2; Prohibitin 2, 12q31.1

## DNA/RNA

### Description

miR-200c belongs to the miR-200 family, which consists of 5 members with two different chromosomal locations: miR-200c and miR-141 are located on chromosome 12p13 and miR-200a, miR-200b and miR-429 are located on 1p36. This family is frequently downregulated upon the progression of tumors and maps to fragile chromosomal regions. Members of this family are important regulators of epithelial-to-mesenchymal transition (EMT) and metastasis.

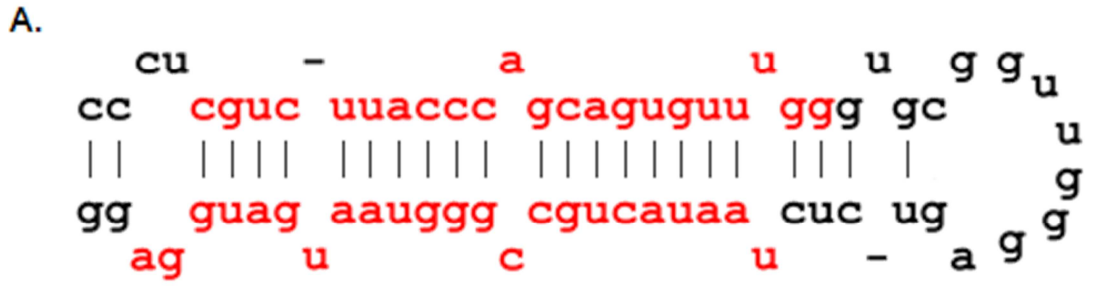
### Transcription

miRNAs are generally transcribed by RNA polymerase II.

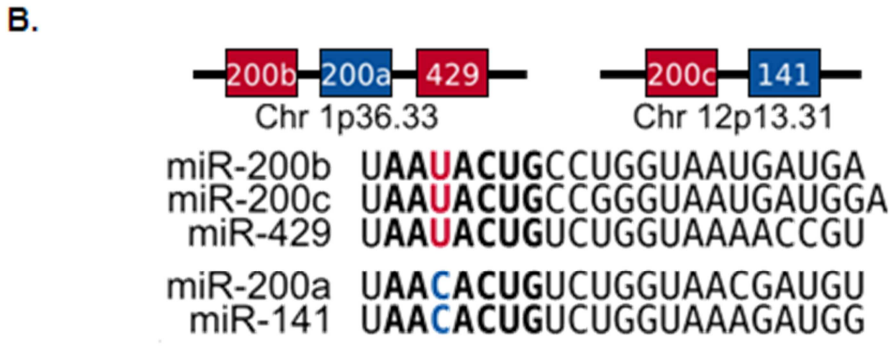
**hsa-mir-200c** (precursor miRNA)
Accession: MI0000650
Length: 68 bp
Sequence:5'-CCCUCGUCUUACCCAGCAGUG UUUGGGUGCGGUUGGGAGUCUCUAAUACUGC CGGGUAAUGAUGGAGG-3'
**hsa-miR-200c** (mature miRNA)
Accession: MIMAT0000617
Length: 23
Sequence: 5'-UAAUACUGCCGGGUAAUGAU GGA-3'

### Pseudogene

No reported pseudogenes.




**A.** Stem-loop structure of hsa-mir-200c (precursor miRNA).




**B.** The miR-200 family members. The human miR-200 family is located in two fragile chromosomal regions on 1p36.33 (200b, 200a and 429) and 12p13.31 (200c and 141), respectively. It consists of two clusters based on seed sequence similarity: miR-200bc/429 (red) and 200a/141 (blue), distinguished by a single nucleotide change (U to C). (Source: Uhlmann et al., 2010, Oncogene).

# Protein

**Note**
microRNAs are not translated into amino acids.

# Mutations

**Note**
Gene mutations have not been described.

# Implicated in

## *Bladder cancer*

**Prognosis**
Loss of miR-200c expression was found to be associated with disease progression and poor outcome in 100 stage T1 bladder tumor patients (Wiklund et al., 2011).

**Oncogenesis**
Deep sequencing of nine bladder urothelial carcinomas and matched normal urothelium revealed that the miR-200c/141 cluster is upregulated in bladder cancer (Han et al., 2011). Consistently, a study comparing miRNA expression patterns by microarray in 27 invasive and 30 superficial bladder tumors with 11 normal urothelia found that miR-200c was upregulated in bladder tumors compared to normal urothelium; however, expression of miR-200c was reduced in invasive compared to non-invasive tumors due to promoter hypermethylation (Wiklund et al., 2011). Furthermore, microarray miRNA analysis of 43 primary tumors (10 colon, 10 bladder, 13 breast and 10 lung cancers) and matched lymph node metastases revealed that miR-200c and other miR-200 family members are downregulated in metastases compared to primary tumors (Baffa et al., 2009). This suggests that while miR-200c may have oncogenic function in bladder cancer, it interferes with invasion and metastasis.
Mechanistically, miR-200c has been implicated in the regulation of epithelial-to-mesenchymal transition (EMT) in bladder cancer cells. A comparison of nine bladder cancer cell lines revealed a correlation between high expression of miR-200c (and fellow miR-200 family member miR-200b) and epithelial phenotype (Adam et al., 2009). The same study also reported that miR-200c expression reverses resistance to anti-EGFR therapy in bladder cancer cell lines through targeting ERRFI-1.

## *Breast cancer*

**Oncogenesis**
A double-negative feedback loop between ZEB family transcription factors and the miR-200 family was shown to regulate EMT in different cell systems, including breast cancer cells (Burk et al., 2008). Moreover, expression of miR-200c was revealed to be activated by p53, resulting in induction of EMT in mammary epithelial cells upon loss of p53 (Chang et al., 2011). Loss of p53 was positively correlated with expression of ZEB1 and negatively correlated with expression of miR-200c and E-Cadherin in 106 breast tumor specimens.
miRNA microarray analysis of 43 primary tumors (10 colon, 10 bladder, 13 breast and 10 lung cancers) and matched lymph node metastases revealed that miR-200c and other miR-200 family members are downregulated in metastases compared to primary tumors (Baffa et al., 2009). Moreover, miR-200c and other miR-200 family members were shown to be underexpressed in the aggressive claudin-low subtype of breast cancer, which displays an EMT-like gene expression signature (Herschkowitz et al., 2011). In contrast, luminal breast cancers, which have a more epithelial-like phenotype and a better clinical prognosis, express high levels of miR-200c (Bockmeyer et al., 2011).
Re-expression of the miR-200 family in aggressive breast cancer cells was shown to inhibit experimental lung metastasis (Ahmad et al., 2011). In contrast, another study reported that miR-200c promotes colonization of breast cancer cells (Dykxhoorn et al., 2009). In in vitro assays, miR-200c suppresses migration and invasion of breast cancer cells through various mechanisms, including targeting of

ZEB1/ZEB2, PLCG1, moesin and fibronectin (Korpal et al., 2008; Uhlmann et al., 2010; Howe et al., 2011).
miR-200c also targets stem cell factors such as BMI1, and downregulation of miR-200c was shown to be characteristic of breast cancer stem cells (Shimono et al., 2009). Furthermore, miRNA microarray analysis revealed that miR-200c is downregulated in breast cancer cells with acquired resistance to cisplatin (Pogribny et al., 2010).

## Colorectal cancer

**Prognosis**
Kaplan-Meier survival analysis of 24 colorectal cancer patients suggested that high expression of miR-200c was associated with decreased overall survival (Xi et al., 2006).

**Oncogenesis**
Analysis of miR-200c expression in 24 colorectal cancer biopsies and matched normal samples by qRT-PCR revealed that miR-200c is overexpressed in colorectal tumors compared to normal tissue (Xi et al., 2006). Furthermore, microarray miRNA analysis of 43 primary tumors (10 colon, 10 bladder, 13 breast and 10 lung cancers) and matched lymph node metastases revealed that miR-200c and other miR-200 family members are downregulated in metastases compared to primary tumors (Baffa et al., 2009).

## Endometrial cancer

**Disease**
Endometrial carcinoma; endometrial carcinosarcoma.

**Oncogenesis**
miRNA microarray analysis of four endometrial endometrioid carcinomas and four normal endometrial tissue samples showed that miR-200c and other miR-200 family members were overexpressed in cancerous compared to normal tissue (Lee et al., 2011). Inhibition of miR-200c decreased the growth of endometrial carcinoma cells (Lee et al., 2011). In contrast, an analysis of miR-200c expression levels in five endometrial cancer and normal endometrial cell lines suggested that miR-200c is lower in cell lines derived from aggressive cancer compared to those derived from less aggressive cancer or normal endometrial epithelium (Cochrane et al., 2009). Restoration of miR-200c expression in aggressive endometrial cancer cells reduced their migration and invasion and increased their sensitivity to microtubule-targeting chemotherapeutic agents, at least in part through targeting TUBB3 (Cochrane et al., 2009; Cochrane et al., 2010; Howe et al., 2011). In a panel of 23 endometrial carcinosarcomas, which are composed of mixed populations of epithelial-like and mesenchymal-like cells, miR-200c and other miR-200 family members were found to be downregulated in the mesenchymal components of the tumors compared to the epithelial components (Castilla et al., 2011); this is consistent with the established role of the miR-200 family in suppression of epithelial-to-mesenchymal transition.

## Esophageal cancer

**Prognosis**
In a panel of 98 esophageal cancer patients treated with preoperative chemotherapy and surgery, expression of miR-200c was associated with shortened overall survival and poor response to chemotherapy, potentially through upregulation of the Akt signaling pathway (Hamano et al., 2011).

**Oncogenesis**
qRT-PCR analysis of miR-200 expression levels in 17 patients with Barrett's esophagus and 20 patients with esophageal adenocarcinoma indicated that miR-200c is downregulated during cancer progression from normal epithelium through Barrett's esophagus to esophageal adenocarcinoma (Smith et al., 2011). In contrast, another study on 98 esophageal cancer patients treated with preoperative chemotherapy and surgery found that miR-200c was expressed at higher levels in the tumor than in normal tissue (Hamano et al., 2011).

## Germ cell tumors

**Disease**
Germinoma; yolk sac tumors.

**Oncogenesis**
**Diagnosis**. Microarray analysis of 25 germ cell tumors and subsequent validation by qRT-PCR in 10 independent samples identified miR-200c as overexpressed in yolk sac tumors compared to germinoma (Murray et al., 2010).

## Head and neck cancer

**Disease**
Squamous cell carcinoma; spindle cell carcinoma.

**Oncogenesis**
miR-200c was significantly downregulated in a panel of 30 spindle cell carcinomas (which display a mesenchymal-like phenotype) compared to normal mucosa as determined by qRT-PC (Zidar et al., 2011). In contrast, expression levels of miR-200c in 30 squamous cell carcinomas were comparable to normal tissue.

## Liver cancer

**Oncogenesis**
**Diagnosis**. Due to its low expression in liver compared to other tissues, miR-200c has been suggested as a biomarker to distinguish hepatocellular carcinoma from liver metastases (Barshack et al., 2010).
miRNA microarray analysis of 92 primary hepatocellular carcinomas and 9 hepatocellular carcinoma cell lines identified miR-200c as a microRNA that is upregulated by p53 (Kim et al., 2011). Increased expression of miR-200c results in downregulation of transcriptional repressors ZEB1

and ZEB2, suggesting a role for p53-mediated regulation of miR-200c in suppression of EMT. miR-200c was reported to be underexpressed in benign liver tumors compared to hepatocellular carcinoma (Ladeiro et al., 2008); miR-200c levels were determined by qRT-PCR in two sets of tumors (first set: 18 benign tumors, 28 hepatocellular carcinomas; second set: 12 benign tumors, 22 hepatocellular carcinomas).

## Lung cancer

**Prognosis**

qRT-PCR analysis of miR-200c expression levels in 70 non-small cell lung cancer (NSCLC) patients revealed that high expression of miR-200c was associated with reduced overall survival (Liu et al., 2011).

**Oncogenesis**

Treatment of immortalized human bronchial epithelial cells with tobacco carcinogens was shown to induce an EMT-like phenotype and stem-cell like properties (Tellez et al., 2011). Quantification of miRNA levels by qRT-PCR in combination with bisulfite sequencing and chromatin immunoprecipitation revealed that these changes are accompanied by epigenetic silencing of miR-200c and other EMT-regulating microRNAs, suggesting that loss of miR-200c contributes to transformation of lung epithelial cells. In contrast, miRNA microarray analysis of six NSCLCs and matched adjacent normal tissue revealed that miR-200c is upregulated in NSCLC compared to healthy tissue (Liu et al., 2011). This finding was further validated in 70 lung carcinomas and matched normal tissue by qRT-PCR.

Several studies have reported that miR-200c can repress invasion and metastasis of lung cancer cells. Firstly, low expression of miR-200c and other miR-200 family members was associated with increased metastatic potential in a syngeneic mouse model of lung adenocarcinoma, and re-expression of miR-200 family members in these cell lines prevented EMT and metastasis (Gibbons et al., 2009). Secondly, miR-200c was shown to be downregulated by promoter hypermethylation in invasive NSCLC cell lines, and re-expression of miR-200c reduced the invasive potential of these cell lines (Ceppi et al., 2010). Furthermore, microarray miRNA analysis of 43 primary tumors (10 colon, 10 bladder, 13 breast and 10 lung cancers) and matched lymph node metastases revealed that miR-200c and other miR-200 family members are downregulated in metastases compared to primary tumors (Baffa et al., 2009). Finally, low expression of miR-200c in 69 primary lung tumors was correlated with lymph node metastases (Ceppi et al., 2010).

Mechanistically, the Notch ligand Jagged2 was shown to suppress expression of miR-200 family members, resulting in induction of EMT and increased metastatic potential (Yang et al., 2011). Moreover, miR-200c and fellow miR-200 family member miR-200b target VEGFR, which also contributes to invasion and metastasis (Roybal et al., 2011).

## Malignant pleural mesothelioma

**Oncogenesis**

**Diagnosis**. miR-200c has been proposed as a biomarker to distinguish malignant pleural mesothelioma from lung adenocarcinoma and lung metastases of other carcinomas. miRNA microarray expression profiling of 10 lung adenocarcinomas and 15 mesotheliomas revealed that miR-200c is reduced in mesothelioma (Gee et al., 2010). This result was further confirmed by qRT-PCR in a set of 100 mesotheliomas and 32 lung adenocarcinomas. Similarly, microRNA microarray analysis of 7 malignant pleural mesotheliomas and 97 carcinomas of various origins also identified miR-200c as underexpressed in mesotheliomas compared to the carcinoma samples, and differential expression levels of miR-200c and two other microRNAs could successfully be used to distinguish between malignant pleural mesothelioma and other types of cancer (Benjamin et al., 2010).

## Melanoma

**Oncogenesis**

Analysis of miR-200c expression levels in a panel of 10 melanoma cell lines by qRT-PCR showed that miR-200c is overexpressed in many of these cell lines compared to normal melanocytes (Elson-Schwab et al., 2010). Overexpression of miR-200c in melanoma cell lines resulted in a shift towards amoeboid type of migration, possibly through targeting of MARCKS.

## Ovarian cancer

**Prognosis**

High expression of miR-200c was found to be correlated with decreased progression-free and overall survival in a panel of 20 serous ovarian cancer patients (Nam et al., 2008). In contrast, a study investigating microRNA expression profiles in a total of 144 patients with epithelial ovarian cancer found that low expression of miR-200c was associated with increased progression-free and overall survival (Marchini et al., 2011). Similarly, high expression of miR-200c was correlated with response to chemotherapy and decreased risk of disease recurrence in a panel of 57 patients with serous ovarian carcinoma (Leskela et al., 2010).

**Oncogenesis**

miR-200c was found to be overexpressed in a panel of 20 serous ovarian carcinomas compared to 8 normal ovarian tissues by miRNA microarray analysis (Nam et al., 2008). Similarly, increased expression of miR-200c compared to normal ovary (n=15) was reported for serous, endometroid and clear cell ovarian carcinoma in a series of 69 cancer specimens.

Expression of miR-200c was correlated with E-Cadherin levels in 36 primary ovarian carcinomas (Park et al., 2008). The regulatory effect of miR-200c on EMT has been shown to be mediated through targeting of ZEB1 and ZEB2, which transcriptionally

repress E-Cadherin (Gregory et al., 2008; Korpal et al., 2008; Park et al., 2008). Re-expression of miR-200c in aggressive ovarian cancer cell lines was shown to reduce their migratory capacity; however, this effect appears to be independent of E-Cadherin expression (Cochrane et al., 2010). Furthermore, forced expression of miR-200c has been reported to sensitize ovarian cancer cells to paclitaxel treatment due to downregulation of miR-200c target gene TUBB3 (Cochrane et al., 2009; Cochrane et al., 2010).
miR-200c was also shown to be downregulated in a subpopulation of the ovarian cancer cell line OVCAR3 expressing the cancer stem cell marker CD133 (Guo et al., 2011).

## Pancreatic cancer

**Prognosis**
In a panel of 99 pancreatic cancer patients, high expression of miR-200c was associated with increased overall survival (Yu et al., 2010).

**Oncogenesis**
Downregulation of miR-200c and other miR-200 family members has been observed in gemcitabine-resistant pancreatic cancer cell lines (Li et al., 2009; Ali et al., 2010). miR-200c has also been suggested to have a stemness-inhibiting function in pancreatic cancer cells through targeting of stem cell factors such as Bmi1 (Wellner et al., 2009).
A double-negative feedback loop between ZEB family transcription factors and the miR-200 family was shown to regulate EMT in different cell systems, including pancreatic cancer cells (Burk et al., 2008). Consistently, high expression of miR-200c was shown to be associated with decreased invasive behavior in a panel of six pancreatic cancer cell lines, and miR-200c expression was correlated with E-Cadherin levels in pancreatic cancer specimens and cell lines (Yu et al., 2010). Overexpression of miR-200c in pancreatic cancer cell lines resulted in upregulation of E-Cadherin expression and reduced invasion but stimulated proliferation.
miRNA expression profiling of various stages in a mouse model of multistep tumorigenesis of the pancreas revealed that miR-200c is downregulated in metastases and metastasis-like tumors (Olson et al., 2009). Moreover, miR-200c also targets components of the Notch pathway, which is aberrantly activated in pancreatic cancer (Brabletz et al., 2011). Undifferentiated, aggressive pancreatic adenocarcinomas were shown to have higher expression of ZEB1 and Notch pathway components and lower expression of miR-200c compared to differentiated tumors.
In contrast to the studies described above, which suggest a metastasis-suppressing function for miR-200c in pancreatic cancer, a comparison of 16 pancreatic ductal adenocarcinoma cell lines found that miR-200c expression was upregulated in the highly metastatic cell lines (Mees et al., 2010).

## Prostate cancer

**Oncogenesis**
Prostate cancer cells with EMT phenotype were found to have stem-cell like properties and express low levels of miR-200 family members (Kong et al., 2010). Overexpression of miR-200c reversed EMT and stem-cell like properties, in part due to targeting of Notch-1. miR-200c was also shown to target the Notch ligand Jagged1, resulting in decreased proliferation of metastatic prostate cancer cells (Vallejo et al., 2011).

## Renal cancer

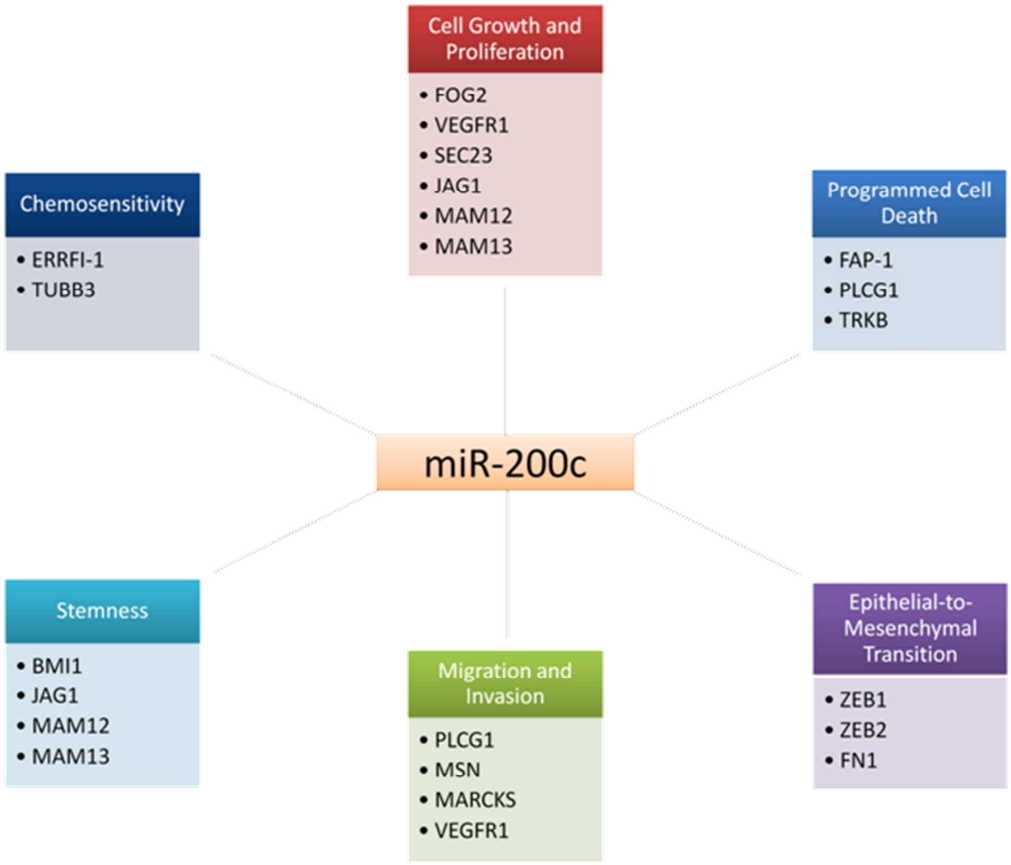
**Disease**
Clear cell carcinoma (CCC); Chromophobe renal cell carcinoma (ChCC).

**Oncogenesis**
**Diagnosis**. miR-200c has been found to be specifically expressed in chromophobe renal cell carcinoma and has been suggested as one of a set of microRNAs that can be used to distinguish between renal cell carcinoma subtypes (Fridman et al., 2010).
miR-200c was found to be significantly downregulated in clear cell carcinoma compared to normal kidney in a panel of 16 CCCs, 4 ChCCs and 6 normal kidneys both by microarray analysis and by qRT-PCR (Nakada et al., 2008). Furthermore, miR-200c expression was inversely correlated with expression of its target gene ZEB1 in these specimens. The downregulation of miR-200c in CCC was also confirmed by a second study comparing a total of 25 clear cell carcinomas and matched adjacent normal tissue (Liu et al., 2010).

## Thyroid carcinoma

**Oncogenesis**
The expression of miR-200 family members, including miR-200c, was found to be downregulated in undifferentiated, aggressive anaplastic thyroid carcinoma compared to both normal tissue and well-differentiated papillary and follicular thyroid carcinomas (Braun et al., 2010). Overexpression of the miR-200 family induced mesenchymal-to-epithelial transition and reduced invasion of ATC cells.

### *Various cancers*




miR-200c target genes regulate numerous processes involved in cancer development and progression.

## References

Xi Y, Formentini A, Chien M, Weir DB, Russo JJ, Ju J, Kornmann M, Ju J. Prognostic Values of microRNAs in Colorectal Cancer. Biomark Insights. 2006;2:113-121

Burk U, Schubert J, Wellner U, Schmalhofer O, Vincan E, Spaderna S, Brabletz T. A reciprocal repression between ZEB1 and members of the miR-200 family promotes EMT and invasion in cancer cells. EMBO Rep. 2008 Jun;9(6):582-9

Gregory PA, Bert AG, Paterson EL, Barry SC, Tsykin A, Farshid G, Vadas MA, Khew-Goodall Y, Goodall GJ. The miR-200 family and miR-205 regulate epithelial to mesenchymal transition by targeting ZEB1 and SIP1. Nat Cell Biol. 2008 May;10(5):593-601

Korpal M, Lee ES, Hu G, Kang Y. The miR-200 family inhibits epithelial-mesenchymal transition and cancer cell migration by direct targeting of E-cadherin transcriptional repressors ZEB1 and ZEB2. J Biol Chem. 2008 May 30;283(22):14910-4

Ladeiro Y, Couchy G, Balabaud C, Bioulac-Sage P, Pelletier L, Rebouissou S, Zucman-Rossi J. MicroRNA profiling in hepatocellular tumors is associated with clinical features and oncogene/tumor suppressor gene mutations. Hepatology. 2008 Jun;47(6):1955-63

Nakada C, Matsuura K, Tsukamoto Y, Tanigawa M, Yoshimoto T, Narimatsu T, Nguyen LT, Hijiya N, Uchida T, Sato F, Mimata H, Seto M, Moriyama M. Genome-wide microRNA expression profiling in renal cell carcinoma: significant down-regulation of miR-141 and miR-200c. J Pathol. 2008 Dec;216(4):418-27

Nam EJ, Yoon H, Kim SW, Kim H, Kim YT, Kim JH, Kim JW, Kim S. MicroRNA expression profiles in serous ovarian carcinoma. Clin Cancer Res. 2008 May 1;14(9):2690-5

Park SM, Gaur AB, Lengyel E, Peter ME. The miR-200 family determines the epithelial phenotype of cancer cells by targeting the E-cadherin repressors ZEB1 and ZEB2. Genes Dev. 2008 Apr 1;22(7):894-907

Adam L, Zhong M, Choi W, Qi W, Nicoloso M, Arora A, Calin G, Wang H, Siefker-Radtke A, McConkey D, Bar-Eli M, Dinney C. miR-200 expression regulates epithelial-to-mesenchymal transition in bladder cancer cells and reverses resistance to epidermal growth factor receptor therapy. Clin Cancer Res. 2009 Aug 15;15(16):5060-72

Baffa R, Fassan M, Volinia S, O'Hara B, Liu CG, Palazzo JP, Gardiman M, Rugge M, Gomella LG, Croce CM, Rosenberg A. MicroRNA expression profiling of human metastatic cancers identifies cancer gene targets. J Pathol. 2009 Oct;219(2):214-21

Cochrane DR, Spoelstra NS, Howe EN, Nordeen SK, Richer JK. MicroRNA-200c mitigates invasiveness and restores sensitivity to microtubule-targeting chemotherapeutic agents. Mol Cancer Ther. 2009 May;8(5):1055-66

Dykxhoorn DM, Wu Y, Xie H, Yu F, Lal A, Petrocca F, Martinvalet D, Song E, Lim B, Lieberman J. miR-200 enhances mouse breast cancer cell colonization to form distant metastases. PLoS One. 2009 Sep 29;4(9):e7181

Gibbons DL, Lin W, Creighton CJ, Rizvi ZH, Gregory PA, Goodall GJ, Thilaganathan N, Du L, Zhang Y, Pertsemlidis A,

Kurie JM. Contextual extracellular cues promote tumor cell EMT and metastasis by regulating miR-200 family expression. Genes Dev. 2009 Sep 15;23(18):2140-51

Li Y, VandenBoom TG 2nd, Kong D, Wang Z, Ali S, Philip PA, Sarkar FH. Up-regulation of miR-200 and let-7 by natural agents leads to the reversal of epithelial-to-mesenchymal transition in gemcitabine-resistant pancreatic cancer cells. Cancer Res. 2009 Aug 15;69(16):6704-12

Olson P, Lu J, Zhang H, Shai A, Chun MG, Wang Y, Libutti SK, Nakakura EK, Golub TR, Hanahan D. MicroRNA dynamics in the stages of tumorigenesis correlate with hallmark capabilities of cancer. Genes Dev. 2009 Sep 15;23(18):2152-65

Shimono Y, Zabala M, Cho RW, Lobo N, Dalerba P, Qian D, Diehn M, Liu H, Panula SP, Chiao E, Dirbas FM, Somlo G, Pera RA, Lao K, Clarke MF. Downregulation of miRNA-200c links breast cancer stem cells with normal stem cells. Cell. 2009 Aug 7;138(3):592-603

Wellner U, Schubert J, Burk UC, Schmalhofer O, Zhu F, Sonntag A, Waldvogel B, Vannier C, Darling D, zur Hausen A, Brunton VG, Morton J, Sansom O, Schüler J, Stemmler MP, Herzberger C, Hopt U, Keck T, Brabletz S, Brabletz T. The EMT-activator ZEB1 promotes tumorigenicity by repressing stemness-inhibiting microRNAs. Nat Cell Biol. 2009 Dec;11(12):1487-95

Ali S, Ahmad A, Banerjee S, Padhye S, Dominiak K, Schaffert JM, Wang Z, Philip PA, Sarkar FH. Gemcitabine sensitivity can be induced in pancreatic cancer cells through modulation of miR-200 and miR-21 expression by curcumin or its analogue CDF. Cancer Res. 2010 May 1;70(9):3606-17

Benjamin H, Lebanony D, Rosenwald S, Cohen L, Gibori H, Barabash N, Ashkenazi K, Goren E, Meiri E, Morgenstern S, Perelman M, Barshack I, Goren Y, Edmonston TB, Chajut A, Aharonov R, Bentwich Z, Rosenfeld N, Cohen D. A diagnostic assay based on microRNA expression accurately identifies malignant pleural mesothelioma. J Mol Diagn. 2010 Nov;12(6):771-9

Barshack I, Meiri E, Rosenwald S, Lebanony D, Bronfeld M, Aviel-Ronen S, Rosenblatt K, Polak-Charcon S, Leizerman I, Ezagouri M, Zepeniuk M, Shabes N, Cohen L, Tabak S, Cohen D, Bentwich Z, Rosenfeld N. Differential diagnosis of hepatocellular carcinoma from metastatic tumors in the liver using microRNA expression. Int J Biochem Cell Biol. 2010 Aug;42(8):1355-62

Braun J, Hoang-Vu C, Dralle H, Hüttelmaier S. Downregulation of microRNAs directs the EMT and invasive potential of anaplastic thyroid carcinomas. Oncogene. 2010 Jul 22;29(29):4237-44

Ceppi P, Mudduluru G, Kumarswamy R, Rapa I, Scagliotti GV, Papotti M, Allgayer H. Loss of miR-200c expression induces an aggressive, invasive, and chemoresistant phenotype in non-small cell lung cancer. Mol Cancer Res. 2010 Sep;8(9):1207-16

Cochrane DR, Howe EN, Spoelstra NS, Richer JK. Loss of miR-200c: A Marker of Aggressiveness and Chemoresistance in Female Reproductive Cancers. J Oncol. 2010;2010:821717

Elson-Schwab I, Lorentzen A, Marshall CJ. MicroRNA-200 family members differentially regulate morphological plasticity and mode of melanoma cell invasion. PLoS One. 2010 Oct 4;5(10)

Fridman E, Dotan Z, Barshack I, David MB, Dov A, Tabak S, Zion O, Benjamin S, Benjamin H, Kuker H, Avivi C, Rosenblatt K, Polak-Charcon S, Ramon J, Rosenfeld N, Spector Y. Accurate molecular classification of renal tumors using microRNA expression. J Mol Diagn. 2010 Sep;12(5):687-96

Gee GV, Koestler DC, Christensen BC, Sugarbaker DJ, Ugolini D, Ivaldi GP, Resnick MB, Houseman EA, Kelsey KT, Marsit CJ. Downregulated microRNAs in the differential diagnosis of malignant pleural mesothelioma. Int J Cancer. 2010 Dec 15;127(12):2859-69

Kong D, Banerjee S, Ahmad A, Li Y, Wang Z, Sethi S, Sarkar FH. Epithelial to mesenchymal transition is mechanistically linked with stem cell signatures in prostate cancer cells. PLoS One. 2010 Aug 27;5(8):e12445

Leskelä S, Leandro-García LJ, Mendiola M, Barriuso J, Inglada-Pérez L, Muñoz I, Martínez-Delgado B, Redondo A, de Santiago J, Robledo M, Hardisson D, Rodríguez-Antona C. The miR-200 family controls beta-tubulin III expression and is associated with paclitaxel-based treatment response and progression-free survival in ovarian cancer patients. Endocr Relat Cancer. 2011;18(1):85-95

Liu H, Brannon AR, Reddy AR, Alexe G, Seiler MW, Arreola A, Oza JH, Yao M, Juan D, Liou LS, Ganesan S, Levine AJ, Rathmell WK, Bhanot GV. Identifying mRNA targets of microRNA dysregulated in cancer: with application to clear cell Renal Cell Carcinoma. BMC Syst Biol. 2010 Apr 27;4:51

Mees ST, Mardin WA, Wendel C, Baeumer N, Willscher E, Senninger N, Schleicher C, Colombo-Benkmann M, Haier J. EP300--a miRNA-regulated metastasis suppressor gene in ductal adenocarcinomas of the pancreas. Int J Cancer. 2010 Jan 1;126(1):114-24

Murray MJ, Saini HK, van Dongen S, Palmer RD, Muralidhar B, Pett MR, Piipari M, Thornton CM, Nicholson JC, Enright AJ, Coleman N. The two most common histological subtypes of malignant germ cell tumour are distinguished by global microRNA profiles, associated with differential transcription factor expression. Mol Cancer. 2010 Nov 8;9:290

Pogribny IP, Filkowski JN, Tryndyak VP, Golubov A, Shpyleva SI, Kovalchuk O. Alterations of microRNAs and their targets are associated with acquired resistance of MCF-7 breast cancer cells to cisplatin. Int J Cancer. 2010 Oct 15;127(8):1785-94

Uhlmann S, Zhang JD, Schwäger A, Mannsperger H, Riazalhosseini Y, Burmester S, Ward A, Korf U, Wiemann S, Sahin O. miR-200bc/429 cluster targets PLCgamma1 and differentially regulates proliferation and EGF-driven invasion than miR-200a/141 in breast cancer. Oncogene. 2010 Jul 29;29(30):4297-306

Yu J, Ohuchida K, Mizumoto K, Sato N, Kayashima T, Fujita H, Nakata K, Tanaka M. MicroRNA, hsa-miR-200c, is an independent prognostic factor in pancreatic cancer and its upregulation inhibits pancreatic cancer invasion but increases cell proliferation. Mol Cancer. 2010 Jun 28;9:169

Ahmad A, Aboukameel A, Kong D, Wang Z, Sethi S, Chen W, Sarkar FH, Raz A. Phosphoglucose isomerase/autocrine motility factor mediates epithelial-mesenchymal transition regulated by miR-200 in breast cancer cells. Cancer Res. 2011 May 1;71(9):3400-9

Bockmeyer CL, Christgen M, Müller M, Fischer S, Ahrens P, Länger F, Kreipe H, Lehmann U. MicroRNA profiles of healthy basal and luminal mammary epithelial cells are distinct and reflected in different breast cancer subtypes. Breast Cancer Res Treat. 2011 Mar 17;

Brabletz S, Bajdak K, Meidhof S, Burk U, Niedermann G, Firat E, Wellner U, Dimmler A, Faller G, Schubert J, Brabletz T. The ZEB1/miR-200 feedback loop controls Notch signalling in cancer cells. EMBO J. 2011 Feb 16;30(4):770-82

Castilla MÁ, Moreno-Bueno G, Romero-Pérez L, Van De Vijver K, Biscuola M, López-García MÁ, Prat J, Matías-Guiu X, Cano

A, Oliva E, Palacios J. Micro-RNA signature of the epithelial-mesenchymal transition in endometrial carcinosarcoma. J Pathol. 2011 Jan;223(1):72-80

Chang CJ, Chao CH, Xia W, Yang JY, Xiong Y, Li CW, Yu WH, Rehman SK, Hsu JL, Lee HH, Liu M, Chen CT, Yu D, Hung MC. p53 regulates epithelial-mesenchymal transition and stem cell properties through modulating miRNAs. Nat Cell Biol. 2011 Mar;13(3):317-23

Guo R, Wu Q, Liu F, Wang Y. Description of the CD133+ subpopulation of the human ovarian cancer cell line OVCAR3. Oncol Rep. 2011 Jan;25(1):141-6

Hamano R, Miyata H, Yamasaki M, Kurokawa Y, Hara J, Moon JH, Nakajima K, Takiguchi S, Fujiwara Y, Mori M, Doki Y. Overexpression of miR-200c induces chemoresistance in esophageal cancers mediated through activation of the Akt signaling pathway. Clin Cancer Res. 2011 May 1;17(9):3029-38

Han Y, Chen J, Zhao X, Liang C, Wang Y, Sun L, Jiang Z, Zhang Z, Yang R, Chen J, Li Z, Tang A, Li X, Ye J, Guan Z, Gui Y, Cai Z. MicroRNA expression signatures of bladder cancer revealed by deep sequencing. PLoS One. 2011 Mar 28;6(3):e18286

Herschkowitz JI, Zhao W, Zhang M, Usary J, Murrow G, Edwards D, Knezevic J, Greene SB, Darr D, Troester MA, Hilsenbeck SG, Medina D, Perou CM, Rosen JM. Comparative oncogenomics identifies breast tumors enriched in functional tumor-initiating cells. Proc Natl Acad Sci U S A. 2011 Jun 1;

Howe EN, Cochrane DR, Richer JK. Targets of miR-200c mediate suppression of cell motility and anoikis resistance. Breast Cancer Res. 2011 Apr 18;13(2):R45

Kim T, Veronese A, Pichiorri F, Lee TJ, Jeon YJ, Volinia S, Pineau P, Marchio A, Palatini J, Suh SS, Alder H, Liu CG, Dejean A, Croce CM. p53 regulates epithelial-mesenchymal transition through microRNAs targeting ZEB1 and ZEB2. J Exp Med. 2011 May 9;208(5):875-83

Lee JW, Park YA, Choi JJ, Lee YY, Kim CJ, Choi C, Kim TJ, Lee NW, Kim BG, Bae DS. The expression of the miRNA-200 family in endometrial endometrioid carcinoma. Gynecol Oncol. 2011 Jan;120(1):56-62

Liu XG, Zhu WY, Huang YY, Ma LN, Zhou SQ, Wang YK, Zeng F, Zhou JH, Zhang YK. High expression of serum miR-21 and tumor miR-200c associated with poor prognosis in patients with lung cancer. Med Oncol. 2011 Apr 24;

Marchini S, Cavalieri D, Fruscio R, Calura E, Garavaglia D, Nerini IF, Mangioni C, Cattoretti G, Clivio L, Beltrame L, Katsaros D, Scarampi L, Menato G, Perego P, Chiorino G, Buda A, Romualdi C, D'Incalci M. Association between miR-200c and the survival of patients with stage I epithelial ovarian cancer: a retrospective study of two independent tumour tissue collections. Lancet Oncol. 2011 Mar;12(3):273-85

Roybal JD, Zang Y, Ahn YH, Yang Y, Gibbons DL, Baird BN, Alvarez C, Thilaganathan N, Liu DD, Saintigny P, Heymach JV, Creighton CJ, Kurie JM. miR-200 Inhibits lung adenocarcinoma cell invasion and metastasis by targeting Flt1/VEGFR1. Mol Cancer Res. 2011 Jan;9(1):25-35

Smith CM, Watson DI, Leong MP, Mayne GC, Michael MZ, Wijnhoven BP, Hussey DJ. miR-200 family expression is downregulated upon neoplastic progression of Barrett's esophagus. World J Gastroenterol. 2011 Feb 28;17(8):1036-44

Tellez CS, Juri DE, Do K, Bernauer AM, Thomas CL, Damiani LA, Tessema M, Leng S, Belinsky SA. EMT and stem cell-like properties associated with miR-205 and miR-200 epigenetic silencing are early manifestations during carcinogen-induced transformation of human lung epithelial cells. Cancer Res. 2011 Apr 15;71(8):3087-97

Vallejo DM, Caparros E, Dominguez M. Targeting Notch signalling by the conserved miR-8/200 microRNA family in development and cancer cells. EMBO J. 2011 Feb 16;30(4):756-69

Wiklund ED, Bramsen JB, Hulf T, Dyrskjøt L, Ramanathan R, Hansen TB, Villadsen SB, Gao S, Ostenfeld MS, Borre M, Peter ME, Ørntoft TF, Kjems J, Clark SJ. Coordinated epigenetic repression of the miR-200 family and miR-205 in invasive bladder cancer. Int J Cancer. 2011 Mar 15;128(6):1327-34

Yang Y, Ahn YH, Gibbons DL, Zang Y, Lin W, Thilaganathan N, Alvarez CA, Moreira DC, Creighton CJ, Gregory PA, Goodall GJ, Kurie JM. The Notch ligand Jagged2 promotes lung adenocarcinoma metastasis through a miR-200-dependent pathway in mice. J Clin Invest. 2011 Apr 1;121(4):1373-85

Zidar N, Boštjančič E, Gale N, Kojc N, Poljak M, Glavač D, Cardesa A. Down-regulation of microRNAs of the miR-200 family and miR-205, and an altered expression of classic and desmosomal cadherins in spindle cell carcinoma of the head and neck--hallmark of epithelial-mesenchymal transition. Hum Pathol. 2011 Apr;42(4):482-8

*This article should be referenced as such:*

Jurmeister S, Uhlmann S, Sahin Ö. MIR200C (microRNA 200c). Atlas Genet Cytogenet Oncol Haematol. 2012; 16(2):92-99.