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Gene Section
Short Communication

MIR145 (microRNA 145)

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Identity

Other names: MIRN145, miR-145, miRNA145

HGNC (Hugo): MIR145

Location: 5q32

DNA/RNA

Description

miR-145 is located on chromosome 5 (5q32-33) within a 4.09 kb region (miRBase).

The pri-microRNA structure of miR-145 has not been identified, yet it is suggested that it co-transcribed with miR-143.

This gene has been implicated as both tumor and metastasis suppressor in multiple tumor types (Sachdeva and Mo, 2010a).

Transcription

miR-145 is transcribed by RNA pol-II into pri-miRNA sequence, which is first processed to pre-miRNA (~88 bp long) involving RNA cutting and exporting, and finally to mature miR-145. miR-145 is a p53-regulated gene.

Several reports suggest that miR-145 can be induced transcriptionally by p53 in response to stress such as serum starvation or anticancer drugs (Sachdeva et al., 2009; Spizzo et al., 2010).

Interestingly, another report showed a novel mechanism of posttranscriptional regulation of miR-145 that occurs via p53-mediated RNA processing (Suzuki et al., 2009).

Recently, a study demonstrates that activated Ras can suppress miR-143/145 cluster through Ras-responsive element-binding protein (RREB1), which represses the miR-143/145 promoter (Kent et al., 2010).

Pseudogene

There is no pseudogene reported for this gene.

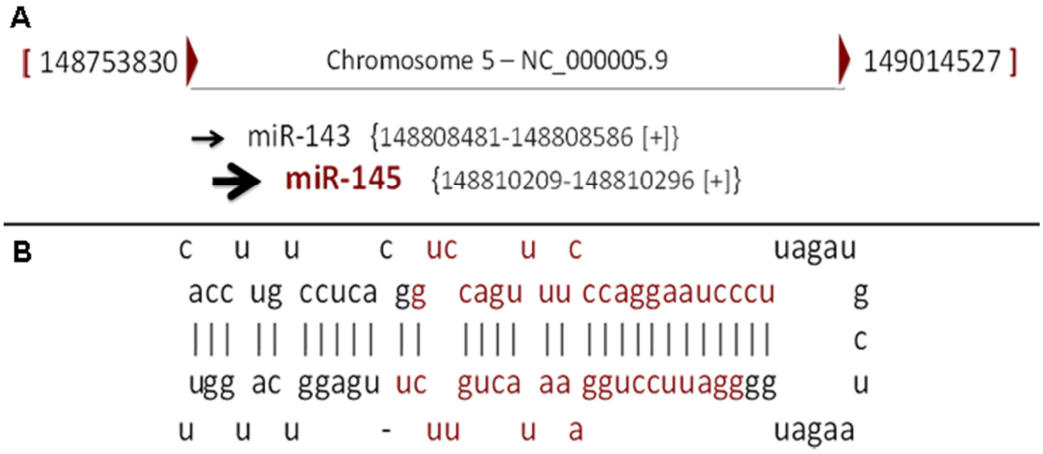

Figure 1: A) Genomic localization of miR-145 gene on chromosome 5q32. B) Stem-loop structure of miR-145 (Red: mature miR-145 sequence).

Protein

Note
Non-coding RNA.

Mutations

Note
No mutations have been found in mature miR-145 sequence; however, a study suggests that OVCAR8 (ovary) and NCI-H727 (lung) cells harbor mutations in pri-miR-145, i.e., C-133A/pri-microRNA/homozygous and G-5R (G/A)/pri-microRNA/heterozygous, respectively. Yet, these mutations do not have any effect on microRNA processing (Diederichs and Haber, 2006).

Implicated in

Cancer

Note
Downregulation of miR-145 has been found in cancers of many tissue types including colon, breast, prostate, pancreas, etc. (Sachdeva et al., 2009; Bandres et al., 2006; Michael et al., 2003). For example, in situ hybridization detected accumulation of miR-145 in normal colon epithelia with no signal from adenocarcinomas cells. Loss of miR-145 in various tumors suggests its role as a tumor suppressor. In fact, miR-145 has been well documented as a tumor suppressor gene in multiple tumor types because of its anti-proliferative and pro-apoptotic effects. It is shown that miR-145 can negatively regulate multiple oncogenes such as MYC, Kras, IRS-1, ERK5, etc. involved in cell proliferation and survival (Sachdeva et al., 2009; Kent et al., 2010; Shi et al., 2007; Ibrahim et al., 2011).

Metastasis

Note
Several reports suggest that miR-145 is a suppressor of metastasis. For example, mir-145 negatively regulates MUC1 and suppresses invasion and metastasis of the breast cancer cells (Sachdeva and Mo, 2010b). Similar findings in prostate cancer and in gliomas have further confirmed the role of miR-145 as a metastasis suppressor by targeting genes including FASCN1 and SOX2, respectively (Fang et al., 2011; Watahiki et al., 2011; Leite et al., 2011).

Stem cells and differentiation

Note
A study has shown that miR-145 is induced during differentiation, and it directly silences the stem cell self renewal and pluripotency program by suppressing multiple pluripotent genes such as OCT4, SOX2 and KLF4 (Xu et al., 2009).

Vascular smooth muscle cells

Note
The role of miR-145 in differentiation of vascular smooth muscle cell (VSMC) has been recently investigated. A report demonstrated that miR-145 is the most enriched microRNA in arteries and its expression is significantly downregulated in vascular walls with neointimal lesions (Chen et al., 2004). Similarly, another group, using transgenic mouse model with miR-145 promoter fused to β-galactosidase gene, found that miR-145 is cardiac-specific and smooth-muscle specific microRNA regulated by serum response factor, myocardin and Nkx2-5 (NK2 transcription factor related, locus 5) (Cordes et al., 2009). Further evidence from the miR-43/miR-145 KO rats suggests that this microRNA cluster is expressed mostly in the SMC compartment in vessels and SMC-containing organs and their loss induces an incomplete differentiation of VSMCs (Elia et al., 2009).

5q syndrome

Note
A comprehensive study using clinical samples combined with mouse models have found that deletion of chromosome 5q correlates with loss of two miRNAs that are abundant in hematopoietic stem/progenitor cells (HSPCs), miR-145 and miR-146a. In addition, they observed that miR-145 is highly expressed in primitive lin- (mouse) and CD34+ (human) bone marrow cells than committed cells and stable knockdown of miR-145 in these cells in mouse marrow results in 5-q syndrome (Starczynowski et al., 2010). Similar work from another group in patients with del (5q) have decreased expression of miR-145 and increased expression of Fli-1 (Kumar et al., 2011). They found that miR-145 functions through repression of Fli-1, a megakaryocyte and erythroid regulatory transcription factor and thus, cells lacking miR-145 have impaired megakaryocyte and erythroid differentiation.

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