

Gene Section

Review

MIR126 (microRNA 126)

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Identity

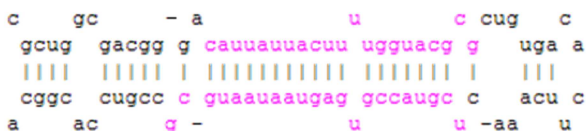
Other names: hsa-mir-126; microRNA 126; miR-126; MIRN126; miRNA126

HGNC (Hugo): MIR126

Location: 9q34.3

Note: The MiRNA126 are located in intron 7 of the epidermal growth factor (EGF)-like-domain, multiple 7 (EGFL7) gene. In addition, the antisense sequence to MIR126 within the hairpin pre-miRNA is also processed as a minor sequence miRNA, designated miRNA126*.

DNA/RNA



Stem loop structure of MiR-126.

Description

MiRNAs can be located within their own open reading frame (ORF) or within the intron of a host gene. Those miRNAs that are located within an intron are dependent on the transcriptional regulation of its host gene. In the human genome, miR-126 is found on chromosome 9 within intron 7 of the EGFL7 gene. An alternative miR-126 transcript from this region has also been reported and is designated miR-126*. Notably, EGFL7 expression is undetectable in normal brain tissue but is deregulated in malignant glioblastoma tumor cells as well as vascular endothelium cells within the tumor (Huang et al., 2010). EGFL7 is also secreted by endothelium and regulates angiogenesis. Recent studies demonstrate that both miR-126 and its host gene EGFL-7 harbor CpG islands invoking epigenetic

regulation as one potential mechanism for the observed deregulation of miR-126 in both solid and hematologic malignancies (Saito et al., 2009).

Transcription

MiRNAs are transcribed as a longer primary mRNA transcript which is called a pri-miR. The pri-miRs are processed mRNA molecules containing a 5' cap and a poly A tail and can range from hundred to thousand nucleotides (Nana-Sinkam et al., 2009). Currently the pri-miR for miR-126 is unknown. In the nucleus, the processing of the pri-miRs by the RNase enzyme, Drosha, to a smaller pre-miR molecule occurs (Nana-Sinkam et al., 2009). The pre-miR forms a stem loop structure to facilitate its transport to the nucleus. For miR-126, it is processed to an 85 nucleotide pre-miR that is then transported to the cytoplasm. Once in the cytoplasm, the pre-miR is incorporated in the RNA-inducible silencing complex (RISC). The RISC contains an RNase III endonuclease, Dicer, which further cleaves the pre-miR to the mature miRNA and minor antisense miRNA.

The pre-miR sequence for miR-126 is

5'-
GCTGGCGACGGGACATTATTACTTTTGGTACGC
GCTGTGACACTTCAAACCTCGTACCGTGAGTAAT
AATGCGCCGTCCACGGCA-3'.

The mature sequence for miR-126 is 52-
ucguaccgugaguauaauaugcg-73.

Minor miRNA sequence:

In some cases, the antisense sequence to the mature miRNA in the hairpin structure is also processed to a minor miRNA. A minor miRNA sequence has been identified for miR-126 and is designated MiR-126*.

- ID: hsa-miR-126*,

- miRBASE Accession #: MI0000444,

- Sequence: The mature sequence for miR-126* is 14-
cauuuuuacuuuugguacg-35.

Protein

Note

MicroRNAs are not translated to protein.

Mutations

Note

No mutations have been identified.

Implicated in

Various cancers

Note

Deregulation of miR-126 has been described in several solid and hematologic malignancies including lung, prostate, breast, renal cell, cervical, thyroid cancers and Acute Leukemias. Furthermore, it has been implicated in regulating processes fundamental to tumor development and progression.

Lung cancer: non-small cell cancer

Disease

Several studies have demonstrated that miR-126 is reduced in lung cancer tissue compared to uninvolved adjacent lung tissue (Yanaihara et al., 2006).

Prognosis

A recent study examining miR-126 expression in 335 lung cancer tissues revealed that elevated miR-126 along with VEGF were negative prognostic factors. Of note, miR-126 expression was of significant predictive value in squamous histology and in cases with lymphatic metastases (Donnem et al., 2011). A separate study identified up-regulation of miR-126 in metastatic sites of lung cancer (Barshack et al., 2010).

Therapeutic Implications: miR-126 represented one of a panel of miRNAs up-regulated in lung tumors from radiosensitive patients. Further investigation demonstrated that miR-126 could augment the apoptotic effects of irradiation in vitro (Wang et al., 2011).

Oncogenesis

Tumor invasion and growth: miR-126 alters processes fundamental to tumor development and progression. In vitro gain of function reduced migratory and invasive capacity as well as proliferation. The CRK adapter protein, VEGF and the miR-126 host gene EGFL-7 are potential functional targets (Crawford et al., 2008; Liu et al., 2009).

Lung cancer: small cell cancer

Oncogenesis

MiR-126 gain of function in vitro reduced small cell cancer cell proliferation and induced G1 arrest (Miko et al., 2011).

Colorectal carcinoma

Disease

In a cohort of 66 colorectal carcinomas, miR-126 expression is reduced in colon cancer compared to 10 adjacent non tumor tissues (Li et al., 2010).

Oncogenesis

MiR-126 has been shown to regulate the PI3-kinase signaling cascade through direct targeting of the p85beta subunit. This targeting resulted in an in vitro reduction in colon carcinoma cell growth (Guo et al., 2008).

Breast cancer

Note

Diagnostic: MiR-126 represented one of several miRNAs whose expression distinguished myoepithelial breast cancer from basal type breast cancer (Bockmeyer et al., 2011). A separate study suggested that miR-126 may serve as a non-invasive biomarker for breast cancer. Patients with breast cancer had lower circulating levels of miR-126 when compared to normal controls (Wang et al., 2010). Lastly, analysis for miR-126 single nucleotide polymorphisms (SNPs) in a cohort of 6042 patients did not identify an associated breast cancer risk (Wang et al., 2010).

Disease

miR-126 has been shown to be down-regulated in breast cancer tissues.

Oncogenesis

Tumor growth and Metastasis: In vitro, high metastatic breast cancer cell lines had lower levels of miR-126. MiR-126 gain of function reduced both breast cancer cell growth in vitro and metastases in vivo. Furthermore, miR-126 expression was inversely correlated with presence of metastases in a cohort of breast cancer patients (Tavazoie et al., 2008). Insulin Receptor Substrate (IRS-1) has been implicated as a functional target for miR-126 (Zhang et al., 2008).

Gastric carcinoma

Prognosis

In a cohort of 100 patients with gastric cancer miR-126 was one of a seven-miRNA signature that correlated with survival (Li et al., 2010).

Oncogenesis

In vitro, miR-126 reduced gastric cancer cell proliferation (Otsubo et al., 2011; Feng et al., 2010). The transcriptional factor SOX2 has been suggested as one target.

Renal cancer

Note

Diagnostic: Early studies suggest that miR-126 expression may have diagnostic utility in renal

carcinoma. In one study, miR-126 expression distinguished clear cell from renal cell carcinoma (Powers et al., 2011).

Bladder cancer

Note

Diagnostic: Investigators examined urinary miRNA expression patterns in a cohort of patients (N=36) and showed that the ratio of miR-126 to miR-152 could accurately diagnose bladder cancer with a specificity of 82% and sensitivity of 72% (Hanke et al., 2010).

Leukemia

Note

Diagnostic: Expression miRNA profiling in a cohort of 47 primary AML specimens followed by qPCR validation revealed that miR-126 and miR-126* could be used to distinguish subgroups of AML with highest expression occurring in core-binding factor (CBF) AML. Allied in vitro and in vivo studies demonstrated that miR-126 could induce proliferation of murine bone marrow progenitor cells in the presence of the AML1-ETO (AE) fusion gene (Li et al., 2008). The association between miR-126 and AML1/ETO rearrangements was further confirmed in a separate cohort of 29 AML samples (Cammarata et al., 2010). Low expression of miR-126 as part of a panel of miRNAs has been shown to correlate with CNS relapse in ALL (Zhang et al., 2009).

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