MIR22 (microRNA 22)

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Identity

Other names: MIR22, hsa-mir-22, miR-22
HGNC (Hugo): MIR22
Location: 17p13.3
Local order: Based on Mapviewer (Master Map: Genes on sequence), genes flanking miR-22 oriented from centromere to telomere on 17p13.3 are:
- PRPF8 (17p13.3): PRP8 pre-mRNA processing factor 8 homolog
- TLCD2 (17p13.3): TLC domain containing 2
- MIR22HG (17p13.3): MIR22 host gene
- MIR22 (17p13.3): microRNA22
- WDR81 (17p13.3): WD repeat domain 81

DNA/RNA

Description

Mir-22 was originally identified in HeLa cells (an immortal cell line derived from cervical cancer cells), but was later found to be ubiquitously expressed in various tissues.

The gene encoding miR-22 is found on the short arm of chromosome 17, in a minimal loss of heterozygosity region.

Figure 1. A. Stem-loop structure of miR-22. B. Genomic localization of miR-22 (MIRN22), miR-22HG (MIRN22HG) on chromosomal band 17p13.3.
**Transcription**
In general, the microRNA genes are transcribed by RNA polymerase II, whereas RNA polymerase III is also responsible for transcription of some other microRNAs.

**Pre-microRNA 22 (Precursor microRNA)**
- Accession: MI0000078.
- Length: 85 bp.
- Sequence:
  
  5' - GGCUAGCGCCAGUAGUUCUUCAGUGGCAAGCUUUUAUGUCCUGACCCAGCUAAAGCUGCCAGUUGAAGAACUGUUGCCCUCUGCC - 3'

**Mature miR-22**
Accession: MIMAT0000077.
Length: 22 nucleotides.
Sequence:

53 -AAGCUGCCAGUUGAAGAACUGU- 74

**Pseudogene**
No pseudogenes were reported for mir-22.

**Protein**

**Note**
MicroRNAs are not translated into amino acids.

**Implicated in**

**Breast carcinoma**

**Note**
Recently, researchers have found that microRNAs (miRNAs) may play important roles in cancer development. After verification in many clinical samples, among all the miRNAs, there is a significantly inverse association between the miR-22 level and ERα protein expression. Estrogen receptors (ERs) are composed of a group of ligand-activated nuclear receptors that regulate diverse gene expression and are implicated in cancers by stimulating cell proliferation and tumor growth. All experimental data demonstrate that ERα is a direct target of miR-22. Taken together, it indicates that miR-22 is frequently downregulated in ERα-positive human breast cancer cell lines and clinical samples. Because ERα expression level is routinely detected in breast cancer samples as a prognostic marker, that miR-22 is directly involved in the regulation of ERα may be one of the mechanisms through which miR-22 could play a pivotal role in the pathogenesis of breast cancer. The expression of the tumor suppressor miR-22 is consistently downregulated in metastatic breast cancer cells. Oncogenes ERBB3, CDC25C and EVI-1 are abundant in metastatic breast cells. Introduction of miR-22 reduces the level of ERBB3 and EVI-1 as well as phosphor-AKT, an EVI-1 downstream target. It suggests that metastatic cancer cells increase specific oncogenic signaling factors through downregulating of miRNA.

**Ovarian cancer**

**Note**
miR-22 level is decreased in ovarian cancer cells which have high invasiveness. Both gain-of-function and loss-of-function study display a negative effect of miR-22 on cell invasion and migration in vitro. Bioinformatics analyses show that miR-22 may regulate multiple pro-metastatic genes. Particularly, Tiam1 is a direct target of miR-22. Alteration of miR-22 expression level has a negative regulatory effect on Tiam1 protein level and mRNA level. Taken together, all findings suggest that miR-22 might be involved in inhibiting ovarian cancer metastasis, probably by targeting Tiam1.

**Hepatocellular carcinoma**

**Note**
In present study, a functional role of miR-22 in hepatocellular carcinoma (HCC) development has been identified. It exists in a large proportion of HCC tissues that miR-22 level is downregulated. Epigenetic alternations in cancer often mediate the deregulation of tumor suppressors or oncogenes, and HDAC4 expression targeted by miR-22 may further aggravate the epigenetic changes in HCC. In vivo and in vitro, the anti-tumor effect of miR-22 in HCC is validated. Restoration of miR-22 expression suppresses cell proliferation and tumourigenicity. In addition to HDAC4, miR-22 can also repress Max expression and cell cycle progression regulated by Myc-Max complex. Thus, accumulation of all targets of miR-22 constitutes the phenotype of miR-22 restoration in HCC. Furthermore, miR-22 may have considerable potential in identification of HCC and therapy for HCC.

**Tumor suppressor**

**Note**
Oncogenic c-Myc can modulate the expression of a subset of miRNAs, including miR-22, conversely, miR-22 represses the c-Myc-binding protein MYCBP, a positive regulator of c-Myc. MYCBP is a direct target of miR-22. Moreover, repression of MYCBP by miR-22 downregulates a subset of E-box-containing c-Myc target genes.

**Cellular senescence**

**Note**
Generally, it is believed that microRNA is associated with cell proliferation, cell differentiation and other biological phenomena. MicroRNA will increase when the aged normal cells stop dividing. Aging extent of cancer cell is suppressed when miR22 is added into cultured breast and cervical cancer cells. It is also found that metastasis of breast cancer is controlled in mouse experiments. Cell aging is a self-defense mechanism which prevents development of cancer in organism. Cell aging will be interfered when microRNA decreases, thus, it promoting cancer cytogenesis. However, aging process in organism
restores after addition of miR22, and then proliferation of cancer cell is inhibited.

References


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