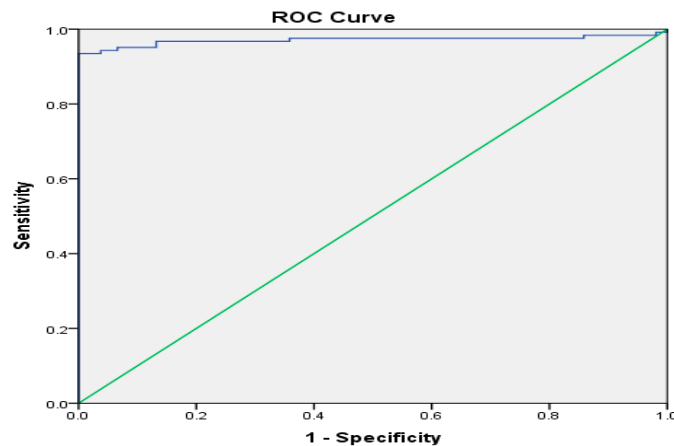
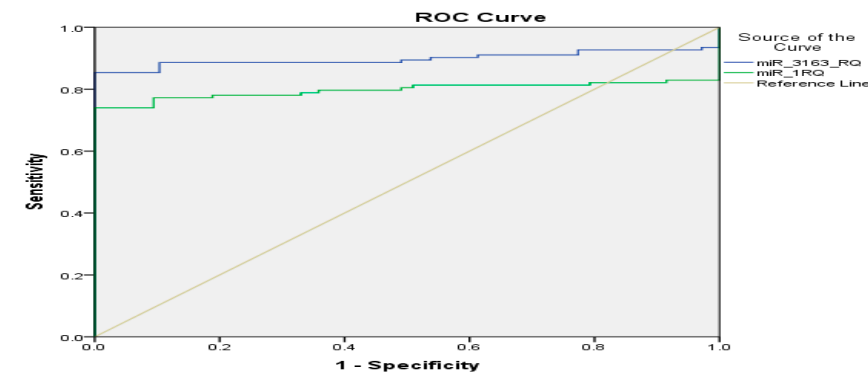


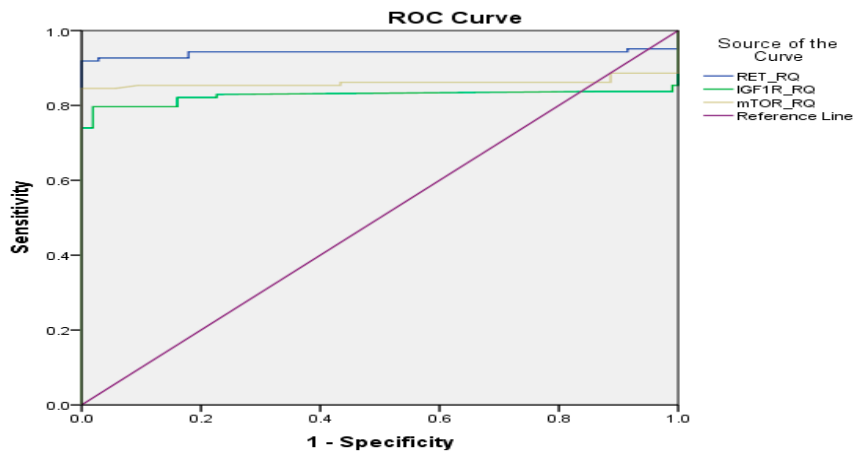
figure S1: ROC curve analysis for differential expression of investigated network panel between T2DM and control



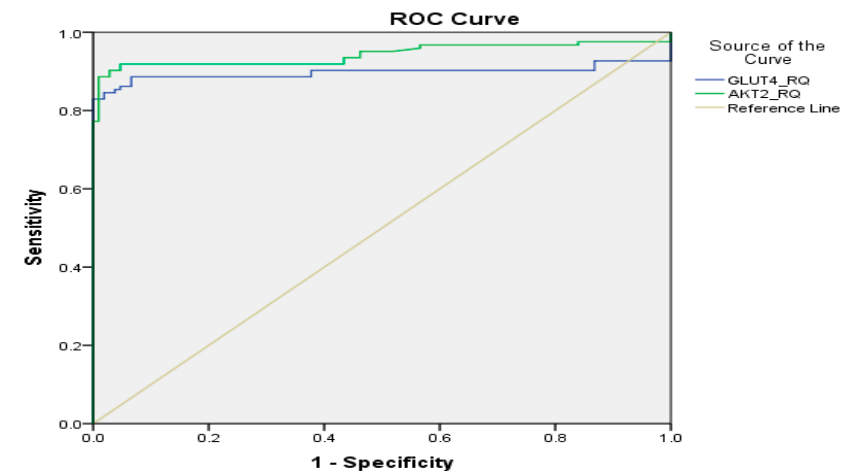
ROC curve of *RP11-773H22.4 lncRNA* (AUC: 0.971, 95% CI: 0.944-0.998, $P < 0.01$).



ROC curve of *miR-3163 miRNA* (AUC: 0.898, 95% CI: 0.848-0.948, $P < 0.01$). and *mir-1* (AUC: 0.797, 95% CI: 0.729-0.865, $P < 0.01$)



ROC curve for *RET mRNA* (AUC: 0.941, 95% CI: 0.900-0.981, $P < 0.01$), *IGF1-R* (AUC: 0.826, 95% CI: 0.761-0.892, $P < 0.01$) and *m-TOR* (AUC : 0.860, 95% CI: 0.800-0.920, $P < 0.01$).



ROC curve for *GLUT4 mRNA* (AUC: 0.897, (95% CI: 0.846-0.948, $P < 0.01$), *AKT-2* (AUC: 0.943, 95% CI: 0.908-0.978, $P < 0.01$).

Table S1: Comparison between lymphocytes' count and viability among the 3 investigated cell line groups:

Dependent Variable	(I) Cell Lines	(J) Cell Lines	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Lymphocytes Count (x10*4)	T2DM lymphocytes without Cas9 editing	T2DM lymphocytes with Cas9 editing	5.000	2.735	NS .117	-1.69	11.69
		Healthy Control lymphocytes	-6.667	2.735	.051	-13.36	.03
	T2DM lymphocytes with Cas9 editing	T2DM lymphocytes without Cas9 editing	-5.000	2.735	NS .117	-11.69	1.69
		Healthy Control lymphocytes	-11.667*	2.735	.005**	-18.36	-4.97

	Healthy Control lymphocytes	T2DM lymphocytes without Cas9 editing	6.667	2.735	.051	-.03	13.36
		T2DM lymphocytes with Cas9 editing	11.667*	2.735	.005**	4.97	18.36
Lymphocytes Viability (%)	T2DM lymphocytes without Cas9 editing	T2DM lymphocytes with Cas9 editing	1.5000	.6242	.053	-.027	3.027
		Healthy Control lymphocytes	-1.6333*	.6242	.040*	-3.161	-.106
	T2DM lymphocytes with Cas9 editing	T2DM lymphocytes without Cas9 editing	-1.5000	.6242	.053	-3.027	.027
		Healthy Control lymphocytes	-3.1333*	.6242	.002**	-4.661	-1.606
	Healthy Control lymphocytes	T2DM lymphocytes without Cas9 editing	1.6333*	.6242	.040*	.106	3.161
		T2DM lymphocytes with Cas9 editing	3.1333*	.6242	.002**	1.606	4.661

One-way ANOVA, Post Hoc test, p: NS, not significant (>0.05), **p < 0.01: is highly significant, *p<0.05: is significant.

figure S2(a): Expression of *RET mRNA* in insulin resistance and T2DM in Gene Atlas Database. Snapshot shows the expression of *RET* gene in T2DM (*available at <https://www.ebi.ac.uk>*) accessed on 9th of June 2017.

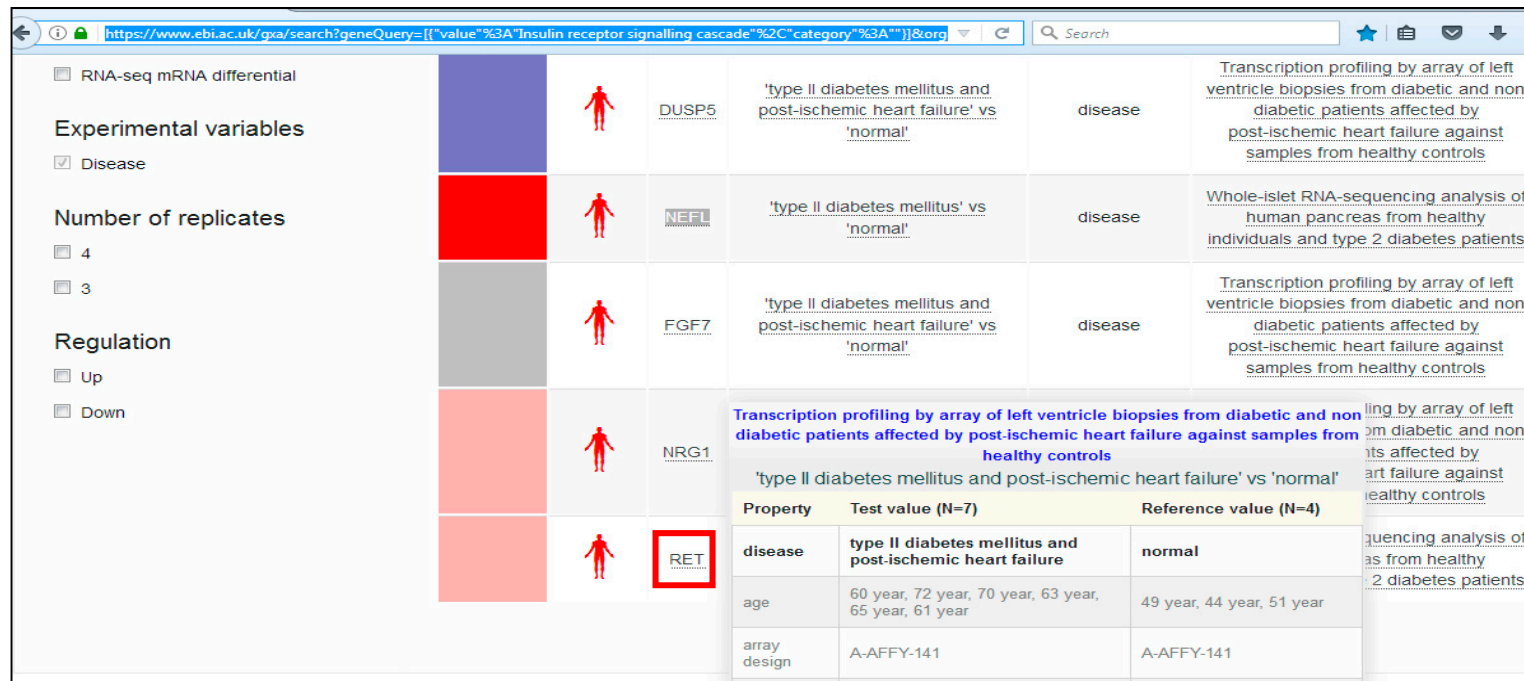


figure S2(b): Differential expression of *RET* mRNA in normal adipose and skeletal muscle in Protein Atlas Database . Snapshot shows the expression of *RET* mRNA in normal skeletal muscle and adipose tissue (available at <https://www.proteinatlas.org/>) accessed on 6th of September 2017.

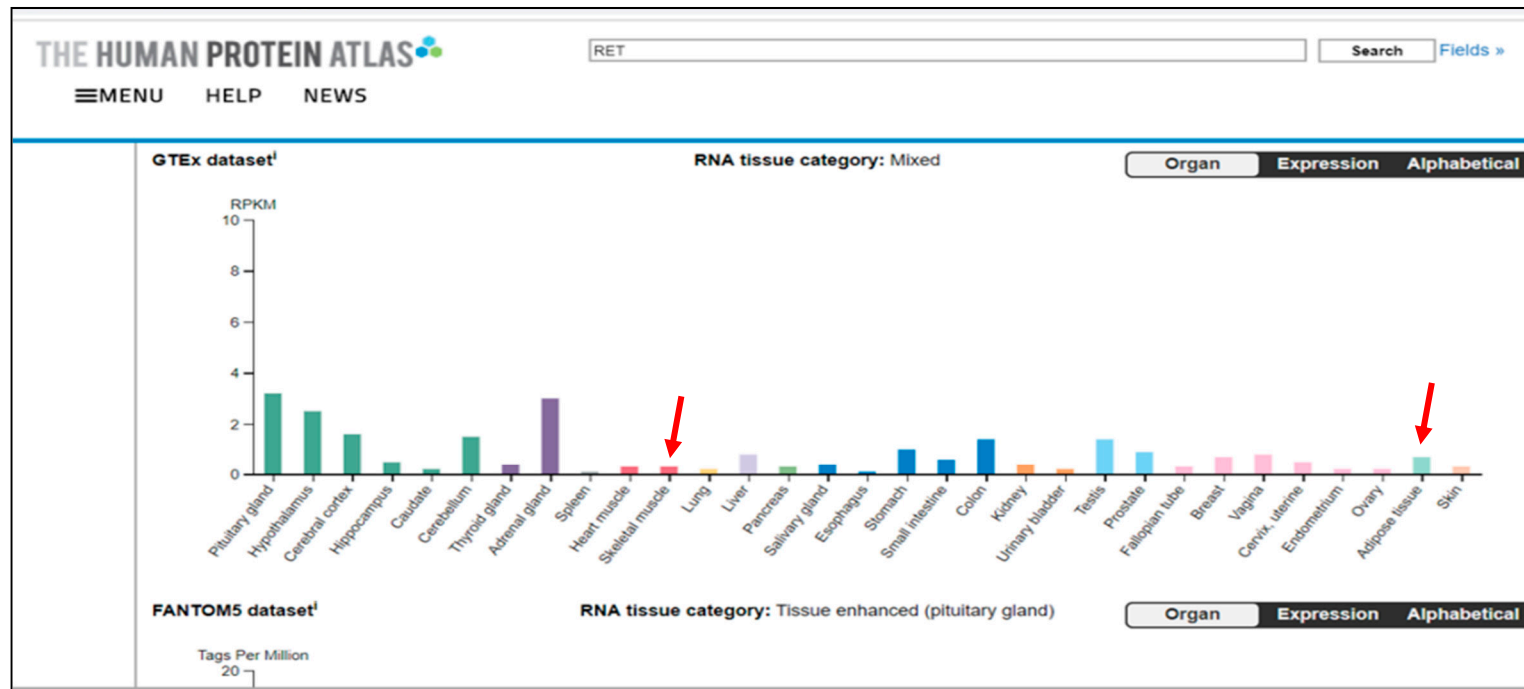


figure S2(c): Verification of expression of *RET* mRNA in normal skeletal muscle, adipose tissue and in WBCs. Snapshot shows the verification of expression of *RET* mRNA in normal skeletal muscle and adipose tissue and in WBCs (*available at <https://www.genecards.org/>*)

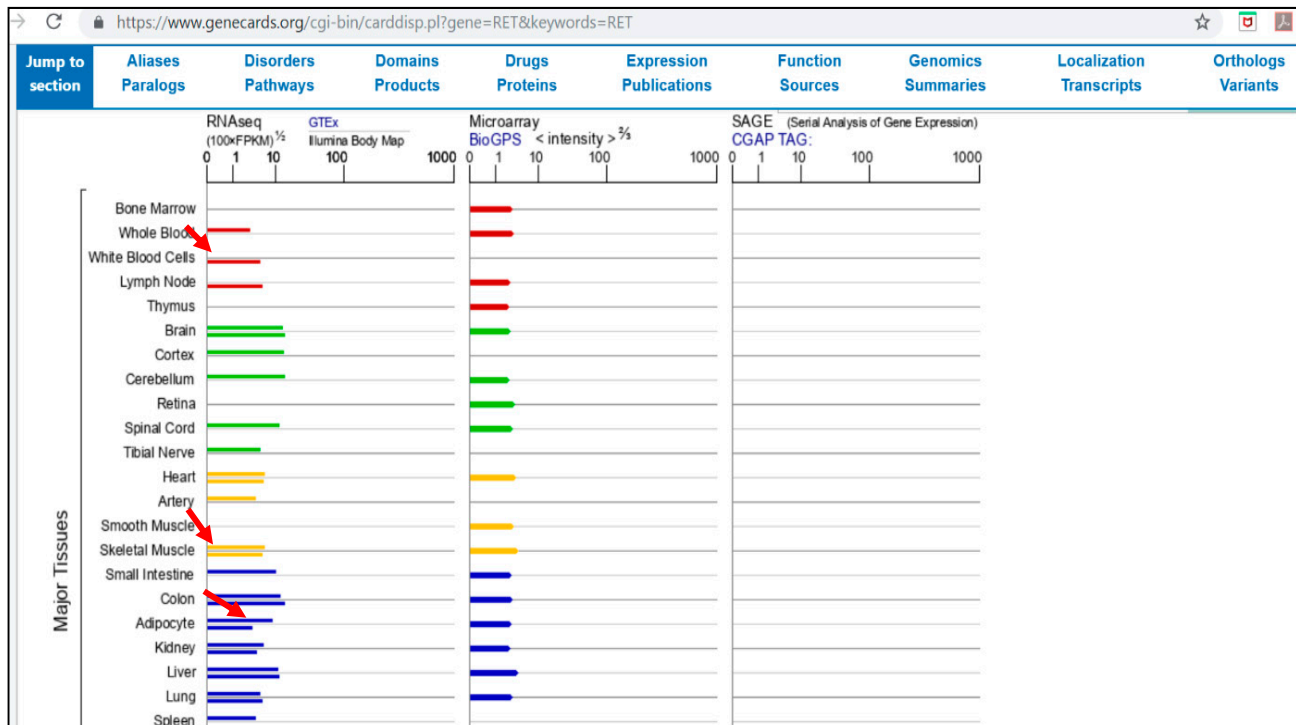


figure S2(d): Expression of *mTOR* mRNA in insulin resistance and T2DM in Gene Atlas Database (figure 4s). Snapshot shows the expression of *mTOR* gene in IR (*available at <https://www.ebi.ac.uk>*)

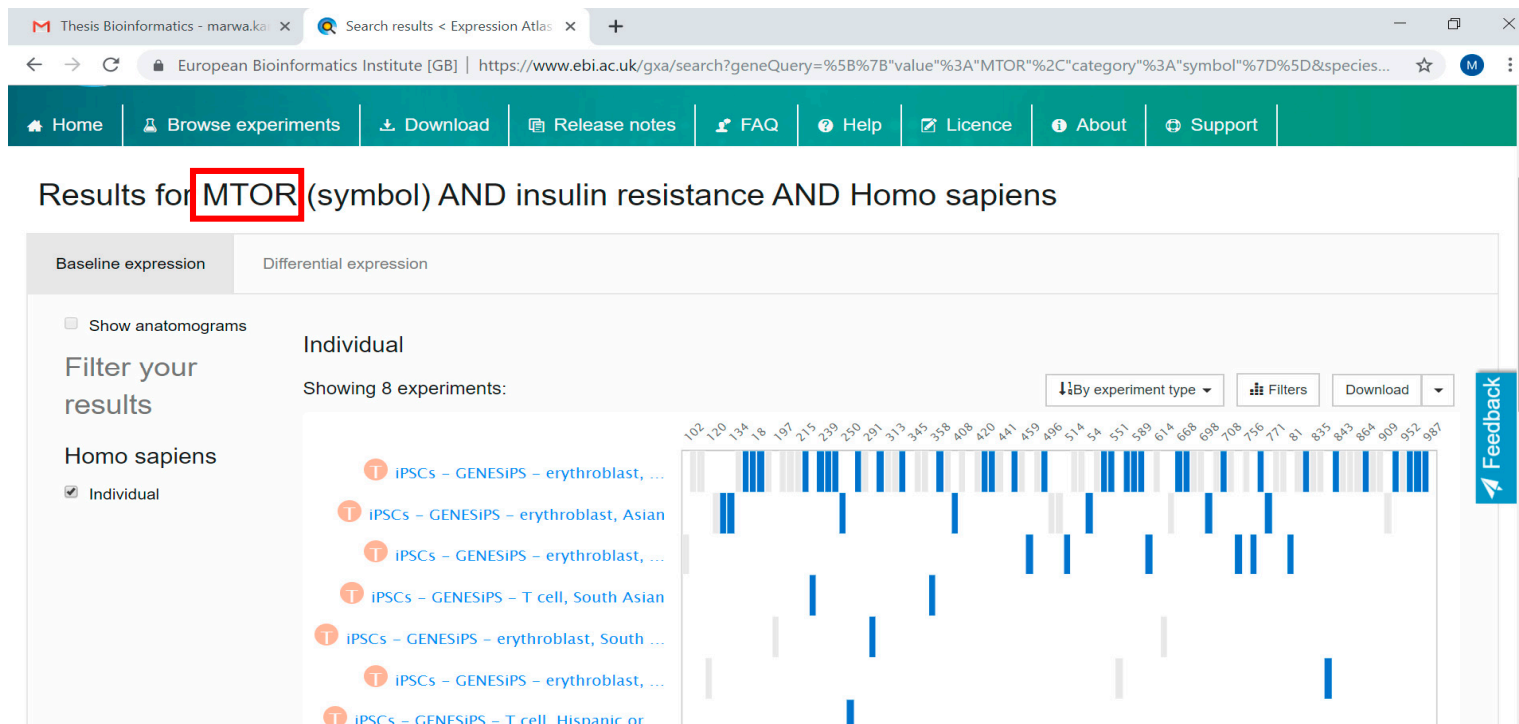


figure S2(e): k map and string map show involvement of *mTOR* gene in insulin signaling pathway and its relation to *RET* gene in insulin resistance in T2DM. Snapshot verifying that the identified *mTOR* gene is linked to IR in T2DM (*available at <http://www.kegg.jp/>*)

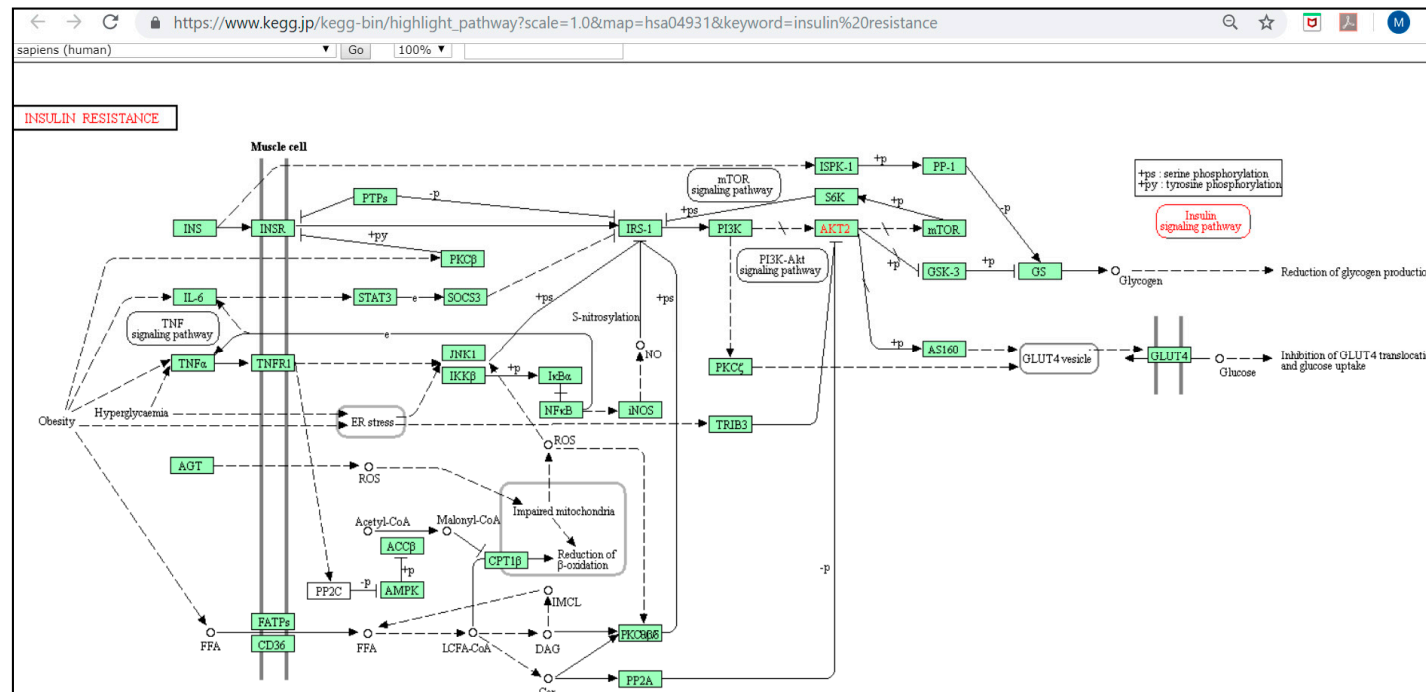


figure S2(f): Snapshot shows verification of the identified candidate genes interaction in the pathogenesis of IR in T2DM (available at: <http://string-db.org/>)

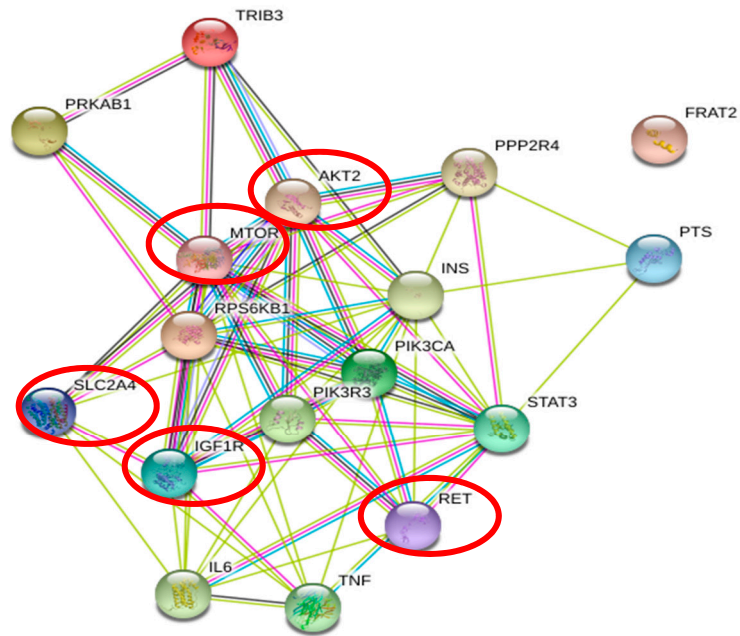


figure S2(g): Retrieval of long non-coding RNA *LncRNA-RP11-773H22.4* and the associated miRNAs: *miR-3163* & *miR-1* that acting as ceRNAs for *RET* mRNA through Database of LncRNA acting as competing endogenous. Snapshot shows search for *LncRNA-RP11-773H22.4*(ENSG00000266969) and *miR-3163* miRNA (available at <http://gyanxet-beta.com/lncdb/index.php>) accessed on 18th of July 2017.

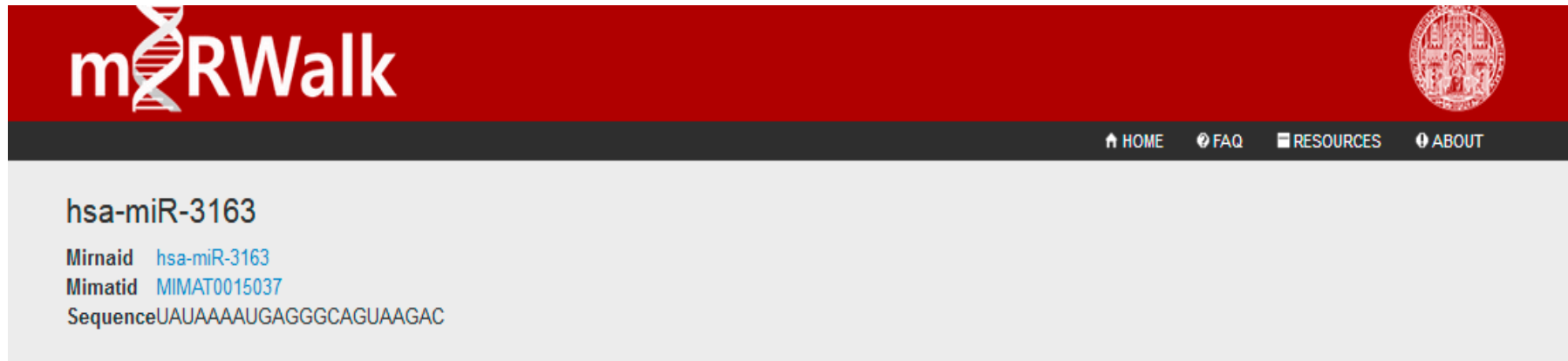
HOME BROWSE DOWNLOAD FAQ CONTACT US FEEDBACK						
Resulting ceRNAs for the mRNA NM_020975(RET)						
The ceRNAs are sorted according to the number of shared miRNAs. The ceRNA score (calculated from the ratio of shared MREs with the total number of regulating MREs) gives the likelihood of the pair for being ceRNAs. Click the serial number of any entry to view the expression heatmap of the lncRNA-mRNA pair. Click the lncRNA or mRNA transcript id to view all miRNA target sites of that transcript.						
Showing results 1 to 30 of 654						
Page 1 of 22						
Serial no.	lncRNA transcript_id	mRNA Accession	Number of common miRNAs	ceRNA score	P-value	common miRNAs
1	ENST0000058585.1	NM_020975	3	0.375	0.301066871362	hsa-miR-128, hsa-miR-3163, hsa-miR-885-5p.
2	ENST00000586787.1	NM_020975	3	0.375	0.197570199090	hsa-miR-128, hsa-miR-4312, hsa-miR-885-5p.
3	ENST00000549854.2	NM_020975	3	0.375	0.606013058817	hsa-miR-128, hsa-miR-3163, hsa-miR-885-5p.
4	ENST00000584772.1	NM_020975	3	0.375	0.311418832516	hsa-miR-128, hsa-miR-3163, hsa-miR-885-5p.
5	ENST00000577287.1	NM_020975	3	0.375	0.334425541818	hsa-miR-128, hsa-miR-3163, hsa-miR-885-5p.
6	ENST00000429988.2	NM_020975	3	0.375	0.576246393802	hsa-miR-128, hsa-miR-3163, hsa-miR-885-5p.
7	ENST00000583712.1	NM_020975	3	0.375	0.079405444990	hsa-miR-128, hsa-miR-3163, hsa-miR-4312.

HOME BROWSE DOWNLOAD FAQ CONTACT US FEEDBACK						
636	ENST00000580022.1	NM_020975	1	0.125	0.742223270147	hsa-miR-3163.
637	ENST00000581080.1	NM_020975	1	0.125	0.635840286825	hsa-miR-3163.
638	ENST00000581719.1	NM_020975	1	0.125	0.854628916757	hsa-miR-3163.
639	ENST00000582527.1	NM_020975	1	0.125	0.883395048378	hsa-miR-3163.
640	ENST00000583138.1	NM_020975	1	0.125	0.331510826388	hsa-miR-3163.
641	ENST00000584382.1	NM_020975	1	0.125	0.894852455022	hsa-miR-3163.
642	ENST00000584805.1	NM_020975	1	0.125	0.908090519951	hsa-miR-3163.
643	ENST00000585381.1	NM_020975	1	0.125	0.429288963975	hsa-miR-3163.
644	ENST00000586053.1	NM_020975	1	0.125	0.514542529301	hsa-miR-3163.
645	ENST00000586727.1	NM_020975	1	0.125	0.465318880983	hsa-miR-3163.
646	ENST00000587344.1	NM_020975	1	0.125	0.92550339304	hsa-miR-3163.
647	ENST00000588211.1	NM_020975	1	0.125	0.265688769353	hsa-miR-3163.
648	ENST00000588900.1	NM_020975	1	0.125	0.488074106037	hsa-miR-3163.
649	ENST00000589040.1	NM_020975	1	0.125	0.464411816257	hsa-miR-3163.
650	ENST00000590739.1	NM_020975	1	0.125	0.482244262612	hsa-miR-3163.
651	ENST00000591368.1	NM_020975	1	0.125	0.548582114311	hsa-miR-3163.
652	ENST00000594810.1	NM_020975	1	0.125	0.417233159017	hsa-miR-3163.

figure S2(h): Snapshot shows identification of *miR-1* miRNA related to *LncRNA-RP11-773H22.4* in T2DM (available at <http://gyanxet-beta.com/lncedb/index.php>) accessed on 18th of July 2017.

HOME BROWSE DOWNLOAD FAQ CONTACT US FEEDBACK					
miRNA targets on lncRNA RP11-773H22.4 (ENST00000588211.1)					
Showing results 1 to 30 of 88					
Serial no.	miRNA Name	Target	Number of target sites	miRNA seed type	Predicted from Ago interaction sites
1	hsa-miR-1	ENST00000588211.1	1	6-mer,	no
2	hsa-miR-101-5p	ENST00000588211.1	1	6-mer,	no
3	hsa-miR-1193	ENST00000588211.1	1	7-merm8,	no
4	hsa-miR-1224-5p	ENST00000588211.1	1	7-merA1,	no
5	hsa-miR-1234-3p	ENST00000588211.1	1	6-mer,	no
6	hsa-miR-1290	ENST00000588211.1	1	6-mer,	no
7	hsa-miR-1292-5p	ENST00000588211.1	1	7-merm8,	no
8	hsa-miR-1299	ENST00000588211.1	1	7-merm8,	no
9	hsa-miR-145-5p	ENST00000588211.1	1	8-mer,	no

figure S2(i): Verification of *miR-3136* and *miR-1* *miRNAs* that act as epigenetic regulators for *RET* and *mTOR mRNAs* in IR in T2DM. Snapshot shows identification of *m-TOR mRNA* related to *miR-3163miRNA* in IR and in T2DM (available at <http://mirwalk.umm.uni-heidelberg.de/>) accessed on 23rd of December 2017.



hsa-miR-3163

Mirnaid [hsa-miR-3163](#)
Mimatid [MIMAT0015037](#)
Sequence [UAUAAAUGAGGGCAGUAAGAC](#)

Interactions:

Mirna	Ensemblid	Genesymbol	Score	Position	Binding Site	Au	Me	N Pairings	Targetscan	Mirdb	Mirtarbase
hsa-miR-3163	ENST00000270776	PGD	0.92	CDS	1390,1408	0.47	-19.424	14	—	—	—
hsa-miR-3163	ENST00000377036	DFFA	0.92	3UTR	2141,2154	0.53	-16.49	12	—	—	—
hsa-miR-3163	ENST00000377022	CASZ1	0.92	CDS	2963,3003	0.34	-17.11	10	—	—	—
hsa-miR-3163	ENST00000344008	CASZ1	0.92	CDS	2963,3003	0.34	-17.11	10	—	—	—
hsa-miR-3163	ENST00000376936	EXOSC10	1.00	CDS	2136,2174	0.48	-17.11	13	—	—	—
hsa-miR-3163	ENST00000361445	MTOR	1.00	CDS	1664,1674	0.37	-17.11	9	—	—	—
hsa-miR-3163	ENST00000361445	MTOR	0.92	CDS	1331,1344	0.47	-17.11	12	—	—	—
hsa-miR-3163	ENST00000294484	DISP3	0.92	CDS	1555,1569	0.43	-16.623	12	—	—	—
hsa-miR-3163	ENST00000376770	FBXO44	1.00	5UTR	323,347	0.48	-6.515	13	—	—	—
hsa-miR-3163	ENST00000376768	FBXO44	0.92	3UTR	1457,1474	0.35	-17.11	10	—	—	—
hsa-miR-3163	ENST00000376590	MTHFR	0.85	3UTR	2922,2935	0.43	-14.908	12	—	—	—
hsa-miR-3163	ENST00000376590	MTHFR	0.85	CDS	616,628	0.35	-19.935	10	—	—	—

figure S2(j): Verification of expression of *LncRNA-RP11-773H22.4* in normal skeletal muscle, adipose tissue and in WBCs. Snapshot shows the verification of expression of *LncRNA-RP11-773H22.4* or ENSG00000266969 in normal skeletal muscle, adipose tissue and in WBCs (available at <http://www.noncode.org/>)

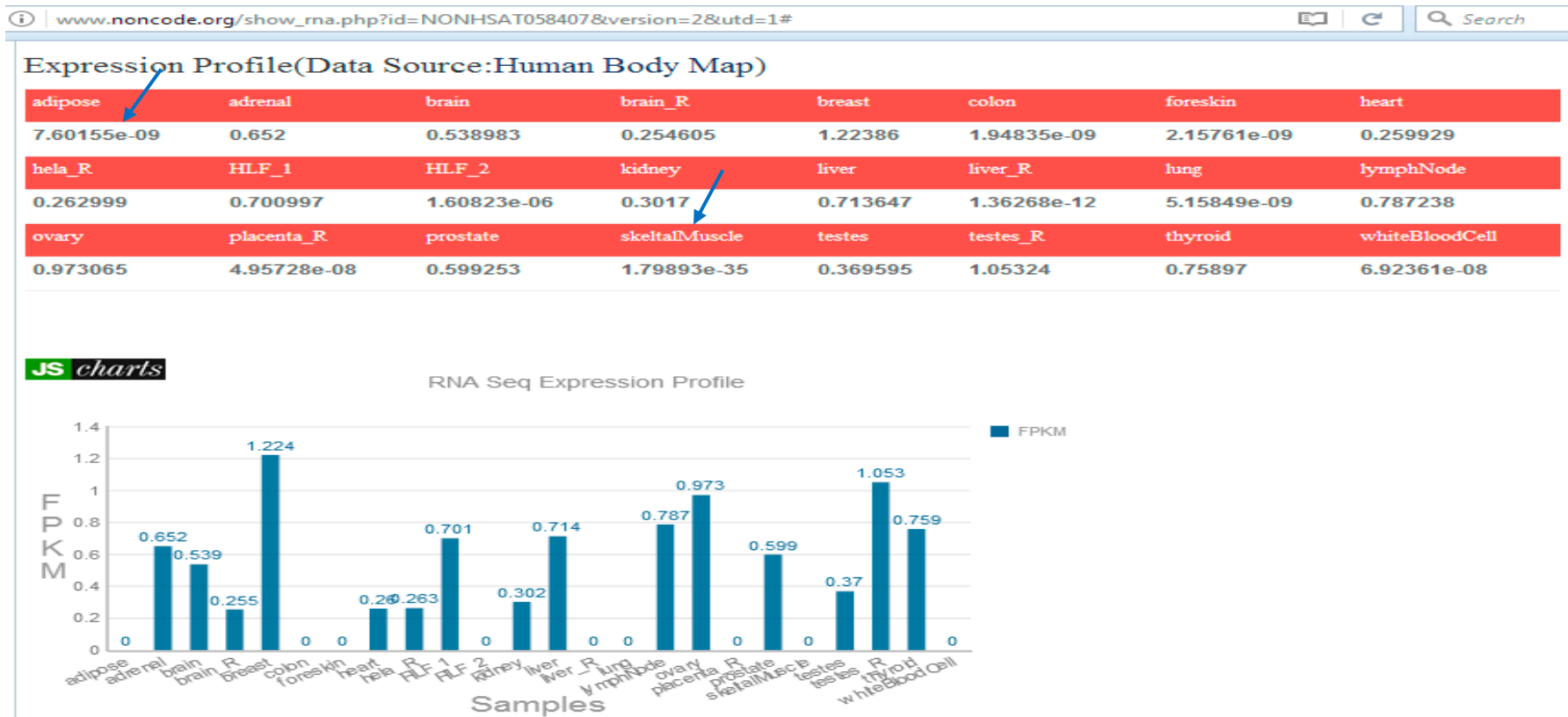
Isoforms

Transcript ID

Data Sources

Source Name	Old Id
PMID26117828	PNCT_HSA052403
NAME	RP11-773H22.4
ensembl	ENST00000588211
PMID26117828	TCONS_00018126
gencode	ENST00000588211.1
NONCODEv4	NONHSAT058407
Incipedia	lnc-PTPN2-6-1_dup1

figure S2(k): Verification of expression of *miR-3163* miRNA in normal skeletal muscle and adipose tissue.



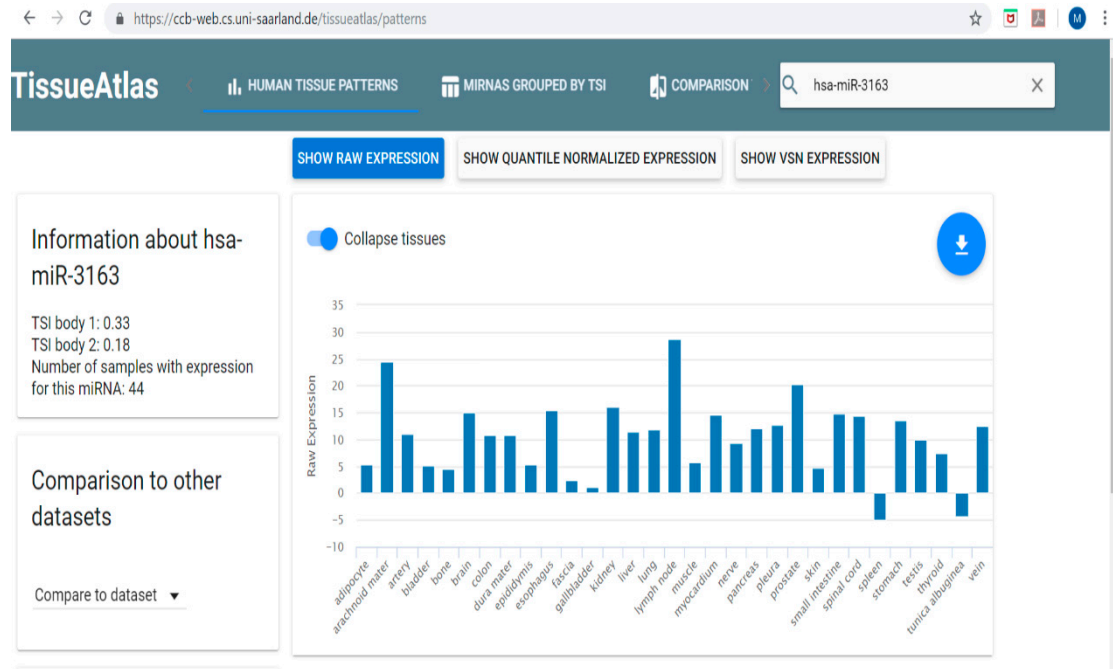


figure S2(l): Alignment between *LncRNA-RP11-773H22.4* and *miR-3163 miRNA* (available at <https://www.ebi.ac.uk>)

<div><div>← → ↺ 🏠</div><div>🔒 https://www.ebi.ac.uk/Tools/services/web/toolresult.ebi?jobId=eml <div>📄 🗨️ ⭐ 🔍 Search</div></div><div><div>Download 📄 🗨️ ⭐</div><div>Feedback rShare</div></div></div>			
Protein alignment	Nucleotide alignment	Web services	Help & Documentation
EMBOSS_001	1 TTIGAAGCGAGGAAGCCGCGCCCTGCGAGTCCGAGGAGGAAATGGAG	50	
EMBOSS_001	1 -----	0	
EMBOSS_001	51 CTCTGCGCTGCGTGGGACCCGSGGGACGGCTCCCGITGGCGCCGCTTCA	100	
EMBOSS_001	1 -----	0	
EMBOSS_001	101 AGGTAAGGGATTAAGAGGCCGAGAGAGATATCGTCTGCGAGGGTGAGGAT	150	
EMBOSS_001	1 -----	0	
EMBOSS_001	151 ACTGAGGTTGGCAGTGTCAACATCGCAAGAGTGCCTACCAgaggagga	200	
EMBOSS_001	1 -----	0	
EMBOSS_001	201 ggaggaggaggaaggagCTGGGCATAACTGGACCATCTCGATCCAGCCCG	250	
EMBOSS_001	1 -----	0	
EMBOSS_001	251 TGGGGAATCCAGAGGGGATAACAAGAGGATA-TAACCACAGGACAATTCA	299	
EMBOSS_001	1 -----UAUAAAUGAGGGCAGUAA-----GAC-----	22	
EMBOSS_001	300 TTAGGCTGTGTTTGGAGTTTCCTGAATTCTATTCCAAATTATTACAAA	349	
EMBOSS_001	23 -----	22	
EMBOSS_001	350 GGCATATTAAAATAATTTTATCTTACAAATTCACATATTTAAAATTGAA	399	
EMBOSS_001	23 -----	22	
EMBOSS_001	400 CATGGAACAGACTCTAGATGACATCAAATATTCCTTATTATGATATACA	449	
EMBOSS_001	23 -----	22	
EMBOSS_001	450 AGAATGTAACATATGCTAAATATTC	474	

figure S2(m): Snapshot shows alignment of *miR-1* *miRNA* with *LncRNA-RP11-773H22.4*
(available at <https://www.ebi.ac.uk>) accessed on 11th April 2019.

Protein alignment	Nucleotide alignment	Web services	Help & Documentation	Bioinformatics Tools FAQ	Feedback	Share
EMBOSS_001	101 AGGTAAGGGATTAAAGAGCCGAGAGAGATATCGTCTGCGAGGGTGAGGAT	150				
EMBOSS_001	1 -----	0				
EMBOSS_001	151 ACTGGAGGTTGGCAGTGTACGATCGCAAGAGTGCTCTACAgaggagga	200				
EMBOSS_001	1 -----	0				
EMBOSS_001	201 ggaggaggaggaaggagCTGGGCATAACTGGACCATCTCGATCCAGCCCG	250				
EMBOSS_001	1 -----	0				
EMBOSS_001	251 TGGGGAATCCAGAGGGGATAACAAGAGGATATAACCACAGGACAATTTCAT	300				
EMBOSS_001	1 -----	0				
EMBOSS_001	301 TAGGCTGTGTTTGACGTTTCTGAATTCTATTCCAATTATTCACAAAG	350				
EMBOSS_001	1 -----UG---	2				
EMBOSS_001	351 GCATATTAATAATTTTATCTTACAAATTCACATATTTAAATTTGAAC	400				
EMBOSS_001	3 --GGAAACAUAUCUUAUAUAGCC--CAUAUAGGACCUGCUAAGCUAUG- ::: :: ::: :: ::: ::: ::: ::: ::: ::: :::	47				
EMBOSS_001	401 ATGGAAACAGA---CTCTAGATGACATCAAAATATTCCTTAT---TATGA	443				
EMBOSS_001	48 -----GAUUGUAA-AGAAGUAUG----UAUUCUA :: :: ::: ::: ::: ::: ::: ::: :::	71				
EMBOSS_001	444 TATACAAGAAATGTAACA----TATGCTAAATAT-TC-	474				

figure S2(n): Alignment between *mTOR mRNA miR-3163* (available at <https://www.ebi.ac.uk>)

← → ↺ European Bioinformatics Institute [GB] | https://www.ebi.ac.uk/Tools/services/web/toolresult.ebi?jobId=emboss_needle-I20190707-113825-0229-36509602-p2m ☆ M ⋮

Input form	Web services	Help & Documentation	Bioinformatics Tools FAQ	Feedback	Share
EMBOSS_001	301	tactcgcttcctatgaccaactgaaccatcacatttttgaattgggttcca	350		
EMBOSS_001	1	-----	0		
EMBOSS_001	351	gctcagatgccaatgagaggaaagggtgcatcttggccatagctagcctc	400		
EMBOSS_001	1	-----	0		
EMBOSS_001	401	ataggagtgggaagtggaatgccaccgaattggcagatttgccaacta	450		
EMBOSS_001	1	-----	0		
EMBOSS_001	451	tcttcggaacctctccctccaatgaccagttgtcatggaatggcat	500		
EMBOSS_001	1	-----	0		
EMBOSS_001	501	ccaaggccattggcgtcttggcatggcaggggacattttaccgtgag	550		
EMBOSS_001	1	-----UAAUA	4		
EMBOSS_001	551	tacgtggaatttgaggtgaagcgagccctggaatggctgggtgctgaccg	600		
EMBOSS_001	5	AAAUAGAGGCGAGUAAGAC-----	22		
EMBOSS_001	601	caatgagggtcg-gagacatgagctgtcctggttctcctgagctggcc	649		
EMBOSS_001	23	-----	22		
EMBOSS_001	650	atcagcgtccctaccttcttcttccagcaagtgaacccttctttgacaa	699		
EMBOSS_001	23	-----	22		
EMBOSS_001	700	catttttggcgtgtgggaccccaacaggccatccgtgaggagctg	749		
EMBOSS_001	23	-----	22		
EMBOSS_001	750	tagccgcccttcgtgctgtgtgatttcacaaccagcgtgagccgaag	799		
EMBOSS_001	23	-----	22		

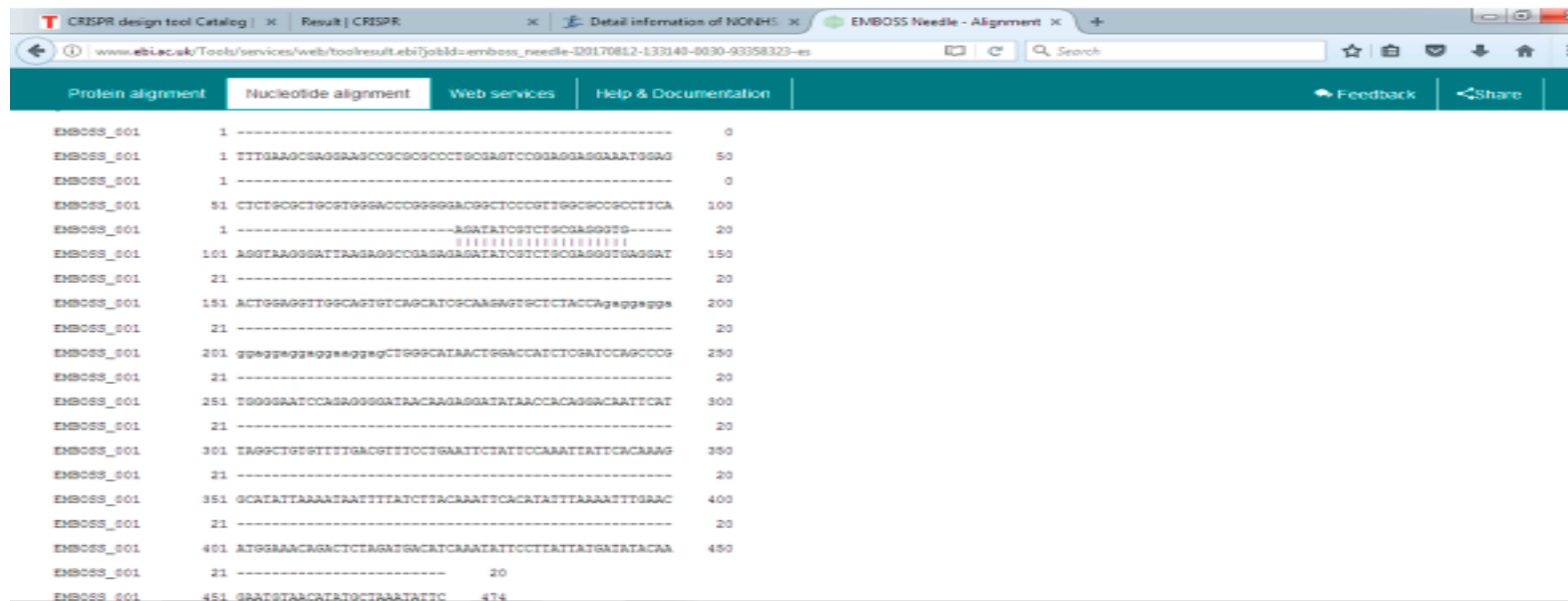
Figure S2(o): Snapshot shows alignment of *miR-1* miRNA with *mTOR* mRNA (available at <https://www.ebi.ac.uk>)

European Bioinformatics Institute [GB] | https://www.ebi.ac.uk/Tools/services/web/toolresult.ebi?jobId=emboss_needle-l20190707-111209-0231-78967558-p2m

Input form	Web services	Help & Documentation	Bioinformatics Tools FAQ	Feedback	Share
EMBOSS_001	1201	gtgttcagagacttgatggaggagaaatttgatcaggtgtgccagtggg	1250		
EMBOSS_001	1	-----	0		
EMBOSS_001	1251	tgctgaaatgcaggaatagcaagaactcgtgatccaaatgacaatcctt	1300		
EMBOSS_001	1	-----	0		
EMBOSS_001	1301	aatttggtgccccgcttggtgcattccgaccttctgccttcacagatac	1350		
EMBOSS_001	1	-----	0		
EMBOSS_001	1351	ccagtatctccaagataccatgaacctgtcctaagctgtgtcaagaagg	1400		
EMBOSS_001	1	-----	0		
EMBOSS_001	1401	agaaggaaagtacagcggccttccaagccctggggctactttctgtggct	1450		
EMBOSS_001	1	-----UGGGAACAUAC-	12		
EMBOSS_001	1451	gtgaggtctgagtttaaggtctattgcctcgcgtgctggacatcatcg	1500		
EMBOSS_001	13	UUCUUUAUAGCCCAUAGGAC---CUGCUAAGCUAUGGAUUAAGA	58		
EMBOSS_001	1501	agcggccctgccccaaaggacttcgccataaaggcagaaggcaalgc	1550		
EMBOSS_001	59	AGUAUGUAUUCUA-----	71		
EMBOSS_001	1551	aggTggatgc-cacagtcttcacttgcatcagcatgctggctcgagcaat	1599		
EMBOSS_001	72	-----	71		
EMBOSS_001	1600	ggggccaggcatccagcaggatatcaaggagctgctggagcccatgctgg	1649		
EMBOSS_001	72	-----	71		
EMBOSS_001	1650	cagtgggactaagccctgccctcactgcagtgtctacacctgagccgt	1699		
EMBOSS_001	72	-----	71		

figure S3: Snapshot shows alignment between lncRNA and the 2 guides, flanking the sequence of lncRNA and miRNAs interaction (available at <https://www.ebi.ac.uk>).

1st guide alignment with lncRNA



The screenshot displays the EMBOS Needle Alignment tool interface. The browser address bar shows the URL: www.ebi.ac.uk/Tools/services/web/toolresult/ebiJobId=emboss_needle-320170812-133140-0030-93358323-es. The interface includes tabs for 'Protein alignment', 'Nucleotide alignment' (selected), 'Web services', and 'Help & Documentation'. There are also links for 'Feedback' and 'Share'.

The alignment results are displayed in a table with three columns: the guide sequence identifier, the alignment score, and the aligned nucleotide sequences. The guide sequence is 'ENSOSS_001' and the lncRNA sequence is '1'. The alignment score is 474.

Guide	Score	Sequence
ENSOSS_001	1	-----
ENSOSS_001	1	TTTGAAGCAGGAGAGCCGCGCGCCTGCGAGTCCGGAGGAGAAATGGAG
ENSOSS_001	1	-----
ENSOSS_001	51	CTCTGCGCTGCGTGGGACCCGCGGACGGCTCCGCTTGGCGCGCCTTCA
ENSOSS_001	1	-----AGATATCTCTGCGAGGGT-----
ENSOSS_001	101	AGGTAAGGATTAGAGGCGCGAGAGATATCTCTGCGAGGGTGAAGAT
ENSOSS_001	21	-----
ENSOSS_001	151	ACTGAGGCTTGGCAGTGTCTAGCATGCGAGGCTCTTACCAgggggga
ENSOSS_001	21	-----
ENSOSS_001	201	ggggggggggggggggCTGGGATAACTGGACCACTCTGATCCAGCCCG
ENSOSS_001	21	-----
ENSOSS_001	251	TGGGGAATCCAGGCGGATACAGAGGATATACCCAGGACATTTCAT
ENSOSS_001	21	-----
ENSOSS_001	301	TAGGCTGTGTTTTGACGTTTCTGAATTCTATCCAAATTAATCAGAG
ENSOSS_001	21	-----
ENSOSS_001	351	GCATATTAAATAATTTTATCTTACAGATTACATATTAAATTTGAC
ENSOSS_001	21	-----
ENSOSS_001	401	ATGGAACAGACTCTAGATGACATCAATATTCCTTATTATGATATACA
ENSOSS_001	21	-----20
ENSOSS_001	451	GGATGTAACATATGCTAAATATTC474

2nd guide alignment with lncRNA

CRISPR design tool Catalog Detail information of NONHE Result CRISPR EMBOS Needle - Alignment				
www.ebi.ac.uk/Tools/services/web/toolresult.xbit?jobId=emboss_needle-120170812-133513-9694-95386942-ey				
Protein alignment	Nucleotide alignment	Web services	Help & Documentation	Feedback Share
EMBOS_001	1 TTTGAAGCGAGGAAGCGCGCGCCCTGCGAGTCCGGAGGAGGAATGGAG	50		
EMBOS_001	1 -----	0		
EMBOS_001	51 CTCTGCGCTGCGTGGGACCCGCGGGACCGCTCCCGTTGGCGCGCCCTTCA	100		
EMBOS_001	1 -----	0		
EMBOS_001	101 AGGTAAAGGGATTAAAGAGCCGAGAGAGATATCGTCTGCGAGGGTGAAGAT	150		
EMBOS_001	1 -----	0		
EMBOS_001	151 ACTGGAGGTTGGCAGTGTGAGCATGCGAAGAGTGCCTACCAgggggga	200		
EMBOS_001	1 -----	0		
EMBOS_001	201 ggggggggaggaggagCTGGGCATAACTGGACCATCTGATCCAGCCCG	250		
EMBOS_001	1 -----	0		
EMBOS_001	251 TGGGGATCCAGAGGGGATACAGAGGATATAACCCAGGACATTCAT	300		
EMBOS_001	1 -----	0		
EMBOS_001	301 TAGGCTGGTTTTTGAGGTTTCTGAAATTCATGCAAAATTCACAAAG	350		
EMBOS_001	1 -----	0		
EMBOS_001	351 GCATATTAAATTAATTTTATCTTACAAATTCACATATTTAAATTTGAC	400		
EMBOS_001	1 -----CTGCGAGCGATATC-----TCTCT-----	20		
EMBOS_001	401 ATGGAAACAGACTC-TAGATGACATCAAAATATTC-CTTATTATGATATAC	448		
EMBOS_001	21 -----	20		
EMBOS_001	449 AAGAAATGTAAATATGCTAAATATTC	474		

Table S2: Sequences of the forward and reverse primers of the 2 guide RNAs:

<u>Sequence</u>	<u>Primer name</u>	<u>GUIDE</u>
TAATACGACTCACTATAGAGATATCGTCTG CGAG	IVT-NONHSAT0584-gRNA- T1- <u>fwd</u>	<u>1st guide</u>
TTCTAGCTCTAAAACCCCTCGCAGACGA TATC	IVT-NONHSAT0584-gRNA- T1- <u>rev</u>	
TAATACGACTCACTATAGCTCGCAGACGAT ATCT	IVT-NONHSAT0584-gRNA- T5- <u>fwd</u>	<u>2nd guide</u>
TTCTAGCTCTAAAACAGAGAGATATCGTCT GCGA	IVT-NONHSAT0584-gRNA- T5- <u>rev</u>	