MicroRNAs (miRNAs) are a class of small regulatory RNAs (20-23 nucleotides long) that have been found to play a critical role in the wide spectrum of biological processes. These small endogenous noncoding RNAs are able to negatively regulate gene expression by pairing with the 3'-untranslated region (3'-UTR) of their target mRNA. miR-150 is a short and single-stranded miRNA, encoded by a gene located at 19q13.33 in Homo sapiens, which is processed to two mature forms (miR-150-5p and miR-150-3p). It has proven to be a pivotal miRNA engaged in the development of hematologic malignancies, normal haematopoiesis, differentiation of B and T cells, and a number of tumours including breast, osteosarcoma, lung, gastric cancer and etc.

Keywords
MicroRNAs, hsa-miR-150

Identity
Other names: MIRN150, hsa-mir-150
HGNC (Hugo): MIR150
Location: 19q13.33
Local order
chr19: 49500785-49500868 (according to GRCh38). Based on Mapviewer Genes on Sequence, genes surrounding the MIR150 on 19q13.33 includes:
DNA/RNA

Description

RNA polymerase II produces the primary miRNA transcripts (Lee et al., 2004) what will result in hairpin loop structures by microprocessor complex (Cai et al., 2004; Lee et al., 2003; Gregory et al., 2006). The stem-loop structure has a two-nucleotide overhang at its 3’ end and termed as a pre-miRNA (precursor-miRNA). Pre-miRNAs will be exported to cytoplasm through the nucleocytoplasmic shuttler Exportin-5 (XPO5), in an energy dependent mechanism (Auyeung et al., 2013; Murchison et al., 2004).

In the cytoplasm, the pre-miRNA hairpin is cleaved to a miRNA:miRNA* duplex by the endoribonuclease Dicer (Lund et al., 2006; Park et al., 2011). Potentially, either strand of the duplex could be a functional miRNA, however only one strand usually interacts with mRNA target through the RNA-induced silencing complex (RISC) (Filipowicz et al., 2008). The sequence of has-miRNA-150, through the above mentioned mechanism, will be transcribed to a stem-loop structure (Reuter et al., 2010) which finally will matures to MIR150-5p and MIR150-3p.

Protein

microRNAs are not translated into amino acids.

Implicated in

Megakaryocytosis

MIR150 drives megakaryocyte-erythocyte progenitors (MEPs) differentiation toward megakaryocytes at the expense of erythroid cells, and the transcription factor MYB is a critical target of MIR150 in this regulation (Lu et al., 2008). Thrombopoietin (THPO) down-modulates MYB expression through induction of MIR150 (Barroga et al., 2008). MIR150 is expressed in mature B and T cells and regulates their differentiation; MIR150 blocks the transition of pro-B to pre-B cells (Xiao et al., 2007).

Cell-cell signaling

Some cells secrete miRNAs as cell-cell signaling molecules (intercellular/interorgan) (Azimzadeh et al., 2014). Human THP-1 cells selectively package MIR150 into active microvesicles in vitro. These secreted microvesicles are delivered specifically into human HMEC-1 cells and induce their migration as an inflammatory response (Zhang et al. 2010).

Pancreatic Cancer

MUC4, a member of Mucins family, is a glycoprotein upregulated in pancreatic tumors. Silencing of MUC4 results in the suppression of cell growth and metastasis in pancreatic tumors (Singh et al., 2004). The binding site of MIR150 is located at the 3’ UTR of MUC4, which leads to the downregulation of MUC4 expression. The overexpression of MIR150 mitigates the malignant behavior of pancreatic cancer cells (Srivastava et al., 2011).
Colorectal cancer
In a work aiming to figure out the altered miRNAs in colorectal cancer (CRC) through characterization of the miRNA profiles of serum exosomes, Ogata-Kawata et al. has showed that the serum exosomal levels of seven miRNAs, including MIR150, were significantly higher in primary CRC patients compared to healthy controls, and were significantly down-regulated after tumor surgery (Ogata-Kawata et al., 2014). However, miRNA expression profiling using qRT-PCR assays in 1) normal colorectal tissues, 2) adenoma and 3) CRC, MIR150 was found low down-regulated in all three groups and tumour tissue had reduced levels of MIR150 expression compared with paired non-cancerous tissue (Ma et al., 2012).

Esophageal cancer
MIR150 expression is significantly lower in esophageal squamous cell carcinoma (ESCC) samples compared with the normal esophageal mucosa levels (P < 0.001) (Yokobori et al., 2013). It has been supposed that MIR150 suppresses tumor proliferation by degradation the Zinc finger E box binding homeobox 1 (ZEB1).

Gastric cancer
The probability of survival in gastric cancer is significantly lower in patients with high expression levels of MIR150 (Katada et al., 2009). MIR150 increases the proliferation rate of gastric cancer cells by targeting the tumor-suppressor early growth response factor 2 (EGR2) (Wu et al., 2010).

Breast cancer
High levels of MIR150 have been found in breast cancer tissues. The application of MIR150 inhibitors against breast cancer cell lines leads to apoptosis. There is a highly conserved MIR150-binding motif at the 3'UTR of P2X7 receptor (P2RX7 ID: 41623+); MIR150 down-regulates the P2X7 protein levels and therefore causes the cancerous cells to escape from P2X7 pro-apoptotic control (Huang et al., 2013).

Lung cancer
Application of antisense oligonucleotide (ASO) against MIR150 in lung carcinoma cells A549 has induced the reduction of cell proliferation rates and increased apoptosis. Up-regulation of TP53 was detected after ASO treatment (Li et al., 2012). MIR150 is upregulated in lung cancer and correlates negatively with the expression of TP53 (Zhang et al., 2013). MIR150 regulates the expression of TP53 through binding to its 3'-UTR, thus inhibition of MIR150 leads to reduction of cell proliferation and increases apoptosis and expression of TP53. In another study, it was demonstrated that MIR150 represses SRC Kinase Signaling Inhibitor 1 (SRCIN1) which leads to the activation of the Src/focal adhesion kinase (PTK2 or FAK) and Src/Ras/extracellular signal-regulated kinase (ERK) pathway, and enhances the migration and proliferation rate of A549 cells (Cao et al., 2014). Moreover, GU XY et al. showed that the overexpression of MIR150 in non-small-cell lung cancer (NSCLC) is associated with alterations in the expression of human BR11-associated receptor kinase 1 (BAK1), so that inhibition of MIR150 reduces cell proliferation and promotes cell apoptosis (Gu et al., 2014). However, it has been argued that the expression level of MIR150 in patients with small-cell lung cancer (SCLC) is much lower than normal lung samples (Bi et al., 2014).

Liver cancer
It has been suggested that MIR150 could be a suitable candidate to discriminate tumoural versus normal human primary hepatocytes (Di Masi et al., 2010). In addition, it has been confirmed that the overexpression of MIR150 down-regulates MYB protein levels and causes a significant reduction of CD133+ cells and the suppression of cell growth/tumorsphere formation (Zhang et al., 2012). It is suggested that MIR150 may be engaged in the self-renewal of liver cancer stem cells through modulation of the downstream target MYB.

Osteosarcoma
A nearly 50-fold overexpression of MIR150 in osteosarcoma samples compared to normal osteoblasts, has been reported (Lulla et al., 2011). Upregulation of MIR150 may cause the down-regulation of P2X7 receptor and therefore an uncontrolled growth of osteosarcoma cells. Other study has argued that MIR150 inhibits cell proliferation and metastasis in osteosarcoma and stimulates cell apoptosis by regulating the expression of SP1 (Li et al., 2015). Recently, it has been reported that MIR150 functions as a tumor suppressor in osteosarcoma partially by targeting the IGF2 mRNA-binding protein 1 (IGF2BP1) (Qu et al., 2016).

Hepatocellular carcinoma
In a recent attempt to identifying the role of miRNAs in hepatocellular carcinoma (HCC) progression, researchers have shown that there are low levels of miR-150-5p in cancerous samples, and determined that the inhibition of miR-150-5p has a drastic effect on hepatoma cell migration and invasion, whereas its overexpression shows reverse results (Li et al., 2014). It was also confirmed that miR-150-5p inhibits the matrix metalloproteinase 14 (MMP14) expression in hepatoma cells.
**Prostate cancer**

The high expression levels of MIR150 is positively correlated with tumor recurrence or metastasis (p=0.010) (Dezhong et al., 2015). It was shown that prostate cancer patients with high MIR150 expression have significantly poorer overall survival and poorer disease-free survival compared those with low MIR150 expression. Furthermore, increased MIR150 expression might participate in the development and progression of human prostate cancer stem cells (CSC) via suppressing p27Kip1 (CDKN1B) (Liu et al., 2015).

**Intrahepatic cholangiocarcinoma**

MIR150 is significantly downregulated in intrahepatic cholangiocarcinoma (ICC) tissues; however its expression level in the blood samples of ICC patients is significantly higher than in controls (Wang et al., 2015).

**Burkitt lymphoma (BL)**

MIR150 is dramatically down-regulated in BL patients; MYB and Survivin (BIRC5) are the targets of MIR150 (Wang et al., 2014). In addition, MIR150 can induce Epstein Barr virus-positive BL differentiation by targeting MYB (Chen et al., 2013).

**Cervical cancer**

Interacting with 3' UTR of FOXO4, MIR150 reduces FOXO4 expression level and thereby regulates several cell cycle- and apoptosis-related genes (CyclinD1 (CCND1), p27, BCL2L11 (BIM), and FASLG), and leads to cervical cancer cell growth and survival (J Li et al., 2015).

**Bladder cancer**

An in vitro investigation to figuring out the role of MIR150 in cells has shown that MIR150 functions as a tumor promoter in reducing chemo-sensitivity and promoting invasiveness of muscle-invasive bladder cancer cells via targeting programmed cell death 4 protein (PDCD4) (Y Lei et al., 2014).

**Epithelial ovarian cancer**

A significant low expression level of MIR150 have been reported in epithelial ovarian cancer (EOC) tissues and patients' serum (Vang et al, 2013; Shapira et al., 2014). MIR150 may function as a tumor suppressor and modulate EOC cell proliferation, and invasion by directly and negatively regulating Zinc Finger E-Box Binding Homeobox 1 (ZEB1) (Jin et al., 2014).

**Influenza**

Patients with severe A/H1N1 disease exhibited a significant over-expression of circulating MIR150 than patients with milder disease, suggesting that the up-regulation of MIR150 is engaged with poorer outcomes of A/H1N1 infection (Morán et al., 2015).

**Acquired immune deficiency syndrome (AIDS)**

Down regulation of MIR150 during HIV infection and its lower level in CD4+ T cells of chronic HIV patients compared to healthy controls has been reported (Witwer et al., 2012; Swaminathan et al., 2009).

It has been speculated that the suppression of MIR150 promotes HIV-1 infection (X Wang et al., 2009). HIV positive patients can be grouped based on the MIR150 levels of their peripheral blood mononuclear cells or their plasma, suggesting MIR150 as a new biomarker for HIV progression, therapy and resistance (Munshi et al., 2014).

**Dengue haemorrhagic fever (DHF)**

The downregulation of suppressors of cytokine signaling 1 (SOCS1) proteins through transfection of a MIR150 mimic into CD14(+) cells infected with DENV-2, suggests that augmented MIR150 expression with depressed SOCS1 expression in CD14(+) cells is associated with the pathogenesis of DHF (RF Chen et al., 2014).

**Cardiovascular Diseases**

Low expression levels of MIR150 is associated with acute myocardial infarction, atrial fibrillation, dilated cardiomyopathy, ischaemic cardiomyopathy and various mouse heart failure models (Devaux et al., 2013; Liu et al., 2012; Topkara et al., 2011; Duan et al., 2013). MIR150 could be a better biomarker for HF than other markers used in clinic (Ellis et al., 2013). MIR150 has a pivotal role as a regulator of cardiomyocyte survival during cardiac injury (Tang et al., 2015). Reduced circulating MIR150 levels are associated with poor survival in pulmonary arterial hypertension (Rhodes et al., 2013).

**Systemic sclerosis**

MIR150 may play an important role in the pathogenesis of Systemic Sclerosis (SSc) via overexpression of integrin β 3 (ITGB3) (Honda et al., 2013). MIR150 expression level is decreased in SSc fibroblasts and the treatment of normal fibroblasts with MIR150 inhibitor promotes the expression of integrin β3, phosphorylated SMAD3, and type I collagen. SSc patients with lower serum MIR150 levels show more severe clinical manifestations.

**Multiple sclerosis (MS)**

MIR150 is down-regulated in peripheral blood mononuclear cells and T cells from MS patients (Martinelli-Boneschi et al., 2012; Freiesleben et al., 2016).

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