

SUPPLEMENTARY DATA

Supplementary Table 1. List of oligonucleotide primer pairs used in real time RT-PCR.

Gene	Forward primer	Reverse primer	Size (bp)
IRAK1	GCTGTGGACACCGATACCTT	GGTCACTCCAGCCTCTTCAG	141
TRAF6	GATCGGGTTGTGTGTGTCTG	AGACACCCCAGCAGCTAAGA	178
ADAMTS3	AGCAAGTACTGCCTGGGAGA	TGACAGACTCGGGCTTTTCT	180
iNOS	TGGTGGTGACAAGCACATTT	AAGGCCAAACACAGCATAACC	119
TNF- α	ACGGCATGGATCTCAAAGAC	GTGGGTGAGGAGCACGTAGT	116
IL-1 β	GGGCCTCAAAGGAAAGAATC	TACCAGTTGGGGA ACTCTGC	183
YM1	GAAGGAGCCACTGAGGTCTG	CACGGCACCTCCTAAATTGT	141

Supplementary Table 2. List of miRNA primers used in real-time RT-PCR.

miRNAs	Company	Catalog number
mmu-miR-146a-5p	Applied Biosystems	4427975 (ID#000468)
U6 snRNA	Applied Biosystems	4427975 (ID#001973)
cel-miR-39	Applied Biosystems	4427975 (ID#000200)

Supplementary Table 3. Antibodies used for Western blotting.

Antibody name	Company and catalog number
anti- β -actin	Abcam, ab6276
anti-Arginase-1	Santa Cruz, SC-18351
anti-YM1	R&D Systems, AF2446
anti-TNF- α	Abbiotec, 250844
anti-iNOS	EMD Millipore, ABN26
anti-IL-1 β	Abcam, ab9787
anti-IRAK1	Santa Cruz, SC-7883
anti-NF- κ B p65	Abcam, ab7970
anti-TRAF6	Santa Cruz, SC-7221
anti-ADAMTS3	Santa Cruz, SC-21486
anti-PGP9.5	MILLIPORE, NE1013

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Supplementary Table 4. Morphomeric changes of myelinated sciatic nerves.

Property	db/m(20w)	db/m(28w)	db/db(20w)	db/db+miR con	db/db+miR-146a
Axon diameter(μm)	5.23±0.26	5.18±0.14	5.22±0.11	4.70±0.08##	5.18±0.09**
Fiber diameter(μm)	8.60±0.18	8.66±0.17	7.88±0.11†	7.54±0.14###	8.70±0.16***
myelin thickness(μm)	1.78±0.07	1.74±0.06	1.62±0.04†	1.42±0.03###	1.75±0.05***
g ratio	0.58±0.01	0.59±0.01	0.60±0.005	0.62±0.005#	0.59±0.006**

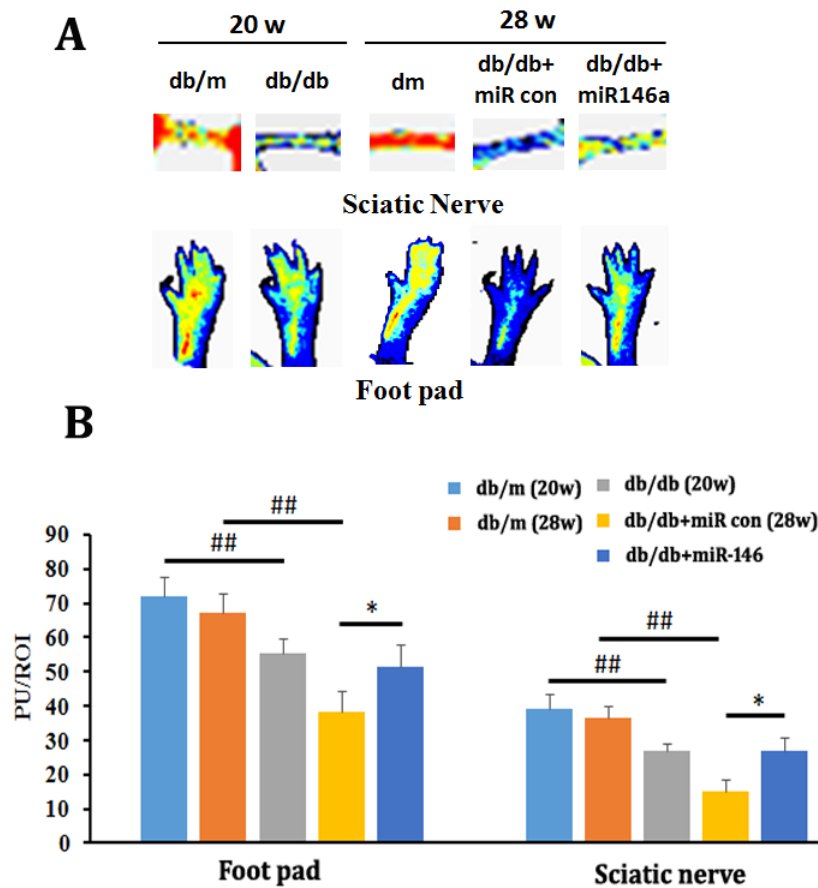
Values are mean±SE.

† P<0.05 vs db/m (20w)

P<0.05, ## P<0.01, ### P<0.001 vs db/m (28w)

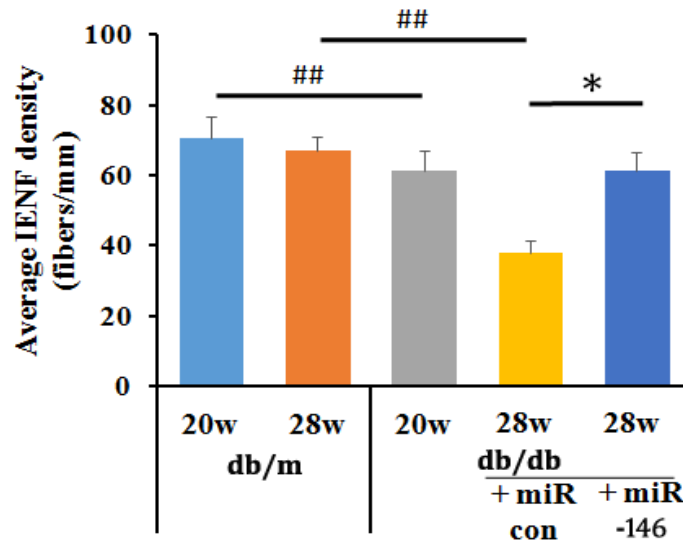
** P<0.01, *** P<0.001 vs db/db+miR con

Supplementary Figure 1. Regional blood flow was reduced at different ages of diabetic mice. Regional blood flow within the sciatic nerve and foot pad tissues was significantly reduced compared with db/m mice aged 20 weeks (A, B). Db/db mice at 28 weeks displayed a significant blood flow deficiency compared with db/db mice aged 20 weeks (A, B). miR-146a treatment significantly increased regional blood flow at the sciatic nerve tissue and foot pads of db/db mice aged 28 weeks compared to the miR-67 mimic treatment (A, B). * P<0.05 vs db/db + miR con; ## P<0.01 vs db/m.



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Supplementary Figure 2. The effect of diabetes on the number of intraepidermal nerve fibers (IENFs). The amount of IENFs in foot-pads stained by the antibody against PGP9.5 was significantly reduced in db/db mice compared with db/m mice aged 20 weeks. Db/db mice aged 28 weeks treated with cel-miR-67 mimics showed approximately a 50% decrease in the number of IENF, compared to age matched non-diabetic db/m mice. Compared with db/db mice aged 20 weeks, db/db mice at 28 weeks displayed a significant reduction of IENF number. * P<0.05 vs db/db + miR con; ## P<0.01 vs db/m.



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Supplementary Figure 3. Morphomeric change of myelinated sciatic nerves. Representative images of semi-thin toluidine blue-stained transverse sections of sciatic nerves derived from non-diabetic (db/m, A) and diabetic mice (db/db, B) aged 20 weeks. Bar=25 μ m.

