SUPPLEMENTARY DATA

Supplementary Figures

Supplementary Figure S1-The map of pHBAAV-U6-MCS-CMV-EGFP vector



Supplementary Figure S2 Sequence alignment of qPCR products in metabolic tissues with full length of lnc866 after Sanger sequencing. A-C: Upper panel, the sequence of lnc866 in islets, skeletal muscle and perirenal adipose tissue; lower panel, sequence alignment. D-F: Sanger sequence results with no matching sequences of lnc866 in liver, peritesticular adipose tissue, and brown adipose tissue.



Supplementary Figure S3-Identification of human homologous sequences of Inc866. (A) Searching for human homologous sequences using NCBI-BLAST. (B) Upper panel, Sanger sequencing results of qPCR product of human islets; lower panel, sequence alignment of qPCR products with full length of AL137118.20.

A

	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
•	Human DNA sequence from clone RP11-108P5 on chromosome 13q14.12-21.1, com	Homo sapiens	141	263	39%	7e-28	65.32%	162446	AL137118.20

Human DNA sequence from clone RP11-108P5 on chromosome 13q14.12-21.1, complete sequence Sequence ID: AL137118.20 Length: 162446 Number of Matches: 3

Range 1	: 143638 t	:o 144449 <u>(</u>	GenBank Graphics		▼ <u>Next Match</u> ▲ <u>Prev</u>	<u>vious Match</u>
Score		Expect	Identities	Gaps	Strand	
141 bits	s(155)	7e-28	550/842(65%)) 51/842(6%)	Plus/Minus	
Query	2152	ATCAAGTC	TTTGCTTTCTTTGG	ACAGCAACTATCCCTATTTI	TA-ACTACTTTTTGAAGT	2210
Sbjct	144449	ATCGAGCA	TTTGCTTTCTTTGG	PCAGCAGCTGTTC-TCTTTG	SCAGACCACTTCCTGTGGT	144391
Query	2211	TTCTTGAA	CCATGATCAAATAA	TTTATTTCCCTCAGTGI	CATGTTTGGATAATATTT	2267
Sbjct	144390	CCCCCTAA	CCATGATCAAATCA	CCATTCATTTCTCCCA-TGI	CTTATTTAGATAAGATTT	144332
Query	2268	TCCTGTAG	AAATCGTCTGTAAA	GACATTAATAGCACTAGTTI	GAGAAGTAGCATTCCTAC	2327
Sbjct	144331	GCTTC-AG	AAATGAATTGCCAA	GACATTCACAATGTTCATTI	GGGAAGTGGCATTTCTTC	144273
Query	2328	ACAATAAC	CTTTGAAAGGGTTG	AGAATATACTCAC-AG	aaaaaaaCCAGGATATGC	2382
Sbjct	144272	ACAGTGAC	TTCCCCAAGACTTG	AGAAAGCCCATATGGAGTAG	GAAAGACTCTGGATACAC	144213
Query	2383	CTGCCCCC	AGTTTACTCCTCCT	CCTCCAAACATCATTCAGAG	TCTTTCTCGGCTGCTTTA	2442
Sbjct	144212	CAGATCCC	AGCTCATTCCTTT	ACTCAACAAAAT-CACAG	CTTTTTCCTACTGCCTCA	144156
Query	2443	TTCCAATC	ACCAAGCTGAAGAC	AGTTCTAGCTCTGGTGCCCI	TTCCTCCAATATGA	2498
Sbjct	144155	TTCCAAAA	GCCCAGCTGTGGAA	IGTTCTGGCTGCTGTGCCCA	ATTTCTTCCTCTAATATTA	144096
Query	2499	GTCATGAA	TCTTCTCCAGTAAT	TTTCAGCCGTAGGTGTATCI	GATA-ACATGAGGTATCT	2557
Sbjct	144095	GTTCTGAA	TTCTCTCGAGTAGG	CTCAAGTAATAGGTATAGTA	AATTTATTTCAATAACT	144036
Query	2558	CCCTTTTG	AAATGGATAGTTTG	IGTTCATGGAAGGCAATGTI	CTGCTT-GTCTTAGTTTA	2616
Sbjct	144035	TTCCATTA	AAATTTGTAATGTA	IGCTTATGGAGATCAATGTI	CTATTGCGTGCTATTTTA	143976
Query	2617	TGATGATT	TTGGTCTTGGACTT:	IGCTTGTGAGTTTCTGAATI	GGGTCTGAGTAATTGTCT	2676
Sbjct	143975	TACTTT	TTAGTCTTGGAGTC:	IGCTCCATCTATT-TGAATG	AGGTTTGGATAGATGTTT	143919
Query	2677	GCCTTTGT	GTCTTTTAATACAT	GCCACAAACTCGGGGGGAAAA	AAGAAAACCACCTGACAC	2736
Sbjct	143918	GCCTTGGT	GTTTCTTAATATAT	ICCTTAAGCCTGAACAA	AAGCCTGACA-	143870
Query	2737	AGTAATCA	TGGGCTCATCAT:	ICTCTTCTCATCAGGAACAG	CTTTGCACAGTAATAAAG	2794
Sbjct	143869	TGACAA	TGCCCACTCATCAT:	TTTCTTCTCTTCAGGAATTG	STTTTGTGCAATAATAAAA	143812
Query	2795	TTCTGTTG	CTTTAGTCATTT(GCTTGTGTCAGAAGAGCCAA	AAAACGTATTGGACTGGA	2852
Sbjct	143811	TGCTATTG	CTTCTTAGTGATTT	GTATGTGGCAAAAGAGCCAA	AAAATTATATCTG-CTGGA	143753
Query	2853	GGAAGAGC	TTGTTTGCCTTAGA	AACAAAAGT-CACTCCTTCC	CAAACCTAATAAAACTCTG	2911
Sbjct	143752	тс	TTGTTTGCCTTAAA	AACAAAATTCCGTTTCTTTC	AGGTATGATATAA-TTTG	143700
Query	2912	GC-TGTTG	TAGTCTTCATGGGT	GTTACACTTTCGTCTTCATI	TTTCCAAGGTCTGATACA	2970
Sbjct	143699	ACTTGTCT	TATTCTTCATGGAT	ATTACATTTTCATCTTTGTT	TTTCTGAATTCTGACATA	143640
Query	2971	GT 2972				
Sbjct	143639	GT 1436	38			

Range 2	: 146533	to	146662	GenBank	Graphics
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▼ Next Match ▲ Previous Match ▲ First Match

Score		Expect	Identities	Gaps	Strand
63.5 bits(69)		2e-04	93/130(72%)	4/130(3%)	Plus/Minus
Query	373	TATCGTTGCT	STGGTTGTTATTCT(GCAAGTGAGATAATTAAG	GTTTAGAAGAGTCTAAAG
Sbjct	146662	TATCATTGTT	GGTTGTTATTT	ACGAATGAGAGAATTCAG	CTTTGGGCTGGTCTAACA
Query	433	TCATTTAACTO	GACAAGGGACAGGA	CTGGAATTCTAACCAAG-	-CTACCTGACATCGGCA-
Sbjct	146602	ACACTTAGCT	ACTAAGTGGCAGAA	CTAGAATTGTAGCCCAGG	CCTGTCTGACATCAGTAA
Query	490	-TGTTCTTGA	498		
Sbjct	146542	CTGTTCTTGA	146533		

Range 3: 145118 to 145375 GenBank Graphics

Next Match A Previous Match A First Match

Score		Expect	Identities	Gaps	Strand	
59.0 bit	ts(64)	0.002	178/269(66%)	26/269(9%)	Plus/Minus	
Query	1530	TGATCATTT	CTGTACTCTCTGCAAAG	TACCAGCCTAACTGT	CCAACTTCCTCCGGAACCT	1589
Sbjct	145375	TGATCATTT	TTGTTTCTTCTGTTCAT	TACCAGCCTAACAGG	STCACTTCACCTGGGCCCT	145310
Query	1590	GAGGG-CAC	TTTAAACTTCTTTGTTA	GCCTTGCCAGCATTT	CCCCTTTGATTCAGGTTGA	1648
Sbjct	145315	TGGAGACAC	TTTGGACATTCTTGTTA	GACTTTTCAGACCTA	ACCCTTTGGTTCAGGTTGA	145250
Query	1649	AATAGTTAA	CCTAGAATTGGAT	CTCAGCCTGGTGAGA	ACTTCCTCTGAAGTTCATG	1704
Sbjct	145255	AATGATTGT	TCCAGAGCTTCCTGAAT	CTCAGCCTGTTG	TTTCTTCAGTA-TTC-TG	145202
Query	1705	TTATGTCTT	TTAACCAAATC-CCCCT	TGTATC	CCTCAAAGAGAAATTCTC	1754
Sbjct	145201	TTGTGCCTC	TTAATCAAGTCTCCACT	CCCAGGCTCTTTCTC	CCTCAGAAAAATTCTC	145144
Query	1755	CTTCAATGG	TCGTGGCATTCCTTCCT	TTA 1783		
Sbjct	145143	CCTCAG	TGATTGCATGCCTTTCT	TTA 145118		





Lage Antices Lage

Human DNA sequence from clone RP11-108P5 on chromosome 13q14.12-21.1, complete sequence Sequence ID: AL137118.20 Length: 162446 Number of Matches: 1

Range	Range 1: 143963 to 144121 GenBank Graphics							
Score		Expect	Identities	Gaps	Strand			
279 bi	ts(309)	5e-71	158/159(99%)	1/159(0%)	Plus/Plus			
Query	10	AGACTAAAA-GTAT	AAAATAGCACGCAATAGA	ACATTGATCTCCATAAGCA	TACATTACA 68			
Sbjct	143963	AGACTAAAAAGTAT	AAAATAGCACGCAATAGA	ACATTGATCTCCATAAGCA	TACATTACA 1440)22		
Query	69	AATTTTAATGGAAA	GTTATTGAAAATAAATTT	ACTATACCTATTACTTGAG	CCTACTCGA 128			
Sbjct	144023	AATTTTAATGGAAA	GTTATTGAAAATAAATTI	ACTATACCTATTACTTGAG	CCTACTCGA 1440	082		
Query	129	GAGAATTCAGAACT	AATATTAGAGGAAGAAAT	GGGCACA 167				
Sbjct	144083	GAGAATTCAGAACT	AATATTAGAGGAAGAAAT	GGGCACA 144121				

Supplementary Figure S4-Confocal image of GFP investigation in pancreas sections after injection of sh866-V or shNC-V into mice via an intraductal route. Quantification of the GFP signals was performed using NIH Image J 1.52 software. Graph representing the number of pancreas with GFP expression in whole area. Scale bar: 200 µm. shNC-V, the negative control shRNA engineered into the AAV9 vector; sh866-V, AAV9 vector carrying shRNA-lnc866. Representative image of 3 independent experiments.



shNC-V

sh866-V

Supplementary Figure S5-Effect of AL137118.20 Smart Silencer on stearic acid-impaired GSIS. *P < 0.05, **P < 0.01 versus the ss-NC group; P < 0.05, $^{\sim}P < 0.01$ versus the SA+ss-AL group. SA, stearic acid; ss-AL, Smart Silencer for AL137118.20; ss-NC, negative control of ss-AL. n = 5 samples from normolipidemic individuals.



Supplementary Figure S6-Inhibitoty efficiency of Smart Silencer for AL137118.20 in the absence and presence of stearic acid. *P < 0.05, **P < 0.01 versus the ss-NC group; P < 0.05, $^{\sim}P < 0.01$ versus the SA+ss-AL group. SA, stearic acid; ss-AL, Smart Silencer for AL137118.20; ss-NC, negative control of ss-AL. n = 5 samples from normolipidemic individuals.



Supplementary Figure S7-The co-expression network of lnc866, miR-297b-5p, and relevant mRNAs. Yellow circle: lnc866; pink circle: miR-297b-5p; green circle: mRNAs; black line: negative relationship.



Supplementary Figure S8-Inhibitory effect of Smart Silencer for lnc866 on miR-297b-5p expression in β -TC6 cell. *P < 0.05 versus the ss-NC group. ss-866, Smart Silencer for lnc866; ss-NC, the negative control of Smart Silencer. n = 3 independent cell cultures per group.



Supplementary Figure S9-Change in the expression of hsa-miR-297 after knockdown of AL137118.20 in the presence of stearic acid.*P < 0.05, **P < 0.01 versus the ss-NC group; P < 0.05, P < 0.01 versus the SA+ss-AL group. SA, stearic acid; ss-AL, Smart Silencer for AL137118.20; ss-NC, negative control of ss-AL. n = 5 samples from normolipidemic individuals.



Supplementary Figure S10-Effect of AMO-297 on GSIS and inflammatory factors level in β -TC6 cells without stearic acid treatment. (*A*) miR-297b-5p expression after the transfection of miR-297b-5p mimic or AMO-297b-5p in β -TC6 cells. (*B*) Insulin concentration after the transfection of a miR-297b-5p mimic or AMO-297b-5p in β -TC6 cells. (*C*) Western blots showing the protein expression of NF κ B p65, IL6, and TNF- α following the transfection of a miR-297b-5p mimic or AMO-297b-5p in β -TC6 cells. **P*<0.05, ***P*<0.01 versus the AMO-NC group; **P*<0.05, ^*P* < 0.01 versus the stearic acid AMO-297 group. AMO-297, anti-miR-297b-5p oligonucleotides; AMO-NC, negative control of AMO-297; 297mimic, miR-297b-5p mimics. *n* = 3 independent cell cultures per group.



Supplementary Figure S11-Role of miR-297b-5p in stearic acid treated mouse islets. (A) Protection of the stearic acid–impaired glucose-stimulated insulin secretion (GSIS) after the transfection of a miR-297b-5p mimic. (B) Western blot showing the effects of miR-297b-5p on the expressions of NF κ B p65, IL6, TNF- α and SAA3 following stearic acid treatment. *P < 0.05, **P < 0.01 versus the 297NC group; $^{P} < 0.05$, $^{\sim}P < 0.01$ versus the SA+297NC group. SA, stearic acid; 297NC, negative control of miR-297b-5p; 297mimic, miR-297b-5p mimics. n = 3 independent cell cultures per group.



Supplementary Figure S12-Changes in expressions of hsa-miR-297 and SAA1 in islets from patients with hyperlipidemia. *P < 0.05, **P < 0.01 versus the N groups. N, normal lipidemic participants; H, hyperlipidemic patients. n=13 and 9 samples in N and H group, respectively.



Supplementary Figure S13-Involevement of SAA3 in stearic acid treated mouse islets. (*A*) Restoration of the stearic acid–impaired glucose-stimulated insulin secretion (GSIS) after the knocking down of *Saa3*. (*B*) Effects of si-*Saa3* on NF κ B p65, IL6, TNF- α and SAA3 protein expression in the presence of stearic acid. SA, stearic acid; si-*Saa3*, siRNA for *Saa3*; si-NC, negative control of si-*Saa3*. **P*<0.05, ***P*<0.01 *versus* the si-NC group; **P*<0.05, ***P*<0.01 *versus* the SA+si-*Saa3* group. *n* = 3 independent cell cultures per group.



Supplementary Figure S14-Sequence alignment of human SAA1 in islets with

mouse *Saa3*. (A) Sanger sequencing results of *SAA1* in human islets. (B) Upper panel, searching for the mouse homologous sequence of qPCR product of human *SAA1* in islets; lower panel, sequence alignment of qPCR product of human *SAA1* in islets with mouse *Saa3*.



B

Seq	Sequences producing significant alignments Download 🗡 New Select columns 🗡 Show 🗌										
	select all 10 sequences selected	Ger	Bank	Grap	hics	Distanc	e tree of	f results	New MSA Viewer		
	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession		
	Trans	cripts									
~	Mus musculus serum amyloid A 3 (Saa3). mRNA	Mus musculus	133	133	83%	4e-29	83.33%	531	NM_011315.3		
~	Mus musculus serum amyloid A 2 (Saa2), transcript variant 4, mRNA	Mus musculus	123	123	76%	7e-26	83.48%	822	NM_001379269.1		
~	Mus musculus serum amyloid A 2 (Saa2), transcript variant 1, mRNA	Mus musculus	123	123	76%	7e-26	83.48%	609	NM_011314.3		
~	Mus musculus serum amyloid A 2 (Saa2). transcript variant 2. mRNA	Mus musculus	123	123	76%	7e-26	83.48%	606	NM_001357491.2		
~	Mus musculus serum amyloid A 2 (Saa2), transcript variant 3, mRNA	Mus musculus	123	123	76%	7e-26	83.48%	825	NM_001379268.1		
~	PREDICTED: Mus musculus serum amyloid A 1 (Saa1). transcript variant X2. mRNA	Mus musculus	114	114	78%	1e-23	81.36%	1026	XM_006540725.2		
~	PREDICTED: Mus musculus serum amyloid A 1 (Saa1), transcript variant X1, mRNA	Mus musculus	114	114	78%	1e-23	81.36%	1029	XM_006540724.2		
~	Mus musculus serum amyloid A 1 (Saa1), transcript variant 1, mRNA	Mus musculus	114	114	78%	1e-23	81.36%	609	NM_009117.4		
~	Mus musculus serum amyloid A 1.(Saa1). transcript variant 2. mRNA	Mus musculus	114	114	78%	1e-23	81.36%	612	NM_001357493.1		
~	Mus musculus strain C57BL/6J chromosome 7, GRCm39	Mus musculus	107	410	55%	1e-21	88.10%	144995196	NC_000073.7		

▲ Download ➤ GenBank Graphics

Mus musculus serum amyloid A 3 (Saa3), mRNA.

Sequence ID: <u>NM_011315.3</u> Length: 531 Number of Matches: 1

Range	1: 18	1 to 306	<u>GenBank</u>	Graphics				1	Next M
Score			Expect	Identities	;		Gaps	S	trand
133 bi	ts(147	7)	4e-29	105/126	5 (83%)		0/126(0%)	P	lus/Plus
Query	24	CTCAGAC	AAATACTT		GGGAACT.	ATGATGCT	GCCAAAAGGGG,	ACCTGGGG	G 83
Sbjct	181	CTCAGAC	AAATACTT	CCATGCTCGG	GGGAACT.	ATGATGCT	GCCCGGAGGGG	receeded	Ġ 240
Query	84	TGCCTGG	GCTGCAGA			GAGAGAAT		CTTTGGCC	CA 143
Sbjct	241	AGCCTGG	ĠĊŦĠĊŦĂĂ	ÁGTCÁTCÁGC	GATGCCA	GAGAGGCT	GTTĊĂĠĂAGŤŤO	ĊACGĠĠĂĊ	CÁ 300
Query	144	TGGTGC	149						
Sbjct	301	TGGAGC	306						

Supplementary Tables

name	sequence
Promoter of U6	GAGGGCCTATTTCCCATGATTCCTTCATATTTGCA
	TATACGATACAAGGCTGTTAGAGAGATAATTGGA
	ATTAATTTGACTGTAAACACAAAGATATTAGTAC
	AAAATACGTGACGTAGAAAGTAATAATTTCTTGG
	GTAGTTTGCAGTTTTAAAATTATGTTTTAAAATG
	GACTATCATATGCTTACCGTAACTTGAAAGTATTT
	CGATTTCTTGGCTTTATATATCTTGTGGAAAGGA
	С
EGFP	ATGGTGAGCAAGGGCGAGGAGCTGTTCACCGG
	GGTGGTGCCCATCCTGGTCGAGCTGGACGGCGA
	CGTAAACGGCCACAAGTTCAGCGTGTCCGGCGA
	GGGCGAGGGCGATGCCACCTACGGCAAGCTGA
	CCCTGAAGTTCATCTGCACCACCGGCAAGCTGC
	CCGTGCCCTGGCCCACCCTCGTGACCACCCTGA
	CCTACGGCGTGCAGTGCTTCAGCCGCTACCCCG
	ACCACATGAAGCAGCACGACTTCTTCAAGTCCG
	CCATGCCCGAAGGCTACGTCCAGGAGCGCACCA
	TCTTCTTCAAGGACGACGGCAACTACAAGACCC
	GCGCCGAGGTGAAGTTCGAGGGCGACACCCTG
	GTGAACCGCATCGAGCTGAAGGGCATCGACTTC
	AAGGAGGACGGCAACATCCTGGGGCACAAGCT
	GGAGTACAACTACAACAGCCACAACGTCTATAT
	CATGGCCGACAAGCAGAAGAACGGCATCAAGG
	TGAACTTCAAGATCCGCCACAACATCGAGGACG
	GCAGCGTGCAGCTCGCCGACCACTACCAGCAGA
	ACACCCCCATCGGCGACGGCCCCGTGCTGCTGC

Supplementary Table S1 The details of sh866-V and shNC-V

	CCGACAACCACTACCTGAGCACCCAGTCCGCCC
	TGAGCAAAGACCCCAACGAGAAGCGCGATCAC
	ATGGTCCTTAAGGAGTTCGTGACCGCCGCCGGG
	ATCACTCTCGGCATGGACGAGCTGTACAAGTAA
siRNA for shNC-V	TTCTCCGAACGTGTCACGTAA
shRNA for shNC-V	Top strand:
	GATCCGTTCTCCGAACGTGTCACGTAATTCAAG
	AGATTACGTGACACGTTCGGAGAATTTTTTC
	Bottom strand:
	AATTGAAAAAATTCTCCGAACGTGTCACGTAAT
	CTCTTGAATTACGTGACACGTTCGGAGAACG
siRNA for sh866-V	CAGCCTGGTGAGAACTTCCTCTGAA
shRNA for sh866-V	Top strand:
	AATTCGCAGCCTGGTGAGAACTTCCTCTGAATT
	CAAGAGATTCAGAGGAAGTTCTCACCAGGCTGT
	TTTTTG
	Bottom strand:
	GATCCAAAAAACAGCCTGGTGAGAACTTCCTCT
	GAATCTCTTGAATTCAGAGGAAGTTCTCACCAG
	GCTGCG
viral titer for sh866-V	1.2*10^12 μg/mL
viral titer for shNC-V	3.5*10^12 μg/mL

shNC-V, the negative control shRNA engineered into the AAV9 vector; sh866-V, AAV9 vector carrying shRNA-lnc866; EGFP, enhanced green fluorescent protein; AAV9, Adeno-Associated Virus serotype 9.

Ingredients	Low fat diet	High SA diet
Cornstarch (g/kg)	367.5	40
Casein (g/kg)	213.465	258.45
Dextrinized cornstarch (g/kg)	121.53	121.53
Sucrose (g/kg)	88.91	88.91
Lard (g/kg)	0	316.6
Soybean oil (g/kg)	51	32.31
Fiber (g/kg)	40	64.61
Mineral mix (AIN-93G-MX) (g/kg)	12.92	12.92
Vitamin mix (AIN-93G-VX) (g/kg)	12.92	12.92
L-cystine (g/kg)	3.88	3.88
Choline bitartrate (g/kg)	2.58	2.58
Calcium carbonate (g/kg)	16.8	16.8
Calcium hydrogen phosphate (g/kg)	7.11	7.11
Potassium citrate(g/kg)	21.32	21.32
Edible blue dye (g/kg)	0.065	0.065
Energy (kcal/kg)	3851.82	5242.95

Supplementary Table S2 The composition of the diet for mice

SA: stearic acid

Gene	sequences
siRNA-1 target sequence	CTGCAAGTGAGATAATTAA
siRNA-2 target sequence	GCATTCCTTCCTTTAAACA
siRNA-3 target sequence	GAGAATATACTCACAGAAA
antisense oligonucleotides target sequence-1	ACGGCTTCCAGATCTGTCTT
antisense oligonucleotides target sequence-2	CGCAGCACATACCTCACATT
antisense oligonucleotides target sequence-3	CCTCCTCCTCCAAACATCAT

Supplementary Table S3 Target sequences of Smart Silencer for mouse lnc866

Supplementary Table S4 Target sequences of Smart Silencer for human

Gene	sequences
siRNA-1 target sequence	GCAATTCATTTCTGAAGCA
siRNA-2 target sequence	GGAGCAGACTCCAAGACTA
siRNA-3 target sequence	CACTAAGAAGCAATAGCAT
antisense oligonucleotides target sequence-1	ATCATACCTGAAAGAAACGG
antisense oligonucleotides target sequence-2	GGCATTGTCATGTCAGGCTT
antisense oligonucleotides target sequence-3	TAGATGGAGCAGACTCCAAG

AL137118.20

Supp	lementary	y Table S	S5 Tar	get sec	juences	of siRN	JAs ı	ised :	in 1	this	stud	y
												. /

name	sequences
siRNA-Saa3	GGAGTTGACAGCCAAAGAT
siRNA- <i>Rela</i>	GAAGCACAGATACCACCAA
siRNA- <i>116</i>	GGACTGATGCTGGTGACAA
siRNA- <i>Tnfa</i>	GACAACCAACTAGTGGTGC

Gene		sequences (5' to 3')
TCONS_00077866-1	Forward	TGTTCCTTCGTGATTCCAGCATCG
(mouse)	Reverse	GCAGCCAGCAGAGATCACATCG
TCONS_00077866-2	Forward	TCAGCAACGGCTTCCAGATC
(mouse)	Reverse	AACGATAGCAGCCACTAGGTGG
AL137118.20	Forward	TCCAAACCTCATTCAAATAG
(human)	Reverse	TGTGCCCATTTCTTCCTC
TCONS_00089573	Forward	ATCAACTCAGCACACTGGAGCATG
(mouse)	Reverse	CAGAAGCGACAGGCATCAGCAG
TCONS_00230830	Forward	GCTGTCTCATTCACCGCCAGTC
(mouse)	Reverse	CGGGAAGTCAAAGGAGAGGCAG
TCONS_00230836	Forward	AACCACAGGCTTCGGGATAGTC
(mouse)	Reverse	CAAGCATAACAGGCGGGAAGTC
TCONS_00252600	Forward	CCGGAGCATTGTCCAGTATACC
(mouse)	Reverse	GCGTCCGTGATAATTGGATGTG
miR-297b-5p	Reverse transcription	GTCGTATCCAGTGCGTGTCGTGGAGTC
		GGCAATTGCACTGGATACGACACATGT
	Forward	GGGGATGTATGTGTGCATGA
	Reverse	GTATCCAGTGCGTGTCGTG
hsa-miR-297	Reverse transcription	GTCGTATCCAGTGCGTGTCGTGGAGTC
		GGCAATTGCACTGGATACGACCATGCA
	Forward	AUGUAUGUGUGCAUGUGCAUG
	Reverse	GTATCCAGTGCGTGTCGTG
U6	Reverse transcription	CGCTTCACGAATTTGCGTGTCAT
	Forward	GCTTCGGCAGCACATATACTA
	Reverse	CGCTTCACGAATTTGCGTGTC
Saa3 (mouse)	Forward	GAAGTTCACGGGACATGGAG
	Reverse	TTCAGCACATTGGGATGTTT

Supplementary Table S6 Primer sequences used for qRT-PCR in this study

SAA1 (human)	Forward	TCGGGACATGTGGAGAGCCTAC
	Reverse	CGCACCATGGCCAAAGAATC
Il6 (mouse)	Forward	TGTGACTCCAGCTTATCTCTTGG
	Reverse	TGATGGATGCTACCAAACTGGA
<i>Tnf-</i> α (mouse)	Forward	ACAAGGTACAACCCATCGGC
	Reverse	CCCTCACACTCACAAACCAC
Rela (mouse)	Forward	GAGGGGAAACAGATCGTCCA
	Reverse	ATTTCCGCCTCTGGCGAATG
Actb (mouse)	Forward	GGTCAGAAGGACTCCTATGTGG
	Reverse	TGTCGTCCCAGTTGGTAACA
ACTB (human)	Forward	ATGGATGATGATATCGCC
	Reverse	GATGCCTCTCTTGCTCTG

_

hsa: human

name	Regulation	log ₂ fold change	P value
TCONS_00088788	Down	-2.093	3.10E-66
TCONS_00038546	Ups	2.027	1.38E-45
TCONS_00184470	Down	-2.262	2.48E-33
TCONS_00233737	Down	-1.935	3.26E-28
TCONS_00100616	Down	-5.992	4.43E-28
TCONS_00233734	Down	-1.596	4.06E-24
TCONS_00128285	Ups	1.645	1.53E-17
TCONS_00098808	Ups	4.455	1.47E-15
TCONS_00139241	Ups	2.896	7.29E-14
TCONS_00164947	Down	-4.105	1.10E-12
TCONS_00077866	Ups	4.055	1.21E-12
TCONS_00250720	Down	-3.783	3.50E-12
TCONS_00146205	Ups	1.012	9.31E-12
TCONS_00184468	Down	-2.351	1.99E-11
TCONS_00068951	Ups	1.519	3.83E-11
TCONS_00239172	Down	-3.593	4.32E-11
TCONS_00004655	Ups	3.733	4.55E-11
TCONS_00078259	Down	-3.770	7.39E-11
TCONS_00057572	Down	-2.086	1.33E-10
TCONS_00102704	Ups	2.883	1.77E-10
TCONS_00009134	Ups	1.060	2.22E-10
TCONS_00088298	Ups	1.537	4.73E-10
TCONS_00088299	Ups	1.679	7.43E-10
TCONS_00195490	Ups	1.567	8.60E-10
TCONS_00239170	Down	-2.512	1.45E-09
TCONS_00088303	Ups	1.598	1.50E-09

Supplementary Table S7 The log₂ fold change of differentially expressed lncRNAs that were exclusively expressed in the stearic acid compared with control group.

TCONS_00119905	Ups	3.432	7.65E-09
TCONS_00088508	Ups	1.307	9.09E-09
TCONS_00252600	Down	-2.123	9.87E-09
TCONS_00185019	Down	-1.554	1.63E-08
TCONS_00214621	Down	-1.027	5.73E-08
TCONS_00230409	Down	-1.190	1.51E-07
TCONS_00148776	Down	-1.313	1.72E-07
TCONS_00216021	Down	-3.085	2.69E-07
TCONS_00233223	Ups	1.471	3.98E-07
TCONS_00230836	Ups	1.328	5.06E-07
TCONS_00266371	Down	-3.003	6.33E-07
TCONS_00277357	Down	-1.996	7.77E-07
TCONS_00281906	Ups	1.972	9.00E-07
TCONS_00081253	Ups	2.272	9.17E-07
TCONS_00139248	Ups	2.864	9.90E-07
TCONS_00140517	Ups	2.042	1.08E-06
TCONS_00180861	Ups	2.938	1.19E-06
TCONS_00075608	Down	-2.929	1.24E-06
TCONS_00039986	Ups	2.724	1.81E-06
TCONS_00002604	Ups	1.124	3.00E-06
TCONS_00150272	Ups	1.401	3.34E-06
TCONS_00206490	Down	-1.346	4.48E-06
TCONS_00277850	Down	-2.785	4.65E-06
TCONS_00102063	Ups	2.781	4.93E-06
TCONS_00167285	Down	-1.892	4.94E-06
TCONS_00195486	Ups	1.810	6.28E-06
TCONS_00055673	Down	-1.121	6.39E-06
TCONS_00129289	Ups	2.737	6.83E-06
TCONS_00078368	Ups	1.220	7.33E-06

TCONS_00057680	Ups	2.550	7.71E-06
TCONS_00080826	Down	-2.643	8.01E-06
TCONS_00249717	Down	-1.194	8.76E-06
TCONS_00178715	Ups	1.903	9.69E-06
TCONS_00139249	Ups	2.677	1.09E-05
TCONS_00009803	Ups	2.530	1.19E-05
TCONS_00147061	Down	-2.392	1.38E-05
TCONS_00112651	Ups	1.420	1.86E-05
TCONS_00230832	Down	-2.552	1.96E-05
TCONS_00128361	Ups	1.675	2.02E-05
TCONS_00130143	Ups	2.403	2.02E-05
TCONS_00132360	Ups	2.084	2.20E-05
TCONS_00006080	Down	-2.089	2.47E-05
TCONS_00001016	Ups	1.209	2.60E-05
TCONS_00252056	Down	-2.549	2.91E-05
TCONS_00102705	Ups	2.367	3.07E-05
TCONS_00045226	Ups	1.695	3.08E-05
TCONS_00233739	Down	-1.961	3.09E-05
TCONS_00150270	Ups	2.395	3.62E-05
TCONS_00079147	Down	-1.064	3.69E-05
TCONS_00069352	Ups	2.515	3.76E-05
TCONS_00148782	Down	-1.258	3.78E-05
TCONS_00252654	Ups	1.088	4.03E-05
TCONS_00111794	Down	-2.504	4.05E-05
TCONS_00055672	Down	-1.016	5.07E-05
TCONS_00214972	Down	-1.347	5.22E-05
TCONS_00006084	Down	-1.362	5.23E-05
TCONS_00144520	Ups	1.982	5.54E-05
TCONS_00230831	Ups	2.460	5.75E-05

TCONS_00099264	Ups	2.457	5.77E-05
TCONS_00008230	Ups	1.518	6.26E-05
TCONS_00150267	Ups	2.437	6.65E-05
TCONS_00056121	Ups	2.382	6.67E-05
TCONS_00249350	Down	-1.122	7.18E-05
TCONS_00099186	Down	-1.258	7.76E-05
TCONS_00196774	Down	-1.515	8.59E-05
TCONS_00099319	Down	-1.694	9.01E-05
TCONS_00260686	Down	-1.056	9.60E-05
TCONS_00203893	Down	-1.488	1.04E-04
TCONS_00230830	Down	-1.491	1.05E-04
TCONS_00008865	Down	-1.238	1.13E-04
TCONS_00068952	Ups	1.280	1.14E-04
TCONS_00036859	Ups	2.358	1.14E-04
TCONS_00120345	Down	-1.381	1.27E-04
TCONS_00177728	Ups	1.819	1.29E-04
TCONS_00003674	Ups	2.087	1.35E-04
TCONS_00088499	Ups	2.115	1.51E-04
TCONS_00180688	Ups	1.904	1.64E-04
TCONS_00043156	Down	-1.683	1.76E-04
TCONS_00077760	Ups	1.852	1.99 E-04
TCONS_00080805	Down	-1.004	2.09E-04
TCONS_00247074	Down	-2.243	2.14E-04
TCONS_00131805	Down	-2.195	2.24E-04
TCONS_00002586	Ups	1.032	2.32E-04
TCONS_00088531	Ups	1.649	2.41E-04
TCONS_00233736	Down	-1.577	2.53E-04
TCONS_00040100	Ups	1.475	2.69E-04
TCONS_00157692	Ups	1.773	2.71E-04

TCONS_00236795	Ups	1.303	2.96E-04
TCONS_00145605	Down	-2.209	3.00E-04
TCONS_00027006	Ups	1.276	3.02E-04
TCONS_00163485	Ups	1.973	3.02E-04
TCONS_00184225	Down	-1.336	3.30E-04
TCONS_00184460	Down	-2.135	3.34E-04
TCONS_00178829	Down	-2.188	3.41E-04
TCONS_00252057	Ups	2.183	3.49E-04
TCONS_00129531	Down	-2.024	3.49E-04
TCONS_00217905	Ups	1.042	3.53E-04
TCONS_00088238	Ups	2.083	3.60E-04
TCONS_00056019	Down	-1.220	3.64E-04
TCONS_00248344	Down	-1.730	3.81E-04
TCONS_00263683	Down	-2.162	4.00E-04
TCONS_00203344	Down	-1.467	4.06E-04
TCONS_00266071	Down	-1.156	4.14E-04
TCONS_00281912	Ups	1.232	4.28E-04
TCONS_00123053	Down	-1.189	4.34E-04
TCONS_00278906	Ups	2.1430	4.44E-04
TCONS_00121253	Down	-1.672	4.45E-04
TCONS_00161581	Down	-1.077	4.54E-04
TCONS_00129760	Down	-1.096	4.61E-04
TCONS_00002601	Ups	1.053	4.92E-04
TCONS_00047022	Down	-2.109	4.95E-04
TCONS_00196773	Down	-1.474	5.32E-04
TCONS_00221124	Ups	1.403	5.74E-04
TCONS_00111420	Down	-1.016	6.20E-04
TCONS_00006072	Ups	2.078	6.44E-04
TCONS_00195489	Ups	1.218	6.53E-04

TCONS_00123093	Ups	1.197	6.54E-04
TCONS_00108495	Down	-1.327	6.58E-04
TCONS_00235952	Down	-1.130	6.92E-04
TCONS_00114840	Ups	2.036	7.07E-04
TCONS_00180689	Ups	1.160	8.48E-04
TCONS_00128357	Ups	1.885	9.01E-04
TCONS_00080780	Down	-1.600	9.45E-04
TCONS_00278334	Ups	1.024	9.49E-04
TCONS_00182959	Down	-1.124	9.90E-04
TCONS_00252601	Down	-1.588	1.04E-03
TCONS_00202594	Ups	1.993	1.06E-03
TCONS_00249723	Down	-1.327	1.10E-03
TCONS_00026862	Ups	1.985	1.10E-03
TCONS_00089573	Down	-1.976	1.10E-03
TCONS_00217223	Down	-1.980	1.14E-03
TCONS_00002528	Ups	1.987	1.14E-03
TCONS_00077762	Ups	1.398	1.17E-03
TCONS_00236022	Down	-1.770	1.24E-03
TCONS_00148773	Down	-1.079	1.29E-03
TCONS_00053707	Down	-1.355	1.30E-03
TCONS_00103585	Ups	1.734	1.30E-03
TCONS_00078111	Down	-1.919	1.31E-03
TCONS_00129930	Ups	1.349	1.32E-03
TCONS_00176551	Ups	1.032	1.33E-03
TCONS_00158955	Ups	1.949	1.34E-03
TCONS_00249349	Down	-1.754	1.42E-03
TCONS_00197656	Ups	1.480	1.44E-03
TCONS_00077761	Ups	1.082	1.52E-03
TCONS_00114790	Ups	1.909	1.65E-03

TCONS_00110262	Down	-1.907	1.67E-03
TCONS_00088377	Down	-1.082	1.73E-03
TCONS_00213910	Ups	1.880	1.80E-03
TCONS_00035996	Ups	1.877	1.84E-03
TCONS_00237351	Ups	1.324	1.87E-03
TCONS_00026810	Down	-1.875	1.87E-03
TCONS_00078108	Down	-1.900	1.88E-03
TCONS_00001993	Ups	1.502	1.94E-03
TCONS_00247953	Ups	1.749	2.01E-03
TCONS_00274730	Ups	1.884	2.03E-03
TCONS_00103408	Ups	1.885	2.04E-03
TCONS_00163455	Ups	1.455	2.09E-03
TCONS_00260769	Down	-1.851	2.10E-03
TCONS_00057573	Ups	1.846	2.13E-03
TCONS_00205706	Ups	1.214	2.14E-03
TCONS_00023590	Ups	1.443	2.24E-03
TCONS_00038441	Down	-1.850	2.29E-03
TCONS_00009804	Ups	1.778	2.33E-03

name	Regulation	log ₂ fold change	P value
TCONS_00088788	Down	-1.332	1.03E-86
TCONS_00233737	Down	-1.448	1.59E-46
TCONS_00088299	Ups	1.540	1.48E-20
TCONS_00184470	Down	-1.512	2.64E-19
TCONS_00038546	Ups	1.172	1.70E-18
TCONS_00009134	Ups	1.080	9.36E-15
TCONS_00184468	Down	-1.755	2.23E-12
TCONS_00088303	Ups	1.641	1.66E-11
TCONS_00195490	Ups	1.395	3.95E-11
TCONS_00139241	Ups	2.208	4.84E-10
TCONS_00119905	Ups	2.697	7.69E-10
TCONS_00068951	Ups	1.274	3.08E-09
TCONS_00233736	Down	-1.391	3.22E-09
TCONS_00184465	Down	-2.134	1.52E-08
TCONS_00088298	Ups	1.152	1.85E-08
TCONS_00147061	Down	-2.362	5.54E-08
TCONS_00239170	Down	-1.748	1.21E-07
TCONS_00216021	Down	-2.326	1.31E-07
TCONS_00167285	Down	-1.996	1.65E-07
TCONS_00089983	Ups	1.093	1.96E-07
TCONS_00279975	Ups	2.262	2.85E-07
TCONS_00102704	Ups	2.031	4.12E-07
TCONS_00139249	Ups	2.194	6.35E-07
TCONS_00132357	Ups	1.913	8.57E-07
TCONS_00077761	Ups	1.229	8.97E-07
TCONS_00251038	Down	-2.123	1.36E-06

Supplementary Table S8 The log₂ fold change of differentially expressed lncRNAs that were exclusively expressed in the palmitic acid compared with control group.

TCONS_00233223	Ups	1.230	1.60E-06
TCONS_00161572	Down	-1.988	5.68E-06
TCONS_00195486	Ups	1.422	6.51E-06
TCONS_00185019	Down	-1.072	7.83E-06
TCONS_00078368	Ups	1.114	1.08E-05
TCONS_00034820	Ups	1.866	1.88E-05
TCONS_00260772	Ups	1.862	2.03E-05
TCONS_00251541	Ups	1.846	2.78E-05
TCONS_00248344	Down	-1.620	3.17E-05
TCONS_00004655	Ups	1.799	4.15E-05
TCONS_00006080	Down	-1.186	4.52E-05
TCONS_00009803	Ups	1.776	5.55E-05
TCONS_00140517	Ups	1.530	5.98E-05
TCONS_00176551	Ups	1.137	8.62E-05
TCONS_00281906	Ups	1.400	1.32E-04
TCONS_00260686	Down	-1.035	1.45E-04
TCONS_00003674	Ups	1.644	1.52E-04
TCONS_00002586	Ups	1.005	1.59E-04
TCONS_00132360	Ups	1.493	1.60E-04
TCONS_00045226	Ups	1.384	1.69E-04
TCONS_00150272	Ups	1.138	1.96E-04
TCONS_00201964	Ups	1.523	2.12 E-04
TCONS_00034821	Down	-1.043	2.44 E-04
TCONS_00026344	Ups	1.599	2.71 E-04
TCONS_00027006	Ups	1.071	3.27E-04
TCONS_00203893	Down	-1.186	3.59E-04
TCONS_00177728	Ups	1.469	3.91E-04
TCONS_00102705	Ups	1.550	4.36E-04
TCONS_00068931	Down	-1.019	4.44E-04

TCONS_00057680	Ups	1.533	5.03E-04
TCONS_00200419	Ups	1.442	5.37E-04
TCONS_00216016	Ups	1.515	5.70E-04
TCONS_00099319	Down	-1.252	6.11E-04
TCONS_00006281	Ups	1.115	7.06E-04
TCONS_00121322	Ups	1.404	7.10E-04
TCONS_00184054	Down	-1.047	7.67E-04
TCONS_00088531	Ups	1.288	8.41E-04
TCONS_00132387	Ups	1.463	8.78E-04
TCONS_00065563	Ups	1.387	1.12E-03
TCONS_00233739	Down	-1.167	1.29E-03
TCONS_00277357	Down	-1.094	1.45E-03
TCONS_00043156	Down	-1.218	1.51E-03
TCONS_00088300	Ups	1.349	1.53E-03
TCONS_00144481	Down	-1.085	1.54E-03
TCONS_00281912	Ups	1.034	1.63E-03
TCONS_00098803	Ups	1.376	1.67E-03
TCONS_00078337	Ups	1.354	1.99E-03
TCONS_00045330	Ups	1.332	2.04E-03
TCONS_00200446	Down	-1.265	2.09E-03
TCONS_00142000	Down	-1.268	2.19E-03
TCONS_00008230	Ups	1.072	2.25E-03
TCONS_00149049	Ups	1.344	2.29E-03
TCONS_00266371	Down	-1.338	2.37E-03
TCONS_00149141	Ups	1.198	2.49E-03
TCONS_00129208	Ups	1.331	2.54E-03

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name	Regulation	log ₂ fold change	P value
TCONS_00088523	Down	-2.749	1.72E-11
TCONS_00142000	Ups	2.128	2.08E-07
TCONS_00230836	Ups	1.015	5.45E-07
TCONS_00145596	Down	-1.995	1.13E-06
TCONS_00039055	Down	-1.807	2.96E-06
TCONS_00089573	Down	-1.733	1.68E-05
TCONS_00039236	Ups	1.708	2.06E-05
TCONS_00252600	Down	-1.375	3.14E-05
TCONS_00247138	Ups	1.634	4.35E-05
TCONS_00139202	Ups	1.592	5.99E-05
TCONS_00034820	Down	-1.599	6.24E-05
TCONS_00167853	Ups	1.622	6.65E-05
TCONS_00230830	Down	-1.179	8.27E-05
TCONS_00201321	Down	-1.549	1.04E-04
TCONS_00077866	Ups	1.586	1.07E-04
TCONS_00281901	Down	-1.521	2.05E-04
TCONS_00002278	Down	-1.471	2.07E-04

Supplementary Table S9 The log2 fold change of differentially expressed lncRNAs

In the steame were group compared with panning were group.	in the stearic	acid s	group	com	pared	with	palmitic	acid	group
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FFAs (µg/ml)	Normal mice	HSD mice	
C14:0, MA	4 151 0 500	7 7 7 7 7 6 6 6 4***	
(Myristic acid)	4.151±0.508	/.23/±0.654	
C16:0, PA	120.002 - 22.200	261 122 - 25 007***	
(Palmitic acid)	138.903±22.389	261.133±25.807	
C16: 1, PLA		4 000 1 (000**	
(Palmitoleic acid)	9.266±1.207	4.922±1.622**	
C18: 0, SA			
(Stearic acid)	63.812±7.864	178.928±27.844	
C18: 1, OA		110.339±20.038***	
(Oleic acid)	58.269±14.821		
C18: 2, LA		***	
(Linoleic acid)	115.355±11.066	138.366±13.582	
γ-C18:3, γ-LNA			
(y-Linolenic acid)	4.707±0.236	8.267±1.585	
C18: 3, LNA		**	
(Linolenic acid)	82.182±13.182	40.567±15.673	
C20: 2, EDA			
(Eicosadienoic acid)	6.601±0.774	7.178±0.781	
C20: 4, AA		110.817±28.302***	
(Arachidonic acid)	80.679±10.041		
C20: 5, EPA		&	
(Eicosapentaenoic acid)	6.172±1.111	2.681±0.669***	
C22: 5, DPA			
(Docosapentaenoic acid)	1.673±0.623	1.675 ± 0.828	
C22: 6, DHA			
(Docosahexaenoic acid)	151.763±15.323	150.278±13.046	

Supplementary Table S10 The composition of fasting serum NEFAs profile in

normal and HSD mice at 22 weeks

Saturated fatty acids	206.867±26.340	447.298±38.126***
Total fatty acids	608.180±47.674	$897.074 \pm 56.754^{***}$
Percentage of SA (%)	10.484 ± 0.873	19.998±3.231***
Percentage of PA (%)	22.796±2.821	29.113±2.228***
PA/SA ratio	2.193:1	1.489:1*

Values are means \pm SD. n = 35 mice in each group. *P < 0.05, **P < 0.01, ***P < 0.001, compared with the value of normal mice group. **HSD**, high stearic acid diet.

chr14 (qD3) 14qA1 qA2 14qA3 14qB 14qC1 C2 qC3 14qD1 D2 14qD3 E1 14qE2.1 qE2.3 E3 14qE4 E5
Scale chr14: 1 kb mm10 72,982,500 72,983,000 72,983,000 72,984,000 72,985,000 72,986,000 72,986,000 72,986,500 72,986,000 72,986,500 72,986,000 <t< td=""></t<>
YourSeq GENCODE VM23 Comprehensive Transcript Set (only Basic displayed by default) NCBI RefSeq genes, curated subset (NM_*, NP_* or YP_*) - Annotation Release GCF_000001635.25_GRCm38.p5 (2017-08-04) Mouse ESTs That Have Been Spliced
TGCAATGGTACCTGTGTGTGTGGTAGTGGTGGTGGTGTGGGAGGGA
TATACACAGGGACTTCCAGGTGAGCAGCCACAGGCCCCTGAGCAAGCTGAGAAGGTAATATCCCACACTG
TTCTTTGAACAGCTTCAGCAAC <mark>GG</mark> CTTCCAGATCTGTCTTTCTGCTCTGGCCCCAGGGATGTTATATTTC
ACTGGCCGTTGAAATCAGTGCCTGTCATTTTCCAGGCTGACGCTGCTCACTGGGTGAGTCAGTTGTTTGG
GTATGAACAGCAAAGCCTCGGATGCAGCTGCCAAAAGGGTGTGTTTGCCTTCACTTCCGGGGACTCTCTC
TCAGCTGCCACCTAGT <mark>GG</mark> CTGCTATCGTTGCTGTGGTTGTTATTCTGCAAGTGAGATAATTAAGGTTTAG
AAGAGTCTAAAGTCATTTAACTGACAAGGGACAGGACTGGAATTCTAACCAAGCTACCTGACATCGGCAT
GTTCTTGACTCTTCCCATCATAATGGATGCTCTTTGCGTCTGTGTTCCTTCGTGATTCCAGCATCGGCTC
ATCTTCCAAACATCTATGAAGTCCCAGGATTGGCCCCATTGGTCCGATGTGATCTCTGCTGGCTG
CTTTTATGAAGGACTTATATACTCGAGGAGAGAGGACAAAGAAAAGCAAAACAAGAAGTTTTTGTGTGCGTT
GATGCTACACTGAGATGAGCTCCTAGAGCTAAGAGTCATGTGGAGCAAACAGGTTTGATCCCCTGGAGAG
GGGACCAATTATTCCTATGAGATAAATGGAAATTAGGAAGGCCCAAGAAAGA
CCTCCATGAAGAATAAGCAGCCCATAAGACATCCCAGGACCCAGAAGGTCATTCTGGGACACAAGTCACA
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GAAAAAATAAATTAATTAATTAATTAATTAATTAATTAA
TCTTCCCTTGGAGACCTAGAATATGCATGGAATGCTGTCCTGGACTATGGTGGGAAGTCTGGTTGGCTGT
GTGTCATAGCTCTAGGCTCACCCATCCCTCAGAACCTCATAGTATCATGTGCATAACTTAAAACTGTAGA
GGATGAATTACTGTCCCATTGGGTATAGACTAAGGGCTAGGGTCTCCTGCTGAATGTTGGTGGTATCTTC
TAAACACAATGCAAAGGGACAGGAGTGGGGGGGGGGAGGAATCTTTGTTAAAGTATCTGACTGGGCGGGGCACAT
TTTCATTCTCATCGCCCAGCTATCTCCCCAATGTTACAGCTTCACTGATCCAAAAAGCCATTTTGCCAAAT
TATAAGAACCACGAAGACAGGCCCGCAGCACATACCTCACATTCTGCTGGCTG
GTACTCTCTGCAAAGTACCAGCCTAACTGTCCAACTTCCTCCGGAACCTGAGGGCACTTTAAACTTCTTT
GTTAGCCTTGCCAGCATTTCCCCTTTGATTCAGGTTGAAATAGTTAACCTAGAATTGGATCTCAGCCTGG
TGAGAACTTCCTCTGAAGTTCATGTTATGTCTTTTAACCAAATCCCCCTTGTATCTCCTCAAAGAGAAAT
TCTCCTTCAATGGTCGTGGCATTCCTTCCTTTAAACATTTCTAGTAAGCTACTACAATGGGGAATCACTA
AATCTTGCTGACAGTGGTCACATTCAGGGCAGGTTACTGTGTACATTGCTGAGGAGTCTGGAAGAACAGA
CAGCCATTCTTCTAACTTCTCCTGACGTGTCTCATCCTCTTAAGTGTCCTCCACGGTGTGGTGACGAGGA
TCTTGAAGATGTGTACTTACATTCTGTGCCAGCCATTTTAATAATAGTGGGTAATTTCCTTAGTCCCCTT
GTGCCTCATCTTCTTTGCCTATAAAAGCTACCGTCACATACTGGGCTCACTAGATTGTCTTTGGTATTGG
GAGGACAGGAATCACATGGCACCAACAAAAAGATCTGGCCATCTACACATCATCAAGTCTTTGCTTTCTT
TGGACAGCAACTATCCCTATTTTTAACTACTTTTTGAAGTTTCTTGAACCATGATCAAATAATTTATTT
CCTCAGTGTCATGTTTGGATAATATTTTCCTGTAGAAATCGTCTGTAAAGACATTAATAGCACTAGTTTG
AGAAGTAGCATTCCTACACAATAACCTTTGAAAGGGTTGAGAATATACTCACAGAAAAAAACCAGGATAT
GCCTGCCCCAGTTTACTCCTCCTCCTCCAAACATCATTCAGAGTCTTTCTCGGCTGCTTTATTCCAATC
ACCAAGCTGAAGACAGTTCTAGCTCTGGTGCCCTTTCCTCCAATATGAGTCATGAATCTTCTCCAGTAAT
TTTCAGCCGTAGGTGTATCTGATAACATGAGGTATCTCCCTTTTGAAATGGATAGTTTGTGTTCATGGAA
GGCAATGTTCTGCTTGTCTTAGTTTATGATGATTTTGGTCTTGGACTTTGCTTGTGAGTTTCTGAATTGG

Supplementary Table S11 Full sequence of lnc866

Red font represents the start and end base of each exon of lnc866.

Characteristics	Normolipidemic	Hyperlipidemic
Characteristics	(n=13)	(n=9)
Age (years)	53.08±9.71	56.44±6.06
Sex (female/male)	8/5	4/5
BMI (kg/m ²)	22.10±2.10	25.17±2.06
Glucose (mmol/L)	5.07±0.82	6.09 ± 0.97
TC (mmol/L)	4.46±1.44	$6.77 {\pm} 1.07^{**}$
TG (mmol/L)	1.29 ± 0.22	$2.94{\pm}0.60^{**}$
HDL-C (mmol/L)	$1.34{\pm}0.46$	$0.78{\pm}0.24^{*}$
LDL-C (mmol/L)	2.36±0.83	4.07±0.66**

Supplementary Table S12 Characteristic and serum analysis of normolipidemic and hyperlipidemic participants

P*<0.05; *P*<0.01, compared with the value of normolipidemic participants.

Characteristics	shNC-V+C	shNC-V+HSD	sh866-V+HSD	sh866-V+C
Body weight (g)	30.646±4.567	47.415±1.386***	47.279±2.523***	30.620±2.219 ^{^^}
Glucose (mmol/l)	4.840±1.056	10.239±2.24**	7.385±0.63*^	4.900±0.533 ^{^^}
TC (mmol/l)	2.963±0.143	6.014±0.679***	$6.000{\pm}0.657^{***}$	2.657±0.506 ^{^^}
TG (mmol/l)	0.786±0.122	$1.755 \pm 0.090^{**}$	$1.704 \pm 0.120^{**}$	0.742±0.099 ^{^^}
HDL-C (mmol/l)	2.403±0.125	$4.281 \pm 0.380^{**}$	4.560±0.489**	2.195±0.457 ^{^^}
LDL-C (mmol/l)	0.218±0.033	$1.180 \pm 0.305^{**}$	1.210±0.233**	0.154±0.017 ^{^^}
Insulin (pmol/l)	106.683±0.316	298.09±0.151*	208.569±0.039*^	98.476±0.012 ^{^^}
Food intake (g/d)	3.928±0.459	3.651±0.923	3.669±0.824	3.861±0.522

Supplementary Table S13 Body weight and serum analysis in normal and HSD mice

at 22 weeks.

After feeding for 22 weeks, the food intake, body weight, fasting blood glucose, plasma insulin levels, TC, TG, LDL-C and HDL-C levels were measured in C57BL/6J mice. All the parameters were detected and calculated in the fasting state. Displayed mode was mean \pm SD, n=35 mice per group. **P*<0.05; ***P*<0.01, ****P*<0.001, compared with the value of shNC-V+C mice. ^*P*<0.05; ^**P*<0.01, ^^*P*<0.001, compared with the value of shNC-V+HSD mice. TC, total cholesterol; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; sh866-V+C, 6 weeks after sh866-V injection, mice were fed with chow diet. shNC-V, the negative control shRNA engineered into the AAV9 vector; sh866-V, AAV9 vector carrying shRNA-lnc866; C, chow diet; HSD, high stearic acid diet; shNC-V+C, 6 weeks after shNC-V injection, mice were fed

with chow diet; **shNC-V+HSD**, 6 weeks after shNC-V injection, mice were fed with HSD; **sh866-V+HSD**, 6 weeks after sh866-V injection, mice were fed with HSD.

		WOIK		
miRNA	mRNA	PCC	P value	
mmu-miR-297b-5p	ENSMUST00000022531	-0.995	3.69E-05	
mmu-miR-297b-5p	ENSMUST00000050785	-0.995	4.47E-05	
mmu-miR-297b-5p	ENSMUST00000074898	-0.992	1.01E-04	
mmu-miR-297b-5p	ENSMUST0000020190	-0.992	1.02E-04	
mmu-miR-297b-5p	ENSMUST00000159720	-0.991	1.08E-04	
mmu-miR-297b-5p	ENSMUST0000006956	-0.986	3.00E-04	
mmu-miR-297b-5p	ENSMUST00000181286	-0.985	3.34E-04	
mmu-miR-297b-5p	ENSMUST0000036188	-0.984	3.79E-04	
mmu-miR-297b-5p	ENSMUST00000181169	-0.983	4.48E-04	
mmu-miR-297b-5p	ENSMUST0000068830	-0.982	4.60E-04	
mmu-miR-297b-5p	ENSMUST00000166854	-0.979	6.58E-04	
mmu-miR-297b-5p	ENSMUST0000086399	-0.978	7.04E-04	
mmu-miR-297b-5p	ENSMUST0000023994	-0.977	8.13E-04	
mmu-miR-297b-5p	ENSMUST0000027748	-0.975	9.10E-04	
mmu-miR-297b-5p	ENSMUST00000131456	-0.968	1.50E-03	
mmu-miR-297b-5p	ENSMUST0000067495	-0.966	1.69E-03	
mmu-miR-297b-5p	ENSMUST00000140373	-0.965	1.78E-03	
mmu-miR-297b-5p	ENSMUST00000102745	-0.954	3.16E-03	
mmu-miR-297b-5p	ENSMUST0000040750	-0.949	3.91E-03	
mmu-miR-297b-5p	ENSMUST00000171621	-0.947	4.10E-03	
mmu-miR-297b-5p	ENSMUST0000031565	-0.944	4.66E-03	
mmu-miR-297b-5p	ENSMUST00000101094	-0.937	5.86E-03	
mmu-miR-297b-5p	ENSMUST0000096232	-0.937	5.87E-03	
mmu-miR-297b-5p	ENSMUST00000147988	-0.929	7.46E-03	
mmu-miR-297b-5p	ENSMUST00000094760	-0.929	7.46E-03	
mmu-miR-297b-5p	ENSMUST00000106373	-0.926	7.98E-03	

Supplementary Table S14 The negative relationship between miR-297b-5p and 31

mRNAs in co-expression network

mmu-miR-297b-5p	ENSMUST00000110323	-0.924	8.47E-03
mmu-miR-297b-5p	ENSMUST00000149874	-0.908	1.21E-02
mmu-miR-297b-5p	ENSMUST00000194644	-0.902	1.38E-02
mmu-miR-297b-5p	ENSMUST00000135828	-0.896	1.57E-02
mmu-miR-297b-5p	ENSMUST00000143213	-0.887	1.84E-02

PCC, Pearson correlation coefficients

Supplementary Table S15	The negative relationsh	nip between TCONS	_00077866
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and minu-mix-2970-5p in co-expression network			
miRNA	mRNA	PCC	P value
mmu-miR-297b-5p	TCONS_00077866	-0.964	1.93E-03

and mmu-miR-297b-5p in co-expression network

PCC, Pearson correlation coefficients

lncRNA	mRNA	PCC	P value
TCONS_00077866	ENSMUST00000022531	0.967	1.46E-03
TCONS_00077866	ENSMUST00000050785	0.967	1.67E-03
TCONS_00077866	ENSMUST00000074898	0.977	8.04E-04
TCONS_00077866	ENSMUST00000020190	0.965	1.82E-03
TCONS_00077866	ENSMUST00000159720	0.985	3.48E-04
TCONS_00077866	ENSMUST0000006956	0.943	4.85E-03
TCONS_00077866	ENSMUST00000181286	0.924	8.47E-03
TCONS_00077866	ENSMUST00000036188	0.983	4.14E-04
TCONS_00077866	ENSMUST00000181169	0.929	7.31E-03
TCONS_00077866	ENSMUST00000068830	0.971	1.23E-03
TCONS_00077866	ENSMUST00000166854	0.974	1.01E-03
TCONS_00077866	ENSMUST0000086399	0.969	1.47E-03
TCONS_00077866	ENSMUST00000023994	0.998	4.19E-06
TCONS_00077866	ENSMUST00000027748	0.998	4.32E-06
TCONS_00077866	ENSMUST00000131456	0.993	7.50E-05
TCONS_00077866	ENSMUST00000067495	0.865	2.61E-02
TCONS_00077866	ENSMUST00000140373	0.880	2.09E-02
TCONS_00077866	ENSMUST00000102745	0.943	4.77E-03
TCONS_00077866	ENSMUST00000040750	0.992	9.84E-05
TCONS_00077866	ENSMUST00000171621	0.848	3.30E-02
TCONS_00077866	ENSMUST00000101094	0.894	1.63E-02
TCONS_00077866	ENSMUST00000096232	0.994	5.14E-05
TCONS_00077866	ENSMUST00000147988	0.901	1.42E-02
TCONS_00077866	ENSMUST00000094760	0.983	4.41E-04
TCONS_00077866	ENSMUST00000106373	0.992	8.79E-05
TCONS_00077866	ENSMUST00000110323	0.948	3.94E-03

Supplementary Table S16 The positive relationship between lnc866 and 31 mRNAs

in co-expression network

TCONS_00077866	ENSMUST00000149874	0.864	2.63E-02
TCONS_00077866	ENSMUST00000194644	0.935	6.29E-03
TCONS_00077866	ENSMUST00000031565	0.988	2.12E-04
TCONS_00077866	ENSMUST00000135828	0.913	1.11E-02
TCONS_00077866	ENSMUST00000143213	0.959	2.49E-03

lnc866: TCONS_00077866; PCC, Pearson correlation coefficients.

Supplementary Table S17 RNA-seq showing the log ₂ fold change of differential
expression of 31 mRNAs in co-expression network in stearic acid-treated β -TC6

	cells			
Ensemble ID	Gene name	Regul	log ₂ fold	P value
ENSMUST00000022531	large tumor suppressor 2	Up	2.445	1.57E-07
	(Lats2)			
ENSMUST00000050785	lipocalin 2 (Lcn2)	Up	5.881	4.66E-53
ENSMUST00000074898	Haptoglobin (Hp)	Up	6.940	7.85E-126
ENSMUST0000020190	vanin 3 (Vnn3)	Up	3.151	9.46E-15
ENSMUST00000159720	alpha-kinase 1(Alpk1)	Up	4.294	8.75E-25
ENSMUST0000006956	serum amyloid A 3 (Saa3)	Up	6.127	5.32E-112
ENSMUST00000181286	Gm16685	Up	2.886	8.01E-26
ENSMUST0000036188	zinc finger CCCH type	Up	2.420	1.55E-22
	containing 12A (Zc3h12a)			
ENSMUST00000181169	Not in the database	Up	3.502	3.23E-26
ENSMUST0000068830	cannabinoid receptor 2	Up	2.178	1.95E-06
	(macrophage) (Cnr2)			
ENSMUST00000166854	transmembrane protein	Up	2.584	2.69E-08
	39a (Tmem39a)			
ENSMUST0000086399	intercellular adhesion	Up	6.190	3.98E-73
	molecule 1 (Icam1)			
ENSMUST0000023994	serine (or cysteine)	Up	4.044	1.64E-23
	peptidase inhibitor, clade			
	G, member 1(Serping1)			
ENSMUST0000027748	regulator of G-protein	Up	3.062	4.60E-21
	signaling 16 (Rgs16)			
ENSMUST00000131456	serine (or cysteine)	Up	4.205	1.09E-24
	peptidase inhibitor, clade			

cells

	G, member 1 (Serping1)			
ENSMUST0000067495	wingless-type MMTV	Up	1.460	8.79E-06
	integration site family,			
	member 11 (Wnt11)			
ENSMUST00000140373	sodium channel and	Up	3.528	3.95E-15
	clathrin linker 1 (Sclt1)			
ENSMUST00000102745	tumor necrosis factor,	Up	3.703	1.44E-16
	alpha-induced protein 2			
	(Tnfaip2)			
ENSMUST0000040750	leukemia inhibitory factor	Up	4.082	6.94E-24
	(Lif)			
ENSMUST00000171621	TRAF-interacting protein	Up	6.642	2.47E-67
	with forkhead-associated			
	domain (Tifa)			
ENSMUST0000031565	fascin actin-bundling	Up	2.876	1.59E-13
	protein 1 (Fscn1)			
ENSMUST00000101094	OTU domain, ubiquitin	Up	3.835	7.10E-20
	aldehyde binding 2			
	(Otub2)			
ENSMUST0000096232	CCAAT/enhancer binding	Up	3.551	9.28E-36
	protein (C/EBP), delta			
	(Cebpd)			
ENSMUST00000147988	cilia and flagella	Up	1.888	4.65E-05
	associated protein 44			
	(Cfap44)			
ENSMUST0000094760	SH3 domain containing 21	Up	2.589	2.68E-08
	(Sh3d21)			
ENSMUST00000106373	sulfotransferase family	Up	2.478	1.05E-07
	1A, phenol-preferring,			

	member 1 (Sult1a1)			
ENSMUST00000110323	CDK5 regulatory subunit	Up	2.288	8.94E-07
	associated protein 1-like 1			
	(Cdkal1)			
ENSMUST00000149874	CASP8 and FADD-like	Up	1.943	2.81E-05
	apoptosis regulator (Cflar)			
ENSMUST00000194644	Gm37628	Up	1.050	4.63E-03
ENSMUST00000135828	zinc finger protein 783	Up	1.491	1.20E-03
	(Zfp783)			
ENSMUST00000143213	BTB (POZ) domain	Up	2.747	3.56E-09
	containing 19 (Btbd19)			