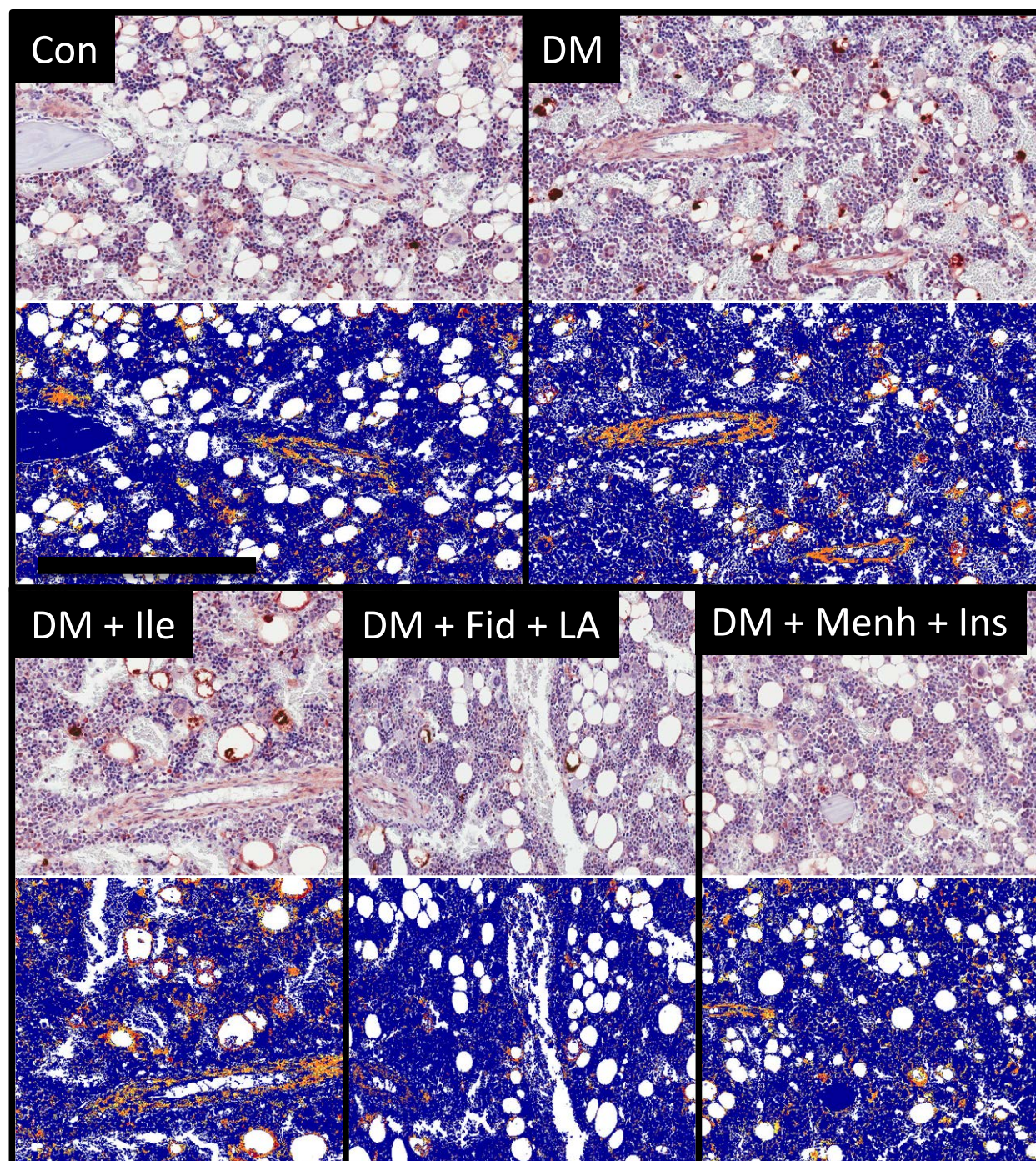


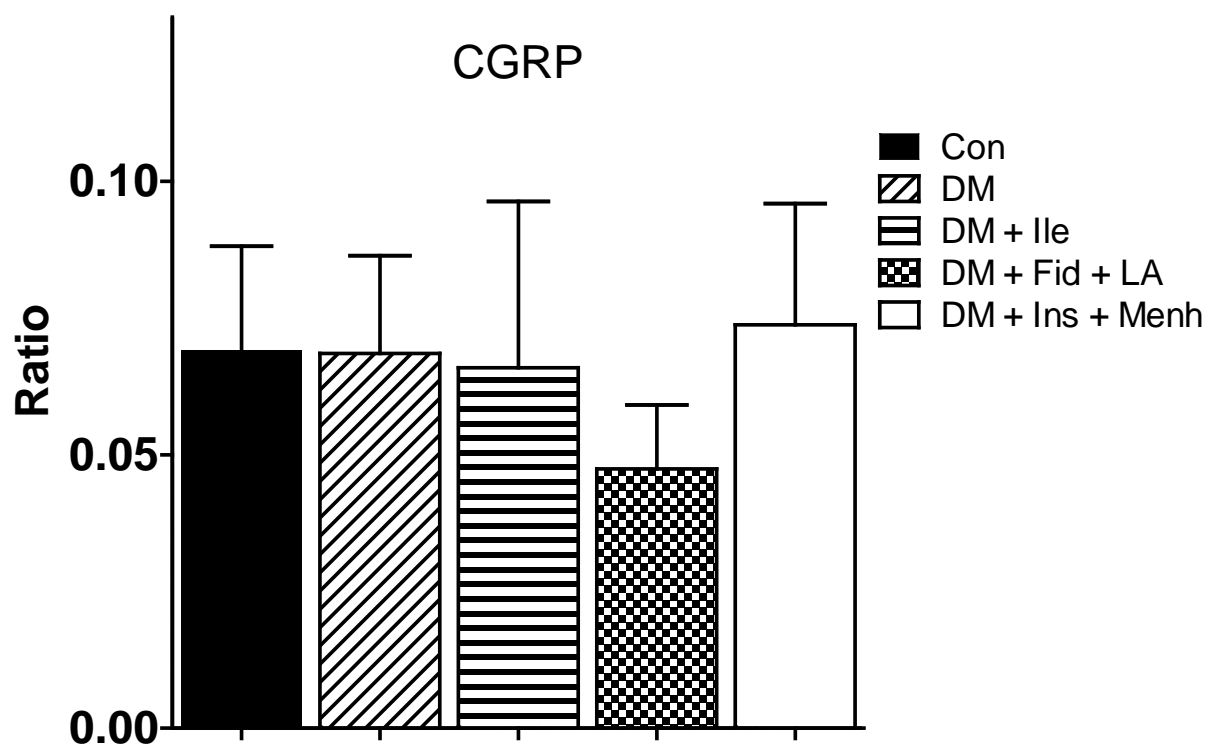
SUPPLEMENTARY DATA

Supplementary Figure 1a. CGRP staining of middle distal femoral marrow. Figures show representative CGRP staining before (top gray images) and after (bottom blue images) quantification by Aperio using the Positive Pixel Count algorithm. In the markup images, positive stain is indicated by yellow (weak positive), orange (middle positive) and red (strong positive). Con, non-diabetic control; DM, diabetic; Ile, ilepatril treatment; Fid + LA, fidarestat and lipoic acid treatment; Menh + Ins, insulin and menhaden oil treatment. Scale bar is 300 μ M. $n = 7$ to 12 animals per group.



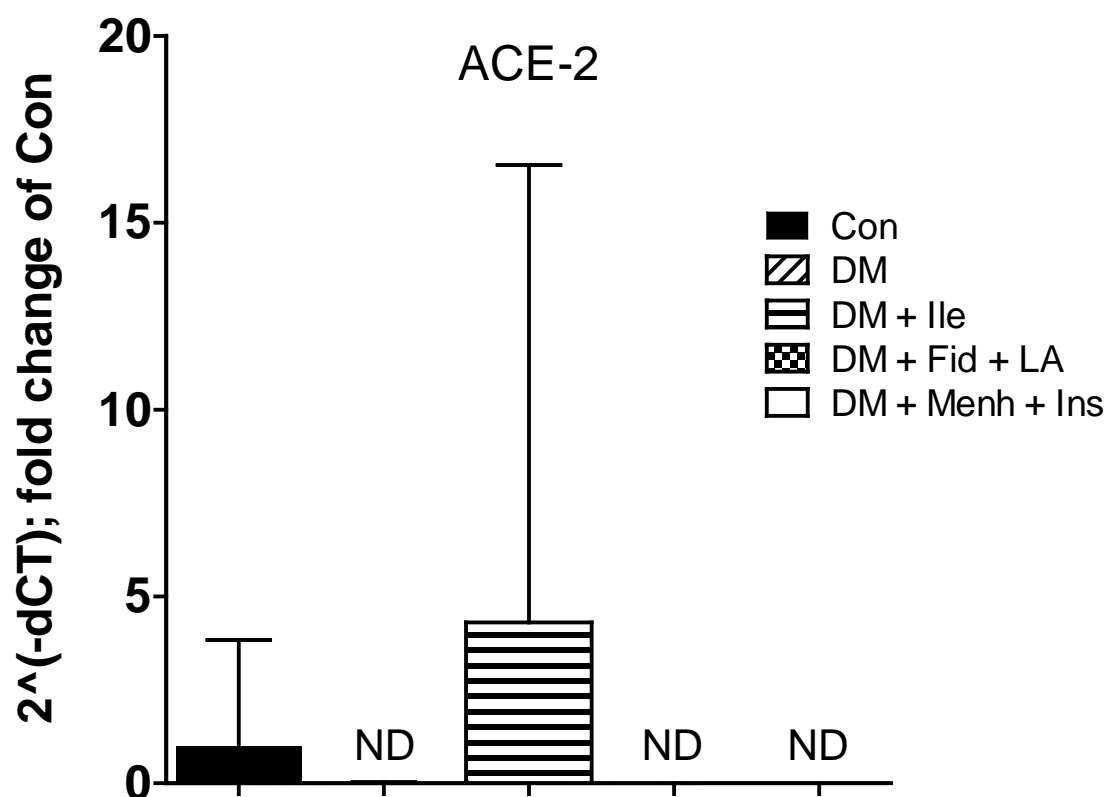
SUPPLEMENTARY DATA

Supplementary Figure 1b. Ratio of strong-positive CGRP pixels to total positive pixels in the middle distal femur. Con, non-diabetic control; DM, diabetic; Ile, ilepatril treatment; Fid + LA, fidarestat and lipoic acid treatment; Menh + Ins, insulin and menhaden oil treatment. Data represent mean \pm SD. There was no statistical significance between groups.



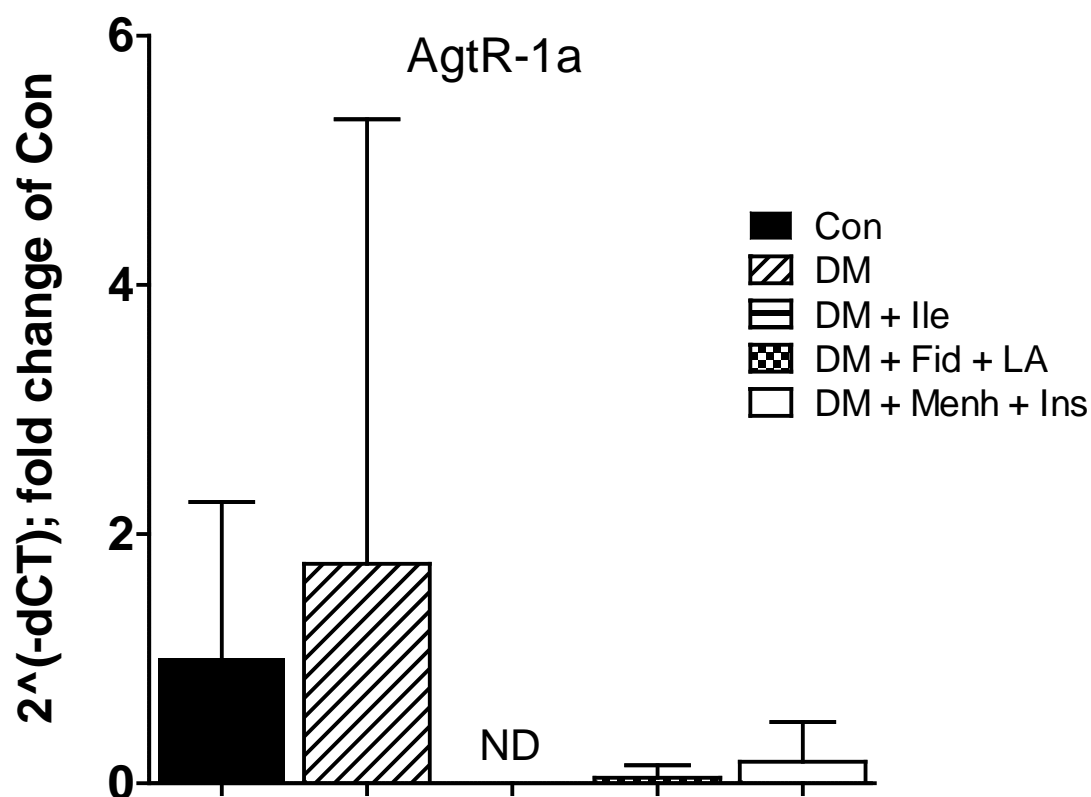
SUPPLEMENTARY DATA

Supplementary Figure 2. Femoral marrow ACE-2. Con, non-diabetic control; DM, diabetic; Ile, ilepatril treatment; Fid + LA, fidarestat and lipoic acid treatment; Menh + Ins, insulin and menhaden oil treatment. Data represent mean \pm SD. ND, not detected. Statistics could not be applied due to low detection in DM and treatment groups.



SUPPLEMENTARY DATA

Supplementary Figure 3. Femoral marrow AgtR-1a. Con, non-diabetic control; DM, diabetic; Ile, ilepatril treatment; Fid + LA, fidarestat and lipoic acid treatment; Menh + Ins, insulin and menhaden oil treatment. Data represent mean \pm SD. ND, not detected. Statistics could not be applied due to low detection in treatment groups.



SUPPLEMENTARY DATA

Supplementary Table 1. Ingested drug, method of delivery and dosage

Agent	Mechanism	Delivery method	Dosage*
Ilepatril	Neutral endopeptidase inhibitor	Chow	500mg
Lipoic acid	Antioxidant	Chow	0.25g
Fidarestat	Aldose reductase inhibitor	Chow	3mg
Menhaden oil	Enriched in EPA and DHA	Chow	25% kCal

Asterisk = Per kilogram chow

Supplementary Table 2. Antigen retrieval protocols

Primary antibody	Pre-treatment reagent	Pre-treatment time
Rabbit anti-neuropeptide Y	Scytek Citrate Plus pH 6.0	Overnight in oven @ 56°C
Rabbit anti-somatostatin	Scytek Citrate Plus pH 6.0	Overnight in oven @ 56°C
Rabbit anti-tyrosine hydroxylase	0.03% Pronase E in TBS	10 minutes @ 37°C
Mouse anti-8-oxo-dG	Scytek Citrate Plus pH 6.0	Overnight in oven @ 56°C
Rabbit anti-CGRP	Scytek Citrate Plus pH 6.0	Overnight in oven @ 56°C

SUPPLEMENTARY DATA

Supplementary Table 3. Primary antibody dilutions

Primary antibody	Clone	Catalog #	Dilution	Vendor
Rabbit anti-neuropeptide Y	Rabbit polyclonal to neuropeptide Y	NBP1-19808	1:200	Novus
Rabbit anti-somatostatin	Rabbit polyclonal to somatostatin	ab103790	1:100	Abcam
Rabbit anti-tyrosine hydroxylase	Rabbit polyclonal to tyrosine hydroxylase	AB152	1:100	Millipore
Mouse anti-8-oxo-dG	2E2	4354-MC-050	1:200	Trevigen
Rabbit anti-CGRP	Rabbit polyclonal to Rat CGRP	PA5-19755	1:200	ThermoFisher