

ESM Table 1. Primer Sequences

Gene name	Forward sequence (5' to 3')	Reverse Sequence (5' to 3')
<i>Eif2alpha</i>	ACGTGGCAGCCTTACTACTAC	CTGACCAGGAAGGACACCAAT
<i>Xbp1</i>	CTGAGTCCGCAGCAGGTG	GGCAACAGTGTCTCAGAGTCCA
<i>Chop</i>	CATGTTGAAGATGAGCGGGTGG	ACCAGGTTCTCTCTCTCAGGT
<i>Spliced xbp1</i>	AGCTTTTACGGGAGAAAACCTCA	GCCTGCACCTGCTGCG
<i>Perk</i>	TCCCCTAGATCCCCTGAACTT	TTTCGAGCTGAGTGCTCTACA
<i>Lnpc</i>	TATCTGTAGGTGCTGCTGCC	AGTCACAGCTGAGAAAAGCG
<i>Irs1</i>	GGACATCACAGCAGCAGAATGAAGAC	CGTGAGGTCCTGGTTGTGAAT
<i>Fat/cd36</i>	TGCACTCTCTCATCGGACTTC	CGTGGCCCGGTTCTACTACTAAT
<i>Lpl</i>	ATCGGGCCCAGCAACATTAT	ACTCCTCTCCATCCAGTTGA
<i>Cyclophilin</i>	GGATTCATGTGCCAGGGTGG	GTTTGGTCCAGCATTTGCCA
<i>Tfam</i>	GGCCATCATTGTCGGC	GACAAGACTGATAGACGAGGGGA
<i>Prkaa1/Ampk alpha 1</i>	AAATCCGCCGGGAGATTGAG	TGATGACCTGGTACAGTTTGATGA
<i>Prkaa2/Ampk alpha 2</i>	GGCAAAGTGAAGACTACCAGG	CGCCATGTTTGCAGATGTAG
<i>Hsl</i>	CGCCAGGACTGGAAAGAATTG	GAACGCTGAGGCTTTGATCT

Genes and their correspondent forward and reverse sequences.

ESM Table 2.

ID	Description	Kegg analysis				
		Gene ratio	Bg ratio	pvalue	p.adjust	qvalue
mmu04510	<b><i>Focal adhesion</i></b>	23/217	208/7783	1.33E-08	1.74E-06	1.44E-06
mmu04512	<b><i>ECM-receptor interaction</i></b>	15/217	88/7783	1.55E-08	1.74E-06	1.44E-06
mmu04151	<b><i>PI3K-Akt signaling pathway</i></b>	26/217	351/7783	4.42E-06	3.32E-04	1.44E-06
mmu04150	<b><i>mTOR signaling pathway</i></b>	10/217	61/7783	6.00E-06	3.37E-04	2.75E-04
mmu05205	<b><i>Proteoglycans in cancer</i></b>	18/217	205/7783	1.50E-05	6.77E-04	5.60E-04
mmu04974	<b><i>Protein digestion and absorption</i></b>	10/217	90/7783	1.88E-04	7.05E-03	5.84E-03
mmu05206	<b><i>MicroRNAs in cancer</i></b>	18/217	276/7783	6.72E-04	1.89E-02	1.57E-02
mmu04919	<b><i>Thyroid hormone signaling pathway</i></b>	10/217	117/7783	1.52E-03	3.81E-02	3.16E-02
mmu05214	<b><i>Glioma</i></b>	7/217	65/7783	2.10E-03	4.72E-02	3.91E-02

Main pathways affected by overexpression of miR-126-3p, including PI3K-Akt and mTOR signaling pathways.

ESM Table 3 - Downregulated proteins considering 0.8 as a cut-off point.

Downregulated proteins after tranfecting 3T3-L1 cells with miR-126-3p mimic	
Protein Name	Ratio H/M normalized
Collagen alpha-2(VI) chain	0.087928
Collagen alpha-2(VI) chain	0.11872
Short/branched chain specific acyl-CoA dehydrogenase, mitochondrial	0.158
Malectin	0.17419
Dystrobrevin alpha;Dystrobrevin beta	0.17813
Collagen alpha-2(IV) chain;Canstatin	0.23754
Lysine-specific demethylase 2A	0.25038
Arginine/serine-rich coiled-coil protein 2	0.26134
Protein canopy homolog 3	0.2671
Testis-expressed sequence 11 protein	0.26782
ATP-binding cassette sub-family B member 7, mitochondrial	0.3332
APC membrane recruitment protein 1	0.34107
Gap junction protein;Gap junction alpha-1 protein	0.35706
Multiple epidermal growth factor-like domains protein 10	0.36137
MAP/microtubule affinity-regulating kinase 3	0.37414
Sphingosine-1-phosphate lyase 1	0.37775
Outer dense fiber protein 2-like	0.37823
Keratin, type II cytoskeletal 2 oral	0.39849
Probable ATP-dependent RNA helicase DDX52	0.3986
Methyl-CpG-binding domain protein 2	0.39945
Transforming growth factor-beta receptor-associated protein 1	0.40149
Plexin-A1;Plexin-A2	0.40198
Phospholipase DDHD2	0.40511
Thioredoxin domain-containing protein 5	0.41024
Ribonuclease T2	0.41858
Tubulin-specific chaperone C	0.4197
NAD kinase (nadk- GTAC)	0.42491
Gamma-glutamylcyclotransferase	0.42609
Neurobeachin	0.42849
Rab-like protein 1	0.44857
Acetyl-coenzyme A transporter 1	0.45529
Retinal dehydrogenase 1	0.4625
Syndecan-3	0.46858
Adenylyltransferase and sulfurtransferase MOCS3;Molybdopterin-synthase adenylyltransferase;Molybdopterin-synthase sulfurtransferase	0.47064
Serine-protein kinase ATM	0.47939
Rho GTPase-activating protein 12	0.48014
Collagen alpha-1(VI) chain	0.48049
Copper-transporting ATPase 1	0.48717
Vascular cell adhesion protein 1	0.49965
E3 ubiquitin-protein ligase UBR2	0.50071
Oligophrenin-1	0.50323
Large neutral amino acids transporter small subunit 1	0.51398
Vacuolar protein sorting-associated protein 18 homolog	0.51894
Histone-lysine N-methyltransferase SETDB1	0.51955
Down syndrome critical region protein 3 homolog	0.52001
Aminopeptidase B	0.52086
Vesicle transport protein GOT1B	0.52214
Ubiquitin-like modifier-activating enzyme ATG7	0.52474

Poly(ADP-ribose) glycohydrolase ARH3	0.52594
Transmembrane 7 superfamily member 3	0.52603
Palladin	0.52732
Integrin-linked protein kinase	0.52858
Ras-related protein Rab-31	0.52925
E3 ubiquitin-protein ligase listerin	0.52943
Protein osteopotenia	0.52968
Unconventional myosin-VIIa	0.52987
Intron-binding protein aquarius	0.53232
cAMP-dependent protein kinase type I-alpha regulatory subunit	0.53497
Sarcosine dehydrogenase, mitochondrial	0.53516
Suppression of tumorigenicity 5 protein	0.5377
Regulatory-associated protein of mTOR	0.53771
Tyrosine-protein kinase Fer	0.54636
Eukaryotic translation elongation factor 1 epsilon-1	0.54846
N-myc-interactor	0.54924
Inhibitor of nuclear factor kappa-B kinase subunit beta	0.55023
Interleukin-1 receptor accessory protein	0.55072
Trafficking protein particle complex subunit 11	0.55192
Alpha-1,2-mannosyltransferase ALG9	0.55467
Poly(ADP-ribose) glycohydrolase	0.5556
Bromodomain adjacent to zinc finger domain protein 2A	0.55696
Serine/threonine-protein kinase Nek7	0.55793
Putative adenosylhomocysteinase 3	0.56154
Twinfilin-2	0.56241
CD151 antigen	0.56351
Thrombospondin-1	0.56498
Tubulin alpha-1A chain;Tubulin alpha-3 chain	0.56955
Protein phosphatase 1F	0.5723
Mitogen-activated protein kinase kinase kinase 7	0.57745
5-3 exoribonuclease 1	0.57925
Stonin-1	0.58006
CD166 antigen	0.5818
Dehydrogenase/reductase SDR family member 9	0.58351
Bromodomain and WD repeat-containing protein 3	0.58353
Ribonucleoside-diphosphate reductase subunit M2	0.58828
Peroxisomal membrane protein PEX14	0.5884
Target of Myb protein 1	0.58948
Oxidized low-density lipoprotein receptor 1;Oxidized low-density lipoprotein receptor 1, soluble form	0.5895
Myomegalin	0.59499
Thioredoxin domain-containing protein 12	0.59751
Neurofibromin	0.60011
Zinc finger SWIM domain-containing protein KIAA0913	0.60122
Huntingtin	0.60282
Sodium/hydrogen exchanger	0.60416
Proteasome subunit beta type-5	0.60532
Actin-related protein 2/3 complex subunit 4	0.60772
Abelson tyrosine-protein kinase 2	0.61042
Trinucleotide repeat-containing gene 6B protein	0.61173
Cytoplasmic polyadenylation element-binding protein 4	0.61665
Sodium-coupled neutral amino acid transporter 2	0.61683

E3 ubiquitin-protein ligase SHPRH	0.61769
Amidophosphoribosyltransferase	0.61834
Aprataxin	0.61902
Protein strawberry notch homolog 1	0.61912
Tyrosine-protein kinase CSK	0.62059
Protein bicaudal C homolog 1	0.62092
Ezrin	0.62172
Hemoglobin subunit beta-1	0.62308
Low-density lipoprotein receptor	0.625
CD9 antigen	0.62519
FERM, RhoGEF and pleckstrin domain-containing protein 2	0.62646
F-box only protein 30	0.62745
Acyl-coenzyme A thioesterase 1	0.62761
Tripeptidyl-peptidase 1	0.62903
Protein kinase C;Protein kinase C alpha type	0.63162
Cone cGMP-specific 3,5-cyclic phosphodiesterase subunit alpha	0.63193
Keratin, type II cytoskeletal 5	0.63285
Mannosyl-oligosaccharide glucosidase	0.6331
ATP-dependent RNA helicase A	0.63438
TRMT1-like protein	0.63512
Mitochondrial dicarboxylate carrier	0.63624
Serine/threonine-protein phosphatase 6 regulatory ankyrin repeat subunit E	0.63889
NEDD8	0.64065
Eukaryotic translation initiation factor 4 gamma 3	0.64071
E3 ubiquitin-protein ligase DZIP3	0.64196
Glucosamine 6-phosphate N-acetyltransferase	0.64323
MAGUK p55 subfamily member 7	0.64404
Double-stranded RNA-specific adenosine deaminase	0.64456
Vacuolar protein sorting-associated protein 53 homolog	0.64487
TBC1 domain family member 1	0.64602
Uncharacterized protein C14orf45 homolog	0.64706
E3 ubiquitin-protein ligase TRIM32	0.64797
Vacuolar protein sorting-associated protein 52 homolog	0.64828
ATP-dependent RNA helicase DDX54	0.64831
ATP-binding cassette sub-family B member 6, mitochondrial	0.64993
Rab5 GDP/GTP exchange factor	0.65166
Lethal(2) giant larvae protein homolog 1	0.6519
Protein sprouty homolog 4	0.65233
Phosphatidate phosphatase LPIN2	0.65309
Proteasome activator complex subunit 4	0.65441
Tensin-3	0.65454
Teashirt homolog 3	0.65541
Coiled-coil domain-containing protein lobo homolog	0.65591
Integrin alpha-V;Integrin alpha-V heavy chain;Integrin alpha-V light chain	0.65611
Amyloid-like protein 2	0.65772
Probable cation-transporting ATPase 13A1	0.65819
M-phase phosphoprotein 6	0.65928
Serine/threonine-protein kinase mTOR	0.65949
Integrator complex subunit 1	0.66009
Sodium-dependent phosphate transporter 2	0.66151
Cyclin-dependent kinase 6	0.66322

Platelet-derived growth factor receptor alpha	0.66427
Enhancer of mRNA-decapping protein 4	0.66472
Collagen alpha-1(V) chain	0.66574
1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase delta-1	0.66681
Thioredoxin domain-containing protein 9	0.66727
Sodium/potassium-transporting ATPase subunit beta-3	0.66792
Phosphatidylinositol transfer protein beta isoform	0.66818
Protein SREK1IP1	0.67058
Glycerol-3-phosphate dehydrogenase, mitochondrial	0.67094
Putative tRNA pseudouridine synthase Pus10	0.67129
Interferon-induced 35 kDa protein homolog	0.67779
Carboxypeptidase Q	0.67801
Probable ATP-dependent RNA helicase DHX36	0.67864
Integrin alpha-1	0.68112
ATP-dependent RNA helicase DDX55	0.6832
Protein jagunal homolog 1	0.68399
Integral membrane protein 2C;CT-BRI3	0.68555
Probable palmitoyltransferase ZDHHC20	0.68591
Glutathione S-transferase A1;Glutathione S-transferase;Glutathione S-transferase A2	0.68662
Peroxisomal carnitine O-octanoyltransferase	0.68958
Plexin-D1	0.69154
39S ribosomal protein L9, mitochondrial	0.69322
Cytosolic acyl coenzyme A thioester hydrolase	0.69585
Phosphoribosylformylglycinamide synthase	0.69612
Protein CLEC16A	0.69627
Ubiquitin/ISG15-conjugating enzyme E2 L6	0.69688
Syndecan-1;Syndecan	0.69756
Annexin A11	0.69938
SRSF protein kinase 2;SRSF protein kinase 2 N-terminal;SRSF protein kinase 2 C-termina	0.70053
Polycystin-2	0.70116
Serine/threonine-protein kinase TAO2	0.70247
tRNA (guanine-N(7)-)-methyltransferase subunit WDR4	0.70329
Transmembrane protein 168	0.70381
Elongation factor 1-alpha	0.70398
E3 ubiquitin-protein ligase HECTD1	0.70574
Alpha-parvin	0.70676
Non-histone chromosomal protein HMG-17	0.70695
Lysosomal-associated transmembrane protein 4A	0.70745
Protein TANC1	0.70841
Zinc transporter 6	0.70884
Asparagine--tRNA ligase, cytoplasmic	0.70983
39S ribosomal protein L16, mitochondrial	0.70988
Protein FAM208A	0.71035
N-acetyllactosaminide alpha-1,3-galactosyltransferase	0.71041
Formin-like protein 3	0.71081
Collagen alpha-2(I) chain	0.71084
Glucosamine-6-phosphate isomerase 1	0.71238
Zinc transporter 1	0.71266
Rho GTPase-activating protein 35	0.71285
Basement membrane-specific heparan sulfate proteoglycan core protein;Endorepellin;LG3 peptide	0.71351
Caspase-3;Caspase-3 subunit p17;Caspase-3 subunit p12	0.71364

Developmentally-regulated GTP-binding protein 2	0.71397
Platelet-activating factor acetylhydrolase IB subunit alpha	0.71441
Chromodomain-helicase-DNA-binding protein 8	0.7146
DNA-directed RNA polymerase I subunit RPA1;DNA-directed RNA polymerase	0.71498
Actin-related protein 2/3 complex subunit 1B	0.71532
Secernin-3	0.7161
Mitochondrial carrier homolog 2	0.71611
Ubiquitin-conjugating enzyme E2 W	0.7173
Proteasome assembly chaperone 2	0.71942
Folate transporter 1	0.71947
Lactoylglutathione lyase	0.72177
Dedicator of cytokinesis protein 7	0.72244
Non-histone chromosomal protein HMG-14	0.72341
SPRY domain-containing protein 4	0.72362
Transducin-like enhancer protein 1;Transducin-like enhancer protein 4;Transducin-like enhancer protein 3	0.72443
Sphingomyelin phosphodiesterase 4	0.72471
Uncharacterized protein C2orf78 homolog	0.72533
5-AMP-activated protein kinase subunit beta-1	0.72566
Protein FAM49B	0.72676
CTP synthase 1	0.72699
CTD small phosphatase-like protein	0.72733
Bcl-2 homologous antagonist/killer	0.72756
Histone-lysine N-methyltransferase SETDB1	0.72848
Ras and Rab interactor 1	0.72908
Uncharacterized protein C1orf198 homolog	0.72998
Ephrin type-B receptor 3	0.73133
MAP kinase-activated protein kinase 3	0.73224
Glucosamine--fructose-6-phosphate aminotransferase [isomerizing] 1	0.73282
Interferon-induced protein with tetratricopeptide repeats 3	0.73309
Probable global transcription activator SNF2L2	0.73316
Collagen alpha-1(XII) chain	0.73332
Fatty acid-binding protein, adipocyte	0.73351
Signal peptide peptidase-like 2B	0.73596
Thrombospondin-2	0.73662
Probable ATP-dependent RNA helicase DDX47	0.73692
NGFI-A-binding protein 1	0.73777
Tetraspanin-6	0.73967
Vacuolar protein sorting-associated protein 13C	0.74047
Cullin-7	0.74255
Transmembrane protein 176B	0.74299
MOB kinase activator 1B	0.74397
Uncharacterized protein KIAA0090	0.74432
FYVE, RhoGEF and PH domain-containing protein 3	0.74453
PRA1 family protein 3	0.74522
Fermitin family homolog 2	0.74619
Protein-associating with the carboxyl-terminal domain of ezrin	0.74634
Importin subunit alpha-7;Importin subunit alpha	0.74652
Pre-mRNA branch site protein p14	0.7471
Centromere protein J	0.74806
Fos-related antigen 2	0.74811
GDP-L-fucose synthase	0.74826

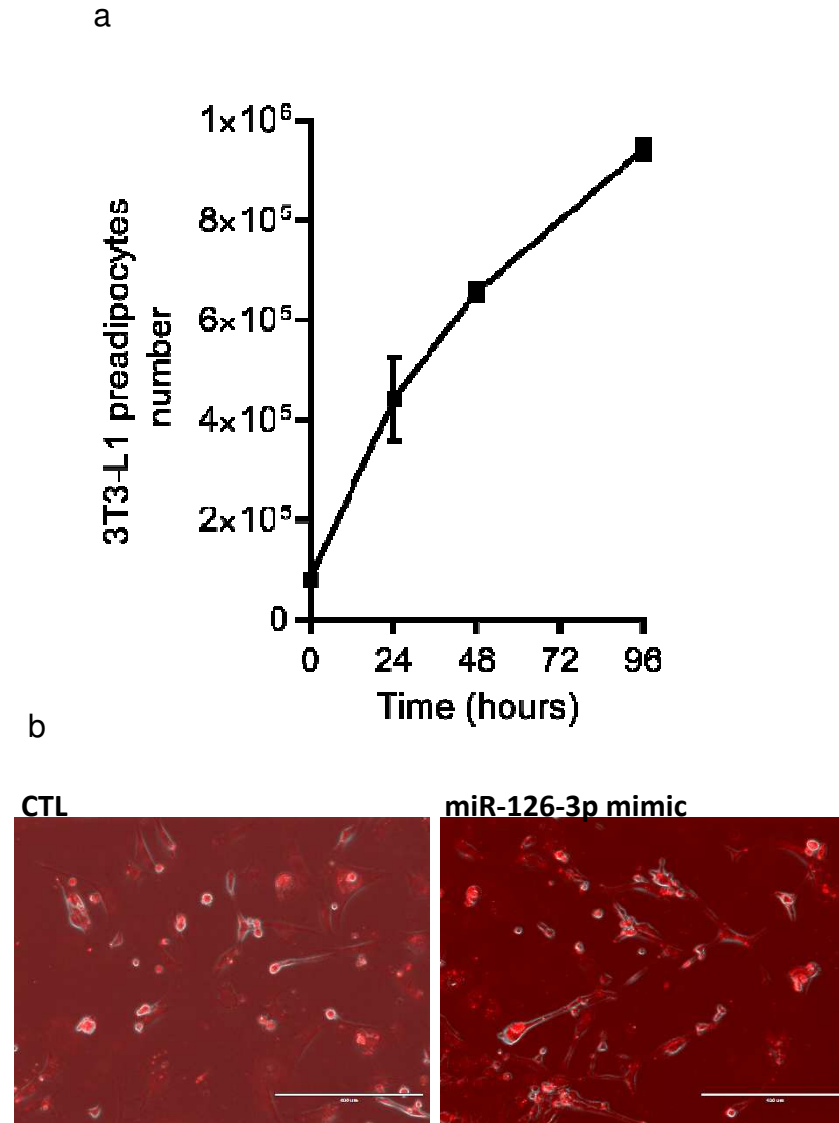
Filamin-A	0.74831
Insulin-like growth factor 2 mRNA-binding protein 2	0.7485
UTP--glucose-1-phosphate uridylyltransferase	0.74873
Polypyrimidine tract-binding protein 3	0.74984
Activator of 90 kDa heat shock protein ATPase homolog 1	0.75056
Mannosyl-oligosaccharide 1,2-alpha-mannosidase IB	0.75096
Unconventional myosin-IXa	0.75246
Methionine--tRNA ligase, cytoplasmic	0.7527
Zinc finger protein 609	0.75323
Poly [ADP-ribose] polymerase 14	0.75358
Aldehyde dehydrogenase, cytosolic 1	0.75408
Transmembrane protein 185B	0.75437
AP-3 complex subunit delta-1	0.75465
Cleavage and polyadenylation specificity factor subunit 5	0.75616
Myotubularin-related protein 3	0.75778
Tripartite motif-containing protein 16	0.75898
Protein YIPF5	0.759
Probable E3 ubiquitin-protein ligase DTX2	0.75983
Protein FAM101B	0.75998
Armadillo repeat-containing X-linked protein 1	0.76013
Quinone oxidoreductase-like protein 1	0.76038
C-Jun-amino-terminal kinase-interacting protein 4	0.7608
ADP-ribosylation factor-binding protein GGA3	0.76083
Pantothenate kinase 4	0.76101
Astrotactin-2	0.76177
CMP-sialic acid transporter	0.76195
Kelch domain-containing protein 4	0.76201
Magnesium transporter protein 1	0.76241
Choline transporter-like protein 1	0.7646
Uncharacterized protein C6orf47 homolog	0.76464
Nuclear pore complex protein Nup133	0.76485
MAPK-interacting and spindle-stabilizing protein-like	0.76491
Dual specificity mitogen-activated protein kinase kinase 1	0.76548
WD repeat-containing protein 92	0.76551
1-acyl-sn-glycerol-3-phosphate acyltransferase delta	0.76562
TSC22 domain family protein 3	0.76578
DnaJ homolog subfamily C member 24	0.76771
Cytospin-B	0.76817
Signal transducer and activator of transcription 5B	0.76825
Uncharacterized protein KIAA0754	0.76847
Beta-parvin	0.76849
Ephrin type-A receptor 2	0.76858
PHD finger protein 10	0.76886
Target of EGR1 protein 1	0.7703
RNA polymerase II elongation factor ELL	0.77073
Mediator of RNA polymerase II transcription subunit 13-like	0.77112
LisH domain and HEAT repeat-containing protein KIAA1468	0.77135
Myosin-14	0.77143
Breast carcinoma-amplified sequence 3 homolog	0.77152
PRELI domain-containing protein 1, mitochondrial	0.77161
Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 2	0.77171

Cystatin-B	0.77217
CD99 antigen-like protein 2	0.7723
Solute carrier family 23 member 2	0.77302
UPF0767 protein C1orf212 homolog	0.77323
Insulin receptor substrate 1	0.77351
CAAX prenyl protease 1 homolog	0.77357
Adenylate cyclase type 9	0.77578
ERO1-like protein alpha	0.77586
1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase gamma-1	0.77724
Amyloid beta A4 protein;N-APP;Soluble APP-alpha;Soluble APP-beta;C99;Beta-amyloid protein 42;Beta-amyloid protein 40;C83;P3(42);P3(40);	0.77753
Tuberin	0.77771
Palmitoyltransferase ZDHHC13	0.778
Eukaryotic translation initiation factor 3 subunit M	0.77867
Importin-13	0.77873
Proteasome-associated protein ECM29 homolog	0.77891
Lysocardiolipin acyltransferase 1	0.7795
Zinc finger homeobox protein 3	0.77957
Rho guanine nucleotide exchange factor 10	0.78016
Neutral amino acid transporter A	0.7818
Nuclear receptor coactivator 5	0.78188
Elongation factor 1-alpha 1;Elongation factor 1-alpha	0.78203
Kinesin-like protein KIF3B	0.78234
Rho GTPase-activating protein 1	0.78276
Small subunit processome component 20 homolog	0.78279
Meiosis arrest female protein 1	0.78298
Unconventional myosin-IXb	0.7833
Carnitine O-palmitoyltransferase 1, liver isoform	0.7834
Unconventional myosin-Ic	0.78369
3-hydroxy-3-methylglutaryl-coenzyme A reductase	0.7839
Protein C8orf37 homolog	0.78449
Probable methyltransferase-like protein 15	0.7849
Protein fat-free homolog	0.78512
Guanosine-3,5-bis(diphosphate) 3-pyrophosphohydrolase MESH1	0.78519
Zinc finger homeobox protein 4	0.78528
Rapamycin-insensitive companion of mTOR	0.78546
Replication protein A 70 kDa DNA-binding subunit	0.78585
Axin-1	0.78619
Fatty acid desaturase 3	0.78639
Protein KIAA0664	0.78668
Coatomer subunit alpha;Xenin;Proxenin	0.78671
Protein lunapark	0.78695
Collagen alpha-1(I) chain	0.78841
Anoctamin-10	0.78878
Tumor necrosis factor alpha-induced protein 2	0.78905
AP-2 complex subunit sigma	0.7895
Glycogenin-1	0.79056
Aspartyl aminopeptidase	0.79159
Ephrin type-B receptor 2	0.79183
Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial	0.79188
Actin, aortic smooth muscle;Actin, gamma-enteric smooth muscle;Actin, alpha cardiac muscle 1;Actin, alpha skeletal muscle	0.79244
Eukaryotic translation initiation factor 4E type 2	0.79284

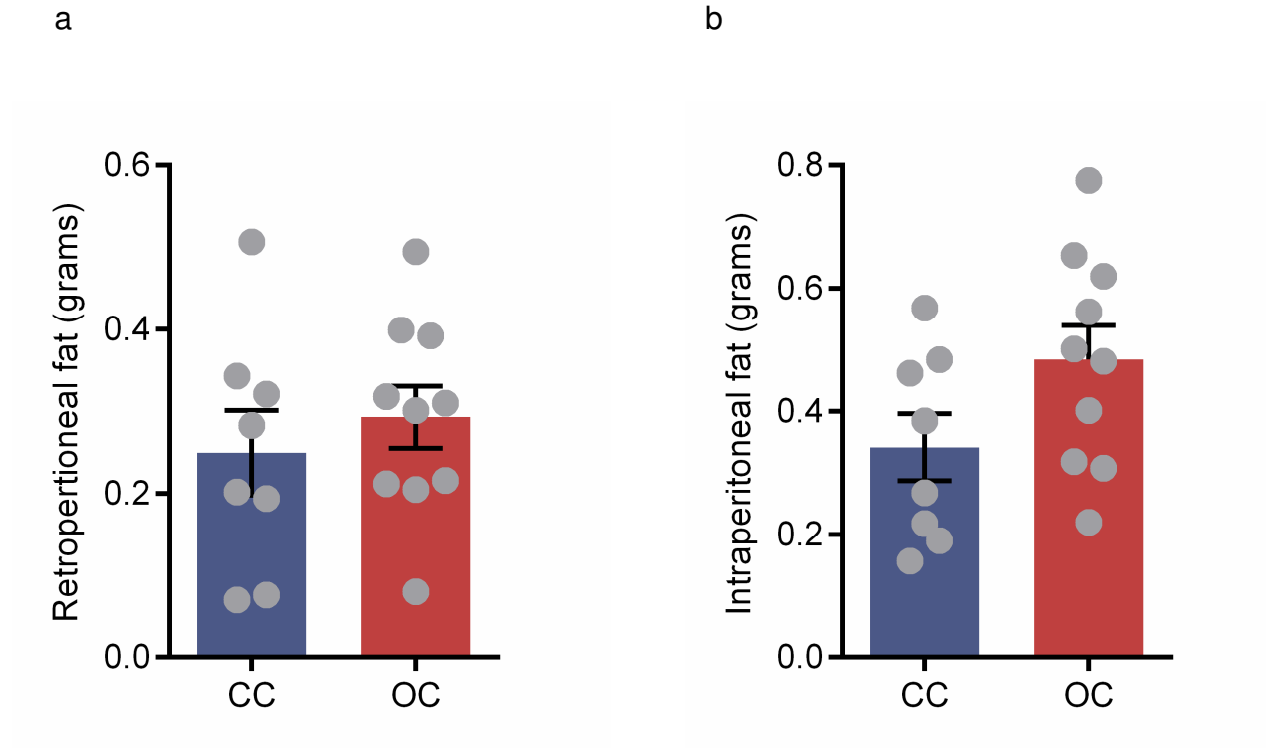


AP-3 complex subunit beta-1	0.7935
PAB-dependent poly(A)-specific ribonuclease subunit 2	0.7942
Nucleolar MIF4G domain-containing protein 1	0.79437
Coatomer subunit beta	0.79462
28S ribosomal protein S2, mitochondrial	0.79467
UPF0711 protein C18orf21 homolog	0.79526
28S ribosomal protein S5, mitochondrial	0.79551
Rho-associated protein kinase 1	0.79578
Dysferlin	0.79629
Kinesin-like protein KIF16B	0.7965
DNA damage-binding protein 1	0.79674
Peripheral plasma membrane protein CASK	0.79738
Beta-enolase;Enolase	0.79772
Dipeptidyl peptidase 9	0.79796
Pseudopodium-enriched atypical kinase 1	0.798
Importin-11	0.79805
Integral membrane protein 2B;BRI2, membrane form;BRI2 intracellular domain;BRI2C, soluble form;Bri23 peptide	0.79851
Biglycan	0.79946
CAP-Gly domain-containing linker protein 2	0.79957

ESM Fig. 1



(a) Cell line turnover was established before miRNA mimic transfection and labelling protocols,  $n=4$  per time point. (b) Representative images of fluorescent mock (Left) or miR-126-3p mimic (Right) transfected 3T3-L1 cells at x10 magnification, taken at 24h after transfection. Scale bars, 400  $\mu\text{m}$ .



Absolute (a) Retroperitoneal and (b) Intraperitoneal fat depots weights of 6 months old male offspring, n=8-11 per group.