

Supplementary Information

MiR-337-3p Promotes Adipocyte Browning by Inhibiting TWIST1

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SUPPLEMENTARY TABLE

Table S1. Anthropometric and clinical characteristics of healthy and metabolic syndrome subjects.

Variables	Non-MetS n=5	MetS n=5	p-Value
Age (years)	53 ± 5	48 ± 2	0.320
BMI (kg/m ²)	22 ± 1	53 ± 4	<0.0001
Waist circumference (cm)	78 ± 2	150 ± 16	<0.0001
SBP (mmHg)	136 ± 4	133 ± 5	0.633
DBP (mmHg)	79 ± 6	79 ± 9	0.971
Triglyceride (mmol/L)	1.0 ± 0.1	1.7 ± 0.2	<0.05
HDL cholesterol (mmol/L)	1.8 ± 0.2	0.5 ± 0.1	< 0.05
Fasting glucose (mmol/L)	5.3 ± 0.1	6.2 ± 0.5	0.131
HbA1c (%)	5.2 ± 0.13	5.9 ± 0.3	0.103
HOMA-IR	1.1 ± 0.3	7.3 ± 2.2	0.067

Data are means ± SEM. Abbreviations: BMI, Body mass Index; DBP, diastolic blood pressure; SBP, systolic blood pressure; HDL, high density lipoprotein; HbA1c, glycosylated Hemoglobin A1C; HOMA- IR, homeostasis model assessment of insulin resistance index. All statistics were performed using Mann Whitney-U test.

Table S2. Strategy used for selecting gene of interest and literature search. Genes and corresponding publications listed below are investigated with the main aim of identifying genes of interest for studying browning. Next by inserting the selected gene miRNA's that target gene of interest are investigated in miRNAviewer Mouse and Rat databases. This led to the identification of Twist-1. The miRNAviewer output helped with composing the list of miRNAs that were assessed in BAT and WAT.

Gene	mirnaviewer Mouse Transcript	mirnaviewer Rat Transcript	Published
Aldh1a1			miR-155 http://www.ncbi.nlm.nih.gov/pubmed/26317551
Atg7	79:miR-24		miR-210 miR-20a MIR137 miR-199a-5p miR-375
Atf4			miR-214 <i>Free Radic Biol Med.</i> 2016 Mar;92:39-49. <i>RNA Biol.</i> 2015;12(3):343-53. <i>J Biol Chem.</i> 2015 Mar 27;290(13):8185-95. <i>Nat Med.</i> 2013 Jan;19(1):93-100.
Eif4ebp1	1: miR-138 , 128: miR-125b , 163: miR-138 , 170: miR-202 , 390: miR-135a , 391: miR-135b	1: miR-138 , 127: miR-125a , 128: miR-125b , 134: miR-18 , 135: miR-18 , 170: miR-202 , 390: miR-135a , 391: miR-135b	miR-125a and miR-125b <i>Oncotarget.</i> 2016 Feb 23;7(8):8726-42. miR-9-5p , miR-675-5p , and miR-138-5p <i>Int J Mol Sci.</i> 2016 Feb; 17(2): 236. miR-34c-3p <i>Cell Prolif.</i> 2015 Oct;48(5):582-92. miR-768-3p <i>Oncogene.</i> 2014 May 15;33(20):2577-88
Eif4ebp2	128: miR-96 , 1112: miR-330 , 1123: miR-214 , 1572: miR-145 , 2016: miR-125b , 2017: miR-125a	32: miR-18 , 128: miR-96 , 436: miR-185 , 792: miR-324-3p , 1112: miR-330 , 1183: miR-214 , 1209: let-7b , 1229: miR-185 , 1833: miR-331	
Id1	250:miR-326	250:miR-326	miR-381 <i>J Thorac Oncol.</i> 2012 Jul;7(7):1069-77. miR-29b <i>Oncogene.</i> 2012 Sep 20;31(38):4221-32.
Ikbke	92: let-7c , 92: let-7b , 92: let-7f , 92: let-7a , 93: let-7e , 93: miR-98 , 94: let-7g , 96: let-7i , 99: let-7d	92: let-7c , 92: let-7b , 92: let-7f , 92: let-7a , 93: let-7e , 93: miR-98 , 94: let-7g , 96: let-7i , 99: let-7d , 150: miR-324-5p	miR-155-5p <i>Oncotarget.</i> 2016 Mar 29;7(13):16567-80. <i>Neoplasia.</i> 2009 Feb;11(2):167-76 let-7e-5p , miR-98-5p and miR-145a-5p <i>Biochim Biophys Acta.</i> 2015 Aug;1852(8):1585-98 <i>Hsa-miR-4717-5p</i> <i>Am J Med Genet B Neuropsychiatr Genet.</i> 2015 Jun;168B(4):296-306 let-7b and let-7i <i>Biochem Biophys Res Commun.</i> 2015 Mar 6;458(2):307-12. miR-296 <i>RNA.</i> 2012 Jan;18(1):135-44.
Mstn	550:miR-29a	550:miR-29a	miR-27 <i>Biomed Res Int.</i> 2015;2015:391306. <i>Am J Physiol Cell Physiol.</i> 2011 Jan;300(1):C124-37. <i>PLoS One.</i> 2014 Jan 31;9(1):e87687. <i>BMC Genomics.</i> 2013 Mar 19;14:194. miR-128 <i>Cell Signal.</i> 2015 Sep;27(9):1895-904.
Prlr	35: miR-142-3p , 135: miR-185 , 426: miR-122a , 499: miR-30a-5p , 503: miR-30e , 840: miR-124a	1: miR-138 , 127: miR-125a , 128: miR-125b , 134: miR-18 , 135: miR-18 , 170: miR-202 , 390: miR-135a , 391: miR-135b	miR-135a <i>DNA Cell Biol.</i> 2015 Aug;34(8):534-40.
p107	12: miR-302b , 12: miR-302 , 12: miR-20 , 465: miR-122a	12: miR-302b , 12: miR-302	miR-888 <i>Cell Cycle.</i> 2014;13(2):227-39 MiR-17 , MiR-20a , and MiR-106b <i>PLoS One.</i> 2011 Jan 20;6(1):e16138. miR-106b-5p <i>Oncogene.</i> 2014 Oct 2;33(40):4813-22.

<p>113:miR-324-5p, 153:miR-326, 278:miR-138, 1184:miR-204, 1184:miR- 211, 1477:miR-15b, 1617:miR-23b, 1780:miR-342, 1781:miR-377, 2827:miR-18, 2849:miR-18, 3101:miR- 346, 3562:miR-377, 3653:miR-377, 4071:miR-185, 4336:miR-15a, Smad3 4542:miR-302b*, 4607:miR-28</p>	<p>855:miR-199a, 855:miR-199b, 1576:miR-412, 3903:miR-145</p>	<p>MiR-23a-3p Biochem Biophys Res Commun. 2016 Jun 16. miR-23b PLoS One. 2015 Jul 8;10(7):e0131867. miR-145 and miR-203 Lung Cancer. 2016 Jul;97:87-94. Cell Mol Biol (Noisy-le-grand). 2015 May 8;61(3):12-6. Biochem Biophys Res Commun. 2015 Mar 27;459(1):49-53. MiR-195 Int J Gynecol Cancer. 2016 Jun;26(5):817-24 miR-16-5p Curr Pharm Des. 2015;21(35):5160-7. miR-199a-5p Biochem Biophys Res Commun. 2016 May 13;473(4):859-66 miR-21 Clin Sci (Lond). 2015 Dec;129(12):1237-49. miR-323-3p Oncotarget. 2016 Mar 22;7(12):14912-24. miR-590-5p Cell J. 2016 Spring;18(1):7-12 miR-708 Sci Rep. 2016 Mar 2;6:22599.MiR-23a-3p Biochem Biophys Res Commun. 2016 Jun 16. miR-23b PLoS One. 2015 Jul 8;10(7):e0131867. miR-145 and miR-203 Lung Cancer. 2016 Jul;97:87-94. Cell Mol Biol (Noisy-le-grand). 2015 May 8;61(3):12-6. Biochem Biophys Res Commun. 2015 Mar 27;459(1):49-53. MiR-195 Int J Gynecol Cancer. 2016 Jun;26(5):817-24 miR-16-5p Curr Pharm Des. 2015;21(35):5160-7. miR-199a-5p Biochem Biophys Res Commun. 2016 May 13;473(4):859-66 miR-21 Clin Sci (Lond). 2015 Dec;129(12):1237-49. miR-323-3p Oncotarget. 2016 Mar 22;7(12):14912-24. miR-590-5p Cell J. 2016 Spring;18(1):7-12 miR-708 Sci Rep. 2016 Mar 2;6:22599.</p>
<p>105:miR-29b, 106:miR-29a, 270:miR- Tnfrsf1a 138</p>		<p>miR-29a World J Gastroenterol. 2016 May 28;22(20):4881-90. miR-511 EMBO Mol Med. 2015 May 20;7(8):1004-17.</p>
<p>Trpv4 1:miR-17-3p 57:miR-151, 68:miR-199a, 68:miR- 199b, 69:miR-337, 253:miR-361, 447:miR-199b, 461:miR-145, 600:miR- 220 420:let-7c, 420:let-7b, 597:miR- 151, 608:miR-199b, 608:miR-199a, 609:miR-337, 793:miR-361</p> <p>Twist1</p>	<p>1:miR-17-3p 14:miR-370, 57:miR-151, 68:miR- 199a, 68:miR-199b, 69:miR-337, 253:miR-361, 461:miR-145, 600:miR-220 15:miR- 370, 72:miR-371, 420:let-7b, 597:miR-151, 608:miR-199b, 608:miR-199a, 609:miR-337, 793:miR-361</p>	<p>miR-203 Arch Oral Biol. 2013 Feb;58(2):192-9. mir-186 Oncotarget. 2016 Apr 21. Oncogene. 2016 Jan 21;35(3):323-32. miR-23a Oncol Rep. 2015 Feb;33(2):942-50. miR-26b-5p Oncotarget. 2016 Mar 24. miR-1271 Biochem Biophys Res Commun. 2016 Apr 1;472(2):346-52 MiR-548c J Exp Clin Cancer Res. ...2016 Jan 13;35:10. miR-33b Sci Rep. 2015 Apr 28;5:9995. MiR-520d-5p Oncotarget. 2014 Dec 15;5(23):12141-50....</p>