

Supplementary Material

Identification of Novel Molecular Network Expression in Acute Myocardial Infarction

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Supplementary Table 1: Study population demographic and clinical characteristics (N=131)

	acute myocardial infarction	non cardiac chest pain	Control
Overall	69	31	31
Type of AMI Anterior stemi(n=31) Inferior stemi(n=24) Non stemi(n=14) $\chi^2(P)$	31(44.9%) 24(34.8%) 14(20.3)	0% 0% 0%	0% 0% 0%
Age More than 55.7 Less than 55.7 $\chi^2(P)$	32(46.4%) 37(53.6%)	17(54.8%) 14(45.2%)	15(48.4%) 16(51.6%)
	.035 (.852)		
Sex Male Female $\chi^2(P)$	55(79.7%) 14(20.3%)	20(64.5%) 11(35.5%)	23(74.2%) 8(25.8%)
	.379 (.538)		
Smoking Positive(n=68) Negative(n=32) $\chi^2(P)$	48(69.6%) 21(30.4%)	24(77.5%) 7(22.5%)	20(64.5%) 11(35.5%)
	.251 (.617)		
Hypertension Positive Negative $\chi^2(P)$	23(33.3%) 46(66.7%)	11(35.5%) 20(64.5%)	8(25.8%) 23(74.2%)
	.567 (.452)		

Diabetes	Positive	24(34.8%)	8(25.8%)	10(32.3%)
	Negative	45(65.2%)	23(74.2%)	21(67.7%)
$\chi^2(P)$.061 (.805)			
Blockers	Positive	41(59.4%)	11(35.5%)	7(22.6%)
	Negative	28(40.6%)	20(64.5%)	24(77.4%)
$\chi^2(P)$	11.630(.001)			
ACEI	Positive	39(56.5%)	2(6.4%)	6(19.4%)
	Negative	30(43.5%)	29(94.6%)	25(80.6%)
$\chi^2(P)$	11.938 (.001)			
Nitrates	Positive	11(15.9%)	7(22.6%)	0(0.0%)
	Negative	58(84.1%)	24(77.4%)	31(100.0%)
$\chi^2(P)$	5.553 (.018)			
Stains	Positive	45(65.2%)	11(35.5%)	1(3.2%)
	Negative	24(34.8%)	20(64.5%)	30(96.8%)
$\chi^2(P)$	33.092 (.000)			
Onset of chest pain Mean \pm S.D		6.52 \pm 2.084	6.4 \pm 1.017	.00
	t(P)	.704 (.484)		
Body mass index Mean \pm S.D		27.1964 \pm 3.13756	27.978 \pm 2.741	26.1613 \pm 2.47786
	t(P)	1.622(.108)		
Cardiac troponin I(ng/ml) Mean \pm S.D		26.000188 \pm 23.6257199	6.8174 \pm 11.24	1.910710 \pm 8.3800879
	t(P)	5.510(.000)		
CK-MB(IU/L) Mean \pm S.D		145.32 \pm 177.501	15.28 \pm 11.25	45.34 \pm 53.295
	t(P)	1.470(.145)		
SGOT (IU/L) Mean \pm S.D		124.99 \pm 151.216	97.874 \pm 28.22	30.77 \pm 24.322
	t(P)	3.440(.01)		
TG(mg/dL) Mean \pm S.D		131.07 \pm 45.046	99.78 \pm 27.67	67.77 \pm 29.654
	t(P)	7.148(.000)		
HDL(mg/dL)		31.67 \pm 6.370	32 \pm 7.85	33.45 \pm 8.258

Mean ± S.D	1.179(.241)		
t(P)			
<u>LDL(mg/dL)</u>	128.94±30.804	119±18.65	118.84±22.056
Mean ± S.D	1.645(.103)		
t(P)			
<u>Cholesterol(mg/dL)</u>	212.4638±33.86330	210.874±30.26	200.4839±28.79105
Mean ± S.D	1.710(.090)		
t(P)			
Serum Creatinine (mg/dL)	1.801362±1.9664037	1.28462±1.87621	1.022581±0.3263022
Mean ± S.D	2.186(.031)		
t(P)			

Supplementary Table 2: Expression of serum RMNAs among the study groups.

		Mean rank	Mean	Std. Deviation	Std. Error	Minimum	Maximum
<i>lncRNA-RP11-175K6</i>	acute myocardial infarction	11.9	.415797	.4028662	.0484994	.0100	2.0300
	non cardiac chest pain	13.1	6.671935	4.2400373	.7615332	.9700	17.8800
	healthy control	11.1	7.183226	4.0800077	.7327910	1.9700	14.2000
	statistics p	<0.01					
<i>RQ-ANPCII mRNA</i>	acute myocardial infarction	12.9	.7248	.71864	.08651	.01	3.41
	non cardiac chest pain	10.6	3.1400	2.39952	.43097	.90	12.04
	healthy control	9.5	4.0129	2.80365	.50355	.90	11.20
	statistics p	<0.01					
<i>R-MIR-106b-5p</i>	acute myocardial infarction	69	148.9561	84.29539	10.14797	18.38	407.31
	non cardiac chest pain	31	3.4965	12.73906	2.28800	.48	72.00
	healthy control	31	2.9784	7.82790	1.40593	.20	44.40

	trol						
	statistics p	<0.01					

Supp Table 3. Positivity rate of the investigated serum RNAs in relation to clinicopathological factors in AMI group.

Clinico-pathological factors	RQ-ANPCII mRNA					R-MIR-106b				
	Median	Mean Rank	Statistics $\chi^2(p)$	N of cases/70 \geq (%)	$\chi^2(p)$	Median	Mean Rank	Statistics $\chi^2(p)$	N of cases/70 \geq (%)	$\chi^2(p)$
Age: ≥ 55.7 years(n=31) < 55.7 years(n=37)	0.6100 0.4410	39.05 30.69	312 (.082)	23(50.0%) 34(64.2%)	1.988(.370)	127.12 136.24	33.73 35.15	549.5(.768)	31(67.4%) 38(71.7%)	.650(.722)
Sex: Male (n=55) Female (n=14)	0.4600 0.5450	34.5 36.96	357.5(.682)	45(57.7%) 13(59.1%)	.003(.954)	116.16 154.89	32.37 45.32	240.5(.031)	55(70.5%) 15(68.2%)	833 .044(
Smoking: Smoker (n=48) Non-Smoker (n=21)	0.4600 0.6100	32.76 40.12	396.5(.161)	40(58.8%) 18(56.2%)	.015(.904)	115.76 153.28	32.83 39.95	400.(.175)	48(70.6%) 22(68.8%)	(.852) (0.035)
Hypertension: Positive (n=23) Negative (n=46)	0.4600 0.5250	34.04 35.48	507.0(.779)	21(67.7%) 37(53.6%)	.961(.327)	121.10 136.71	33.72 35.64	499.5(.707)	24(77.4%) 46(66.7%)	1.178(.278)
Diabetes: Positive (n=24) Negative (n=45)	0.3150 0.6400	25.19 40.23	304.5(.003)	21(61.8%) 37(56.1%)	1.250(.263)	142.66 127.12	40.33 32.16	412.0(.107)	25(73.5%) 45(68.2%)	.306(.580)
Blockers: Positive (n=41) Negative (n=28)	0.5100 0.4900	36.21 33.23	524.5(.545)	31(64.6%) 27(51.9%)	2.685(.101)	127.12 128.90	34.22 36.14	542.0(.696)	41(85.4%) 29(55.8%)	10.447(.001)
ACEI: Positive (n=39) Negative (n=30)	0.5100 0.4900	34.79 35.27	577.0(.923)	33(73.3%) 32(45.5%)	7.302(.007)	137.19 121.94	36.79 32.67	515.0(.397)	40(88.9%) 30(54.5%)	13.901(.00)

Nitrates: Positive (n=11) Negative (n=58)	0.5800 0.4600	40.09 34.03	263.0(.359)	8(72.7%) 50(56.2%)	1.745(.187)	116.16 131.21	37.41 34.54	292.5(.664)	11(100%) 59(66.3%)	5.297(.021)
statins: Positive (n=45) Negative (n=24)	0.4600 0.5800	32.63 39.44	433.5(.180)	39(84.8%) 19(35.2%)	23.964(.00)	127.12 131.21	34.53 35.88	519.0(.791)	46(100%) 24(44.4%)	36.508(.00)

Clinico-pathological factors	lncRNA-RP11-175K6				
	Median	Mean Rank	Statistics	N of cases/70 >1.36(%)	P χ^2 (c)
Age: ≥55.7 years(n=32) <55.7 years(n=37)	0.17 0.40	28.28 40.81	377.0(0.010)	31(67.4%) 36(67.9%)	.479(.787)
Sex: Male (n=55) Female (n=14)	0.29 0.20	36.25 30.11	316.50(0.307)	53(67.9%) 15(68.2%)	.00(.983)
Smoking: Smoker (n=48) Non-Smoker (n=21)	0.30 0.19	37.36 29.60	390.50(0.139)	46(67.6%) 22(68.8%)	.012(.912)
Hypertension: Positive (n=23) Negative (n=46)	0.18 0.31	30.74 37.13	431.0(0.212)	24(77.4%) 44(63.8%)	1.832(.176)
Diabetes: Positive (n=) Negative (n=)	0.29 0.25	36.58 34.16	502.0(0.632)	25(73.5%) 43(65.2%)	.724(.395)
Blockers: Positive (n=41) Negative (n=28)	0.25 0.27	35.26 34.63	563.50(0.898)	39(81.2%) 29(55.2%)	7.448(.006)
ACEI: Positive (n=39) Negative (n=30)	0.31 0.21	36.72 32.77	518.0(0.417)	38(84.4%) 30(54.5%)	10.168(.001)
Nitrates: Positive (n=11) Negative (n=58)	0.27 0.26	40.32 33.99	260.50(0.337)	10(90.9%) 58(65.2%)	2.981(.084)
statins: Positive (n=45) Negative (n=24)	0.29 0.18	37.10 31.06	445.50(0.234)	44(95.7%) 24(44.4%)	29.934(.00)

Supplementary Table 4: Correlation between the investigated serum RNAs among the study group.

Correlations					
			RQ(lncRNA)	RQ-ANPCII mRNA	R-MIR-106b
Spearman's rho	RQ(lncRNA)	Correlation Coefficient	1.000	.629**	-.687-**
		Sig. (2-tailed)	.	.000	.000
		N	131	131	131
	RQ-ANPCII mRNA	Correlation Coefficient	.629**	1.000	-.653-**
		Sig. (2-tailed)	.000	.	.000
		N	131	131	131
	R-MIR-106b	Correlation Coefficient	-.687-**	-.653-**	1.000
		Sig. (2-tailed)	.000	.000	.
		N	131	131	131

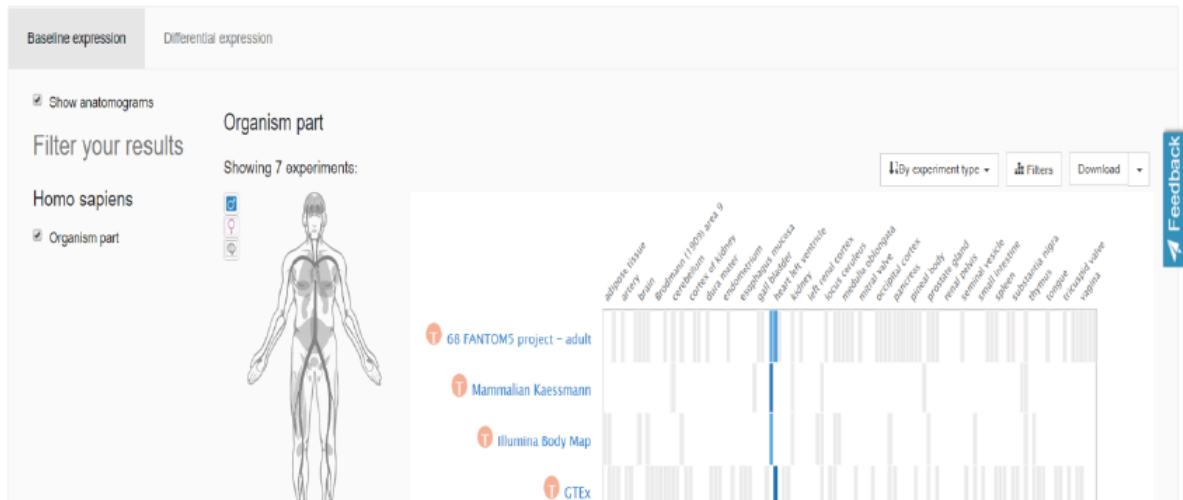
** . Correlation is significant at the 0.01 level (2-tailed).

Supplementary Table 5. Predicted power of the investigated parameter by linear regression analysis.

Model	Variables	Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		Beta			Lower Bound	Upper Bound
1	(Constant)		.987	.326	-.178-	.531
	ANPC	-.047-	-2.023-	.046	-.088-	-.001-
	mirna 106b-5p	.405	4.802	.000	.239	.577
	lncRNA-RP11-175K6	-.035-	-.654-	.0515	-.138-	.070
	cardiac troponin after cut-off	.008	.266	.791	-.050-	.066
	CKMB	.018	1.066	.290	-.014-	.047
	SGOT	.028	1.257	.212	-.015-	.068
	Hypertension	.008	.443	.659	-.027-	.043
	Diabetes	-.026-	-1.579-	.118	-.058-	.007
	Smoking history	.005	.327	.744	-.028-	.038

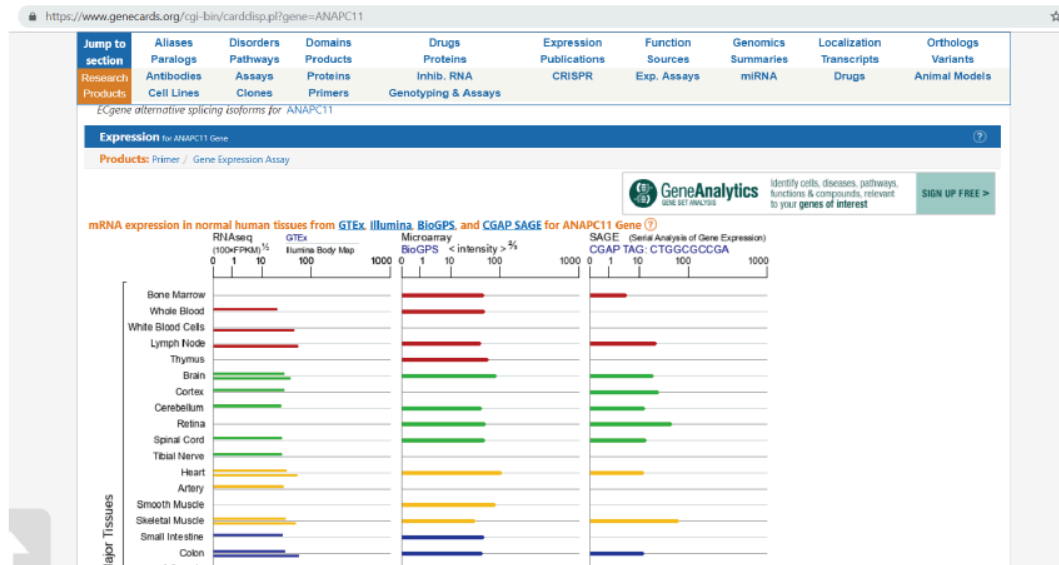
Supplementary figures

Results for ANAPC11 (symbol) AND heart AND Homo sapiens



Supplementary figure 1, Anaphase-promoting complex subunit 11 gene expression in heart that was retrieved from gene atlas expression database available at <https://www.ebi.ac.uk/gxa/home>

Supplementary figure 2, Anaphase-promoting complex subunit 11 gene expression loss is related to heart disease that was retrieved from GEO profile available at <https://www.ncbi.nlm.nih.gov/geoprofiles/66454439>



Supplementary figure 3, Anaphase-promoting complex subunit 11 gene expression in heart that was retrieved from gene card database available at <https://www.genecards.org/cgi-bin/carddisp.pl?gene=ANAPC11>

This screenshot shows the pathway information for ANAPC11 on the GeneCards website. At the top, there's a navigation bar similar to the previous screenshot. Below it, a table lists cellular processes with associated scores and icons:

5	Cellular Senescence (REACTOME)	Cell Cycle, Mitotic	0.85
		Cellular Senescence	0.64
		Senescence-Associated Secretory Phenotype (SASP)	0.56

Below the table, there are sections for 'GenesLikeMe' (Genes that share pathways with ANAPC11), 'Pathways by source for ANAPC11 Gene', and 'GeneGo (Thomson Reuters) pathways for ANAPC11 Gene'. The 'Pathways by source' section includes:

- 1 Sino Biological pathway for ANAPC11 Gene: Canonical Wnt Pathway
- 31 Reactome pathways for ANAPC11 Gene:
 - Activation of APC/C and APC/C-Cdc20 mediated degradation of mitotic proteins
 - Adaptive Immune System
 - Antigen processing- Ubiquitination and Proteasome degradation
 - APC/C-Cdc20 mediated degradation of Cyclin B
 - APC/C-Cdc20 mediated degradation of mitotic proteins
- 5 KEGG pathways for ANAPC11 Gene:
 - Cell cycle
 - Human T-cell leukemia virus 1 infection
 - Oocyte meiosis
 - Progesterone-mediated oocyte maturation
 - Ubiquitin mediated proteolysis

The 'GeneGo' section lists 7 pathways, including 'Cell cycle Regulation of G1/S transition (part 1)', 'Cell cycle Role of SCF complex in cell cycle regulation', and 'Cell cycle Role of APC in cell cycle regulation'. At the bottom, there's a 'UniProtKB/Swiss-Prot' entry for Q9NYG5-APC11_HUMAN with the pathway 'Protein modification; protein ubiquitination'.

Supplementary figure 4, Anaphase-promoting complex subunit 11 gene ontology that was retrieved from gene card database available at <https://www.genecards.org/cgi-bin/carddisp.pl?gene=ANAPC11>

Metal binding ⁱ	58	Zinc 3	By similarity		1
Metal binding ⁱ	59	Zinc 1	By similarity		1
Metal binding ⁱ	73	Zinc 2	By similarity		1
Metal binding ⁱ	76	Zinc 2	By similarity		1

Feature key	Position(s)	Description	Actions	Graphical view	Length
Zinc finger ⁱ	34 – 77	RING-type <small>PROSITE-ProRule annotation</small>	Add BLAST		44

GO - Molecular functionⁱ

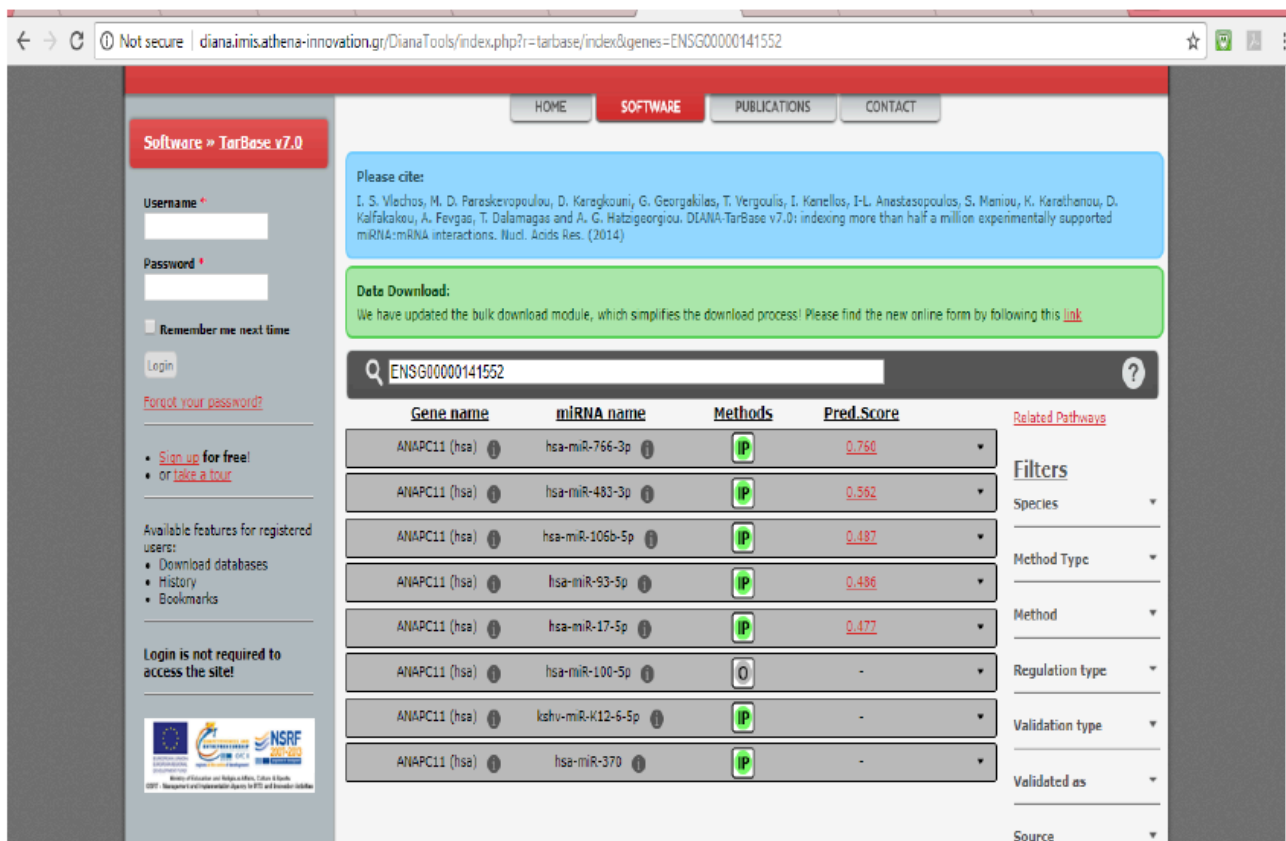
- cullin family protein binding Source: MGI
- metal ion binding Source: UniProtKB-KW
- ubiquitin protein ligase activity Source: MGI
- ubiquitin-ubiquitin ligase activity Source: MGI

Complete GO annotation on QuickGO ...

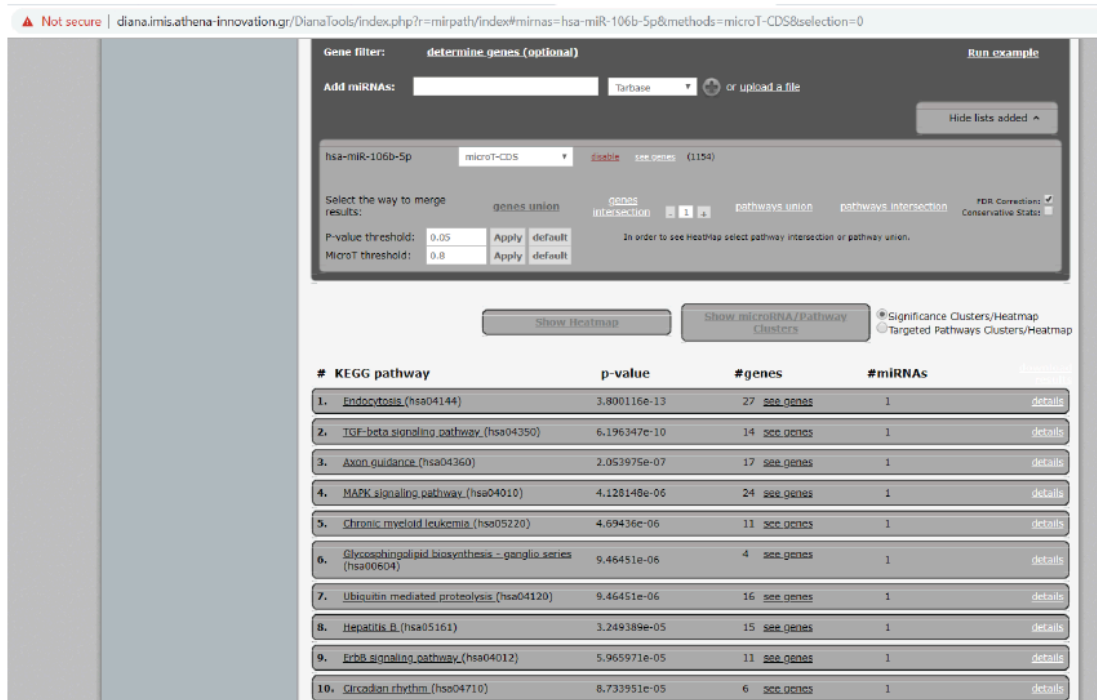
GO - Biological processⁱ

- anaphase-promoting complex-dependent catabolic process Source: Reactome
- cell division Source: UniProtKB-KW
- mitotic cell cycle Source: UniProtKB
- positive regulation of mitotic metaphase/anaphase transition Source: GO_Central
- protein K11-linked ubiquitination Source: UniProtKB
- protein ubiquitination Source: UniProtKB
- regulation of mitotic cell cycle phase transition Source: Reactome
- ubiquitin-dependent protein catabolic process Source: GO_Central

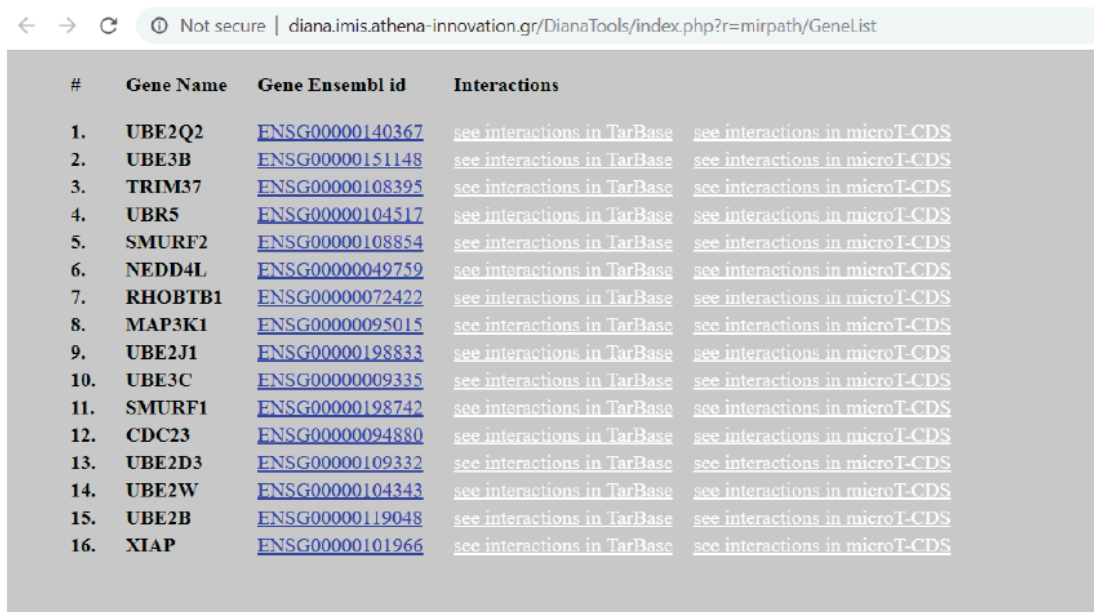
Supplementary figure 5, Anaphase-promoting complex subunit 11 gene ontology that was retrieved from Uniprot database available at <https://www.uniprot.org/uniprot/Q9NYG5>



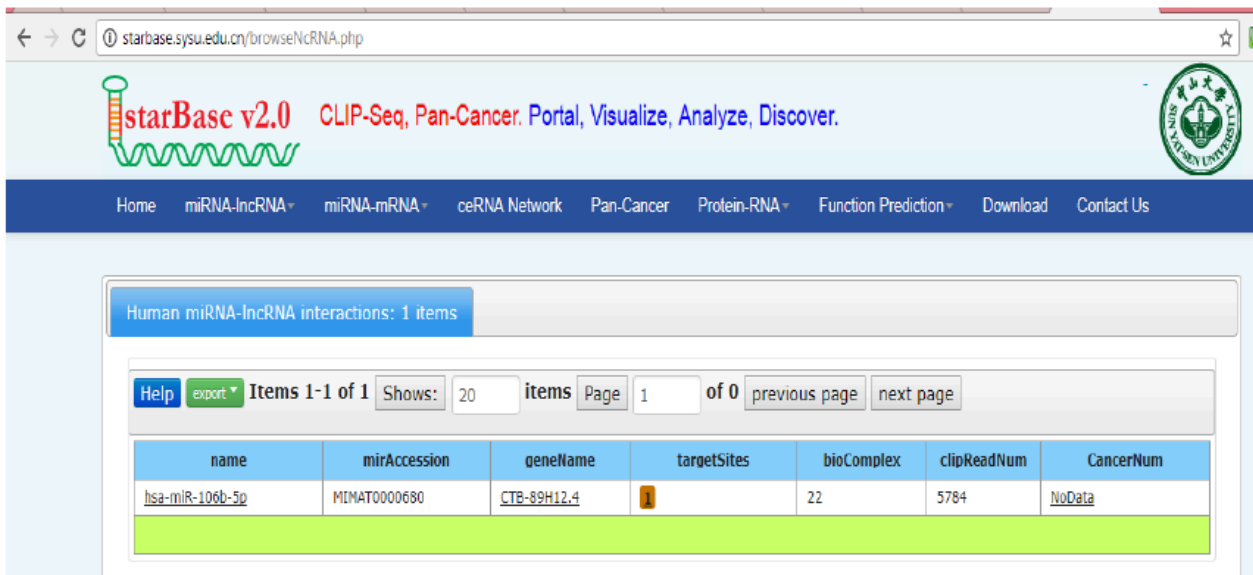
supplementary figure 6, printscreen represents that miR106b-5p is targeting Anaphase-promoting complex subunit 11 with high prediction score that was retrieved from Diana database available at http://diana.imis.athena-innovation.gr/DianaTools/index.php?r=microT_CDS/index



Supplementary figure 7 printscreen shows miR-106b-5p pathway enrichment analysis that was retrieved from Diana database available at <http://www.microrna.gr/miRPathv2>.



Supplementary figure 8 printscreen shows miR-106b-5p pathway enrichment analysis. it revealed that miR-106b-5p has many target genes related to UPS. Data was retrieved from Diana database available at <http://www.microrna.gr/miRPathv2>



The screenshot shows the starBase v2.0 website interface. The header includes the logo and tagline "starBase v2.0 CLIP-Seq, Pan-Cancer. Portal, Visualize, Analyze, Discover." along with the Sun Yat-sen University logo. A navigation bar contains links for Home, miRNA-lncRNA, miRNA-mRNA, ceRNA Network, Pan-Cancer, Protein-RNA, Function Prediction, Download, and Contact Us. The main content area displays "Human miRNA-lncRNA interactions: 1 items". Below this, there is a pagination control showing "Items 1-1 of 1" and "Shows: 20 items Page 1 of 0". A table with 7 columns is shown below the pagination:

name	mirAccession	geneName	targetSites	bioComplex	clipReadNum	CancerNum
hsa-miR-106b-5p	MIMAT0000680	CTB-89H12.4	1	22	5784	NoData

supplementary figure 9, printscreen represents that miR106b-5p is targeting Anaphase-promoting complex subunit 11 with high prediction score that was retrieved from Diana database available at http://diana.imis.athena-innovation.gr/DianaTools/index.php?r=microT_CDS/index

Input form	Web services	Help & Documentation	Bioinformatics Tools FAQ	Feedback	Share
EMBOSS_001	1	-----	0		
EMBOSS_001	151	GTCCCAGGATGCTTTCTGTGCAGACATGATCGCTGGTAACAGATGCTG	200		
EMBOSS_001	1	-----	0		
EMBOSS_001	201	GTTCACTCTCATCCTCGCCATACCTGAGGACTATGCTCCTCTCTAGAA	250		
EMBOSS_001	1	-----	0		
EMBOSS_001	251	TTGGTGCAGTCATCTGACTTAATTGATTCAGCGCATTTATCTGCAGGCT	300		
EMBOSS_001	1	-----	0		
EMBOSS_001	301	GGAGTACAATAGCAGCATCAGCTCACTGCACATCTGCCTCCCGGTT	350		
EMBOSS_001	1	-----	0		
EMBOSS_001	351	CAAGCAATTCCTCTGCCTCAGCTTCCGAGTTGCTGGATTACAGGACCC	400		
EMBOSS_001	1	-----	0		
EMBOSS_001	401	TGCCACCATGCCCACTAATTTTGTATTTTAGTAGAGATGGGTTTCA	450		
EMBOSS_001	1	-----	0		
EMBOSS_001	451	CCATGTTGGTCAGGCTGGCTTGAACCTCTGACCTCAGGTGATCCACTG	500		
EMBOSS_001	1	-----	0		
EMBOSS_001	501	CCTCGGCTCCCAAAGTCTGGGATTACAGGTGTGAGCCACCACCTGG	550		
EMBOSS_001	1 : : .:. : . : : uaaagugcugacagugcagau	21		
EMBOSS_001	551	CCTGTGAGATGGTTTCTGGGTAGAATGAAAGAAGCTTGGCTACTGGGT	600		
EMBOSS_001	22	-----	21		
EMBOSS_001	601	CCATTTTATGTGACATGTTGCTCCCTATTATAGTCAGTCCCTGGAAACC	650		
EMBOSS_001	22	-----	21		

supplementary figure 10 ,printscreen represents that lncRNA-RP11-175K6.1 is targeting miR106b-5p that was retrieved from European Bioinformatic institute using Clustal alligment database available at https://www.ebi.ac.uk/Tools/services/web/toolresult.ebi?jobId=emboss_needle-I20190726-131627-0261-17609716-p2m