

Article

ABHD4-Regulating RNA Panel: Novel Biomarkers in Acute Coronary Syndrome Diagnosis

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Methodology Details

We have used the following products: U6 sn RNA, TaqMan[™] microRNA Control Assay 5X (RT: 001973), hsa-miR-221 TaqMan[™] Advanced miRNA Assay 5X (RT: 00052), hsa-miR-197 TaqMan[™] Advanced miRNA Assay 5X (RT: 000497), ABHD4 TaqMan[™] Gene Expression Assay (FAM) (HS01040459-m1) (Thermo Fisher Scientific, Inc, Waltham, MA, USA), Human FENDRR RT2 lncRNA qPCR Assay (LPH26005A-200), and Hs-ACTB-1-RT2 QuantiTect Primer Assays (Cat. No. QT00095431) (Qiagen, Germany).

Table S1. Study Population Demographic and Clinical Characteristics (*n* = 110).

	Acute myocardial infarction	Non-cardiac chest pain	Control
Overall	68	21	21
Type of ACS			
Unstable angina (<i>n</i> = 21)			
STEMI (<i>n</i> = 31)	21 (30.9%)	0%	0%
Non STEMI (<i>n</i> = 16)	31 (45.6%)	0%	0%
χ^2 (<i>p</i>)	16 (23.5)	0%	0%
Age			
Mean \pm S.D	55.7 \pm 11.7	56.7 \pm 10.7	54.6 \pm 10.2
		.225 (.779)	
F(<i>p</i>)			
Sex			
Male (<i>n</i> = 87)	54 (79.4%)	16 (72.2%)	17 (81%)
Female (<i>n</i> = 23)	14 (20.6%)	5 (23.8%)	4 (19%)
		.155 (0.925)	
χ^2 (<i>p</i>)			
Smoking			15 (71.4%)

Positive (<i>n</i> = 75)	47 (69.1%)	13 (61.9%)	6 (28.6%)
Negative (<i>n</i> = 35)	21 (30.9%)	8 (38.15%)	
χ^2 (<i>p</i>)	.511 (0.75)		
<u>Hypertension</u>			
Positive (<i>n</i> = 34)	23 (33.8%)	5 (23.8%)	6 (28.6%)
Negative (<i>n</i> = 76)	45 (66.2%)	16(67.2%)	15 (71.4%)
χ^2 (<i>P</i>)	.820 (0.664)		
<u>Diabetes Mellitus</u>			
Positive (<i>n</i> = 38)	24 (35.5%)	5 (23.8%)	9 (42.9%)
Negative (<i>n</i> = 72)	44(64.7%)	16 (67.2%)	12 (56.1%)
χ^2 (<i>p</i>)	1.729 (0.421)		
<u>Onset of chest pain</u>			
Mean \pm S.D	6.8 \pm 1.077	6.22 \pm 1.023	0.00
F (<i>p</i>)	0.604 (.523)		
<u>Body mass index</u>			
Mean \pm S.D	27.2 \pm 3.9	26.6 \pm 2.6	25.4 \pm 1.7
F (<i>p</i>)	5.03 (0.008)		
<u>TG (-mg/dL)</u>			
Mean \pm S.D	132.09 \pm 44.66	66 \pm 29.04	71.1 \pm 28.8
F (<i>p</i>)	33.5 (0.000)		
<u>HDL (-mg/dL)</u>			
Mean \pm S.D	31.7 \pm 6.4	33.2 \pm 7.5	33.4 \pm 9.3
F (<i>p</i>)	0.671(0.53)		
<u>LDL (-mg/dL)</u>			
Mean \pm S.D	128.19 \pm 28.3	119.8 \pm 25.5	124.7 \pm 28.2
F (<i>p</i>)	1.35 (0.262)		
<u>Cholesterol (-mg/dL)</u>			
Mean \pm S.D	211.9 \pm 33.2	201.19 \pm 32.3	201.4 \pm 28.3
F (<i>p</i>)	1.408 (0.249)		
<u>Serum Creatinine (-mg/dL)</u>			
Mean \pm S.D	1.827 \pm 1.9	0.95 \pm 0.38	1.1 \pm 0.3
F (<i>p</i>)	3.04 (0.037)		

S.D.: Standard Deviation, χ^2 : Chi-Square test, *p*: level of significance, F: One Way Anova test.

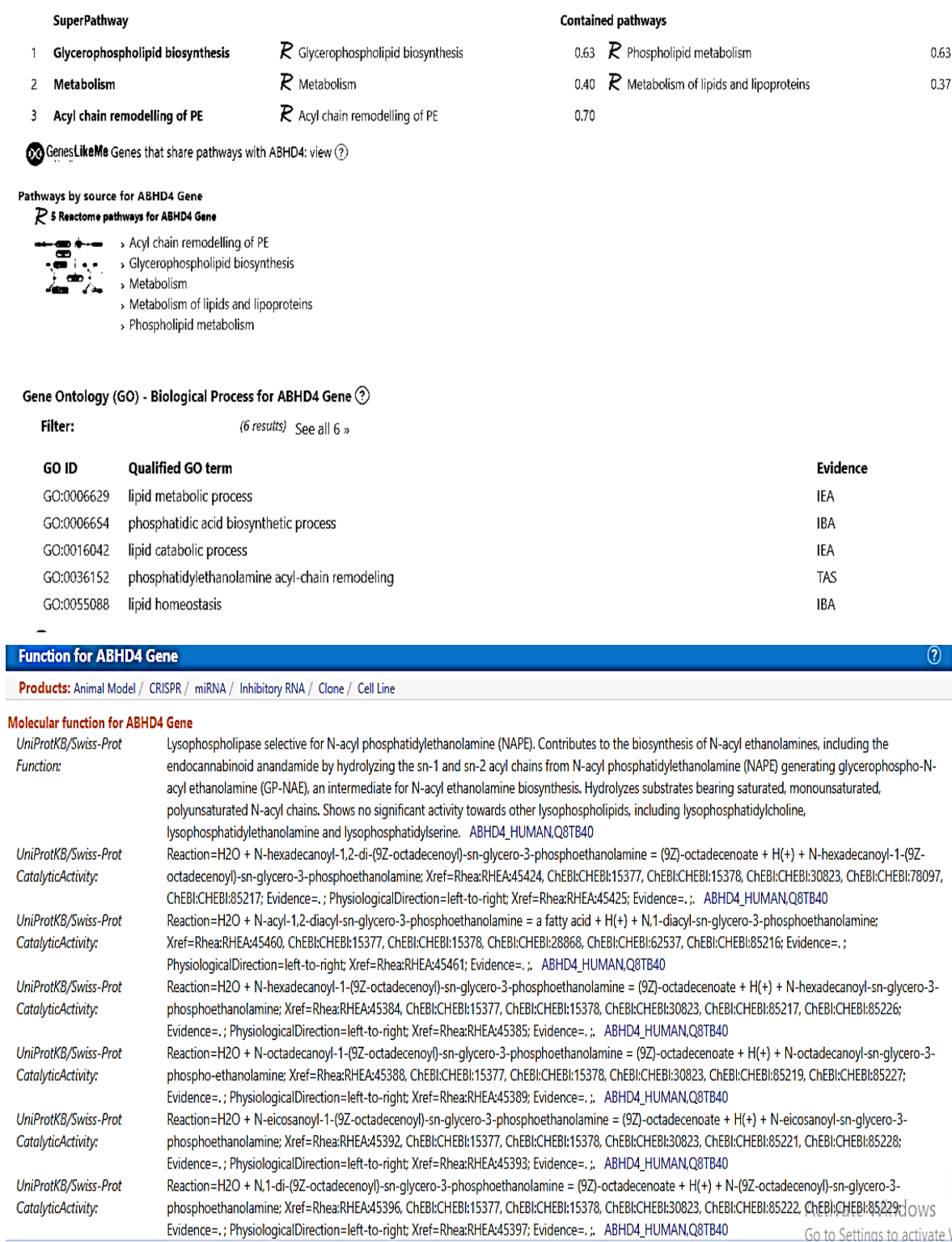


Figure S1. Gene ontology of ABHD4 mRNA by KEGG map that was retrieved from GeneCards®: The Human Gene Database. It shows that ABHD4 mRNA is linked specifically to phospholipid metabolism. Available at (<https://www.genecards.org/cgi-bin/carddisp.pl?gene=ABHD4>, accessed on 21 May 2021)).



Figure S2: Gene expression of ABHD4 mRNA in heart that was retrieved from GeneCards®: The Human Gene Database. It shows basal RNA expression in normal heart. Available at (<https://www.genecards.org/cgi-bin/carddisp.pl?gene=ABHD4>, (accessed on 27 May 2021)). X-axis represents level of RNA expression while Y-axis represents the tissue in which the gene is expressed.

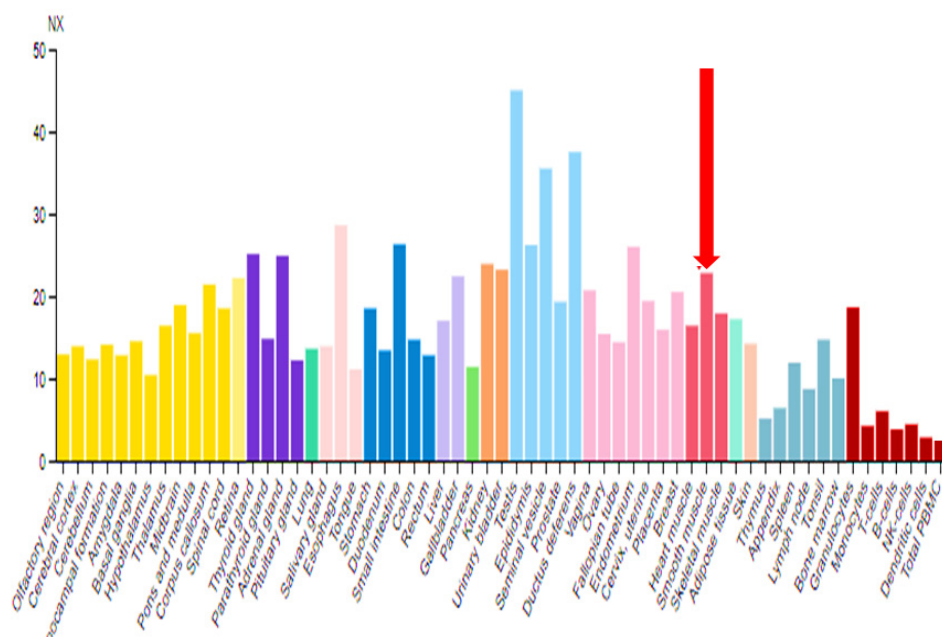


Figure S3. Gene expression of ABHD4 mRNA in heart that was retrieved from The Human Protein Atlas database. It shows the basal expression of ABHD4 mRNA in heart. The red arrow refers to the level of ABHD4 mRNA expression in normal heart. Y-axis represents level of RNA expression while X-axis represents the tissue in which the gene is expressed.

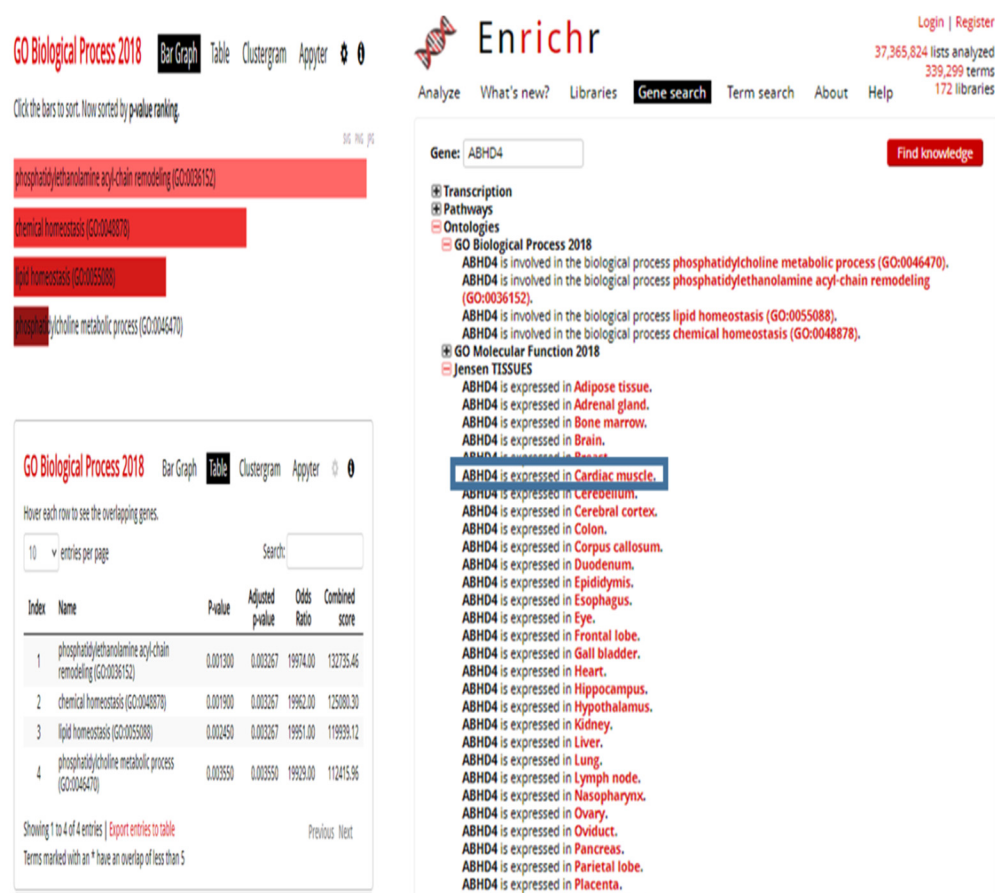



















Figure S4. Gene ontology and expression of ABHD4 mRNA in heart that was retrieved from Enrichr tool (<https://maayanlab.cloud/Enrichr/> (accessed on 1 June 2021)). It shows the expression of ABHD4 mRNA in heart and its link to phospholipid metabolism.

	SuperPathway	Contained pathways			
1	ADP signalling through P2Y purinoceptor 12	<div><div></div>ADP signalling through P2Y purinoceptor 12</div> <div><div></div>G-protein activation</div>	0.73	<div><div></div>Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding</div> <div><div></div>G alpha (z) signalling events</div>	0.57
2	DAG and IP3 signaling	<div><div></div>PLC beta mediated events</div> <div><div></div>G-protein mediated events</div>	0.65	<div><div></div>Opioid Signalling</div> <div><div></div>G Protein Signaling Pathways</div>	0.45
3	GABA receptor activation	<div><div></div>Activation of GABAB receptors</div> <div><div></div>GABA B receptor activation</div>	0.71	<div><div></div>GABA receptor activation</div>	0.56
4	Signaling by GPCR	<div><div></div>GPCR downstream signaling</div> <div><div></div>Signaling by GPCR</div>	0.76	<div><div></div>Signal Transduction</div>	0.44
5	Transmission across Chemical Synapses	<div><div></div>Neurotransmitter Receptor Binding And Downstream Transmission In The Postsynaptic Cell</div> <div><div></div>Transmission across Chemical Synapses</div>	0.67	<div><div></div>Neuronal System</div>	0.71

Gene Ontology (GO) - Biological Process for MIR197 Gene (?)

Filter: (3 results)

GO ID	Qualified GO term	Evidence
GO:0032701	negative regulation of interleukin-18 production	IDA
GO:0035195	gene silencing by miRNA	IDA,IEA
GO:1900015	regulation of cytokine production involved in inflammatory response	IDA

Figure S5. Pathway enrichment analysis of miR-197 by KEGG map that was retrieved from GeneCards®: The Human Gene Database (<https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR197> (accessed on 25 May 2021)). It clarifies the role of miRNA-197 in inflammatory response and diacyl glycerol (DAG) and lipid metabolism that is closely linked to myocardial ischemia.

Items 1 - 25 of 45 < Prev Page 1 of 2 Next >		
Process	Evidence Code	Pubs
gene silencing by miRNA	IDA	PubMed
gene silencing by miRNA	IEA	
gene silencing by miRNA	IGI	PubMed
gene silencing by miRNA	IMP	PubMed
miRNA mediated inhibition of translation	IDA	PubMed
miRNA mediated inhibition of translation	IMP	PubMed
negative regulation by host of viral genome replication	ISS	
negative regulation of ERK1 and ERK2 cascade	IDA	PubMed
negative regulation of TRAIL-activated apoptotic signaling pathway	IDA	PubMed
negative regulation of TRAIL-activated apoptotic signaling pathway	IMP	PubMed
negative regulation of apoptotic process	IDA	PubMed
negative regulation of apoptotic process	IMP	PubMed
negative regulation of cell adhesion molecule production	IGI	PubMed
negative regulation of cell migration involved in sprouting angiogenesis	IGI	PubMed
negative regulation of cell population proliferation	IDA	PubMed
negative regulation of cytokine production involved in inflammatory response	ISS	
negative regulation of double-strand break repair	IDA	PubMed
negative regulation of hematopoietic stem cell proliferation	IDA	PubMed
negative regulation of heterotypic cell-cell adhesion	IDA	PubMed
negative regulation of inflammatory response	IGI	PubMed
negative regulation of interleukin-21 production	IDA	PubMed
negative regulation of leukocyte adhesion to vascular endothelial cell	IGI	PubMed
negative regulation of necroptotic process	IDA	PubMed
negative regulation of sprouting angiogenesis	IGI	PubMed
negative regulation of vascular associated smooth muscle cell differentiation	IMP	PubMed

Figure S6. Pathway enrichment analysis of miR-221-3p by KEGG map that was retrieved from <https://www.ncbi.nlm.nih.gov/gene/407006> (accessed on 28 May 2021). It clarifies the role of miRNA-221 in inflammatory response and apoptosis that is closely linked to myocardial ischemia.

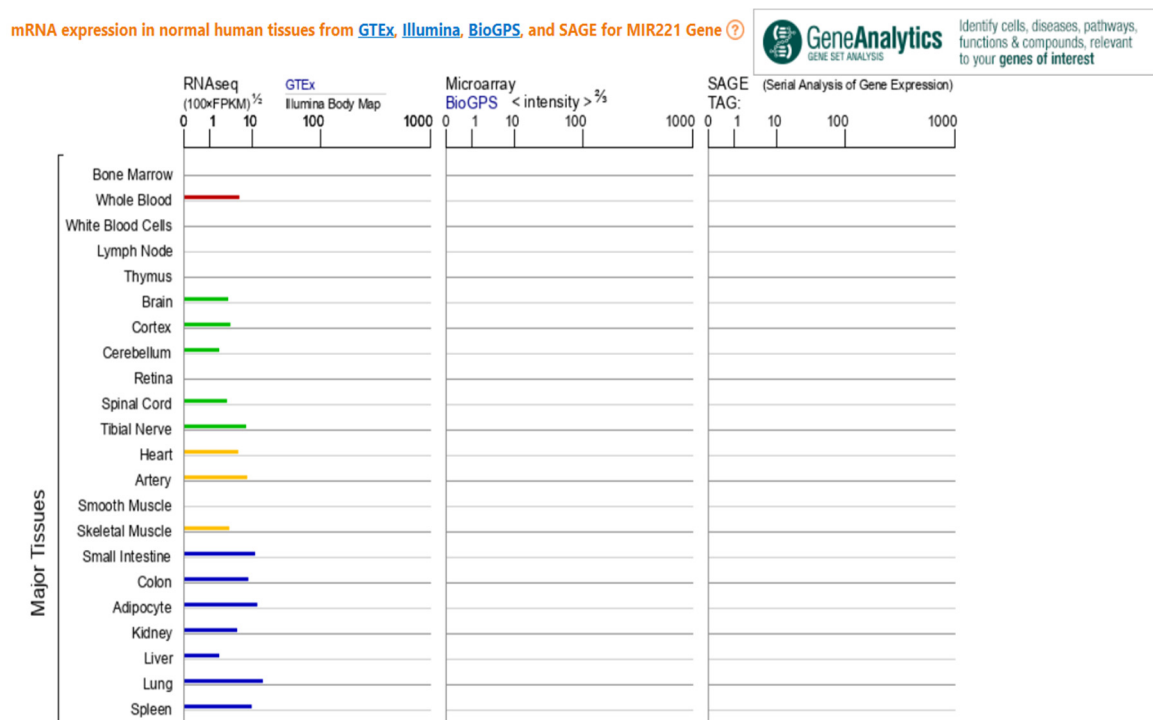


Figure S7: Gene expression of miRNA-221-3p in heart that was retrieved from GeneCards®: The Human Gene Database. Available at (<https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR221> (accessed on 1 June 2021)). It shows the basal expression of miRNA-221 in normal heart. X-axis represents level of RNA expression while Y-axis represents the tissue in which the gene is expressed.

Mirna △	Refseqid △	Genesymbol △	Score △	Position △	Binding Site △	Au △	Me △	N Pairings △	Targetscan △	Mirdb △	Mirtarbase △
hsa-miR-197-5p	NM_022060	ABHD4	0.92	3UTR	2221,2257	0.41	-5.036	20	–	–	–
hsa-miR-197-5p	NM_022060	ABHD4	0.85	3UTR	1144,1168	0.52	-6.937	19	–	–	–
hsa-miR-197-5p	NM_022060	ABHD4	1.00	3UTR	1994,2016	0.43	-9.552	18	–	–	–
hsa-miR-197-3p	NM_022060	ABHD4	1.00	3UTR	2047,2070	0.41	-9.547	17	–	–	–
hsa-miR-198	NM_022060	ABHD4	1.00	3UTR	1425,1445	0.46	-5.083	18	–	–	–
hsa-miR-198	NM_022060	ABHD4	1.00	3UTR	1991,2015	0.43	-5.763	18	–	–	–
hsa-miR-199a-5p	NM_022060	ABHD4	1.00	3UTR	2341,2362	0.34	-6.983	19	–	–	–
hsa-miR-208a-5p	NM_022060	ABHD4	0.92	5UTR	1,43	0.34	-3.938	16	–	–	–
hsa-miR-208a-5p	NM_022060	ABHD4	1.00	CDS	632,649	0.4	-9.22	16	–	–	–
hsa-miR-129-5p	NM_022060	ABHD4	0.92	3UTR	1743,1762	0.46	-15.567	15	–	–	–

Figure S8: ABHD4 mRNA is a direct target of miRNA-197-5p that was retrieved from miRWalk database (accessed on 1 June 2020). It shows direct interaction between miRNA-197-5p and ABHD4 mRNA.

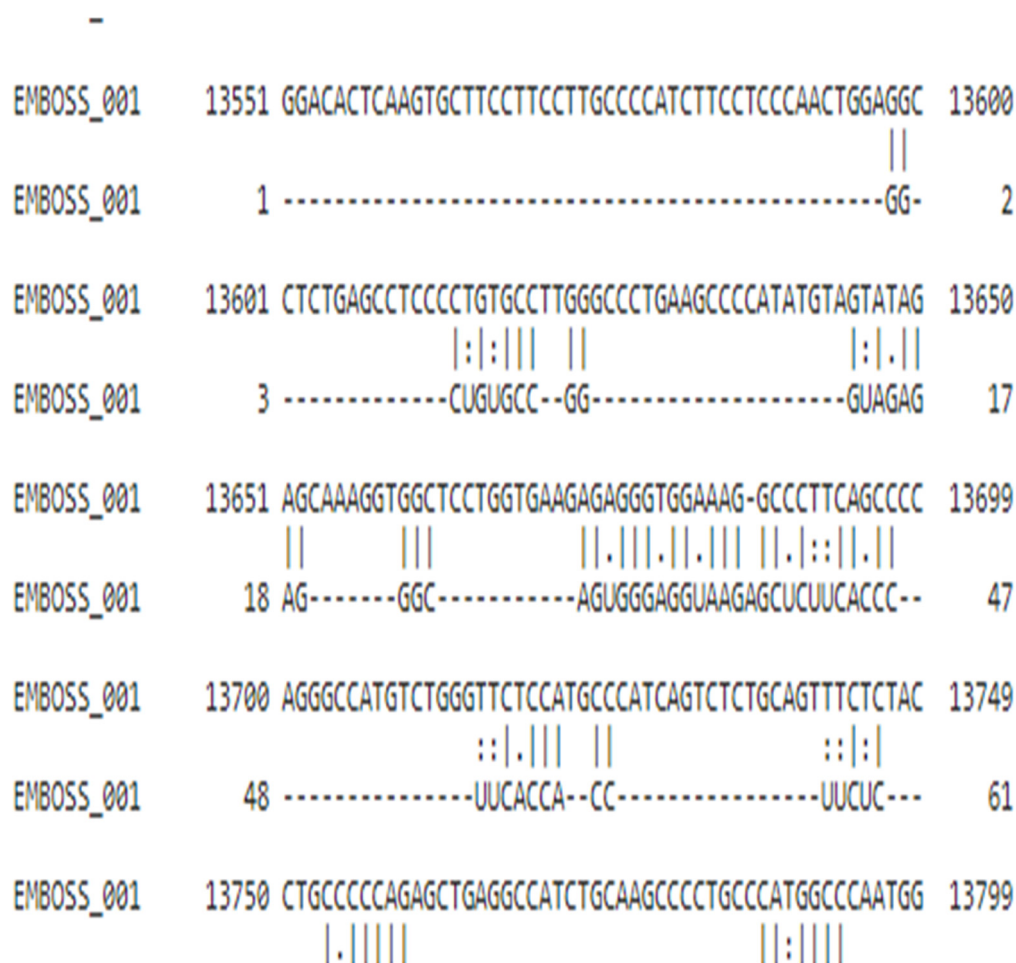


Figure S9. Alignment between ABHD4 mRNA and miRNA-197-5p that was performed using European bioinformatics institute database (accessed on 1 January 2021). It shows direct interaction between miRNA-197-5p and ABHD4 mRNA.

Mirna Δ	Refseqid Δ	Genesymbol Δ	Score Δ	Position Δ	Binding Site Δ	Au Δ	Me Δ	N Pairings Δ	Targetscan Δ	Mirdb Δ	Mirtarbase Δ
hsa-miR-216a-5p	NM_022060	ABHD4	0.81	CDS	89,111	0.35	-10.282	15	—	—	—
hsa-miR-216a-3p	NM_022060	ABHD4	0.85	CDS	292,314	0.41	-10.37	20	—	—	—
hsa-miR-217-5p	NM_022060	ABHD4	0.85	3UTR	2317,2350	0.38	-6.338	19	—	—	—
hsa-miR-218-2-3p	NM_022060	ABHD4	1.00	5UTR	10,54	0.37	-9.609	17	—	—	—
hsa-miR-219a-1-3p	NM_022060	ABHD4	0.81	CDS	412,430	0.43	-10.839	14	—	—	—
hsa-miR-219a-1-3p	NM_022060	ABHD4	0.85	3UTR	1450,1478	0.48	-9.532	17	—	—	—
hsa-miR-221-3p	NM_022060	ABHD4	0.92	3UTR	2016,2051	0.46	-5.714	21	—	—	—
hsa-miR-222-5p	NM_022060	ABHD4	0.85	CDS	369,388	0.38	-10.16	17	—	—	—
hsa-miR-222-3p	NM_022060	ABHD4	0.85	CDS	816,834	0.48	-14.182	15	—	—	—
hsa-miR-222-3p	NM_022060	ABHD4	0.85	3UTR	1455,1483	0.52	-8.406	16	—	—	—

Figure S10: ABHD4 mRNA is a direct target of miRNA-221-3p that was retrieved from miRWalk database. (accessed on 1 June 2021). It shows direct interaction between miRNA-221-3p and ABHD4 mRNA.


```

EMBOSS_001      1 ----- 0
EMBOSS_001      8301 GGGCCGCTCCCAGGCCAGCTTGGGGCAGACAGTTGTTAGGAGATAAAAC 8350
EMBOSS_001      1 -----AGCU-----ACA-UUGU----- 11
EMBOSS_001      8351 TCTTAGCTGCTGGAGTTCTGGGCTTTATTTCTTCTTCAACAAAGCTCTGA 8400
EMBOSS_001      12 -----CUGCUGGGUUC----- 23
EMBOSS_001      8401 CTCAGTTAGGTAAACACAGGCACTAGCAAGCCTGATCATTTCCAGAGAGT 8450
EMBOSS_001      24 ----- 23
EMBOSS_001      8451 TCCCAGGGACAGACACAAAGGAATACAGAAGATAATAGATTAATTAAAC 8500
EMBOSS_001      24 ----- 23
EMBOSS_001      8501 ATGCTGCCCATCTCTAGAGGAAGGCCCTCCCTGTTCCCTACAGGTATGCA 8550
EMBOSS_001      24 ----- 23
EMBOSS_001      8551 ATTGGCCTGATGAACAAGAGTCTGGAAAATATTAATATTTTAAAGATTT 8600
EMBOSS_001      24 ----- 23
EMBOSS_001      8601 TTTTAACTGAAAAATTGATACAAACATGGTATTTTTTTCTTTTTTAGG 8650
EMBOSS_001      24 ----- 23
EMBOSS_001      8651 TCAAAAATAATTAGCAAAAACATGATATTTTCAAAGGAAAGGAAGTCT 8700

```

Figure S11. Alignment between ABHD4 mRNA and miRNA-221-3p that was performed using European bioinformatics institute database (accessed on 1 June 2021). It shows direct interaction between miRNA-221-3p and ABHD4 mRNA.

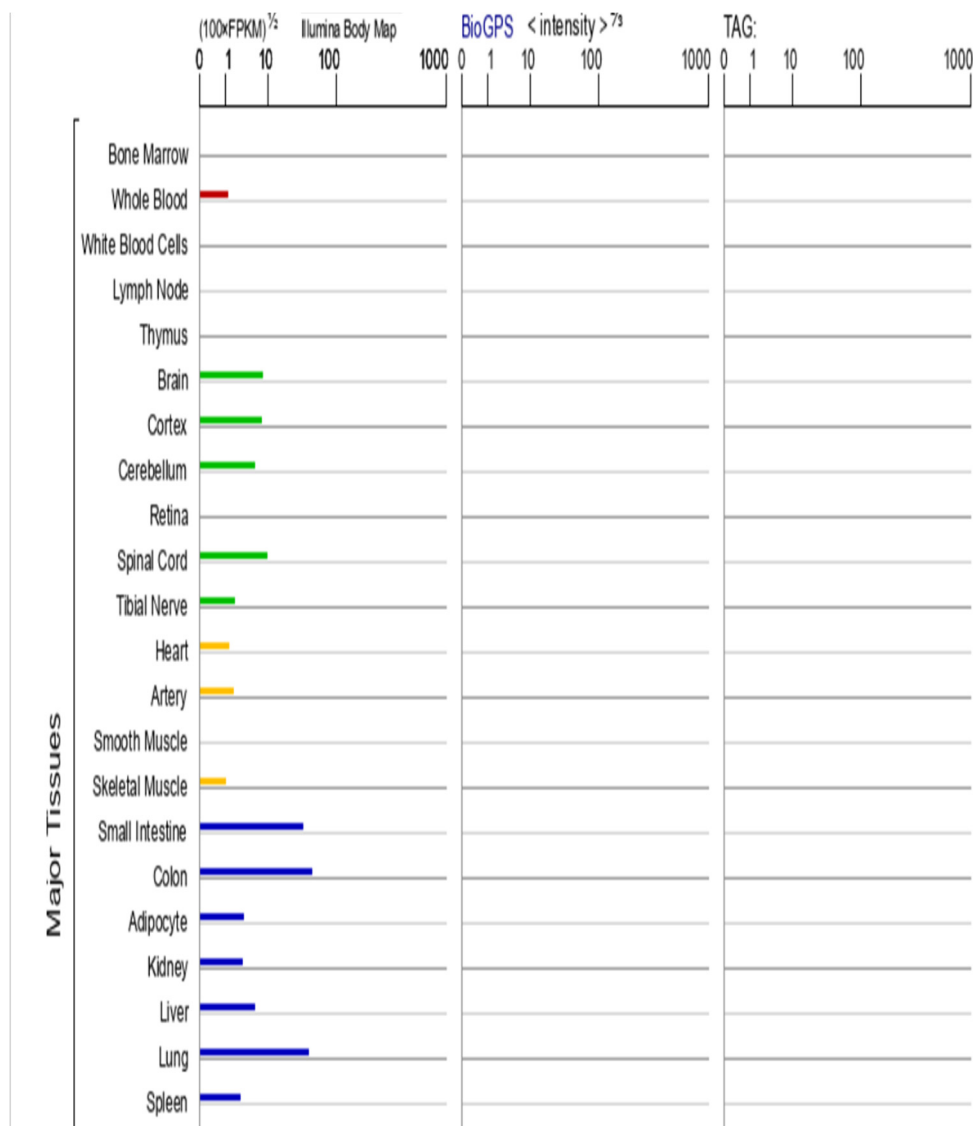
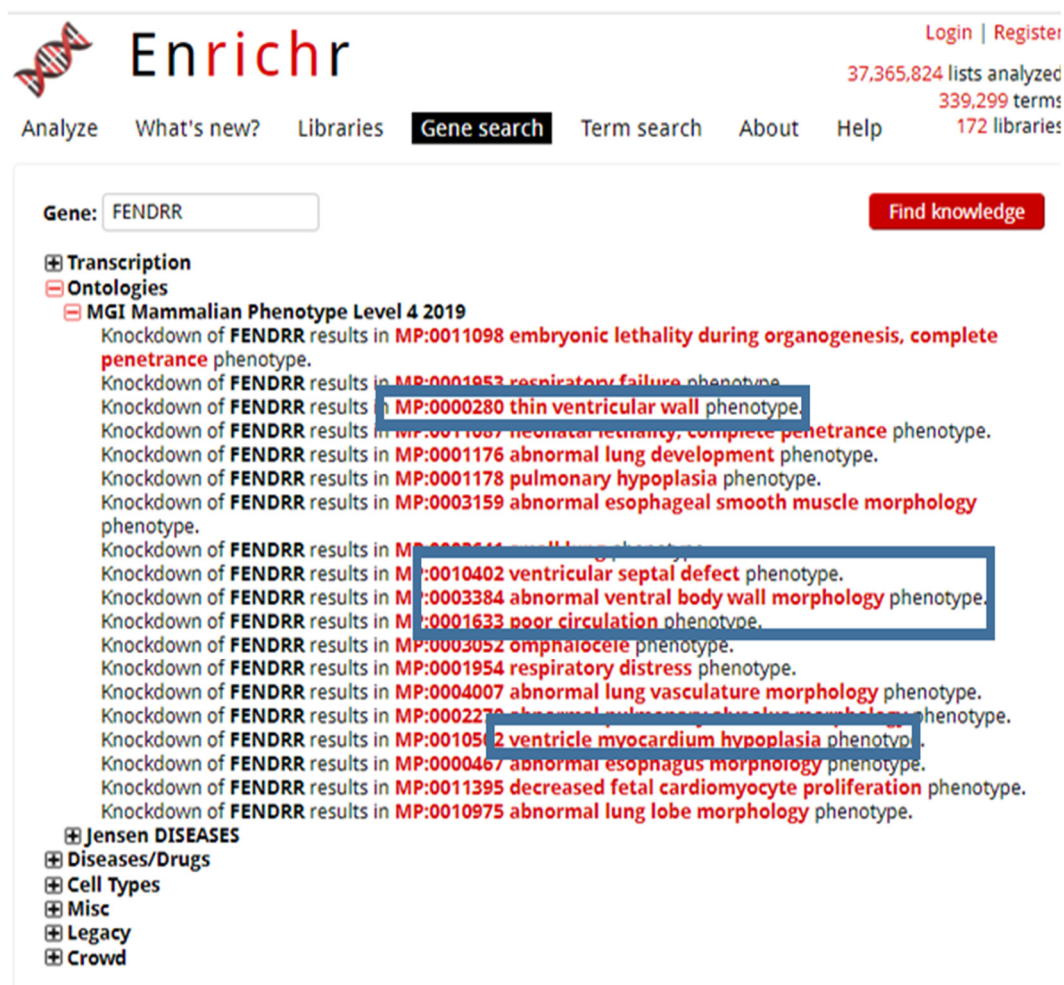


Figure S12. Gene expression of FENDRR lncRNA in heart that was retrieved from GeneCards®: The Human Gene Database. Available at (<https://www.genecards.org/cgi-bin/carddisp.pl?gene=FENDRR&keywords=FENDRR,lncRNA>, accessed on 1 June 2021) It shows the basal expression of FENDRR lncRNA in normal heart. X-axis represents level of RNA expression while Y-axis represents the tissue in which the gene is expressed.



Enrichr Login | Register
37,365,824 lists analyzed
339,299 terms
172 libraries

Analyze What's new? Libraries **Gene search** Term search About Help

Gene: **Find knowledge**

Transcription
Ontologies
MGI Mammalian Phenotype Level 4 2019
Knockdown of **FENDRR** results in **MP:0011098 embryonic lethality during organogenesis, complete penetrance** phenotype.
Knockdown of **FENDRR** results in **MP:0001953 respiratory failure** phenotype.
Knockdown of **FENDRR** results in **MP:0000280 thin ventricular wall** phenotype.
Knockdown of **FENDRR** results in **MP:0011087 neonatal lethality, complete penetrance** phenotype.
Knockdown of **FENDRR** results in **MP:0001176 abnormal lung development** phenotype.
Knockdown of **FENDRR** results in **MP:0001178 pulmonary hypoplasia** phenotype.
Knockdown of **FENDRR** results in **MP:0003159 abnormal esophageal smooth muscle morphology** phenotype.
Knockdown of **FENDRR** results in **MP:0003544 small lung** phenotype.
Knockdown of **FENDRR** results in **MP:0010402 ventricular septal defect** phenotype.
Knockdown of **FENDRR** results in **MP:0003384 abnormal ventral body wall morphology** phenotype.
Knockdown of **FENDRR** results in **MP:0001633 poor circulation** phenotype.
Knockdown of **FENDRR** results in **MP:0003052 omphalocele** phenotype.
Knockdown of **FENDRR** results in **MP:0001954 respiratory distress** phenotype.
Knockdown of **FENDRR** results in **MP:0004007 abnormal lung vasculature morphology** phenotype.
Knockdown of **FENDRR** results in **MP:0002276 abnormal pulmonary vasculature morphology** phenotype.
Knockdown of **FENDRR** results in **MP:0010512 ventricle myocardium hypoplasia** phenotype.
Knockdown of **FENDRR** results in **MP:0000467 abnormal esophagus morphology** phenotype.
Knockdown of **FENDRR** results in **MP:0011395 decreased fetal cardiomyocyte proliferation** phenotype.
Knockdown of **FENDRR** results in **MP:0010975 abnormal lung lobe morphology** phenotype.

Jensen DISEASES
Diseases/Drugs
Cell Types
Misc
Legacy
Crowd

Figure S13. Gene expression of FENDRR lncRNA in heart that was retrieved from Enricher tool database. Available at <https://maayanlab.cloud/Enrichr/> (accessed on 1 June 2021). It shows the FENDRR lncRNA relation to different cardiac disorders.



FENDRR:15	FENDRR	chr16:86487716-86490879	-	2825
FENDRR:16	FENDRR	chr16:86487706-86490879	-	2835
FENDRR:17	FENDRR	chr16:86474539-86477993	-	2138
FENDRR:18	FENDRR	chr16:86490183-86508886	-	563
FENDRR:19	FENDRR	chr16:86490268-86508886	-	969
FENDRR:2	FENDRR	chr16:86490268-86508877	-	960
FENDRR:20	FENDRR	chr16:86474529-86508886	-	3121
FENDRR:21	FENDRR	chr16:86474623-86508886	-	3211
FENDRR:22	FENDRR	chr16:86474623-86508886	-	3606
FENDRR:23	FENDRR	chr16:86478011-86508886	-	731
FENDRR:24	FENDRR	chr16:86487737-86508886	-	2630
FENDRR:25	FENDRR	chr16:86473638-86498552	-	4093
FENDRR:26	FENDRR	chr16:86474623-86498552	-	3164

Figure S14. FENDRR lncRNA detailed isoform that was retrieved from LNCipedia database, (accessed on 1 June 2021). It presents the details of FENDRR lncRNA isoforms.

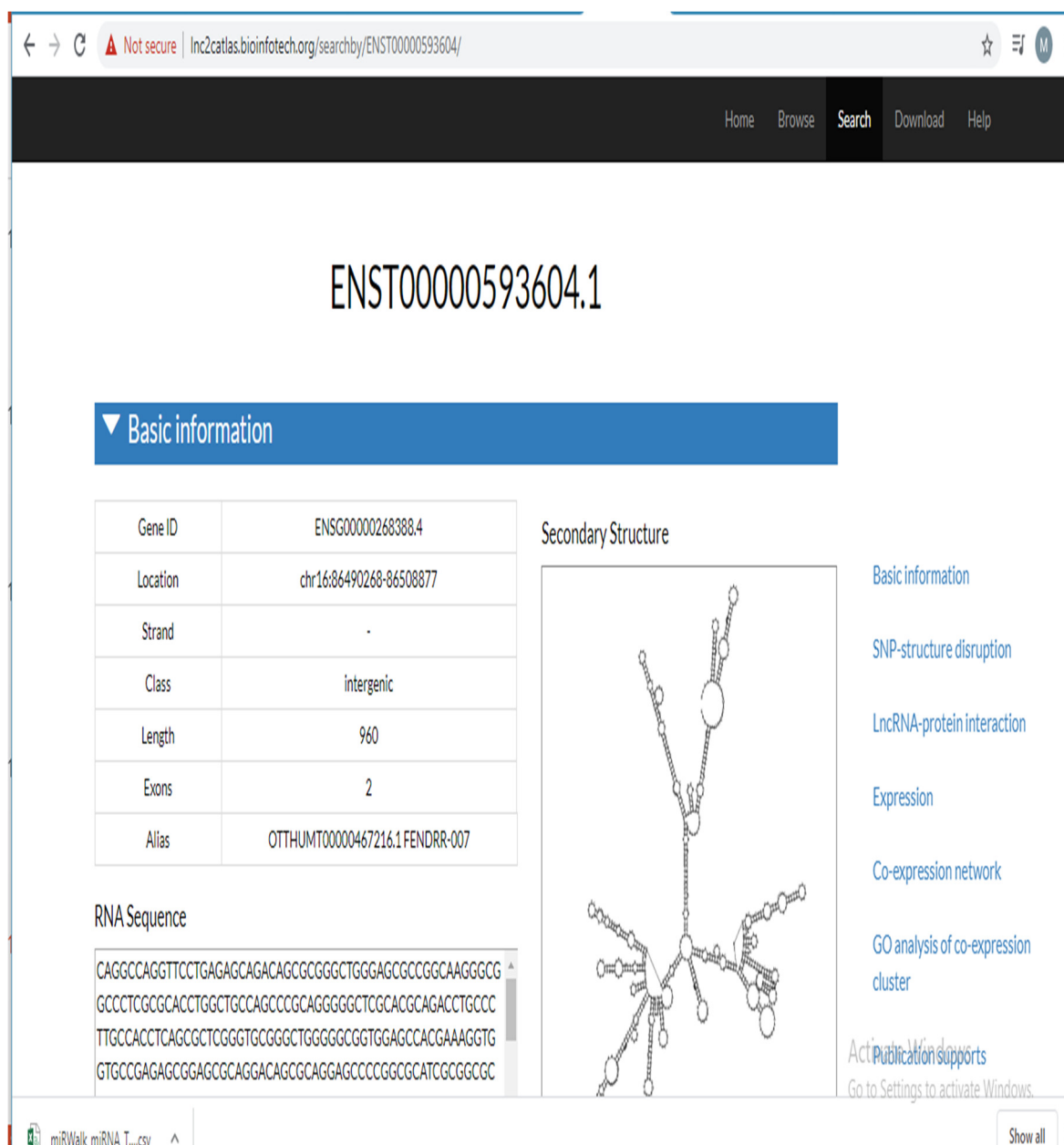


Figure S15. FENDRR lncRNA structure that was retrieved from Lnc2atlas database (accessed on 1 June 2021). It presents the detailed structure of FENDRR lncRNA.

```

EMBOSS_001      151 GACTGTCTGTGGCTGAGGAACAGTTGTAGACACCTTCCCCTCTTCCTTT      200
EMBOSS_001      1  ----- 0
EMBOSS_001      201 TCCAGGTCGGCCTCCGGGAG----GGCGGGGGTGGGTGCGTTGCTTG      245
EMBOSS_001      1  --CAGGCCAGGTTCTGTAGAGCAGACGCGGGCTGGGAGCG----- 41
EMBOSS_001      246 CTTTGCATTGCCCAG-AAGAGGCAGC-----GGCTG--AGCC      280
EMBOSS_001      42 -----CCGGCAAG-GGCGGCCCTCGCGCACCTGGCTGCCAGCC      78
EMBOSS_001      281 TGGGGAGCCATGGGAGACGCGCTCGCCGCGAGCCGGGGATCTGGCTTT      330
EMBOSS_001      79 CG-----CAGGGG-----GCTCGCAGCAGACCTG---CC---CTTG      109
EMBOSS_001      331 CTACCTTAGTCTCGCGAGTGCCCTCATTCTCTCTGGCCTCTGGAGAG      380
EMBOSS_001      110 CCACCTCAG--CGCTCGGTGC-----GGCTGGGG--- 138
EMBOSS_001      381 ATTCCATGTTGATGTGTGAGATCCCGAAAGCAAGCTTGTGGGACGCGGG      430
EMBOSS_001      139 -----GCGGTG---GAGCCACGAAAG-----GTGGTGC-CGAG      167
EMBOSS_001      431 TGCGGAG-GTAG--CAGC-CAGGCGTGCTCGTCTCGACTTGCCCCCAGA      476
EMBOSS_001      168 AGCGGAGCGCAGGACAGCGCAGGAG-----CCCCGG- 198
EMBOSS_001      477 ACGGCAGTCGTGGGGATGGAGAGAGCCTCCTCCCTCCGCCCGGCAAGA-      525
EMBOSS_001      199 --CGCA-TCGCGG-----CGC---GCACAGAC      219
EMBOSS_001      526 -GAAGATGTGGAGAGACTGGAGAGGTCTCCATCGCGCTGAAAT----- 567
EMBOSS_001      220 CCAGGATTG-----TGAAGAGGTGACC-----CAAATTTCAAGA      254

```

Figure S16. Alignment between ABHD4 mRNA and FENDRR lncRNA that was performed using European bioinformatics institute database (accessed on 1 June 2021). It shows putative interaction between ABHD4 mRNA and FENDRR.


```

EMBOSS_001      1 ----- 0
EMBOSS_001    451 GGCAGATAGGGGTTGGTTATCCTATTGTCTTTACTTTTCATATATTTTATT 500
EMBOSS_001      1 ----- 0
EMBOSS_001    501 TTTTCTGTAATAAAACAAATTAAATCACCTGTCGTGACCTCACAGGGGC 550
EMBOSS_001      1 ----- 0
EMBOSS_001    551 CAGTGTGGGTTGTGGCGTGAGGCAGGAAGCTCTGCAGAGTTCCTTGGTCA 600
EMBOSS_001      1 ----- 0
EMBOSS_001    601 AAAGGATTAATTACAAAAGAACTCCATGAACACCGAGAAGAAGAGAAGGG 650
EMBOSS_001      1 ----- 0
EMBOSS_001    651 AATCCTGGCATTAAAGCCACAAAGAACTTGATATGGTCTTGTCTCTCT- 699
EMBOSS_001      1 -----AGCUACA-----UUGUCUGCUG 17
EMBOSS_001    700 --TCTCTCAATTGACAGTGAGAACTGAAGACCAGAGAGGGTGAGTGGTT 747
EMBOSS_001    18 GGUUUC----- 23
EMBOSS_001    748 TACTCAGTTTGGCACAACCTGACCCCAACCTAGCCCTCCATGAGGACTGAG 797
EMBOSS_001    24 ----- 23
EMBOSS_001    798 CGCATGAGAGATCCTGAGCCACAGCCGCCAGCCCTGCTCCTCTCGAATT 847
EMBOSS_001    24 ----- 23
EMBOSS_001    848 TCTGACCTACAGGAAGTGAAGAAGTAATGAAAGACTGCTGTTTAAAGCC 897

```

Figure S17. Alignment between hsa-miRNA-221-3p and FENDRR lncRNA that was performed using European bioinformatics institute database (accessed on 1 January 2021). It shows putative interaction between hsa-miRNA-221-3p and FENDRR.

Query	Length_Query	Target	Length_Target	dG	ndG	Start_Position_Query	End_Position_Query	Start_Position_Target	End_Position_Target
FENDRR	969	hsa-miR-221-3p	23	-7.25	-0.4833	234	256	1	23

Query	Length_Query	Target	Length_Target	dG	ndG	Start_Position_Query	End_Position_Query
Start_Position_Target		End_Position_Target					
FENDRR	969	hsa-miR-221-3p	23	-7.25	-0.4833	234	256
5'	ACTGCGCCAGGCGGCTTCCTGAGAGCAGAGCGGCTGGGAGCGCCAGGCGGCTTCGCGACCTGGCTGCCAGCCGACAGGCGCTCGCAGCAGACCTGCCCTTCCACCTCAGCGCTCGGCTGCGGCTGGGCGGCTGGGAGCCACGAAAGGTGGTGGCAGAGCGGAGCGGAG GACAGCGCAGAGGCGGCGGCGCATCGCGGCGGCGCAGAGCCAGGATTTGTGAAGAGGTGACCCAAATTTCAAGACAATGTTGGATGCAAGGATTTGCCAGCAACTGCATCACTGCAAAACAGCTCTGCCCGTGTCTCCGAGATACCAAGTGAATACATGATGGGATTTACATCTGAA AAACCAAGGCAAGAGGCGCATGGGAAAGGAGGAGGTGGAGCAGGACTGGACAGAGCTGATAAATGGTTGTGCTGAGTACTGGGCGAGATAGGGGTTGGTTATCCTATTGTCTTTACTTTTCATATATTTTATTTTCTGTAATAAAACAAATTAATACCTGCTGAGCTCACAGGCGCAGTG TGGGTTGTGGGCTGAGGCGAGGAGCTCTGAGAGTTCCTTGGTCAAAAGGATTAATTACAAAAGAACTCCATGAACACCGAGAGAGAGAGAGGGAATCCTGGCATTAAAGCCACAAAGAACTTGATATGGTCTTGTCTCTCTCTCAATTGACAGTGAGAACTGAAGACGAGAGGAGT GGTCTACTCAGTTTGGCACAACCTGACCCCAACCTGACCCCTCCATGAGGACTGAGCGCATGAGAGATCCTGAGCCACAGCGCCAGCCCTGCTCTCGAATTTCTGACCTACAGGAAGTGAAGAAGTGAAGAAGTGTCTTTAAAGCCATGCTTTTGGCATGTTTGTATGAGTGTGA GATAACGAGAAACATCGGATTTACATTT 3'						
..... .. .							
3' AGCTACATTGTCTGCTGGGTTTC 5'							

Figure S18. Alignment between hsa-miRNA-221-3p and FENDRR lncRNA that was performed using LncTar: an efficient tool for predicting RNA targets of lncRNAs (<http://www.cuilab.cn/lncTar>, accessed on 1 January 2021). It shows putative interaction between hsa-miRNA-221-3p and FENDRR.

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EMBOSS_001      1 --CAG-GCCAGGTTCTCTGAGAGCAGACAGCGCGGGCTGGGAGCGCCGGCA 47
                  |.| |||.||: ||||..|.|| :||| ||.|
EMBOSS_001      1 GGCUGUGCCGGU-----AGAGAGGGCAG-----UGGGA----GGUA 33

EMBOSS_001      48 AGGG-----CGGCCCTCGCGCACCTGGCTGCCAGCCCGCAGGGGGCTCGC 92
                  ||.| |..||:|.|| ||||: .|: |||.||.|||||
EMBOSS_001      34 AGAGCUCUUCACCCUUCAC-CACCU-UCU-CCACCAGCAUGG----- 73

EMBOSS_001      93 ACGCAGACCTGCCCTTGCCACCTCAGCGCTCGGGTGGGGCTGGGGGCGG 142
                  ||
EMBOSS_001      74 -----CC----- 75

EMBOSS_001      143 TGGAGCCACGAAAGTGGTCCGAGAGCGGAGCGCAGGACAGCGCAGGAG 192

```

Figure S19. Alignment between hsa-miRNA-197-5p and FENDRR lncRNA that was performed using European bioinformatics institute database (accessed on 1 January 2021). It shows putative interaction between hsa-miRNA-197-5p and FENDRR.

Query	Length_Query	Target	Length_Target	dG	ndG	Start_Position_Query	End_Position_Query	Start_Position_Target	End_Position_Target
FENDRR	969	hsa-miR-197-5p	23	-8.44	-1.4067	311	333	1	23

Query	Length_Query	Target	Length_Target	dG	ndG	Start_Position_Query	End_Position_Query
FENDRR	969	hsa-miR-197-5p	23	-8.44	-1.4067	311	333

5'

ACTGCGCGCCAGGCCAGGTTCTTGAGAGCAGACAGCGCGGGCTGGGAGCGCCGCAAGGGCGGCCCTCGCGCACCTGGCTGCGAGCCGCGAGGGGCTGCGACGCACTGCCCCCTTGCCACCTCAGCGCTCGGGTGGCGGGCTGGGGGCGGTGGAGCCACGAAAGTGGTGGAGCGGAGCGCGAGGACGCGCAGGAGCGCCCGCGCATCGCGCGCGCAGACCCAGGATTTGTGAAGAGGTGACCCAAATTTCAAGACAATGTTGGATGCAACGGATTTGCGACCACTGATCACTGTCAAAACAGCTCTGCCGTGTCTCCGAAGATACCAAGTGAATACATGTAGATGGGATTTACATCTGAA

AAACCAAGGCAAGAGGCCATGGGAAGGAGCGAGGTGGAGCAGGACTGGACAGAGCTGATAAATGGTTGTGCTGAGTACTGGGCGAGATAGGGGTGATCCATTGCTTTACTTTTCATATATTTATTTTCTGTAATAAAACAAATTAAGATCACTGTGCTGACCTCAGAGGGGCCAGTG

TGGGTTGTGGCGTGAGGCGAGGAGCTCTGAGAGTTCTTGGTCAAAAGATTAAATACAAAAGAACTCCATGAACACCGAGAGAGAGAGAGGGAATCCTGGCATTAAAGCCACAAAGAACTTGATATGGTCTTGTCTCTCTCAATTGACAGTGAGAACTGAAGACAGAGAGGGTGAGT

GGTTTACTCAGTTTGGCACAACCTGACCCCAACCTAGCCCTCCATGAGGACTGAGGCGATGAGAGATCCTGAGCCACAGCCGCCAGCCCTGCTCTCGAATTTCTGACCTACAGAACTGCAAGAAGTAAAGAAAGACTGCTGTTAAAGCCACTGCATTTTGGCATGTTTGTATGAGTCGTA

GATAACCAAGAAACATCGATTACATTT 3'

.....|||||.....|||

3' GGAGGGTGACGGGAGAGATGGGC 5'

Figure S20 Alignment between hsa-miRNA-197-5p and FENDRR lncRNA that was performed using LncTar: an efficient tool for predicting RNA targets of lncRNAs (<http://www.cuilab.cn/lncTar>, accessed on 1 January 2021). It shows putative interaction between hsa-miRNA-197-5p and FENDRR.