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Gene Section
Review

MIR100 (microRNA 100)

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Identity

Other names: hsa-mir-100, MIRN100, miR-100

HGNC (Hugo): MIR100

Location: 11q24.1

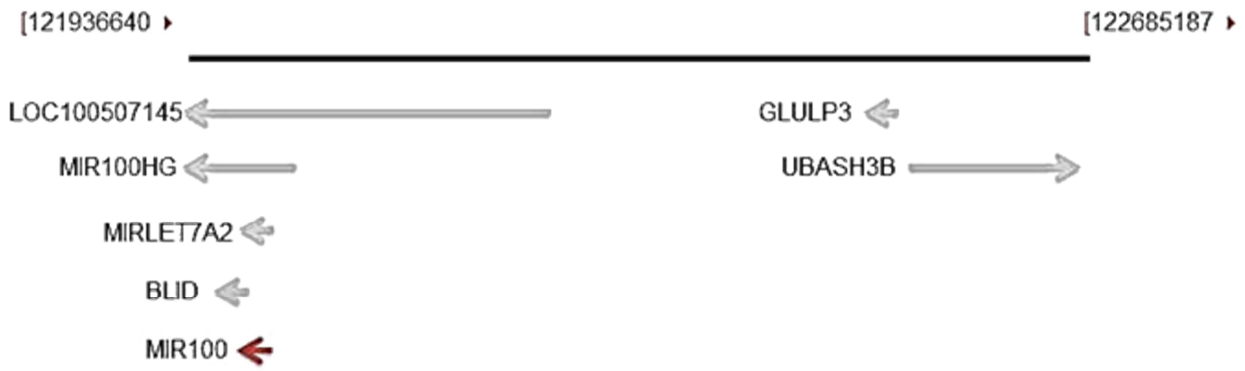
Local order

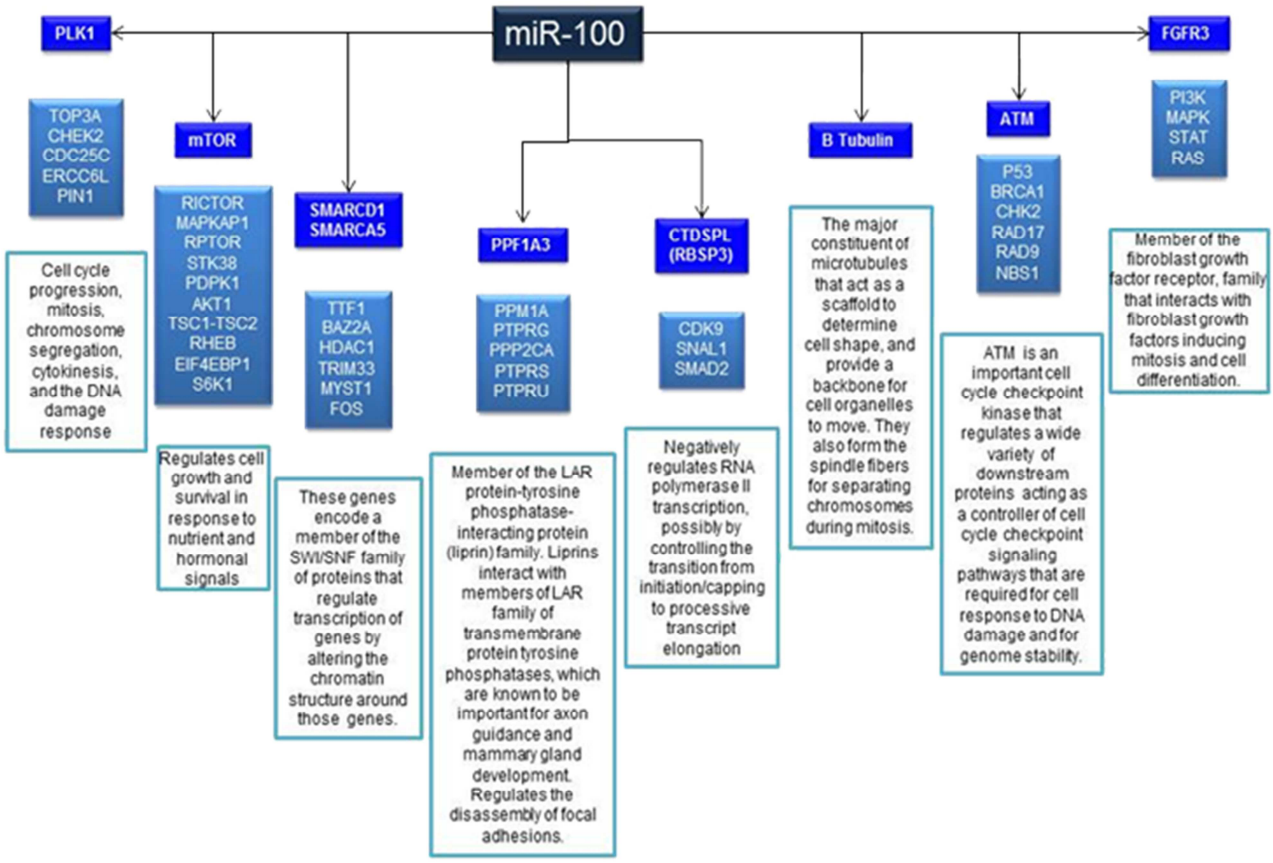
- microRNA 125b-1
- BH3-like motif containing, cell death inducer
- microRNA let-7a-2
- **microRNA 100**
- Glutamate-ammonia ligase (glutamine synthetase) pseudogene 3
- Ubiquitin associated and SH3 domain containing B

Note

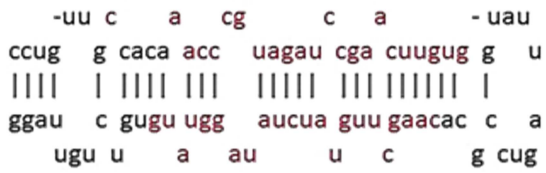
Human chromosome 11 (HSA11), is one of the most gene- and disease-rich chromosomes in humans with a gene density of 11,6 genes per megabase, including 1524 protein-coding, and 69 microRNAs. It represents approximately 4,4% of the human genome. There are hundreds of disorders currently attributed to the chromosome, including cancer susceptibility loci.

miR-100 is part of the family miR-99, that comprehends:
hsa-miR-100 (AACCCGUAGAUCCGAACUUGUG)
hsa-miR-99a (AACCCGUAGAUCCGAUCUUGUG)
hsa-miR-99b (CACCCGUAGAACCGACCUUGCG).
Their predicted targets are:
SMARCD1, SMARCA5, mTOR, PPFIA3 (Sun et al., 2011; Nagaraja et al., 2010), PLK1 (Petrelli et al., 2012; Peng et al., 2012; Feng et al., 2011; Ugras et al., 2011; Li et al., 2011; Shi et al., 2010), CTDSPL (RBSP3) (Zeng et al., 2012), β-tubulin (Lobert et al., 2011), ATM (Ng et al., 2010), PPP3CA (Sylvius et al., 2011), FGFR3 (Cato et al., 2009).





DNA/RNA



RNA - stem-loop.

Description

DNA sequence: hsa-mir-100 MI0000102.
CCUGUUGCCACAAACCCGUAGAUCCGAACUU GUGGUAUUAGUCCGCACAAGCUUGUAUCUAU AGGUAUGUGUCUGUUAGG.

Transcription

Mature sequence: 13 - aacccguagauccgaacuugug - 34.

Protein

Note
microRNAs are not translated into amino acids.

Mutations

Note
Gene mutations have not been described.

Implicated in

Prostate cancer

Disease
miR-100 is down-regulated during the prostate cancer progression, from high grade prostate intraepithelial neoplasia through metastasis (Leite et al., 2011a; Leite et al., 2011b). The same result was posteriorly confirmed by Sun D et al. (2011) that found miR-100 down-expressed in C4-2B, an advanced prostate cancer cell line in comparison with LNCaP an androgen-dependent prostate cancer cell line. Porkka KP et al. have previously related down-expression of miR-100 with hormone-refractory tumors (Porkka et al., 2007).

Prognosis
Contradictorily, lower levels of miR-100 was related to lower rates of biochemical recurrence in patients with localized adenocarcinoma treated with radical prostatectomy in a mean follow up of 58,8 months (Leite et al., 2011c).

Hepatocellular carcinoma

Disease
miR-100 is involved with HCC carcinogenesis being down-regulated early, since the pre-neoplastic lesions. A paralleled increase in polo like kinase 1 (PLK1)

suggests this gene as a target of this miR-100 (Petrelli et al., 2012).

Ovarian cancer

Disease

In a microarray study of 74 ovarian cancer tissue and cell lines miR-100 was shown to be down-regulated in cancer specimens against normal tissue together with miR-199a, miR-140, miR-145, and miR-125b1 (Iorio et al., 2007).

Prognosis

miR-100 is significantly down-expressed in epithelial ovarian cancer and related to FIGO stage, lymph node metastasis, higher CA125 serum levels and shorter overall survival (Peng et al., 2012). Experimental studies with clear cell type ovarian cancer, an aggressive variant of the tumor showed that over-expression of miR-100 enhanced sensitivity to the rapamycin analog RAD001 (everolimus), confirming the key relationship between mir-100 and the mTOR pathway (Nagaraja et al., 2010).

Lung cancer

Note

Drug resistance - miR-100 was shown to be down-regulated in docetaxel-resistant SPC-A1/DTX cells compared with parenteral SPC-A1 cells.

The ectopic miR-100 re-sensitized tumor cells to docetaxel by suppression of cell proliferation, G2/M arrest and induction to apoptosis.

Similar effect was identified knocking down PLK1, reinforcing this mRNA as a miR-100 target (Feng et al., 2011).

Leukemia

Disease

In acute myeloid leukemia (AML) miR-100 was found to promote cell proliferation of promyelocytic blasts and arrest the differentiation to granulocyte/monocyte lineages. RBSP3, a phosphatase-like tumor suppressor, important in cell differentiation is a target of miR-100. miR-100 regulates G1/S transition and blocks the terminal differentiation of cells targeting RBSP3 which in turn modulates pRB/E2F1 (Zeng et al., 2012).

Prognosis

Differently in acute lymphoblastic leukemia (ALL) miR-100 is down-regulated when compared to normal samples.

Also the down-expression is related to higher count of white blood cells and hyperdiploid karyotypes. Increase in miR-100 expression is related to t(12;21), biological feature associated to better outcome (de Oliveira et al., 2012).

On the other hand miR-100 over-expression has been related to vincristine and daunorubicin resistance (Schotte et al., 2011).

Thyroid cancer

Prognosis

miRNA profile was used to differentiate benign and malignant thyroid tumors in specimens obtained by fine-needle aspiration biopsy. Diagnostic accuracy of differentially expressed genes was determined by analyzing receiver operating characteristics (ROC). miR-100 was overexpressed in malignant follicular neoplasia and in Hurthle cell carcinomas (Vriens et al., 2011).

Pancreatic cancer

Disease

miR-100 was shown to be over-expressed in chronic pancreatitis when compared with normal pancreas and also over-expressed in pancreatic cancer versus pancreatitis (Bloomston et al., 2007).

Breast cancer

Note

Drug resistance - Taxanes bind to β subunit of the tubulin heterodimer and reduce microtubule dynamics leading to cell cycle arrest in G2/M. miR-100 is involved in the regulation of the expression of β-tubulin class II and V, and a down-expression of miR-100 is related to increase in the expression of these isoforms of β-tubulin conferring MCF7 breast cancer cell line resistance to paclitaxel (Lobert et al., 2011).

Disease

miR-100 has been described as down-regulated in breast cancer, including male breast cancer (Fassan et al., 2011).

Bladder cancer

Disease

Down-regulation of miR-100 has been described in urothelial carcinomas, having as a main target the mRNA of FGFR3. FGFR3 mutation is characteristics of low-grade, non-invasive urothelial carcinoma, and another possible pathway for bladder cancer development would be the loss of regulation of FGFR3 by down-expression of miR-100 (Dip et al., 2012 in press; Song et al., 2010; Catto et al., 2009).

Head and neck squamous cell carcinoma

Note

Drug resistance - Down-regulation of miR-100 together with miR-130a and miR-197 was related to resistance of UMSCC-1 and SQ20B cell lines to cisplatin, 5-fluorouracil, paclitaxel, methotrexate, and doxorubicin (Dai et al., 2010).

Glioma

Note

Radio resistance - Higher expression of miR-100

confers radio-sensitivy to M059J and M059K human malignant glioma cells, targeting ATM (Ng et al., 2010).

Uterine cervix squamous carcinoma

Disease

The miR-100 expression was shown to be significantly and gradually reduced from low-grade CIN, high-grade CIN to cervical cancer tissues. It was also reduced in HPV positive cervical cancer cell lines. miR-100 down-expression influenced cell proliferation, cycle and apoptosis, and the probable mechanism is the loss of control of PLK1 protein (Li et al., 2011).

Laminin A/C - related muscular dystrophy

Note

Physiopathology - miR-100, toghether with miR-192, and miR-335 participate in muscle differentiation and proliferation and are probably involved in the development of the disease. miR-100 expression induces up-regulation of myogenin and α-actin and down-regulates Ki-67 a protein related to proliferation. Sylvius et al. (2011) show that miR-100 is involved with muscle differentiation by targeting PPP3CA the calcineurin gene. Calcineurin is a component of the calcium-dependent signaling pathways and has been shown to be involved in the regulation of skeletal muscle differentiation, hypertrophy, and fiber-type specification.

Psoriasis

Note

Physiopathology - mir-100 has been described as down-regulated in psoriasis skin. It is probably involved in the disease by repressing mTOR and inhibiting angiogenesis. In this context, miR-100 has been called as a anti-angiomiR (Calin et al., 2011).

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