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Gene Section
Review

MIR146B (microRNA 146b)

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Identity

Other names: MIRN146B, miRNA146B

HGNC (Hugo): MIR146B

Location: 10q24.32

Local order: Based on Mapviewer, gene flanking MIR146B oriented from centromere to telomere on 10q24.32 are**:**
- NFKB2: Nuclear factor of kappa light polypeptide gene enhancer in B-cell 2
- PSD: pleckstrin and Sec7 domain containing
- FBXL15: F-box and leucine-rich repeat protein 15
- CUEDC2: CUE domain containing 2
- **MIR146B: microRNA 146b**
- LOC100505761: hypothetical LOC100505761
- TMEM180: transmembrane protein 180
- ACTR1A: ARP1 actin-related protein 1 homolog A

DNA/RNA

Note
The MIR146B gene is transcribed into a precursor that produces two mature microRNAs, miR-146b-5p and miR-146b-3p.
These microRNAs belong to the miR-146 family, which comprises 2 other members, miR-146a-5p and miR-146a* (recently renamed miR-146a-3p) produced from a gene, MIR146A, localized on chromosome 5.

Description

MIR146B is located in an intergenic region.

Transcription

RNA Polymerase II is suggested to be the most likely enzyme involved in microRNA transcription, leading to the production of a ~1000 nucleotide primary microRNA, in this case pri-miR-146b. The beginning and the end of the pri-miR-146b sequence are unknown.

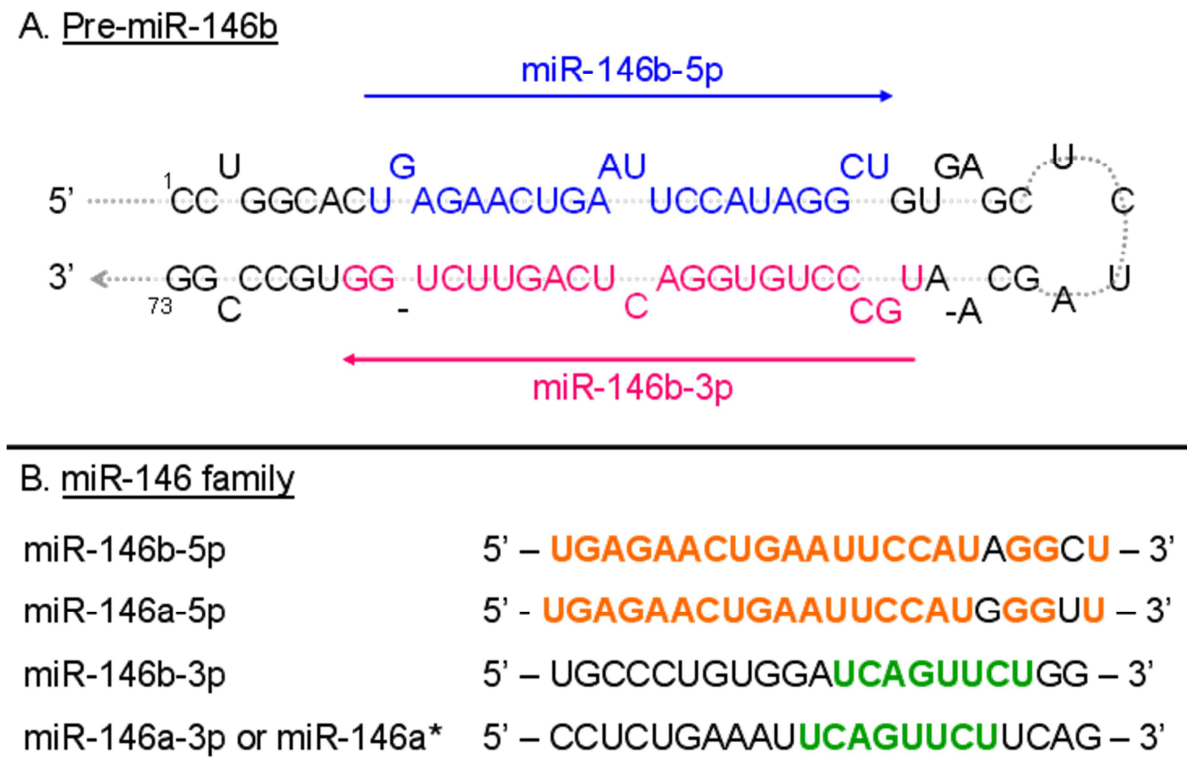
pre-miR-146b
miRBase accession number: MI0003129.
Length: 73 nucleotides.
Sequence: 5'-CCUGGCACUGAGAACUGAAUUCCAUAGGCUGUGAGCUCUAGCAAUGCCCUGUGGACUCAGUUCUGGUGCCCGG-3'

mature miR-146b-5p
miRBase accession number: MIMAT0002809.
Length: 22 nucleotides.
Sequence: 5'-UGAGAACUGAAUUCCAUAGGCU-3'

mature miR-146b-3p
miRBase accession number: MIMAT0004766.
Length: 22 nucleotides.
Sequence: 5'-UGCCCUGUGGACUCAGUUCUGG-3'

Pseudogene

No reported pseudogenes.



A. Homo sapiens stem-loop structure of pre-miR-146b. This figure represents the sequence and structure of the miR-146b precursor (pre-miR-146b). Two different mature miRNAs are produced from this precursor: miR-146b-5p (sequence in blue) and miR-146b-3p (sequence in pink). The orientations 5' to 3' are indicated by the direction of the arrows. **B. The miR-146 family members.** Identities between the sequences of miR-146a-5p and miR-146b-5p are shown in orange and those between the sequences of miR-146a-3p and miR-146b-3p are shown in green. MiR-146a-5p and miR-146b-5p differ by only two nucleotides located outside the seed region, while miR-146a-3p and miR-146b-3p are much more divergent, especially in the seed region.

Protein

Note
microRNAs aren't translated into amino acids.

Mutations

Note
The 1000 Genome project identified a SNV (single nucleotide variation) in one West African individual, a C>T variation at position 104196269 (according to hg19-Feb_2009) in the first nucleotide of pre-miR-146b.
The minor allele frequency is 0.059 in 118 individual samples of a West Africa population. This variation is reported in the NCBI SNP database and referenced with the number rs76149940 (submission in March 2010).

Implicated in

Breast cancer

Prognosis
mir-146b-5p along with other microRNAs may permit to differentiate breast tumour sub-types. However, conflicting results have been obtained. One study, where miR-146b has been analysed in 167 breast cancer cases, showed an elevated expression in triple negative breast tumours.
This study comprised analyses of several different tumour mammary cell lines and miR-146b-5p was found to be the most expressed in basal-like tumour cell lines (Garcia et al., 2011).
A second study, based on 20 samples only, identified specific expression of a set of seven microRNAs (including miR-146b-5p) in normal basal cells but not in basal-like breast cancers, which are close to triple negative breast cancers. miR-146b-5p may have an elevated expression in malignant myoepithelioma of the breast (Bockmeyer et al., 2011).

Oncogenesis
Two studies described a biological role for miR-146b in breast tumour progression.
The BRMS1 (Breast cancer Metastasis Suppressor 1) protein up-regulated the expression of miR-146b in MDA-MB-435, a tumour mammary cell line.
Moreover, the overexpression of this microRNA down-regulated the expression of EGFR (Epidermal Growth Factor Receptor) in another tumour cell line, MDA-MB-231. This study showed an impact, in vitro, of

miR-146b on invasion and migration of cells and on the suppression of metastasis (Bockmeyer et al., 2011).
The second study depicted a direct target of miR-146b-5p, BRCA1 (BReast CAncer 1), one of the two major breast cancer predisposition genes.
The binding of miR-146-5p to the BRCA1 3'UTR decreased the expression of BRCA1, induced cellular proliferation and reduced the homologous recombination rate. miR-146b seemed to have an important role in tumour progression via BRCA1 (Garcia et al., 2011).

Thyroid cancer

Disease
Three studies showed that miR-146b, along with a set of other microRNAs, are overexpressed in tumours versus hyperplasic nodules or versus uncertain malignant potential tumours (Nikiforova et al., 2008; Lassalle et al., 2011; Chen et al., 2008). miR-146b is consistently overexpressed in both papillary and follicular thyroid carcinomas (Chen et al., 2008) and is associated with extrathyroidal invasion (Chou et al., 2010) and with aggressive papillary thyroid carcinoma (Yip et al., 2011). Of note, in these two studies, miR-146b overexpression seems correlated with BRAF mutations.

Prognosis
The expression of miR-146b and of a set of six other microRNAs was able to predict malignancy of thyroid fine needle aspiration specimens (Shen et al., 2012; Agretti et al., 2012).

Oncogenesis
In thyroid follicular cells, miR-146b-5p was shown to bind directly the 3'UTR of SMAD4, an important member of the TGF-β signalling pathway. This modulation of the TGF-β signal confirmed the oncogenic role of miR-146b-5p in thyroid cancers (Geraldo et al., 2012).

Lung cancer

Prognosis
A microarray analysis of 61 squamous cell carcinoma samples versus 10 normal lung samples showed that miR-146b had the strongest prediction accuracy for stratifying Non-Small Cell Lung Cancer (NSCLC) in prognostic groups (Raponi et al., 2009). Another study completed this observation and found a significant reduction of a set of seven microRNAs (including miR-146b) in serum of NSCLC patients (Heegaard et al., 2012).

Oncogenesis
A study analysed the effect of miR-146b overexpression in A549 lung cancer cells. A 3-8-fold increase in the expression of pre-miR-146b did not alter the major cellular functions classically involved in oncogenesis, such as proliferation, migration or invasiveness. This overexpression only impacted the ability to form colonies, perhaps because miR-146b-5p and miR-146b-3p may have opposing effects (Patnaik et al., 2011).

Other cancers

Note
(like prostate, pancreas, kidney, colorectal)

Disease
microRNA profiling by microarrays has shown that miR-146b is overexpressed in many cancer types, such as glioma (Xia et al., 2009), melanoma (Jukic et al., 2010), oesophageal cancer (Zhao et al., 2012), bladder cancer (Pignot et al., 2012), colorectal cancer (Ragusa et al., 2010) or oral cancers (Scapoli et al., 2010). miR-146b seems to be also overexpressed in some prostate and colorectal cancers (Kanaan et al., 2012).

Immunity

Note
Innate immunity and inflammation play an important role in cancer development and it is therefore noteworthy to mention that the miR-146 family is involved in these mechanisms of cell protection. Even if more evidence has been gathered in the case of the former, both miR-146a and miR-146b control Toll-like receptor and cytokine signaling pathways. miR-146b is predicted to bind the 3'UTR of the IL-1 receptor-associated kinase 1 and TNF receptor-associated factor 6 transcripts. The expression of MIR146B is regulated by NF-κB (Taganov et al., 2006).

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