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Gene Section

Mini Review

MIR10B (microRNA 10b)

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Identity

Other names: MIRN10B (microRNA 10b): MIR10B; hsa-mir-10b; mir-10b

HGNC (Hugo): MIR10B

Location: 2q31.1

Local order: Based on Mapviewer Genes on Sequence, genes flanking MIRN10B oriented from centromere to telomere on 2q31.1 are:

HOXD11; Homeobox 11, 2q31.1

HOXD 10; Homeobox 10, 2q31.1

HOXD 9; Homeobox 9, 2q31.1

HOXD 8; Homeobox 8, 2q31.1

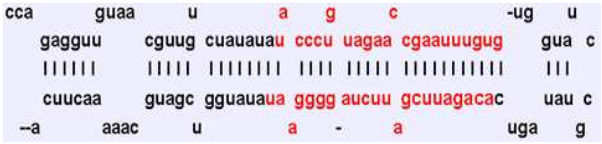
MIRN10B; microRNA 10b, 2q31.1

HOXD 4; Homeobox 4, 2q31.1

HOXD 3; Homeobox3, 2q31.1

MTX2; Metaxin 2, 2q31.1.

DNA/RNA



Stem-loop structure of mir-10b.

Description

In human, microRNA-10 gene has been duplicated. It is now present in the form of two variants as miR-10a and miR-10b located on different chromosomes. miR-10a is located between HOX4B and HOX5B on 17q21, while miR-10b is located between HOXD4 and HOXD8 on 2q31.1. It is believed that, there is a strong correlation between the specific miRs and HOX genes. MIRN10B maps to the HOXD cluster on 2q31.1. HOX genes are a family of transcription factor genes that play crucial roles during normal development and in oncogenesis. HOXD4 expression is deregulated in a variety of solid and hematopoietic cancers.

Transcription

miRNAs are generally transcribed by RNA polymerase II.

There is limited information on how miRNA gene expression is regulated due to lack of basic information of their gene structures. Screening of miRNA putative promoter regions (miPPRs) revealed miPPR-10b for MIRN10B. TWIST1, a metastasis-promoting transcription factor, has been shown to induce miR-10b via binding to the most proximal E-box upstream of the miR-10b hairpin region. This E-box was in the miPPR-10b.

Pri-miRNA (primary) mir-10b: The primary miRNA transcripts are called pri-miRNAs. They contain cap structures and poly(A) tails. If transcribed by RNA polymerase II, primary transcript of mir-10b is not known yet.

Pre-miRNA (precursor) mir-10b: pri-miRNA transcripts are processed by microprocessor complex consisting nuclear RNase enzyme Drosha and the double-stranded RNA binding protein Pasha to generate pre-miRNAs. The precursor mir-10b is 110 nucleotides long. Pre-miR-10b is transferred from nucleus to cytoplasm.

Sequence:

5'-CCAGAGGUUGUAACGUUGUCUAUAUA
UACCCUGUAGAACCGAAUUUGUGUGGUAUCC
GUAUAGUCACAGAUUCGAUUCUAGGGGAAUA
UAUGGUCGAUGCAAAAACUUCA-3'

Mature miR-10b: In the cytoplasm, pre-miRNA molecules are processed into mature miRNA by RNA-

induced silencing complex (RISC). Mature miR-10b is 23 nucleotides long.
Sequence:
5'-UACCCUGUAGAACCGAAUUUGUG-3'

Pseudogene

No reported pseudogenes.

Protein

Note
MicroRNAs are not translated into amino acids.

Mutations

Note
Gene mutations have not been described.

Implicated in

Colorectal neoplasia

Disease
Possible changes in microRNA levels; including miR-10b, was investigated during colorectal tumorigenesis. There was not a significant down-regulation of microRNA 10b in colon tumors to suggest a potential role in colorectal tumorigenesis.

Breast Cancer

Disease
76 breast cancers and 10 normal breast samples were analyzed by microRNA microarray and Northern Blotting to identify miRNAs whose expression is deregulated notably in cancer versus normal breast tissues. According to these results; miR-10b was one of the microRNAs which were down-regulated.

Oncogenesis
Tumor invasion and Metastasis: Although miR-10b was downregulated in nonmetastatic breast cancers in comparison with normal breast tissue, this miRNA was over-expressed in about 50% of metastatic breast cancers. Ectopic expression of miR-10b had no effect on proliferation, but an increase in transwell migration and Matrigel invasion was observed. In vivo ectopic expression of miR-10b conferred invasive properties on otherwise non-invasive breast cancer cells. Although control tumors could not invade surrounding tissues and exhibited poor vascularization, miR-10b over-expressing tumors exhibited an invasive behavior and were highly vascularized. miR-10b promoted metastasis in non-metastatic breast cancer cells. Lung micro-metastasis was detected in miR-10b over-expressing cells while there were no intravasating cells or lung metastases in control tumors.
It was shown that miR-10b expression was induced by transcription factor TWIST allowing miR-10b to inhibit translation of the mRNA encoding homeobox D10 (Figure 2). This resulted in increased expression of a well-characterized prometastatic gene, RHOC (ras homolog gene family member C), thus leading to migration, tumor invasion, and metastasis.

Glioblastoma

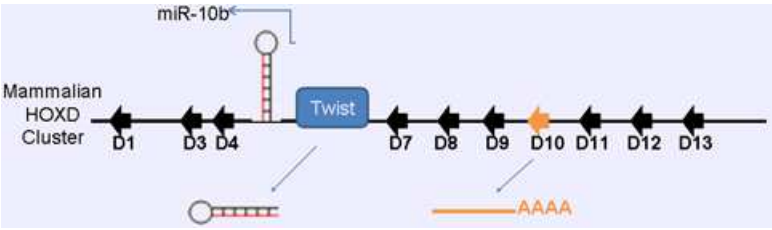
Disease
miR-10b was one of the over-expressed miRNAs in glioblastomas compared to peripheral tissues. According to the microarray studies on glioblastomas, an excess of 1.97- to 13.6-fold increase was observed in 5 in out of 9 samples. This data was further confirmed by Northern blotting. miR-10b was stated to be a candidate oncogene microRNA as it was significantly upregulated in glioblastomas.

Acute Myeloid Leukemia (AML)

Disease
Role of microRNAs in the biology of NPMc+ (nucleophosmin) AML was investigated in 85 adult de novo AML patients. Microarray studies characterized these patients for subcellular localization/mutation status of NPM1 and FLT3 mutations. A strong microRNA expression pattern was identified which differentiated NPMc+ mutated from the cytoplasmic-negative (NPM1 unmutated) cases. According to this pattern, miRNA-10b together with miRNA-10a, let-7 and miR-29 family members were up-regulated. These data was further confirmed by qRT-PCR in 44 AML patients (randomly chosen from the initial cohort). According to the overall results, it was remarkable that miRNA-10b and miRNA-10a expression levels clearly differentiated NPMc+ vs. NPMc- cases.

Central Nervous System (CNS) tumors

Disease
Although, miRNA-10b was not specifically expressed in brain tissue, it was one of the 5 microRNAs which were highly expressed in CNS tumor-derived cell lines compared to normal brain tissue.



Regulation and function of miR-10b in breast cancer metastasis.

Hepatocellular adenomas (HCAs) and Hepatocellular Carcinomas (HCCs)

Disease

Expression of miRNAs was analyzed in a series of 46 malignant and benign hepatocellular tumors compared to 4 normal liver tissues. The most significant deregulated miRNAs were further analyzed in a second series of 43 tumors and 16 non-tumor liver tissues including cirrhosis and chronic hepatitis of various etiologies. miRNA-10b was found to be overexpressed in HCC when compared to benign tumors and non-tumor liver tissues.

Protein synthesis inhibition

Disease

The apolipoprotein B mRNA-editing enzyme catalytic polypeptide-like 3G (APOBEC3G or A3G) and other APOBEC family members were shown to induce protein synthesis by miRNAs such as miR-10b in 293T and HeLa cells. miRNA microarray results suggested overexpression of miR-10b in 293T cells. Luciferase assay showed A3G effects on miRNA mediated translational repression. A3G facilitates recruitment of miRNA-targeted mRNA to polysomes to synthesize more proteins and drives dissociation of miRNA-targeted mRNA from P-bodies.

Megakaryocytopoiesis

Disease

In order to discover regulatory pathways during megakaryocytic differentiation, microRNA expression profiling was performed for in vitro differentiated megakaryocytes derived from CD34+ hematopoietic progenitors. According to the PAM (predictive analysis of microarray), miR-10b was one of the microRNAs which were identified to be involved in megakaryocytic differentiation. Downregulation of miR-10b was shown by microarrays. But Northern blot analysis and q-RT-PCR results showed that miR-10a and miR-130a were the most significantly down-regulated among the examined miRNAs.

Adipogenesis

Disease

miR-10b was shown to be up-regulated during 3T3-L1 pre-adipocyte differentiation. It was stated that this up-regulation may not be related to an actual differentiation process and may be induced by growth arrest and/or hormonal stimulation.

References

Meazza R, Faiella A, Corsetti MT, Airoldi I, Ferrini S, Boncinelli E, Corte G. Expression of HOXC4 homeoprotein in the nucleus of activated human lymphocytes. Blood. 1995 Apr 15;85(8):2084-90

Manohar CF, Salwen HR, Furtado MR, Cohn SL. Up-regulation of HOXC6, HOXD1, and HOXD8 homeobox gene expression in human neuroblastoma cells following chemical induction of differentiation. Tumour Biol. 1996;17(1):34-47

Bernstein E, Caudy AA, Hammond SM, Hannon GJ. Role for a bidentate ribonuclease in the initiation step of RNA interference. Nature. 2001 Jan 18;409(6818):363-6

Lagos-Quintana M, Rauhut R, Meyer J, Borkhardt A, Tuschl T. New microRNAs from mouse and human. RNA. 2003 Feb;9(2):175-9

Michael MZ, O' Connor SM, van Holst Pellekaan NG, Young GP, James RJ. Reduced accumulation of specific microRNAs in colorectal neoplasia. Mol Cancer Res. 2003 Oct;1(12):882-91

Calin GA, Sevignani C, Dumitru CD, Hyslop T, Noch E, Yendamuri S, Shimizu M, Rattan S, Bullrich F, Negrini M, Croce CM. Human microRNA genes are frequently located at fragile sites and genomic regions involved in cancers. Proc Natl Acad Sci U S A. 2004 Mar 2;101(9):2999-3004

Denli AM, Tops BB, Plasterk RH, Ketting RF, Hannon GJ. Processing of primary microRNAs by the Microprocessor complex. Nature. 2004 Nov 11;432(7014):231-5

Lee Y, Kim M, Han J, Yeom KH, Lee S, Baek SH, Kim VN. MicroRNA genes are transcribed by RNA polymerase II. EMBO J. 2004 Oct 13;23(20):4051-60

Ciafrè SA, Galardi S, Mangiola A, Ferracin M, Liu CG, Sabatino G, Negrini M, Maira G, Croce CM, Farace MG. Extensive modulation of a set of microRNAs in primary glioblastoma. Biochem Biophys Res Commun. 2005 Sep 9;334(4):1351-8

Iorio MV, Ferracin M, Liu CG, Veronese A, Spizzo R, Sabbioni S, Magri E, Pedriali M, Fabbri M, Campiglio M, Ménard S, Palazzo JP, Rosenberg A, Musiani P, Volinia S, Nenci I, Calin GA, Querzoli P, Negrini M, Croce CM. MicroRNA gene expression deregulation in human breast cancer. Cancer Res. 2005 Aug 15;65(16):7065-70

Zeng Y, Yi R, Cullen BR. Recognition and cleavage of primary microRNA precursors by the nuclear processing enzyme Drosha. EMBO J. 2005 Jan 12;24(1):138-48

Garzon R, Pichiorri F, Palumbo T, Iuliano R, Cimmino A, Aqeilan R, Volinia S, Bhatt D, Alder H, Marcucci G, Calin GA, Liu CG, Bloomfield CD, Andreeff M, Croce CM. MicroRNA fingerprints during human megakaryocytopoiesis. Proc Natl Acad Sci U S A. 2006 Mar 28;103(13):5078-83

Kajimoto K, Naraba H, Iwai N. MicroRNA and 3T3-L1 pre-adipocyte differentiation. RNA. 2006 Sep;12(9):1626-32

Debernardi S, Skoulakis S, Molloy G, Chaplin T, Dixon-McIver A, Young BD. MicroRNA miR-181a correlates with morphological sub-class of acute myeloid leukaemia and the expression of its target genes in global genome-wide analysis. Leukemia. 2007 May;21(5):912-6

Gaur A, Jewell DA, Liang Y, Ridzon D, Moore JH, Chen C, Ambros VR, Israel MA. Characterization of microRNA expression levels and their biological correlates in human cancer cell lines. Cancer Res. 2007 Mar 15;67(6):2456-68

Huang J, Liang Z, Yang B, Tian H, Ma J, Zhang H. Derepression of microRNA-mediated protein translation inhibition by apolipoprotein B mRNA-editing enzyme catalytic polypeptide-like 3G (APOBEC3G) and its family members. J Biol Chem. 2007 Nov 16;282(46):33632-40

Lui WO, Pourmand N, Patterson BK, Fire A. Patterns of known and novel small RNAs in human cervical cancer. Cancer Res. 2007 Jul 1;67(13):6031-43

Ma L, Teruya-Feldstein J, Weinberg RA. Tumour invasion and metastasis initiated by microRNA-10b in breast cancer. Nature. 2007 Oct 11;449(7163):682-8

Fujita S, Iba H. Putative promoter regions of miRNA genes involved in evolutionarily conserved regulatory systems among vertebrates. Bioinformatics. 2008 Feb 1;24(3):303-8

Garzon R, Garofalo M, Martelli MP, Briesewitz R, Wang L, Fernandez-Cymering C, Volinia S, Liu CG, Schnittger S, Haferlach T, Liso A, Diverio D, Mancini M, Meloni G, Foa R, Martelli MF, Mecucci C, Croce CM, Falini B. Distinctive microRNA signature of acute myeloid leukemia bearing cytoplasmic mutated nucleophosmin. Proc Natl Acad Sci U S A. 2008 Mar 11;105(10):3945-50

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

Ma L, Weinberg RA. MicroRNAs in malignant progression. Cell Cycle. 2008 Mar 1;7(5):570-2

Negrini M, Calin GA. Breast cancer metastasis: a microRNA story. Breast Cancer Res. 2008;10(2):203

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