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REGULATORY MODEL OF miRNA-125 IN LEUKEMIA

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ABSTRACT:

MicroRNAs (miRNAs) are small, subtypes of RNA that are 22-25 nucleotides in length that regulate the gene expression by targeting homologous sequences in messenger RNA (mRNA). Their unusual expressions have been observed in various types of cancers. In this paper we first briefly outline of multiple pairwise alignment of pri-miRNA-125 of three organisms and secondary structure. We then discuss in detail on binding sites of miRNA-125 with different target genes to known the binding energy using computational tool. Finally, we discuss on mechanism of miRNA-125 over-expression causes different types of leukemia due to abnormal expression of gene present on chromosome 21. Thus we have reported that one of the major causes of leukemia is abnormal expression of miRNA-125.

Keywords: *miR-125, Overexpression, cancer, leukemia, oncogene, target gene*

[I] INTRODUCTION

MicroRNAs (miRNAs) are small non-coding, single stranded RNA molecules with 22-25 nucleotides in size, that regulate specific target mRNA by complementary seed region in the 3'untranslated region (UTR) by cleaving or repressing the transition. [4, 1]. miRNA have various functions in gene regulation, including proliferation, differentiation, and apoptosis [38]. Depending up on cellular contents miRNA-125 undergo proliferation and apoptosis in breast cancer, [53, 55, 22, 52, 27,] prostate, [58, 36, 12, 57, 60, 29] hematopoietic stem cells, [21] leukemia [65] and in lung cancer [64]. miR-125b expression regulates cell proliferation by inhibiting osteoblastic differentiation [46].

High expression of miR-125b in mouse activates the actin distribution and the shape of fibroblast [24]. miR-125a-5p expression in liver cell down-regulate the HBV S gene thus reducing the

amount of secreted HBsAg [50]. In rats over-expression of miR-125a regulate hyperglycemic phenotype in adipose and liver tissue [26]. In human neuroblastoma and lung fibroblast cells expression of miR-125b target p53 and induce apoptosis due to stress [35]. Recent studies have shown that miR-125 expression in hippocampal neurons [13], human-astroglial (HAG) cells [49] and glioma stem cell [62, 56].

In this study, we focused on miRNA-125, its regulatory function and analyzed the positive and negative regulation in different types of cells/tissues by using literature studies. We have analyzed the pairwise alignment of pre-miR-125 in human, mouse and rats. Further we find the binding energy of miRNA- target gene. Finally, we are interested in finding the mechanism network due to expression of miR-125 in different types of cells. Altogether the reports explain that miR-125 act as an oncogene and cause leukemia.

[II] METHODS

2.1 Collection of data

Initially, we started with downloading the papers that are available on pubmed, science direct, etc., among the paper retrieves we selected those papers that are mainly concentrating on miRNA-125 in the title of the papers. We studied those papers and started collecting the information of expression of miRNA-125, cell type, and miRNA target gene. During our studies on miRNA-125, we collected some of the information on the available papers then we started with tabulating all the observations and put it into consolidated into a table as shown in Table 1. That contains the information heading as miRNA names in which species studies involved, types of cell study, target gene, expression of miRNA and its functions. We then analyzed regulation of miRNA and classified the tabulation into positive and negative regulation of miRNA. We came across many data which have been explained in result.

2.2 Analysis of sequences

We collected all the sequences of miRNA-125 in pre-mature and mature sequence from miRBase (release 18) for sequence alignment studies. On the other hand, the gene that is target for miRNA-125, those target gene mRNA nucleotides are collected from the database of National Centre of Biotechnology Information (NCBI) (http://www.ncbi.nlm.nih.gov). We used open source MiRanda 3.3 version software to predict miRNA- target sequence alignment (http://www.microrna.org) and also to find binding energy. RNA folding of mir-125 is retrieved by Geneious software.

[III] RESULT AND DISCUSSION

3.1 Identification of miRNA-125

In human miR-125a cluster present on chromosome (chr) 19 which contain three genes of miRNA: miR-125a, miR-let-7e and miR-99b. miR-125b cluster present on chr 21 which contain three genes of miRNA: miR-125b, miR-let-7c and miR-99a. In mouse miR-125a and miR-125b cluster are sited in chr 17 and 16 [23]. The pre-mature miRNA-125 sequences of human, mouse and rat are collected from miRBase-release 18 [33]. We started with analyzing all sequences of miRNA-125a/b of the three organisms by using Geneious 5.6.4.

We performed Global Multiple Sequence Alignment (MSA) with cost matrix: 65% similarity (5.0/-4.0), gap open penalty 12, gap extension penalty 3, for the pre-mir-125 between *Homo sapiens* (human), *Mus musculus* (mouse) and *Rattus norvegicus* (rat). The alignment is shown in Figure 1 (A, B, C) and is highly conserved with transition mutation result in conversation of A ->G and U ->C in all the three sequences. RNA folding of miR-125a/b is shown in Figure 2.

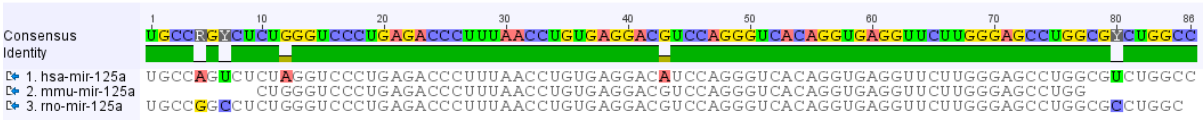
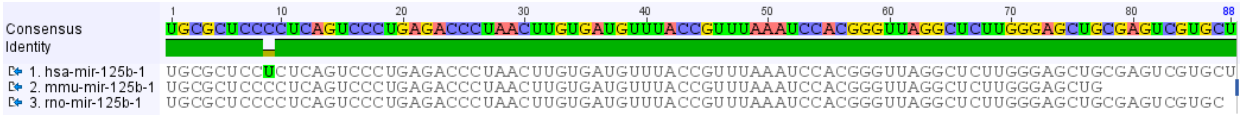
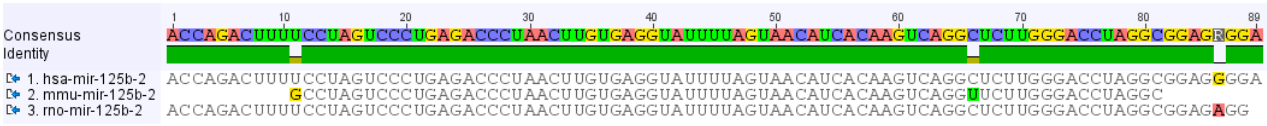


Fig: 1A. multiple Pairwise alignment of pre-mir-125a with Identical Sites: 80 (94.1%), Pairwise % Identity: 96.8%.

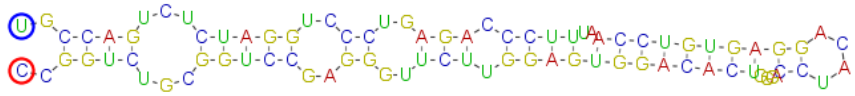


1B. multiple Pairwise alignment of pre-mir-125b-1 with Identical Sites: 86 (98.9%), pairwise % Identity: 99.2%.

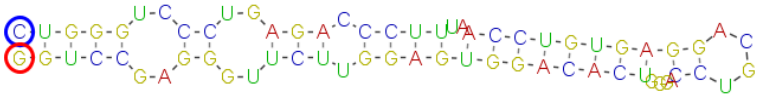


1C. multiple Pairwise alignment of pre-mir-125b-2 with Identical Sites: 85 (96.6%), Pairwise % Identity: 97.8%.

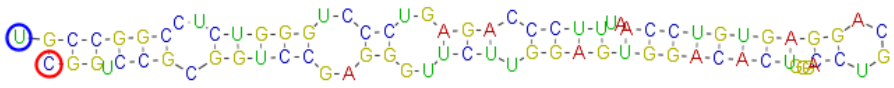
hsa-miR-125a



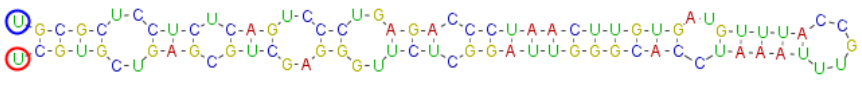
mmu-miR-125a



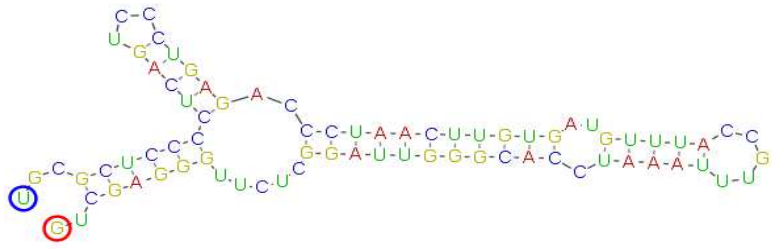
rn-miR-125a



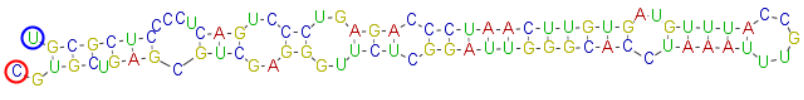
hsa-miR-125b-1



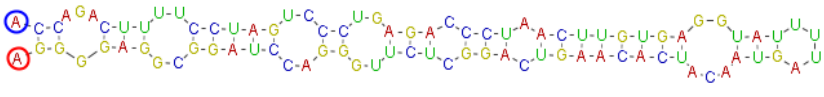
mmu-miR-125b-1



rno-miR-125b-1



hsa-miR-125b-2



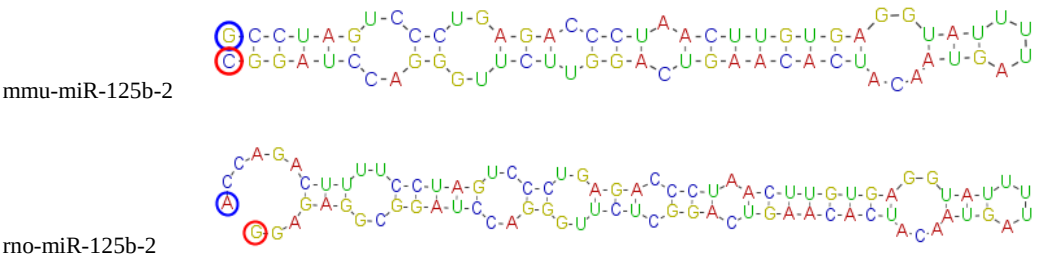


Fig: 2. Secondary structure of the novel miRNA-125. Comparison of secondary structures of miR-125a/b between *Homo sapiens* (hsa), *Mus musculus* (mmu) and *Rattus norvegicus* (rno) that are retrieved by RNA fold have included in the Geneious software package.

3.2 Database of miRNA-125

For this study, first we collected approximately 40 published papers from various schools of thoughts (Table 1) and understood the mechanism and role played by the miRNA in particular cell/ tissues, which has been collated in Table 1.

Organisms	miRNA Name	Oncogenes target (genes)	Cell types	Type of Interactions	Effect of miRNA	References
Mouse	miR-125b	TEF	Fibroblasts	actin distribution and the shape of fibroblast	Over-expression	24
Human	miR-125b	BMPR1B	breast cancer	increased breast cancer risk	downregulation	53
Human	miR-125b	c-raf-1	human breast cancer	Decreases the levels of oncogene proteins and stimulates cell death.	expression	27
Human	miR-125b	Bak1	prostate cancer cells	promotes proliferation	Over-expression	58
Human, Mice	miR-125b	Bak1, Ppp1ca	neuroblastoma cells	pro-apoptosis	expression	34
Human	miR-125b	Tp53, Tp53inp1, Cdc25c, Ppp2ca	neuroblastoma cells	pro-apoptosis	expression	34
Mice	miR-125b	Itch, Puma	neuroblastoma cells	anti-apoptosis	expression	34
Human	miR-125a/b	ERBB2/ ERBB3	breast cancer	suppresses cell proliferation	Over-expression	55
Human	miR-125b	KLF13, CXCL11, FOXA1	oral squamous cell carcinoma (OSCC)	cause cancer because loss of chr in 11q and 21 which regulate the miR125, miR-125 is downregulated	Down-regulation	25
Human	miR-125b	KLF13, CXCL11, FOXA1	oral squamous cell carcinoma (OSCC)	reduced cell proliferation	increase the expression	25
Human	miR-125b-2	lin-28, lin-41	Prostate Cancer	reduced proliferation of differentiated cells.	depletion or down-regulation	36
Human	miR-125a-5p	EGFR	lung cancer cells	migration and invasion of lung cancer cells	Down-regulation	60
Human	miR-125a-5p	IL16, CCL21, CCL4, IGF-2	non-small cell lung cancer (NSCLC)	enhance cell migration and invasion in cancer cell	Down-regulation	29
Mouse	miR-125b-2	-	hematopoietic progenitor cell	leukemia's with the structural ETV6/RUNX1 abnormality	Over-expression	19
Human	miR-125b-2	-	lymphoid progenitors	survival and growth of lymphoid progenitors(suppressing apoptosis and caspase 3 activation)	expression	19
Human	miR-125b-2	-	leukemic cells	ETV6/RUNX1 ALL	expression	19
Human	miR-125b	-	ETV6/RUNX1 leukemia	partial protection from apoptosis	repression after treating with drug	19

Human	miR-125a-5p	HBV S gene (HBV 3037–3065)	liver (hepatic cells)	down-regulate the expression of HBV S gene thus reducing the amount of secreted HBsAg.	expression	50
Mouse	miR-125b	IGF-II	myoblast	myoblast differentiation and muscle regeneration	Down-regulation	18
Mouse	miR-125b	IGF-II	skeletal muscle	skeletal muscle regeneration	Down-regulation	18
Human	miR-125a	p53		reduces p53 protein expression	expression	66
Human	miR-125b	BLIMP-1	germinal centers(GC) phase of B cell	inhibits B cell differentiation and enhances cell death of myeloma cells	Over-expression	23
Mouse	miR-125b	IRF-4	germinal centers(GC) phase of B cell	inhibits B cell differentiation and enhances cell death of myeloma cells	Over-expression	23
Mice	miR-125a	Bak1	hematopoietic stem cells (HSC)	reduction of apoptosis in immature hematopoietic progenitors cells	expression	21
Mice	miR-125b	-	fetal liver cells	increase in WBCs associated with a macrocytic anemia	Over-expression	6
Mice	miR-125b	-	fetal liver cells	B-cell / T-cell acute lymphoblastic leukemia	Over-expression	6
Mice	miR-125b	-	fetal liver cells	induce primary lymphoid or myeloid leukemia by BCR-ABL fusion protein	Over-expression	6
Human	miR-125a	truncated TrkC	medulloblastoma carcinogenesis	promote medulloblastoma cell growth arrest and apoptosis	Down-regulation	16
Human	miR-125a	truncated TrkC	medulloblastoma carcinogenesis	treatment that inhibits tumor growth	Up-regulated by RA (All-trans-retinoic acid)	16
Rats(Goto-Kakizaki [GK] spontaneously diabetic	miR-125a	Slc35c2, Umps, Ptges2, Ppap2c, Sult1a1	adipose and liver tissue	hyperglycemic phenotype	Over-expression	26
Human	miR-125a	HuR	breast cancer	inhibited cell growth via suppression of cell proliferation and promotion of apoptosis and also inhibit cell migration	Over-expression	22
Human	miR-125b	p53	human neuroblastoma cells and lung fibroblast cells	represses apoptosis	increase	35
Human	miR-125b	p53	lung fibroblast cells	induces apoptosis	Down-regulation	35
Human	miR-125b	BAK1	human prostate carcinoma	decrease the apoptosis	increase the expression	12
Human	miR-125b	Bak1	Ovarian Cancer	decreased cisplatin-induced cyto toxicity	Over-expression	32
Human	miR-125b	Bak1	Ovarian Cancer	increased cisplatin sensitivity in cisplatin-resistant cells	Down-regulation	32
Mouse	miR-125b	ErbB2	mesenchymal stem cells	attenuated in osteoblastic-differentiated	expression	46
Mice	miR-125b	p53, puma, bak1	prostate cancer	promotes growth of prostatic xenograft tumors	Over-expression	57
Human	miR-125b	STAT3	osteosarcoma tissue	suppressed proliferation and migration of cell decreased tumor formation	Over-expression	41
Human	miR-125b	STAT3	osteosarcoma tissue	proliferation and migration of cell result in cancer	Down-regulation	41
Human	miR-125b	CBFβ	malignant myeloid cell	Myeloid Cell proliferation and promoting leukemogenesis	expression	39
Human	miR-125b	CBFβ	malignant myeloid cell	promote myeloid differentiation	Down-regulation	39
Human	miR-125b-2	DICER1 ST18	HSPCs (hematopoietic stem and progenitor cells)	increase the proliferation and enhances their ability to self-renew (presumed cells of origin for DS-AMKL/TL) (Down syndrome)-(acute megakaryoblastic leukemia)	Over-expression	31
Human	miR-125b-2	DICER1	HSPCs (hematopoietic stem and progenitor cells)	DS-AMKL (Down syndrome)-(acute megakaryoblastic leukemia)	highly over-expression	31
Human	miR-125b	DICER1	HSPCs (hematopoietic stem and progenitor cells)	inhibits DS megakaryocytic leukemia cell growth.	Down-regulation	31
Mouse	miR-125b	ST18, DICER1	hematopoietic cells	proproliferative effect on hematopoietic progenitor cells	Over-expression	31

Human	miR-125b	MUC1	breast cancer cell	promote DNA damage and increase the apoptotic	Over-expression	52
Human	miR-125b	MUC1	breast cancer cell	result in breast cancer	Down-regulation	52
Human	miR-125b	MLF2	myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) patients	the arrest of maturation by morphology and reduced expression of CD14 in monocytic cells	Up-regulation (from 6- to 90-fold)	7
Human	miR-125b	MCL1	myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) patients	block late stages of differentiation.	Up-regulation	7
Human	miR-125b	notch1, p53	haiey haiey disease (HHD) keratinocytes	keratinocytes proliferation and differentiation	Over-expression	43
Human	miR-125b	NR2A	Hippocampal neurons	long thin protrusions and altered synaptic function	Over-expression	13
Human	miR-125a	ARID3B	ovarian cancer	represses the mesenchymal phenotype and prevent cancer or maintaining an epithelial morphology or induces a mesenchymal-to-epithelial transition.	Over-expression	11
Human	miR-125a	ARID3B	ovarian cancer	mesenchymal morphologies or behaviors in cancer	repression	11
Human	miR-125a-5p	-	lung squamous cell carcinoma (SCC),	in lung SCC	Up-regulation	64
Human	miR-125b	BAK1	pediatric acute promyelocytic leukemia (APL)	reduced apoptosis and enhanced proliferation of leukemic cells and further induce oncogenesis	Over-expression	65
Human	miR-125b	NF-κB	human-astroglial (HAG) cells	increase the neurological disorders including Alzheimer's disease (AD) due iron and aluminum-sulfate metal (reactive oxygen species)	Up-regulation	49
Human	miR-125b	CDK6, CDC25A	Glioma stem cell	induced proliferation	Down-regulation	56
Human	miR-125b	CDK6, CDC25A	Glioma stem cell	proliferation defect	Over-expression	56
Human	miR-125b	CDKN2A	normal human astrocytes(NHA)	IL-6 induce proliferation	Up-regulation	48
Human	miR-125b	Bmf	human glioma cell	proliferation and inhibits all-trans-retinoic acid (ATRA)-induced cell apoptosis(inhibit apoptosis)	Over-expression	62
Human	miR-125b	Bmf	human glioma cell	decreased proliferation and enhanced the sensitivity to all-trans-retinoic acid (ATRA)-induced apoptosis.(promoted the late cell apoptosis)	Down-regulation	62
Mouse	miR-125b	Smo	medulloblastoma (MBs)	Inhibit Hedgehog (Hh) signaling.	Over-expression	17
Mouse	miR-125b	Gli1	undifferentiated granule cell progenitors (GCPs)	delay growth arrest and differentiation	Down-regulation	17
Mouse	miR-125b	Gli1	undifferentiated granule cell progenitors (GCPs)	To reduce the proliferation rate and to differentiate.	Over-expression	17
Human	miR-125b	Bcl-2	hepatocellular carcinoma (HCC)	suppresses HCC cell proliferation and promotes apoptosis	Over-expression	67

Table: 1. Elucidation of miR-125a/b regulation in different cell types with the types of interaction and the target genes.

Of all the published studies, we came across approximately 20% of papers [27, 29, 26, 57, 7, 43] that are proved in computational approach by using following prediction algorithms like TargetScan [37], PicTar [47], miRBase [20] MicroCosm Target databases [20], miRanda [30], 30% proved experimentally [58, 36, 6, 16, 39, 13, 49, 56] and another approximately 50% proved by computational methods followed by experimental methods [24, 34, 55, 50, 18, 66, 22, 32, 12, 41, 31, 52, 11, 65, 48, 62].

During our literature survey, we came across paper showing miRNA- target gene binding

site [9]. miRNA has more than 100 target genes [8]. We adopted the same method as we concentrated on single miRNA. To find out binding energy and miRNA- target gene binding first we downloaded miRNA-125 from miRBase and all target gene sequences were stored in FASTA format. We used miRanda 3.3 with gap open penalty: -9.0, gap extend penalty: -4.0, score threshold: 140.0, energy threshold: 1.0 kcal/mol, scaling parameter: 4.0. Query representing miR-125 and Ref representing target gene sequence name in Supplementary Table 2. After finding the results from miRanda of miRNA-125-binding to the target genes we found that based on the observation seed region if miRNA-125 in human, mouse and rat (Table 3).

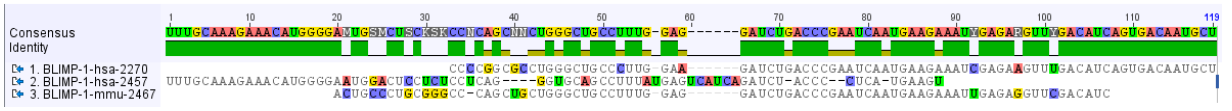
MiRNA Name	Seed regions
hsa-miR-125a-3p	5' CAGGUGA 3'
mmu-miR-125a-3p	5' CAGGUGA 3'
hsa-miR-125a-5p	5' CCCUGAGA 3'
hsa-miR-125b-5p	5' CCCUGAGA 3'
mmu-miR-125b-5p	5' CCCUGAGA 3'
hsa-miR-125b-1-3p	5' CGGGUUA 3'
mmu-miR-125b-1-3p	5' CGGGUUA 3'
hsa-miR-125b-2-3p	5' CACAAGU 3'
mmu-miR-125b-2-3p	5' CAAGUCA 3'

Table: 3. showing miR-125a/b in *Homo sapiens* and *Mus musculus* with seed regions.

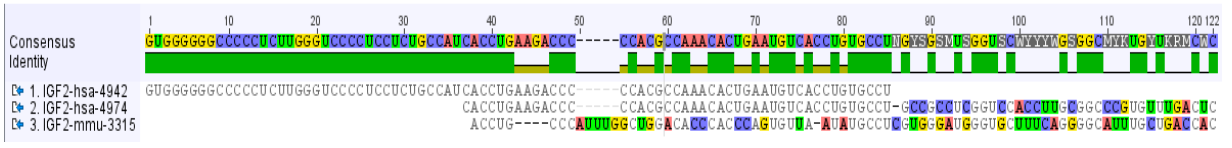
During our analysis we found that some of the genes like Bak1, CDK6, PPP1CA, IGF2, DICER-1, BLIMP-1, and GLI1 are seen in human and mouse which are bound to miRNA-125. We performed MSA of seven genes to identify homology and also the region of miRNA-125 binding. We used multiple alignments from Geneious 5.6.4 with default value as follow cost matrix: 65% similarity (5.0/-4.0), gap open penalty 12, and gap extension penalty 3, alignment type: global alignment with free end gaps. The results are shown in Figure 2.

A)

B)



C)



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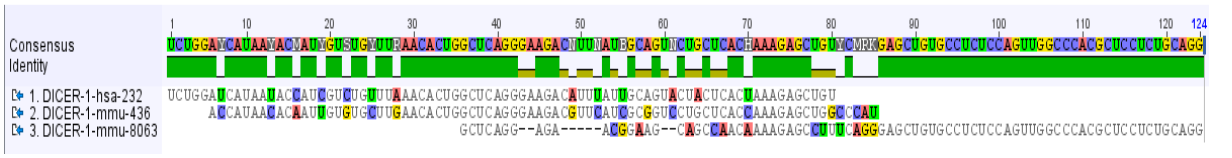

E)

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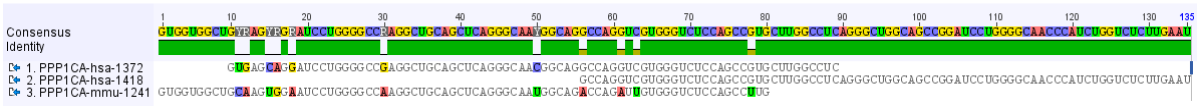
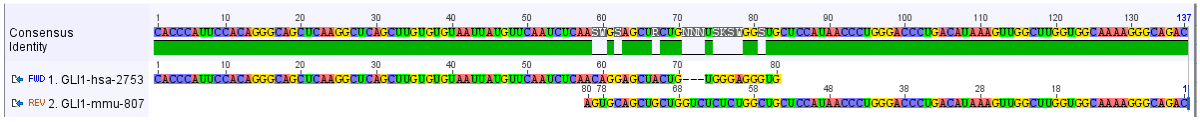
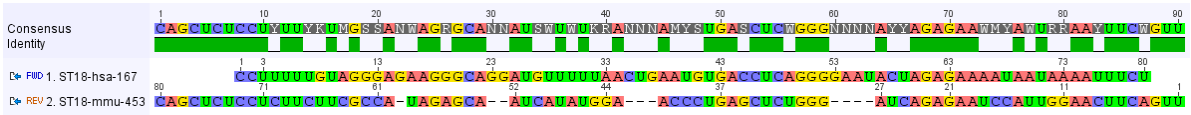


G)



H)



I)

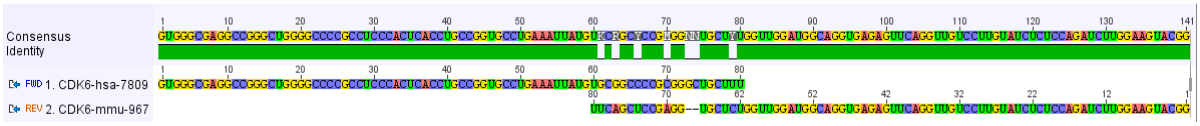


Fig: 2. Showing multiple pairwise alignment of target gene and illustrating identical sites (IS) and pairwise % identity (PI) for A,B,C,D and F respectively BAK1 (IS) 43 (49.4%), (PI) 58.8%, BLIMP1-153 (60.2%), 67.4%, IGF243 (50.0%), 63.3%, DICER-148 (60.0%), 65.9%, PPP1CA69 (86.3%),88.5%, between *Homo sapiens*=hsa and *Mus musculus*=mmu. Pairwise sequence align and illustrating identical sites (IS) and pairwise % identity (PI) for E,G,H and I respective DICER1 75 (94.9%), 94.9%, GLI1 14 (53.8%),53.8%, ST18 42 (52.5%),52.5% and CDK6 14 (66.7%),66.7% between *Homo sapiens*=hsa and *Mus musculus*=mmu.

3.3 Over-expression of miRNA-125

In the cell, improper expression of miRNA alters the regulatory network leading to abnormality in its functions that cause proliferation, production of more protein, signaling etc. and finally resulting in cancer. miRNA have a role in cancer due to deletion, amplification or chromosomal translocation region. In patients carrying the t(2;11)(p21;q23) translocation in myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) have showed the over-expression of miR-125b (6 to 90-fold) than in healthy person which block the process of differentiation in monocytes and granulocytes [7]. In other case, over-expression of miR-125b from 30 to 600-fold in B-acute lymphoid leukemia (ALL) patients due the translocation t (11;14)(q24;q32) [10]. Other studies show that due to distal losses of chr 11q and 21 contribute to the reduced expression of miR-125b that cause oral squamous cell carcinoma (OSCC) [25]. Over-expression of miR-125 in germinal centers (GC) phase of B cell, inhibit B cell differentiation into plasma

cells by targeting BLIMP-1 and IRF-4 transcription factors [23].

ETS2 and ERG are transcription factors of the family ETS are encoded on human chr 21. Similar arrangement in mouse on the chr 16 which is homologous [3]. High level of ERG indicates the cause of AML and ALL [44, 2]. When both mRNAs, ETS2 and ERG high expression has been observed in AML patients with complex karyotypes and abnormal chr 21 [3]. ERG is required for definitive hematoposis and for maintenance of proper platelets number in normal hematopoiesis [44]. Over-expression of ERG, ETS2 and FLI-1 phosphorylated STAT3 that activates JAK/STAT pathway from Gata1- knockdown cells finally result on megakaryocyte malignancies [59]. Megakaryopoies is favor in low levels of c-myb. Further the over-expression of ERG inhibits the expression of c-myb [15]. ERG cooperates with GATA1s [54]. GATA1 mutations cause myeloid leukemia of Downs' syndrome (DS). DS face a 500-fold increased risk for acute megakaryoblastic leukemia (AMKL) [51, 61, 63]. GATA1 binding to RUNX1 has lead to active αIIb integrin megakaryocytic promoter element. Mutation in GATA1 due to deletion of sequence in transcription activation site leads to megakaryocytic Leukemia [61]. The truncated forms of GATA-1 lack RUNX1 which is significant in trisomy 21 [14]. Over-expression of miR-125b-2 cooperates with Gata1s mutation in fetal livers (FLs) progenitors [31]. miR-125b over-expression is associated with oncogenes like BCR-ABL fusion protein to promote leukemia [6].

chr 21 encodes four miRNAs (hsa-mir-99a; hsa-let-7c; hsa-mir-125b-2 and hsa-mir-155). hsa-mir-125b-2 cluster are upregulated in the ETV6/RUNX1 ALL, hsa-mir-155 expressed in all subtype of leukemia cells. Over-expression of miR-125b-2 inhibits the apoptosis and caspase 3 activation in response to IL3 scarcity [19]. IL3 promote cell survival through JAK/STAT pathway [45, 28, 40, 5]. Expression of miR-125b contributes to myeloid cell proliferation and promoting leukemogenesis by down-regulating CBFβ [39]. miR-125a expression down-regulates proapoptotic protein Bak1 (40 - 50%) that reduce apoptosis in immature hematopoietic progenitors cells [65]. Over-expression of miR-125b in pediatric acute promyelocytic leukemia (APL) inhibits Bak1 expression that reduces apoptosis and enhanced proliferation of leukemic cells [48].

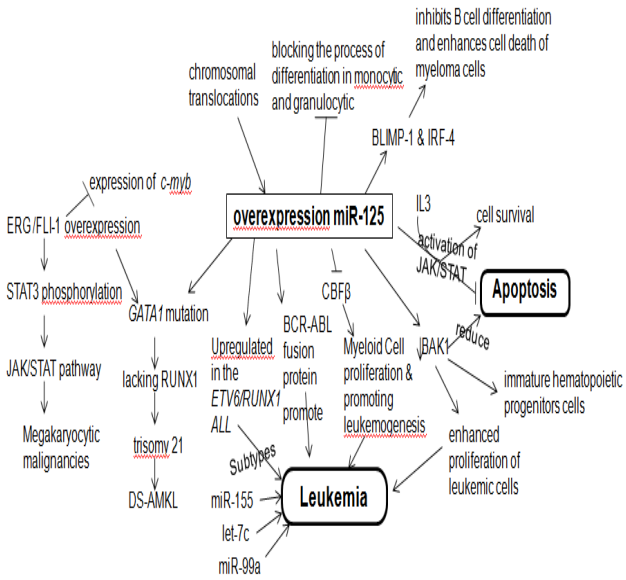


Fig: 3. Potential role of microRNA-125 overexpression in regulatory mechanisms. Mechanism of microRNA-125 mediated gene regulation in different types. miRNA direct targeting the mRNA and regulating the expression of the target gene at post-transcriptional levels (mRNA degradation and inhibit translation). The over-expression of miRNA changes the specific function and lead to cancer (leukemia).

[IV] CONCLUSION

Our studies imply that miR-125 acts as an oncogene. All these reports from Figure 3 entail that miR-125 expression considerably causes different types of cancers mainly leukemia. The abnormality in its functions due to different types of genes and miRNA which is encoded on chr 21 leads to Downs' syndrome, leukemia and other types of cancers. This might be important

factor in clinical therapeutics. In this paper, we studied deeply on miR-125 positive and negative regulation and find the binding energy of miR-125 binding site with different target genes. Different pathways show that over-expression of miR-125 resulting in leukemia.

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miRNA NAME	REGION NUMBER ALIGNMENT	TARGET GENE NAME	BIND SITES	BIND ENERGY
hsa-miR-125a-5p	3002 to 3024 Align	ARID3B	Query: 3' agUGUCCAAUUUCCCAGAGUCCCu 5' :|||| |:| | ||||||| Ref: 5' auGCAGGGGAGA-CGACUCAGGGa 3'	-24.680000 kCal/Mol
hsa-miR-125a-5p	3736 to 3759 Align	ARID3B	Query: 3' aguguccaauuucccAGAGUCCCu 5' |||||||| Ref: 5' uggccaguaugucuuUCUCAGGGg 3'	-19.230000 kCal/Mol
hsa-miR-125a-5p	2124 to 2147 Align	ARID3B	Query: 3' aguguccaauuucccaGAGUCCCu 5' ||||||| Ref: 5' cccagccaccucccagCUCAGGGc 3'	-15.850000 kCal/Mol
hsa-miR-125a-5p	3162 to 3185 Align	ARID3B	Query: 3' aguguccaauuucccaGAGUCCCu 5' ||||||| Ref: 5' cacucagcauucccagCUCAGGGc 3'	-17.430000 kCal/Mol
hsa-miR-125a-3p	639 to 659 Align	ARID3B	Query: 3' ccGAGGGUUCUUGGAGUGGAca 5' ||:|||| :||||||| Ref: 5' ugCUUCCAAG-GCCUCACCUuc 3'	-31.740000 kCal/Mol
hsa-miR-125a-3p	1160 to 1181 Align	ARID3B	Query: 3' ccGAGGGUUCUUGGAGUGGACa 5' |||:: :| ||||||| Ref: 5' ccCUCUUUGGCUACUCACCUGc 3'	-21.680000 kCal/Mol
hsa-miR-125a-3p	3843 to 3864 Align	ARID3B	Query: 3' ccgaGGGUUCUUGGAGUGGACa 5' ||||:| | |||:|||| Ref: 5' uuucCCCAGGCAGCUCGCCUGg 3'	-26.959999 kCal/Mol
hsa-miR-125b-5p	1552 to 1573 Align	BAK1	Query: 3' aguguUCAAUCCCAGAGUCCCu 5' ||||:| |||||||| Ref: 5' uuugcAGUUGGACUCUCAGGGa 3'	-24.700001 kCal/Mol
hsa-miR-125b-5p	2054 to 2075 Align	BAK1	Query: 3' agUGUUCAAUCCCAGAGUCCCu 5' |||: ||||||||::||| Ref: 5' gcACAGCCUAGGGUCUUGGGGg 3'	-33.259998 kCal/Mol
mmu-miR-125b-5p	1477 to 1498 Align	Bak1	Query: 3' aguguUCAAUCCCAGAGUCCCu 5' :| |:| |||||||| Ref: 5' uuggcGGCUGGACUCUCAGGGa 3'	-20.410000 kCal/Mol
hsa-miR-125b-1-3p	2270 to 2290 Align	BLIMP-1	Query: 3' ucGAGGGUUCUCGGAUUGGGCa 5' ||: |||| :||:||||| Ref: 5' ccCUUGGAAGA-UCUGACCCGa 3'	-22.270000 kCal/Mol
hsa-miR-125b-5p	179 to 200 Align	BLIMP-1	Query: 3' agUGUUCAAUCCCAGAGUCCCu 5' :|| |: |||:||||| Ref: 5' caGCACUGUGAGGUUUCAGGGa 3'	-26.350000 kCal/Mol
hsa-miR-125b-5p	2459 to 2480 Align	BLIMP-1	Query: 3' aguguucaaucccaGAGUCCCu 5' ||||||| Ref: 5' aauggacuccucucCUCAGGGu 3'	-13.950000 kCal/Mol
hsa-miR-125a-5p	177 to 200 Align	BLIMP-1	Query: 3' aguguccaAUUUCCCAGAGUCCCu 5' |: : |||:||||| Ref: 5' uccagcacUGUGAGGUUUCAGGGa 3'	-24.480000 kCal/Mol
hsa-miR-125a-5p	2457 to 2480 Align	BLIMP-1	Query: 3' aguguccaauuucccaGAGUCCCu 5' ||||||| Ref: 5' ggaauggacuccucucCUCAGGGu 3'	-14.890000 kCal/Mol
hsa-miR-125a-3p	2215 to 2234 Align	BLIMP-1	Query: 3' ccgaGGGUUCUUGGAGUGGACa 5' |:||||: :||||||| Ref: 5' uagcCUCAAGG--UUCACCUGa 3'	-24.940001 kCal/Mol

mmu-miR-125b-1-3p	2467 to 2488 Align	BLIMP-1	Query: 3' ucGAGGGUUCUCGGAUUGGGCa 5' Ref: 5' gcCUUUGGAGGAUCUGACCCGa 3'	-25.780001 kCal/Mol
mmu-miR-125b-2-3p	2819 to 2840 Align	BLIMP-1	Query: 3' uccAGGGUUCUUGGACUGAACa 5' Ref: 5' ugcUUCUUAGGGUAUGGCUUGg 3'	-17.730000 kCal/Mol
mmu-miR-125b-5p	2948 to 2969 Align	BLIMP-1	Query: 3' aguguucaaucccAGAGUCCCu 5' Ref: 5' aauguuaccaaaaUCUCAGGGc 3'	-15.070000 kCal/Mol
mmu-miR-125b-5p	2657 to 2678 Align	BLIMP-1	Query: 3' aguguucaaucccaGAGUCCCu 5' Ref: 5' aacggccuccucucCUCAGGGu 3'	-15.290000 kCal/Mol
hsa-miR-125b-5p	2218 to 2238 Align	BMF	Query: 3' agUGUUCAAUCCCAGAGUCCCu 5' Ref: 5' ggACAA-AGAAGACCUCAGGGc 3'	-16.049999 kCal/Mol
hsa-miR-125b-5p	2611 to 2632 Align	BMF	Query: 3' agugUUCAAUCCCAGAGUCCCu 5' Ref: 5' gucaGAAUUCUAUUCUCAGGGu 3'	-17.059999 kCal/Mol
hsa-miR-125b-5p	1401 to 1422 Align	BMF	Query: 3' aguguucaaucccaGAGUCCCu 5' Ref: 5' caccuccagcagacCUCAGGGa 3'	-16.809999 kCal/Mol
hsa-miR-125a-5p	2609 to 2632 Align	BMF	Query: 3' aguguccaauuucccAGAGUCCCu 5' Ref: 5' uggucagaauucuauUCUCAGGGu 3'	-17.469999 kCal/Mol
hsa-miR-125a-5p	1399 to 1422 Align	BMF	Query: 3' aguguccaauuucccaGAGUCCCu 5' Ref: 5' gccaccuccagcagacCUCAGGGa 3'	-17.440001 kCal/Mol
hsa-miR-125a-3p	4224 to 4245 Align	BMF	Query: 3' ccgagggUUCUUGGAGUGGACa 5' Ref: 5' uagcaggAAGGGGCUCACCUGu 3'	-23.709999 kCal/Mol
hsa-miR-125b-5p	1706 to 1727 Align	BMPR1B	Query: 3' aguguucaaucccAGAGUCCCu 5' Ref: 5' uucagaccucaccUCUCAGGGa 3'	-17.450001 kCal/Mol
hsa-miR-125b-5p	234 to 255 Align	CBFB	Query: 3' aguguucaaucCCAGAGUCCCu 5' Ref: 5' ccggccggcgcGGCCUCAGGGc 3'	-18.059999 kCal/Mol
hsa-miR-125a-5p	150 to 174 Align	CCL21	Query: 3' agUGUC-CAAUUUCCCAGAGUCCcu 5' Ref: 5' agGCAGUGAUGGAGGGGCUCAGGac 3'	-26.190001 kCal/Mol
hsa-miR-125a-3p	378 to 399 Align	CCL4	Query: 3' ccGAGGGUUCUUGGAGUGGACa 5' Ref: 5' guCUUCAGGGAAGGUCACCUGa 3'	-21.870001 kCal/Mol
hsa-miR-125a-3p	960 to 984 Align	CDC25A	Query: 3' ccGAGGGUUCUUGG---AGUGGACa 5' Ref: 5' cuCUUUUUACACCCCAGUCACCUGu 3'	-20.400000 kCal/Mol
hsa-miR-125a-3p	467 to 489 Align	CDC25A	Query: 3' ccGAGGGUUCUUGG-AGUGGACa 5' Ref: 5' gcCGCCGGGGGACUGUCGCCUGu 3'	-26.190001 kCal/Mol
hsa-miR-125b-5p	1 to 9 Align	CDC25C	Query: 3' aguguucaaucccaGAGUCCCu 5' Ref: 5' -------------gCUCAGGGa 3'	-16.440001 kCal/Mol
hsa-miR-125a-5p	10856 to 10879 Align	CDK6	Query: 3' aguGUCCAAUUUCCCAGAGUCCcu 5' Ref: 5' cucUAAGAAAAAUGGCCUCAGGua 3'	-12.730000 kCal/Mol
hsa-miR-125a-3p	7809 to 7825 Align	CDK6	Query: 3' ccGAGGGUUCUUGGAGUGGACa 5' Ref: 5' gcCUCCCA-----CUCACCUGc 3'	-24.629999 kCal/Mol
hsa-miR-125a-3p	8878 to 8899 Align	CDK6	Query: 3' ccGAGGGUUCUUGGAGUGGACa 5' Ref: 5' uaCCCCCAGGAACAGCACCUGa 3'	-30.760000 kCal/Mol

hsa-miR-125a-3p	2923 to 2944 Align	CDK6	Query: 3' ccGAGGGUUCUUGGAGUGGACa 5' :|::||: : |:|:|||| Ref: 5' uaUUUUCAGUGUCUUUACCUGa 3'	-19.870001 kCal/Mol
mmu-miR-125a-3p	967 to 987 Align	CDK6	Query: 3' ccgaGGGUUCUUGGAGUGGACa 5' ||::| | :||||||| Ref: 5' acaaCCUGA-ACUCUCACCUGc 3'	-24.030001 kCal/Mol
hsa-miR-125a-5p	1340 to 1363 Align	CDKN2A	Query: 3' aguguccaAUUUCCCAGAGUCCCu 5' ||::| ||||||| Ref: 5' uugugaacUAGGGAAGCUCAGGGg 3'	-23.110001 kCal/Mol
mmu-miR-125b-5p	8063 to 8084 Align	DICER-1	Query: 3' agUGUUCAAUCCCAGAGUCCCu 5' |||| || |:||||| Ref: 5' caACAAAAGAGCCUUUCAGGGa 3'	-18.860001 kCal/Mol
mmu-miR-125b-5p	436 to 457 Align	DICER-1	Query: 3' aguguucaauccCAGAGUCCCu 5' | ||||||| Ref: 5' ugcuugaacacuGGCUCAGGGa 3'	-19.320000 kCal/Mol
mmu-miR-125b-1-3p	2196 to 2217 Align	DICER-1	Query: 3' ucGAGGGUUCUCGGAUUGGGCa 5' |||||| |: ||||| Ref: 5' agCUCCCAAAUGUAGAACCCGa 3'	-30.410000 kCal/Mol
mmu-miR-125b-2-3p	5420 to 5437 Align	DICER-1	Query: 3' ucCAGGGUUCUUGGACUGAACa 5' |||:::| ||||||| Ref: 5' ggGUCUUGA----CUGACUUGc 3'	-20.809999 kCal/Mol
mmu-miR-125b-2-3p	686 to 705 Align	DICER-1	Query: 3' ucCAGGGUUCUUGGACUGAACa 5' ||:|: | | |||||| Ref: 5' agGUUCUCAUUA--UGACUUGc 3'	-18.379999 kCal/Mol
mmu-miR-125b-2-3p	9542 to 9563 Align	DICER-1	Query: 3' ucCAGGGUUCUUGGACUGAACa 5' | ||: ||||::|| |||| Ref: 5' auGGCCUCAGAAUUUGCCUUGg 3'	-19.620001 kCal/Mol
hsa-miR-125b-1-3p	1992 to 2013 Align	DICER-1	Query: 3' ucGAGGGUUCUCGGAUUGGGCa 5' ||||:|| || ||||| Ref: 5' agCUCCUAAAUGCAGAACCCGa 3'	-30.240000 kCal/Mol
hsa-miR-125b-1-3p	5471 to 5490 Align	DICER-1	Query: 3' ucGAGGGUUCUCGGAUUGGGCa 5' || |||| | ::||:|||| Ref: 5' aaCUGCCAA-A-UUUAGCCCGg 3'	-21.670000 kCal/Mol
hsa-miR-125b-5p	232 to 253 Align	DICER-1	Query: 3' aguguucaauccCAGAGUCCCu 5' | ||||||| Ref: 5' uguuuaaacacuGGCUCAGGGa 3'	-19.320000 kCal/Mol
hsa-miR-125b-2-3p	4597 to 4618 Align	EGFR	Query: 3' caggguucUCGGACUGAACAcu 5' || ||||||||| Ref: 5' ugagcguuAGACUGACUUGUuu 3'	-17.200001 kCal/Mol
mmu-miR-125b-2-3p	4835 to 4856 Align	ERBB2	Query: 3' uccaggguucuUGGACUGAACa 5' |: ||||||| Ref: 5' agagcauugccAUGUGACUUGu 3'	-13.920000 kCal/Mol
hsa-miR-125a-3p	3413 to 3434 Align	ERBB3	Query: 3' ccGAGGGUUCUUGGAGUGGACa 5' ||:::||| | |||:||| Ref: 5' gcCUUUUAAGUCCAUCAUCUGg 3'	-21.350000 kCal/Mol
hsa-miR-125a-5p	4144 to 4167 Align	ERBB3	Query: 3' agUGUCCAAUUUCCCAGAGUCCCu 5' | || | |:|| |:|||||| Ref: 5' gaAGAGAUGAGAGCUUUUCAGGGg 3'	-18.629999 kCal/Mol
hsa-miR-125a-5p	4308 to 4331 Align	ERBB3	Query: 3' aguguccaauuuCCCAGAGUCCCu 5' || ||||||| Ref: 5' ccugcucccuguGGCACUCAGGGa 3'	-17.340000 kCal/Mol
hsa-miR-125b-2-3p	2753 to 2773 Align	GLI1	Query: 3' caGGGUUCUCGGACUGAACACu 5' |:||| ||: :||||| Ref: 5' agCUCAAG-GCUCAGCUUGUGu 3'	-22.080000 kCal/Mol
mmu-miR-125b-5p	807 to 828 Align	GLI1	Query: 3' aguGUUCAAUCCCAGAGUCCCu 5' :| || ||||| |||| Ref: 5' cuuUAUGUCAGGGUCCCAGGGu 3'	-23.280001 kCal/Mol
hsa-miR-125a-3p	4974 to 4995 Align	IGF2	Query: 3' ccgaggguuCUUGGAGUGGACa 5' |||: ||||||| Ref: 5' ccaaacacuGAAUGUCACCUGu 3'	-19.850000 kCal/Mol
hsa-miR-125a-3p	4942 to 4962 Align	IGF2	Query: 3' ccGAGGGUUCUUGGAGUGGACa 5' ||||: | | ||||||| Ref: 5' ccCUCCUCUG-CCAUCACCUGa 3'	-22.629999 kCal/Mol

mmu-miR-125a-3p	3524 to 3545 Align	IGF2	Query: 3' ccgaggguucuUGGAGUGGACa 5' |: ||||||| Ref: 5' ucgaacgccauAUGUCACCUGu 3'	-19.240000 kCal/Mol
mmu-miR-125a-3p	1390 to 1410 Align	IGF2	Query: 3' ccgAGGGUUCUUGGAGUGGACa 5' |||||| ||:||||:| Ref: 5' cagUCCCAA-AAUCUCACUUuu 3'	-21.799999 kCal/Mol
mmu-miR-125a-5p	3315 to 3338 Align	IGF2	Query: 3' agUGUCCAAUUUCCCAGAGUCCCu 5' :::|| |::: | |:|||||| Ref: 5' ucGUGGGAUGGGUGCUUUCAGGGg 3'	-26.150000 kCal/Mol
hsa-miR-125b-5p	612 to 633 Align	IL16	Query: 3' agUGUUCAAUCCCA-GAGUCCCu 5' :|||| || || |||:||| Ref: 5' gaGCAAG-UACUGUCCUCGGGGu 3'	-20.370001 kCal/Mol
mmu-miR-125b-2-3p	2452 to 2474 Align	IRF4	Query: 3' uccAGGG-UUCUUGGACUGAACa 5' |||| ||||::|| ||||| Ref: 5' gaaUCCCAAAGAGUCUCACUUGc 3'	-23.000000 kCal/Mol
hsa-miR-125b-5p	2057 to 2078 Align	IRF-4	Query: 3' aguguucaaucccAGAGUCCCu 5' |||||||| Ref: 5' ugucugugccauuUCUCAGGGa 3'	-16.790001 kCal/Mol
hsa-miR-125b-2-3p	735 to 755 Align	IRF-4	Query: 3' caggGUUCUCGGACUGAACACu 5' |||| ||| :|||||| Ref: 5' cuggCAAG-GCCCAGCUUGUGa 3'	-22.209999 kCal/Mol
hsa-miR-125b-2-3p	2596 to 2617 Align	ITCH	Query: 3' caGGGUUCUCGGACUGAACAcu 5' ||||: |||| |||||| Ref: 5' uaCCCAGAAGCCAUACUUGUuu 3'	-22.889999 kCal/Mol
hsa-miR-125b-5p	5923 to 5944 Align	KLF13	Query: 3' aguguucAAUCCCAGAGUCCCu 5' ||| || |||||| Ref: 5' agcuuucUUAAGGCCUCAGGGu 3'	-17.750000 kCal/Mol
hsa-miR-125b-5p	1433 to 1454 Align	KLF13	Query: 3' aguguucaaucccAGAGUCCCu 5' |||||||| Ref: 5' guugaaccccccuuUCUCAGGGa 3'	-16.520000 kCal/Mol
hsa-miR-125b-5p	3463 to 3483 Align	KLF13	Query: 3' agUGUUCAAUCCCAGAGUCCCu 5' ||| ||| |||||||| Ref: 5' auACAUUUUA-UGUCUCAGGaa 3'	-17.230000 kCal/Mol
hsa-miR-125b-2-3p	2653 to 2674 Align	KLF13	Query: 3' caggguuCUCGGACUGAACACu 5' || || |:|||||| Ref: 5' gaguguuGACCCAGGCUUGUGg 3'	-18.150000 kCal/Mol
hsa-miR-125b-5p	1531 to 1552 Align	LIN28A	Query: 3' aguguucaaucccAGAGUCCCu 5' |||||||| Ref: 5' gguacaugagcaaUCUCAGGGa 3'	-21.000000 kCal/Mol
hsa-miR-125b-5p	3864 to 3885 Align	MCL1	Query: 3' aguguucaaucccAGAGUCCCu 5' |||||||| Ref: 5' ugucuuacgcuucUCUCAGGGa 3'	-17.770000 kCal/Mol
hum-miR-125b-5p	936 to 957 Align	MLF2	Query: 3' aguguucAAUCCCAGAGUCCCu 5' | :||||||||||| Ref: 5' cucucccUGGGGGUCUCAGGGa 3'	-28.330000 kCal/Mol
hum-miR-125b-5p	697 to 718 Align	MLF2	Query: 3' agUGUUCAAUCCCAGAGUCCCu 5' :|:: ||: | ||||||| Ref: 5' cgGCGGCUUGAGUCCUCAGGGg 3'	-19.400000 kCal/Mol
hsa-miR-125a-3p	1067 to 1088 Align	MLF2	Query: 3' ccGAGGGUUCUUGGAGUGGACa 5' ||:| || |||||||| Ref: 5' auCUUCAAACCCCCUCACCUuu 3'	-18.980000 kCal/Mol
hsa-miR-125a-5p	934 to 957 Align	MLF2	Query: 3' aguguccaauUUCCCAGAGUCCCu 5' ::||||||||||| Ref: 5' accucucccuGGGGGUCUCAGGGa 3'	-28.700001 kCal/Mol
hsa-miR-125b-1-3p	1041 to 1061 Align	NFKB1	Query: 3' ucgagggUUCUCGGAUUGGGCa 5' ||||| ||||:||| Ref: 5' cgggaaaAAGAG-CUAAUCCGc 3'	-19.049999 kCal/Mol
hsa-miR-125b-5p	3624 to 3645 Align	NOTCH1	Query: 3' aguguucaaUCCCAGAGUCCCu 5' :|| ||||||| Ref: 5' cugcccacgGGGCACUCAGGGu 3'	-22.290001 kCal/Mol

hsa-miR-125b-5p	9061 to 9082 Align	NOTCH1	Query: 3' aguguucaaucccaGAGUCCCu 5' Ref: 5' ugccgccugcacucCUCAGGGc 3'	-15.200000 kCal/Mol
hsa-miR-125b-1-3p	409 to 430 Align	NOTCH1	Query: 3' ucgAGGGUUCUCGGAUUGGGCa 5' Ref: 5' ucgUGCCAGCAGGCUGACCCGu 3'	-26.410000 kCal/Mol
hsa-miR-125b-1-3p	166 to 187 Align	NOTCH1	Query: 3' ucgAGGGUUCUCGGAUUGGGCa 5' Ref: 5' cgaUGCCAGGACCCCAACCCGu 3'	-25.600000 kCal/Mol
hsa-miR-125b-1-3p	5926 to 5946 Align	NOTCH1	Query: 3' ucGAGGGUUCUCGGAUUGGGCa 5' Ref: 5' guCUUCC-AGAUCCUGAUCCGg 3'	-27.559999 kCal/Mol
hsa-miR-125b-5p	1418 to 1439 Align	PPP1CA	Query: 3' aguguucaaucCCAGAGUCCCu 5' Ref: 5' cagccgugcuuGGCCUCAGGGc 3'	-17.920000 kCal/Mol
hsa-miR-125b-5p	1372 to 1392 Align	PPP1CA	Query: 3' agugUUCAAUCCCAGAGUCCCu 5' Ref: 5' gccgAGGCUGCAG-CUCAGGGc 3'	-19.910000 kCal/Mol
mmu-miR-125b-5p	1241 to 1262 Align	PPP1CA	Query: 3' aguGUUCAAUCCCAGAGUCCCu 5' Ref: 5' ggcCAAGGCUGCAGCUCAGGGc 3'	-19.969999 kCal/Mol
hsa-miR-125b-2-3p	1977 to 1998 Align	PPP2CA	Query: 3' caggguucucggacUGAACACu 5' Ref: 5' guuuuucauaauaaACUUGUGa 3'	-12.400000 kCal/Mol
rno-mir-125a	1023 to 1046 Align	PTGES2	Query: 3' aguguccaAUUUCCCAGAGUCCCu 5' Ref: 5' ucaagaccUACCUGGUUUCAGGGc 3'	-19.209999 kCal/Mol
mmu-miR-125b-1-3p	275 to 296 Align	PUMA	Query: 3' ucgagggUUCUCGGAUUGGGCa 5' Ref: 5' gcccguaGAGGGUCUAGCCCGc 3'	-31.180000 kCal/Mol
hsa-miR-125b-2-3p	901 to 921 Align	RAF1	Query: 3' caGGGUUCUCGGACUGAACACu 5' Ref: 5' auUUCGA-UGUCAGACUUGUGg 3'	-21.180000 kCal/Mol
hsa-miR-125b-5p	1760 to 1780 Align	RAF1	Query: 3' aguguucaaUCCCAGAGUCCCu 5' Ref: 5' gcccggcagACGG-CUCAGGGa 3'	-18.910000 kCal/Mol
hsa-miR-125a-5p	1758 to 1780 Align	RAF1	Query: 3' aguguccaaUUUCCCAGAGUCCCu 5' Ref: 5' uugcccggcAGACGG-CUCAGGGa 3'	-20.709999 kCal/Mol
hsa-miR-125a-5p	2987 to 3010 Align	RAF1	Query: 3' aguguccaauuuucccAGAGUCCCu 5' Ref: 5' uccgcaucucagcccUCUCAGGGa 3'	-19.610001 kCal/Mol
rno-miR-125b-5p	1649 to 1670 Align	Slc35c2	Query: 3' agGUUUCAAUCCCAGAGUCCCu 5' Ref: 5' agGUGAGGUAGUUUCUCAGGuu 3'	-15.490000 kCal/Mol
rno-mir-125a	1811 to 1834 Align	Slc35c2	Query: 3' agugUCCAAUUUCCCAGAGUCCCu 5' Ref: 5' ucugAGGAUAAAGGGUCUGGGGGu 3'	-30.920000 kCal/Mol
mmu-miR-125b-5p	453 to 473 Align	ST18	Query: 3' aguguucaaUCCCAGAGUCCCu 5' Ref: 5' ucugaucccAGAG-CUCAGGGu 3'	-17.350000 kCal/Mol
hsa-miR-125b-5p	167 to 188 Align	ST18	Query: 3' agUGUUCAAUCCCAGAGUCCCu 5' Ref: 5' uaACUGAAUGUGACCUCAGGGg 3'	-15.120000 kCal/Mol
hsa-miR-125b-5p	3954 to 3973 Align	STAT3	Query: 3' aguGUUCAAUCCCAGAGUCCCu 5' Ref: 5' uguCUGGUUGAG--CUCAGGGa 3'	-19.530001 kCal/Mol
hsa-miR-125b-5p	2220 to 2241 Align	TP53	Query: 3' agUGUUCAAUCCCAGAGUCCCu 5' Ref: 5' agACUUGUUUUAUGCUCAGGGu 3'	-18.690001 kCal/Mol

hsa-miR-125b-5p	1526 to 1545 Align	TP53INP1	Query: 3' agUGUUCAAUCCCAGAGUCCCu 5' Ref: 5' caAAAAUUUA--UUCUCAGGGu 3'	-15.010000 kCal/Mol
hsa-miR-125a-5p	1522 to 1545 Align	TP53INP1	Query: 3' aguguccaauuucccAGAGUCCCu 5' Ref: 5' caagcaaaaauuuauUCUCAGGGu 3'	-15.010000 kCal/Mol

Supplementary Table: 2. Prediction of miRNA binding site with target genes by using miRanda algorithm. The Table showing miR-125–binding site with target mRNA and binding energy query representing miR-125, ref representing sequence of target mRNA.