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Gene Section
Review

MIR296 (microRNA 296)

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Abstract

Review on MIR296, with data on DNA/RNA and where the gene is implicated.

Identity

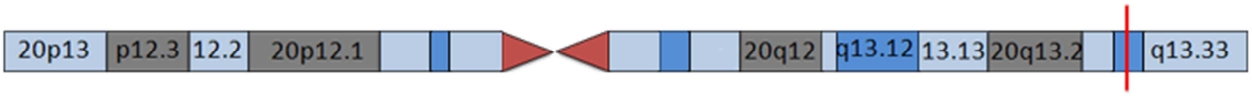
Other names: MIRN296, miRNA296

HGNC (Hugo): MIR296

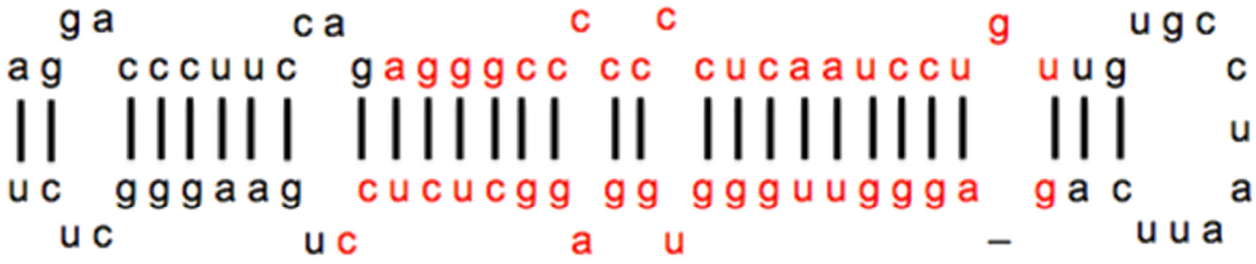
Location: 20q13.32

Local order: Orientation: minus strand.
Based on Mapviewer, genes flanking miR296 on 20q13.32 are: **miR296**; miR298; GNAS-AS1, GNAS antisense RNA 1; GNAS, GNAS complex locus.

Note: miR296 has been implicated in cancerogenesis and it has been reported both over-expressed and lost in different human cancer cell types, suggesting that it functions as an oncogene or an oncosuppressor in different biological settings.
Furthermore, miR296 has been also described to contribute to carcinogenesis by dysregulating p53. miR296 has been named an "angiomiR" because of its role in angiogenesis.



Schematic representation of human chromosome 20 with highlight of miR296 locus (red dash).



Stem-loop structure of miR-296, with mature miR-296-3p and miR-296-5p sequences highlighted in red.

miR-296 plays important roles in different cell types and cellular pathways, regulating several distinct mRNAs.
Recently, miR-296, along with miR-298, has been demonstrated to be part of the GNAS complex locus, a highly complex cluster with imprinted gene expression, coding a stimulatory G-protein alpha subunit (Gs-α), involved in many signal transduction pathways (Robson et al., 2012).
miR-296 was initially found to be specifically expressed in differentiated mouse embryonic stem cells, directly cross-talking with Nanog, Oct4 and Sox2 gene (Houbaviy et al., 2003).
It was also characterized in human embryonic stem cells (Suh et al., 2004; Lakshmipathy et al., 2007).
miR-296 has been involved in antiviral responses induced by IFNα/IFNβ, inhibiting HCV replication directly targeting viral transcripts (Pedersen et al., 2007).
In a large series of human cancer cell lines and carcinoma specimens, miR-296 was identified as a comprehensive regulator of cell tumorigenicity, migration and invasion by inhibition of the expression of one of its targets, Scrib, a cytoplasmic protein that participates in multiprotein complexes (Vaira et al., 2012).

DNA/RNA

Note
Accession: NR_029844

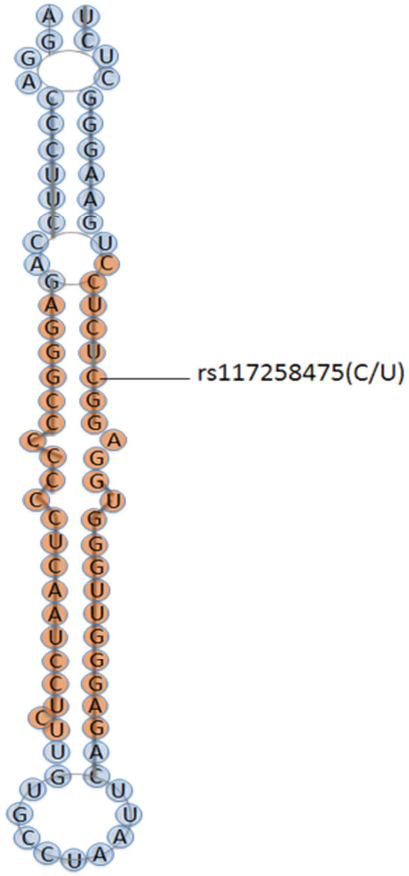
Description

Size: 80 bases.
Sequence: >gi|262206120|ref|NR_029844.1| Homo sapiens microRNA 296 (MIR296), microRNA.
AGGACCCTTCCAGAGGGCCCCCCCTCAATCCT GTTGTGCCTAATTCAGAGGGTTGGGTGGAGGC TCTCCT GAAGGGCTCT.

Transcription

Pre-miR296:
Accession: MI0000747
Sequence:
AGGACCCUUCCAGAGGGCCCCCCCUCAAUCCU GUUGUGCCUAAUUCAGAGGGUUGGGUGGAGG CUCUCCUGAAGGGCUCU
Mature sequence hsa-miR296-5p
Accession: MIMAT0000690
Lenght: 21 nt
Sequence: 14-agggccccccucaauccugu-34
Mature sequence hsa-miR296-3p
Accession: MIMAT0004679
Lenght: 22 nt
Sequence: 48-gaggguuggguggaggcucucc-69

Mutations



Note
SNP ID: rs117258475
Position: chr20:57392686
SNP Loc relative to pre-miR: 64
Ref-allele: C/U

Implicated in

Various cancers

Note
miR-296 is variably expressed in different human cancers, it has been shown to be reduced or over-expressed and to correlate with metastatic disease. miR-296 has an inhibitory function on different targets.

Lung carcinomas

Note
In lung carcinomas, miR-296 is a tumour-suppressive miR as it has been found to be lost.
The loss results in a repression of Numbl expression. Numbl becomes overexpressed and mislocalized in cancer cells from a variety of human tumors (Vaira et al., 2013).

Hepatocellular carcinomas

Note

miR-296 is lost during hepatocellular carcinomas progression. The loss of miR-296 deregulates cell polarity and plasticity. The resulting effect is an over-expression of Scrib. miR296 regulates cell migration, invasion, and tumorigenicity, through the transcriptional repression of Scrib. miR296 or Scrib levels predict tumor relapse in hepatocellular carcinoma patients (Vaira et al., 2012).

Prostate cancers

Note

miR-296 is a specific regulator of the oncogene HMGA1 in prostate cancer cells and is associated with prostate cancer growth and invasion. In this type of cancer there is an inverse correlation between HMGA1 and miR-296 expression levels, and low miR-296 expression levels correlate with advanced tumor grade and stage (Wei et al., 2011).

Parathyroid carcinomas

Note

miR-296 has been found to be down-regulated in parathyroid carcinomas compared to normal parathyroid glands. miR-296 expression levels negatively correlated with hepatocyte growth factor receptor-regulated tyrosine kinase substrate mRNA expression levels. miR-296 might have a role as an oncosuppressor gene in these type of neoplasia (Corbetta et al., 2009).

Esophageal carcinomas

Note

In squamous cell carcinomas of the esophagus, miR-296 is reported to be over-expressed and to have a pro-tumorigenic role. High levels of miR-296 are associated with resistance to chemotherapy, while its forced down-regulation resulted in increased sensitivity to standard chemotherapeutic agents and in decreased tumorigenesis of esophageal carcinoma cell lines, likely through reduction of cyclin D1 and upregulation of p27 (Hong et al., 2010).

Gastric cancers

Note

miR-296-5p overexpression significantly promoted gastric cancer cells growth through repression of Caudal-related homeobox 1 (CDX1), an intestinal-specific transcription factor, reported to have vital roles in gastric intestinal metaplasia (Li et al., 2013).

Colon cancers

Note

Decrease in miR-296 circulating levels, in patients with colon cancer, predicts chemotherapy resistance and is associated with metastasis formation. Low levels of circulating miR-296 in patients with colon cancers reflect more aggressive tumor phenotype and increased tumor cell invasiveness (Shivapurkar et al., 2012).

Immortalized cells

Note

In immortalized cells, miR-296 is frequently upregulated and the over-expression has been reported to determine p53 down-regulation. A number of cancer cells express high levels of miR-296, that downregulates p21WAF1 mRNA expression via interaction with its 3' untranslated region (Yoon et al., 2011).

Angiogenesis

Note

miR-296 was identified in endothelial cells of normal and neoplastic tissues, where it promoted angiogenesis through inhibition of one of its target gene, the hepatocyte growth factor-regulated tyrosine kinase substrate (HGS). HGS normally stimulates degradation of growth factors receptors, such as vascular endothelial receptor-2 (VEGFR2) and platelet derived growth factor receptor β (PDGFR-β) (Wurdinger et al., 2008).

Hypertension

Note

The human with-no-lysine kinase-4 (hWNK4) is a member of the serine-threonine protein kinase family and may be involved in pathophysiological processes of hypertension as it regulates diverse ion transporters. Expression of hWNK4 can be downregulated by miR-296 at the posttranscriptional level in a cell-specific manner (Mao et al., 2010).

Anti-viral defences

Note

Human miR-296-5p inhibits enterovirus EV71 replication by targeting the viral genome. miR-296 has a role as critical effectors in intricate networks of host-pathogen: effectively miR-296-5p was found to be significantly increased in response to EV71 infection. Overexpression of miR296-5p inhibited EV71 infection (Zheng et al., 2013).

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