MIR125B2 (microRNA 125b-2)

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Identity

Other names: MIR125B2 (microRNA 125b-2); MIR125B2; hsa-mir-125b-2; miR-125b-2
HGNC (Hugo): MIR125B2
Location: 21q21.1
Local order: Based on Mapviewer (Master Map: Genes on sequence), genes flanking miR-125b2 oriented from centromere to telomere on 21q21.1 are:

DNA/RNA

- Stem-loop structure of miR-125b2.

Description

The gene is located in the intronic region of C21orf34.

Transcription

Transcription start site for this microRNA is not known.
Pre-miRNA
Pre-miR length: 89 bases
Sequence:
5’-ACCAGACUUUUUCUAGUCCCUGAGACCUCUAACUUGUGAGGUAUUUUAGUAACAUCACAAGUCAGGCUCUUGGGACCUGGGCCGGAGGGGA-3’
Mature miR-125b
Mature miR-125b can originate from two precursor structures: pre-miR-125b1 and pre-miR-125b2. The mature microRNA resides between the 17th and 38th nucleotides of precursor miR-125b2. Mature miR-125b is 22 nucleotides long.
Sequence:
miR-125b (from pre-miR-125B2):
17 - uccucagaccuaacucuuga - 38

Pseudogene

No reported pseudogenes.

Protein

Note
miRNAs are not translated into amino acids.

Implicated in

Breast Cancer

Note
Among differentially expressed microRNAs in cancers, miR-125b is one of the most consistently deregulated microRNAs in breast cancer. Downregulation of miR-125b suggested that it may potentially act as a tumor
suppressor gene. Microarray analysis of 10 normal and 76 neoplastic breast tissues showed downregulation of miR-125 in breast tumors. Although the miR-125b levels in MDA-MB-231 breast cancer cells were comparable to normal breast tissue, in MCF-7, T47D, SK-BR3, BT20 and MDA-MB-175 breast cancer cells showed downregulation of miR-125b. Both microarray analysis and Northern blotting demonstrated low levels of miR-125b transcript in breast cancer cell lines and tumors.

In another study, miR-125b along with its homolog; miR-125a were identified to be significantly downregulated in ERBB2-amplified and overexpressing breast cancers. Ectopic expression of miR-125a and miR-125b in the ERBB2 dependent human breast cancer line, SKBR3, caused suppression of its anchorage-dependent growth and inhibition of its mobility and invasive capabilities. Ectopic expression miR-125a and miR-125b in non-transformed and ERBB2-independent MCF10a cells produced inhibitory effects on its anchorage-dependent growth and no significant impact on the mobility of these non-invasive human breast epithelial cells. Furthermore, miR-125a and miR-125b targets, ERBB2 and ERBB3, were downregulated when these two microRNAs were expressed in SKBR3 cells. Downregulation of ERBB2 and ERBB3 decreased the motility and invasiveness features of SKBR3 cells.

Prostate Cancer

Note

MicroRNA levels were examined by microarrays in 10 benign peripheral zone tissues and 16 prostate cancer tissues. Widespread downregulation of miR-125b was shown in prostate cancer tissues. These results were also verified by qRT-PCR. Among 328 known and 152 novel human microRNAs, miR-125b was one of the most downregulated microRNAs in prostate cancer. Some bioinformatically predicted targets of miR-125b were found to be upregulated in prostate cancer, shown by microarray analysis (EIF4EBP1, RPL29, MGC16063 and PAPB) and immunohistochemistry (RAS, E2F3, BCL-2 and MCL-1). Increased expression EIF4EBP1 was also confirmed through qRT-PCR, in 61 human prostate tumors and 19 normal tissues. Several microRNA paralogous groups, having high levels of sequence similarity, were also found to be downregulated in prostate cancer. Along with miR-125a, and miR-125b, other members of let-7 family microRNAs were also downregulated. This finding indicated that these microRNAs with similar sequences might potentially target similar mRNAs. Interestingly in another study, according to Northern blot analysis in 9 prostatic cell lines, miR-125b was found to be upregulated. 5 fold increase was found in 2 androgen positive prostate cell lines (AI cds1 and AI cds2) compared to androgen negative prostate cell line (AD LN CaP). Moreover, TATA box and Androgen Responsive Elements (AREs) were found in the 5' of the miR-125b gene. Upregulation of miR-125b was also confirmed in response to androgen. Finally, one target of miR-125b, BAK1 (BCL2-antagonist/killer1) was confirmed initially by microarrays and then by luciferase assays. Thus, upregulation of miR-125b in response to androgen resulted with decreased levels of BAK1, an apoptotic protein.

Ovarian Cancer

Note

Through microarray analysis, several microRNAs were found to be deregulated in human ovarian cancer. Among several microRNAs, miR-214, miR-199a and miR-200a were found to be upregulated whereas miR-100, let-7 family members and miR-125b were the most significantly downregulated microRNAs in ovarian cancer. Downregulation of miR-125b was further confirmed by Northern blotting. 5.5 fold downregulation of miR-125b in primary ovarian tumor compared to normal ovary was shown.

Neuroblastoma

Note

miR-125a and miR-125b transcription was elevated in response to retinoic acid (RA) treatment in human neuroblastoma cell line (SK-N-BE), confirmed by Northern blot and qRT-PCR. Neurotrophin Receptor Tropomyosin-Related Kinase C ( NTRK3) is a key regulator protein of the neuroblastoma cell proliferation. Only the truncated form of NTRK3 was found to be a target of both miR-125a and miR-125b. Downregulation of tNTRK3 is critical for growth of neuroblastoma cells. Ectopic expression of miR-125a and miR-125b in primary neuroblastoma cells, (SK-N-BE), resulted in the downregulation of tNTRK3. Downregulation of these microRNAs in neuroblastoma cells resulted in tumor formation whereas upregulation of them resulted in in-vitro neuronal differentiation.

Squamous Cell Carcinoma

Note

Expression levels of 156 human mature microRNAs were analyzed by using real-time quantitative PCR in 20 paired tongue squamous cell carcinoma (SCC) and normal tissues. Apart from the upregulated microRNAs in SCC, miR-125b was one of the downregulated microRNAs. It was found that miR-125b was downregulated 4.7 fold in SCC compared to normal tissue.

Other cancers/Immune System

Note

Deregulation of miR-125b2 in differentiated cancer cells was shown by primer extension assays through comparison of transcript levels. Depletion of miR-125b2 by siRNA in PC-3 (prostate cancer) and HeLa cells (cervical cancer) inhibited cell proliferation.
Further, upregulation of miR-125b was shown in response to retinoic acid treatment during differentiation of cells in culture. Thus, it was concluded that miR-125b was essential for proliferation of differentiated cells.

miR-125b was also reported to have a role in innate immunity. Downregulation of miR-125b was observed in response to lipopolysaccharide (LPS), an endotoxin, stimulation in mouse Raw 264.7 macrophages. Moreover, miR-125b level oscillated in response to TNF-alpha. miR-125b was shown to target 3’ UTR of TNF-alpha, thus interfered with the cellular levels of TNF-alpha. Downregulation of miR-125b in response to LPS was required to increase the cellular levels of TNF-alpha.

**Osteoblastic Differentiation**

**Note**

According to microRNA microarray analysis, miR-125b expression level was found to be weakly downregulated in mouse mesenchymal stem cells. This finding indicated that miR-125b could have a role in osteoblastic differentiation. Expression level of miR-125b was found to be time dependent in ST2 cells (mesenchymal stem cell). Ectopic expression of miR-125b inhibited the proliferation of ST2 cells during differentiation and thus, inhibited the osteoblastic cell differentiation. On the other hand, silencing of miR-125b promoted osteoblastic differentiation.

**References**


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