

Supplementary Figure 1. Characterization of tonsil-derived mesenchymal stem cells (**TMSCs).** (a) Cells were analysed by flow cytometry after labelling with the indicated antibodies (anti-CD34, anti-CD73, anti-CD90, and anti-CD105). The grey and red histograms represent the isotype control and positive reactivity with the indicated monoclonal antibody, respectively. (b) The differentiating ability of TMSCs into adipocytes, chondrocytes, and osteocytes were noted in appropriate culture medium. Image magnification: 200x. The microscopic and flow cytometry images are representatives of three independent experiments.



Supplementary Figure 2. Obesity-associated metabolic pathologies in peripheral tissues were not relieved by TMSCs. Mice were fed a HFD for 6 weeks, and then TMSCs were intraperitoneally injected once every 2 weeks into HFD-induced diabetic mice while a normal or HFD diet was maintained. Mice were sacrificed after 10 weeks of TMSC administration, and liver and adipose tissues were extracted. Real-time polymerase chain reaction of hepatic genes involved in (a) gluconeogenesis and (b) glycogen degradation (n = 5). Fbp1, fructose bisphosphatase 1; Fbp2, fructose bisphosphatase 2; G6pc, glucose-6-phosphatase; Gys2,

glycogen synthase 2; Pepck1, phosphoenolpyruvate carboxykinase 1; Pepck2,

phosphoenolpyruvate carboxykinase 2; Pygb, brain glycogen phosphorylase; Pygl, liver glycogen phosphorylase. Values are mean \pm S.E.M. (n = 5). **P < 0.01. (c) Liver and (d) adipose tissues were stained with haematoxylin and eosin. Image magnification, $100 \times$. The image is a representative image of three independent experiments.



Supplementary Figure 3. Characterization of IGFBP5-knockdown TMSCs. IGFBP5 was downregulated in TMSCs using siRNA treatment. (a) TMSC proliferation for 48 h and (b) TMSC cell death upon palmitate treatment were analysed with MTT assays (n = 4). **P < 0.01, ***P < 0.001. (c) TMSC surface immunophenotypes were analysed by flow cytometry. The

image is representative of three independent experiments. The grey and red histograms represent the isotype control and positive reactivity with the indicated monoclonal antibody, respectively.

Gene	Primer sequence (5'-3')	Reference		
Chop	F: GTCCCTAGCTTGGCTGACAGA	[1]		
	R: TGGAGAGCGAGGGCTTTG			
BiP	F: TCATCGGACGCACTTGGAA	[1]		
	R: CAACCACCTTGAATGGCAAGA			
Hk4	F: GGAACCAACTTCAGGGTGATG	[2]		
	R: CTGGTGTTTCGTCTTCACGCT			
Pdx1	F: TTCCCGAATGGAACCGAGC	[3]		
	R: GCGTGAGCTTTGGTGGATT			
Glut4	GATTCTGCTGCCCTTCTGTC			
	ATTGGACGCTCTCTCTCCAA			
IL-6	CACAAGTCCGGAGAGGAGAC	[4]		
	CAGAATTGCCATTGCACAAC			
Insr	AGGCTCCCGTCTCTTCTTCAA			
	GACATCCCCACATTCCTCGTT			
PPARγ	TGCCAAAAATATCCCTGGTT			
	GAGGCCAGCATCGTGTAGAT			
TNFα	GATCTCAAAGACAACCAACATGTG	[5]		
	CTCCAGCTGGAAGACTCCTCCCAG			
Fbp1	F: GGCTGCTGTATGAGTGCAAC	[6]		
	R: CGGTGGGAACGATGTCTAAT			
Fbp2	F: CAGAAGCCCCTTTGAGACAG	[6]		
	R: AGTTGAGCAGCTGGGTGAGT			
Pepck1	F: ACAGACTCGCCCTATGTGGT	[6]		
	R: TGCAGGCACTTGATGAACTC			
Pepck2	F: CTTTGGACGCTACCTGGAAC	[6]		
	R: CTGCTTCATCTCTCCGGAAC			
G6pc	F: ACTCCAGCATGTACCGGAAG	[6]		
	R: AAGAGATGCAGGAGGACCAA			
Pygl	F: CAAGTGTCCCAAGAGGGTGT	[6]		
	R: ATCGCAGGCATTTTGTAAGC			
Pygb	F: GGACAGTGAGAGGCAGAAGC	[6]		
	R: CGTGAAATGCAGGTGTCTGT			
Gys2	F: CATGCCAGACACCTGACACT	[6]		
	R: GGGCCTGGGATACTTAAAGC			
Gapdh	F: CACTCTTCCACCTTCGATGC	[7]		
	R: CCCTGTTGCTGTAGCCGTAT			

Supplementary table 1. Primers used in real-time PCR

Supplementary table 2. Proteins detected in conditioned medium derived from TMSC (TMSC-

CM). Proteins detected in both TMSC-CM and conditioned medium derived from AMSC

(AMSC-CM) were written in red letters.

Protein name
14-3-3 protein epsilon isoform
71 Kd heat shock cognate protein
Beta-2 microglobulin
C1 esterase
Calcium binding protein Cab45 precursor
Calgizzarin
Calmodulin
Cathepsin D
Cofilin-1
Collagen, type VI, alpha 1
Collagen, type VI, alpha 3
Colligin
Decorin
Fibulin-1D
Glyceraldehyde-3-phosphate dehydrogenase
Hematopoietic Cell-Specific Lyn Substrate 1
Insulin-like growth factor-binding protein 4
Insulin-like growth factor-binding protein 5
Insulin-like growth factor-binding protein 7
Laminin A3
Laminin B1
Laminin B2
Lumican
Matrix metalloproteinase-2
Matrix metalloproteinase-3/Tissue inhibitor of metalloproteinases-1 complex
Nucleobindin
Phospholipase A2
Phospholipid transfer protein
Preprostromelysin
PRO2044
Profilin-1

Pro-matrix metalloproteinase-1 Prosaposin Protease Nexin-1 Pyruvate kinase Quiescent cell proline dipeptidase Quiescin Ras GTPase-activating-like protein S100 calcium-binding protein A6 Stanniocalcin-2 Transforming growth factor induced protein Transketolase Triosephosphate isomerase Vinculin Supplementary table 3. Proteins detected in AMSC-CM. Proteins detected in both TMSC-CM

and A	MSC-	CM w	ere v	vritten	in	red	letters.

Protein name 14.3.3 gamma Beta tubulin C1 inhibitor Calgizzarin Calmodulin Calumenin Cofilin-1 Collagen, type VI, alpha 1 Collagen, type VI, alpha 3 Colligin Fibrillin Follistatin-related protein precursor Glyceraldehyde-3-phosphate dehydrogenase Hematopoietic Cell-Specific Lyn Substrate 1 Initiation factor 4D Intracellular chloride channel p64H1 Laminin B1 Legumain Lumican Mac-2 binding protein Matrix metalloproteinase-2 Matrix metalloproteinase-3/Tissue inhibitor of metalloproteinases-1 complex Nm23 protein, partial Osteoblast specific factor 2 P1725 Pentaxin Phosphoglycerate mutase isozyme B Phospholipase A2 Plasminogen Activator Inhibitor, type 1 Prepro-alpha-1type 1 collagen Prepro-alpha-1 type 3 collagen Prepro-alpha-2type 1collagen Preprocathepsin B

PRO2044 Profilin-1 Prosaposin Prostacyclin-stimulating factor Protease Nexin-1 Pyruvate kinase S100 calcium-binding protein A6 Smooth muscle protein Stanniocalcin-2 Thioredoxin reductase Thrombospondin 2 Thrombospondin-1 Tissue inhibitor of metalloproteinases-2 Transforming growth factor induced protein Triosephosphate isomerase VCP protein Vinculin

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